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The EURL ECVAM - Cosmetics Europe prospective validation study of Reconstructed human Cornea-like Epithelium (RhCE)-based test methods for identifying chemicals not requiring classification and labelling for serious eye damage/eye irritation

Validation Study Report

Barroso J., Alépée N., Cole T., Eskes C., Freeman S. J., Liška R., McNamee P., Pfannenbecker U., Reus A. A., Rubingh C. M., Schaeffer M. W. and Zuang V.

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THE EURL ECVAM - COSMETICS EUROPE

PROSPECTIVE VALIDATION STUDY OF

RECONSTRUCTED HUMAN CORNEA-LIKE EPITHELIUM

(RHCE)-BASED TEST METHODS

FOR IDENTIFYING CHEMICALS NOT REQUIRING CLASSIFICATION

AND LABELLING FOR SERIOUS EYE DAMAGE/EYE IRRITATION

VALIDATION STUDY REPORT

March 2014

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LIST OF ABBREVIATIONS

BLR	Between-laboratory reproducibility
Cat	Category
CLP	EU Regulation 1272/2008 on the Classification, Labelling and Packaging of Substances and Mixtures
DPRA	Direct Peptide Reactivity Assay
EURL ECVAM	European Union Reference Laboratory for Alternatives to Animal Testing
EIVS	EURL ECVAM – Cosmetics Europe Eye Irritation Validation Study
EpiOcular™ EIT	EpiOcular™ Eye Irritation Test
EPRA	Eye irritation Peptide Reactivity Assay
ESAC	EURL ECVAM's Scientific Advisory Committee
EU	European Union
GD	Guidance Document;
GHS	Globally Harmonized System for Classification and Labelling of Chemicals
SkinEthic™ HCE	SkinEthic™ Human Corneal Epithelium
SkinEthic™ HCE LE	SkinEthic™ HCE Long-time Exposure
SkinEthic™ HCE SE	SkinEthic™ HCE Short-time Exposure
SkinEthic™ HCE TS	SkinEthicTM HCE testing strategy (with LE, SE and EPRA)
ICCVAM	US Interagency Coordinating Committee on Validation of Alternative Methods
ITS	Integrated Testing Strategy/ies
MTT	3-[4,5 - dimethylthiazol-2-yl] - 2,5 - diphenyltetrazolium bromide
NC	Negative Control
NICEATM	US National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods
OECD	Organisation for Economic Co-operation and Development
PC	Positive control
PM	Prediction model
REACH	EU Regulation 1907/2006 on the Registration, Evaluation, Authorisation and restriction of Chemicals
RhCE	Reconstructed human Cornea-like Epithelium
SD	Standard Deviation
SOP	Standard Operating Procedures

TG	Test Guideline
UN	United Nations
US	United States
VMG	Validation Management Group
WLR	Within-laboratory reproducibility

LIST OF DEFINITIONS

Complete test sequence: A test sequence (see definition below) is considered complete if it contains three qualified tests (see definition below). Otherwise, the test sequence is considered as incomplete.

EpiOcular™ model: A Reconstructed human Cornea-like Epithelium (RhCE) tissue construct produced by MatTek Corporation, consisting of a non-keratinized multilayered epithelium prepared from non-transformed, human-derived epidermal keratinocytes.

EpiOcular™ Eye Irritation Test (EIT): a test method that predicts the eye irritation potential of chemicals employing the EpiOcular™ RhCE construct as test system and a protocol with different exposure and post-exposure incubations for liquids and solids.

Eye irritation Peptide Reactivity Assay (EPRA): a test method that predicts chemical reactivity, defined as the electrophilic potential of the chemical to react with cysteine or lysine containing peptides (same protocol as DPRA, but a slightly different prediction model).

Negative control (NC): A reference test chemical that does not induce a cytotoxic effect in the treated tissues (i.e., does not reduce their viability). It is used to verify if the viability of the tissues used for testing, as quantified by the MTT assay, is within a defined acceptance range of optical density (OD).

Positive control (PC): A reference test chemical known to induce a cytotoxic effect in the treated tissues as quantified by using the MTT assay. It is used to verify if the tissue batch used for testing is responding to the reference chemical within a defined acceptance range of % viability (relative to NC). It should be noted that the positive control does not need to be an *in vivo* irritant chemical (based on the Draize eye irritation test).

Qualified run: A run (see definition below) is qualified when it meets the test acceptance criteria for the NC and PC, as defined in the corresponding SOP. Otherwise, the run is considered as non-qualified.

Qualified test: A test (see definition below) is qualified when it meets the criteria for an acceptable test, as defined in the corresponding SOP, and is within a qualified run. Otherwise, the test is considered as non-qualified.

Run: A run consists of multiple tests with different test chemicals (one test per test chemical) conducted concurrently with a test with NC and a test with PC, tested by one operator, as defined in the corresponding SOP.

SkinEthic™ Human Corneal Epithelium (HCE) model: a RhCE construct produced by SkinEthic™ Laboratories, consisting of a multilayered epithelium prepared from immortalized human corneal epithelial cells.

SkinEthic™ HCE Long-time Exposure (LE): a test method that predicts the eye irritation potential of chemicals employing the SkinEthic™ HCE RhCE construct as test system and a long-time exposure of test chemicals.

SkinEthic™ HCE Short-time Exposure (SE): a test method that predicts the eye irritation potential of chemicals employing the SkinEthic™ HCE RhCE construct as test system and a short-time exposure of test chemicals.

SkinEthic™ HCE test strategy/method: A test strategy to predict the eye irritation potential of chemicals, consisting of three separate assays (i.e., EPRA, SkinEthic™ HCE SE, and SkinEthic™ HCE LE). In this test strategy, chemical reactivity, as determined by the EPRA, is used to decide if a chemical is tested with SkinEthic™ HCE SE (reactive chemicals) or SkinEthic™ HCE LE (non-reactive or inconclusive chemicals).

Test: A single test chemical concurrently tested in a minimum of two/three tissue replicates as defined in the corresponding SOP. A “test” for a test chemical is defined when the cytotoxic effect by using MTT is quantitatively measured. A reported technical issue before the viability measurement is not considered as a “test” for the test chemical.

Test chemical: Any chemical (substance or mixture) being tested as a single entity.

Test sequence: The total number of tests performed for a single test chemical in a single laboratory, which includes any re-testing. A test sequence may include both qualified and non-qualified tests. The first two tests having technical issues for each test chemical, tests included in the first two runs presenting technical issues, and tests included in the first six non-qualified runs were not considered as part of a test sequence for the purposes of the present validation study.

Executive summary

A prospective validation study of two *in vitro* test methods using Reconstructed human Cornea-like Epithelium (RhCE) models (MatTek EpiOcular™ and SkinEthic™ Human Corneal Epithelium (HCE)) for the identification of chemicals not requiring classification and labelling for serious eye damage/eye irritation, has been conducted by the European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) and Cosmetics Europe - The Personal Care Association. Pre-validation studies with both test methods have served to optimise protocols and refine prediction models, and were able to show that both test methods are able to predict ocular toxicity properties of test substances with a high degree of accuracy, approximately 80% overall. The Eye Irritation Validation Study (EIVS), co-sponsored by EURL ECVAM and Cosmetics Europe, evaluated the validity (relevance and reliability) of these two RhCE test methods to discriminate chemicals not requiring classification and labelling for serious eye damage/eye irritancy (No Category) from chemicals requiring classification and labelling (Category 1 and Category 2) according to the United Nations Globally Harmonized System of Classification and Labelling of Chemicals (UN GHS) and as implemented by the EU Classification, Labelling and Packaging regulation (EU CLP) (UN, 2013; EC, 2008). These RhCE test methods are not intended to differentiate between UN GHS/EU CLP Category 1 (serious eye damage) and UN GHS/EU CLP Category 2 (eye irritation). This differentiation would be left to another tier of a test strategy as described e.g., by Scott *et al*. (2010). The EIVS has been undertaken in accordance with the principles and criteria documented in the OECD Guidance Document on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment (No. 34, OECD, 2005) and according to the Modular Approach to validation (Hartung *et al*., 2004).

The protocols assessed were the original EpiOcular™ Eye Irritation Test (EIT) protocol for liquid chemicals, the original EpiOcular™ EIT protocol for solid chemicals, an EpiOcular™ EIT optimised protocol for solid chemicals, the SkinEthic™ HCE Short-time Exposure (SE) protocol, the SkinEthic™ HCE Long-time Exposure (LE) protocol, and the SkinEthic™ HCE test strategy (TS) combining the SE and LE protocols as well as the Eye irritation Peptide Reactivity Assay (EPRA). Two prediction models, using 50% or 60% mean tissue viability as the threshold differentiating classified (UN GHS Cat 1 and Cat 2) chemicals (mean tissue viability ≤ 50% or 60%) from non-classified (UN GHS No Cat) chemicals (mean tissue viability > 50% or 60%), were evaluated with each of the EpiOcular™ EIT protocols, while a single prediction model using a 50% mean tissue viability cut-off was evaluated with the SkinEthic™ HCE SE, LE and TS. The EpiOcular™ EIT was originally developed by MatTek Corporation with the single threshold of 60% mean tissue viability in the prediction model and the submission of the test method to EURL ECVAM for validation was based on this single prediction model. However, in the beginning of the EIVS and even before training and transferability took place, MatTek Corporation was faced with the necessity to replace the insert membrane used in the production of the EpiOcular™ tissues due to discontinued production of the insert membrane used until then (MTI-001a). A replacement insert membrane (MTI-003) was approved by the Validation Management Group (VMG) for use in EIVS after multiple testing of 94 chemicals at MatTek Corporation and comparative statistical analysis performed by the EURL ECVAM biostatistician on the use of the old MTI-001a insert membrane (discontinued) versus the new MTI-003 insert membrane. The results showed that with the MTI-003 membrane a sensitivity higher than 90% could potentially still be achieved using a 50% cut-off instead of 60%, with a significant gain in specificity.

Considering these new data, the VMG decided to evaluate two prediction models with EpiOcular™ EIT in EIVS, one based on the original cut-off at 60% mean tissue viability as in the submission to EURL ECVAM and a second one based on a cut-off at 50% mean tissue viability.

EIVS included a statistically sufficient number of chemicals, supported by complete and quality assured *in vivo* Draize eye test data, for comparative evaluation of results. A total of 104 selected test chemicals (52 liquids and 52 solids) were distributed as identity coded aliquots for blind ring trial testing as three runs in three laboratories for both test methods. One other chemical (chemical #27; 2-Ethylhexylthioglycolate) was sent to all participating laboratories for testing but was excluded and replaced by another chemical (one of the final 104) at a very early stage of the study on request of one of the SkinEthic™ HCE participating laboratories because it was identified as a very strong MTT reducer. It has therefore been excluded from all the statistics described in the three statistics reports of this study. However, by the time chemical #27 was replaced by another chemical, it had already been tested in a complete test sequence by all three EpiOcular™ EIT participating laboratories. Since in EpiOcular™ EIT chemical #27 only produced minor interference with the MTT assay, it was decided to include it in all the statistics described in this report. Following the ring trial, the 52 solid chemicals were re-tested, with an additional 8 others newly selected (all identity coded i.e., blind testing) in three runs in one laboratory, for validation of an optimised EpiOcular™ EIT solid chemicals protocol. Chemical #37 (PEG-40 hydrogenated castor oil) was originally selected by the EIVS VMG as being solid. However, all three laboratories participating in the main validation study of the EpiOcular™ EIT (Beiersdorf, Harlan and IIVS) independently considered the chemical as being liquid due to its low melting point and testing occurring in the spring/summer period. This chemical was therefore tested during the main part of EIVS using the liquid protocol of EpiOcular™ EIT. However, due to a VMG oversight, chemical #37 was again shipped to Beiersdorf as a solid to be tested during the validation of the EpiOcular™ EIT optimised solid chemicals protocol. Since this time the testing occurred during the autumn/winter, Beiersdorf confirmed the physical state of the chemical as being solid upon receipt and tested it as such. Thus, chemical #37 was tested in both the liquid chemicals and solid chemicals protocols of EpiOcular™ EIT, somewhat in agreement with its borderline physical state. The VMG considered both sets of data (produced with the original liquid chemicals and the optimised solid chemicals protocols) as being valid and these were therefore included in all the statistics analyses. Nevertheless, the EpiOcular™ EIT predictive capacity was also calculated considering only the optimised solids protocol data (excluding the liquid chemicals protocol data) in accordance with the fact that this chemical had been tested *in vivo* as a solid and had been originally considered by the VMG as a solid during chemicals selection for the study.

EpiOcular™ EIT main validation study

The three laboratories participating in the validation of EpiOcular™ EIT, two European, Beiersdorf (the lead laboratory) and Harlan UK (naïve laboratory), and one in the US, IIVS, were trained by MatTek Corporation to assure optimal transfer of the test protocol into their facilities and to guarantee that the Standard Operating Procedure (SOP) did not allow for individual (different) interpretation of the experimental steps. All procedures and assay documentation were discussed and comments and suggestions for improvement and

clarification of the SOP were collected and implemented by MatTek Corporation in a final version of the SOP that was used in the ring trial of the validation study. The nine laboratory technicians assigned to the project (three per laboratory) performed the test method with 8 coded test chemicals (2 liquid No Cat, 2 solid No Cat, 2 liquid Cat 2, 1 solid Cat 2, 1 liquid Cat 1 and 2 solid Cat 1) at their test facility to demonstrate transferability of the test method. The variability of the particular experiments performed by single operators was very low, as judged by the difference in viability between tissue replicates (only 1 out of 108 results showed a difference > 20%). All test chemicals were consistently predicted by the three laboratories and nine operators using 50% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, while, using a 60% cut-off in the prediction model, 1 liquid chemical was predicted differently by one operator in one laboratory. Highly reproducible results were therefore obtained between operators and laboratories in the EpiOcular™ EIT transfer study. All the participating laboratories demonstrated their proficiency in performing the EpiOcular™ EIT and readiness to enter the formal validation study.

Based on the results for the fraction of complete test sequences (99.7% in total), it can be concluded that the validation of the EpiOcular™ EIT was based on high-quality data. The acceptance criterion for this characteristic was unequivocally fulfilled (≥ 85%). One chemical (chemical #33; 2,2'-[[4-[(2-Methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol; INCI name: HC BLUE NO. 11) was considered incompatible with the test method at Beiersdorf due to too high colour interference with the MTT assay and was therefore excluded from the statistical analysis for that laboratory.

The EpiOcular™ EIT test method was found to be highly reproducible. The within-laboratory reproducibility (WLR) (93.6% and 95.2% concordance of classifications for the 50% and 60% cut-offs analysed in this study, respectively) and the between-laboratory reproducibility (BLR) (91.3% and 93.3% concordance of classifications for the 50% and 60% cut-offs analysed in this study, respectively) were significantly above the acceptance criteria set by the VMG (WLR ≥ 85% and BLR ≥ 80%).

Taking 60% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, the overall accuracy (79.0%) and specificity (70.5%) were ‘definitely acceptable’ according to the acceptance criteria as defined by the VMG (overall accuracy ≥ 75%; specificity ≥ 60%), whereas the sensitivity (87.6%) was between the limits of ‘definitely unacceptable’ (< 80%) and ‘definitely acceptable’ (≥ 90%). Considering only the liquid chemicals, the test method fulfilled all of the ‘definitely acceptable’ criteria (overall accuracy of 81.9%; sensitivity of 98.3%; specificity of 66.7%). For the solid chemicals both the overall accuracy (75.9%) and the specificity (74.8%) were ‘definitely acceptable’, whereas the sensitivity (76.9%) was ‘definitely unacceptable’. Of note, the solid chemicals protocol showed balanced predictive capacity values with the 60% cut-off.

Taking 50% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, the overall accuracy (77.9%) and specificity (74.5%) were ‘definitely acceptable’ according to the acceptance criteria defined by the VMG (overall accuracy ≥ 75%; specificity ≥ 60%), whereas the sensitivity (81.4%) was still between the limits of ‘definitely unacceptable’ (< 80%) and ‘definitely acceptable’ (≥ 90%). Again, considering only the liquid chemicals, the test method fulfilled all of the ‘definitely acceptable’ criteria (overall accuracy of 82.5%; sensitivity of

96.2%; specificity of 69.8%), while for the solid chemicals only the specificity (79.7%) was ‘definitely acceptable’. The overall accuracy (73.0%) fell short of ‘definitely acceptable’ (≥ 75%) but surpassed ‘definitely unacceptable’ (< 65%), while the sensitivity (66.7%) was ‘definitely unacceptable’.

Based on these findings the VMG concluded that:

- EpiOcular™ EIT can be easily transferred among properly equipped and staffed laboratories, including those having no prior experience in performance of similar test methods i.e., naïve laboratories. Experienced personnel can readily be trained in the test method, and the necessary equipment and supplies can be readily obtained. The EpiOcular™ EIT SOP is clearly written and the testing and analysis of results can be performed without difficulties.

- The validation study was of high quality due to a near complete dataset with negligible re-testing performed.

- The WLR was well above the acceptance criterion set by the VMG (WLR ≥ 85%), and concordance of classifications within a single laboratory was above 90% for EpiOcular™ EIT in the participating laboratories.

- The BLR was also well above the acceptance criterion set by the VMG (BLR ≥ 80%), and the concordance of final classifications obtained between the different participating laboratories was greater than 90% for EpiOcular™ EIT.

- The EpiOcular™ EIT protocol for liquid chemicals met all of the VMG acceptance criteria for sensitivity, specificity and overall accuracy. The 60% cut-off was considered to be better than the 50% cut-off because it resulted in a better sensitivity and generated no false negatives based on the mode of all predictions (the 50% cut-off generated one false negative for a Category 2B chemical), with similar overall accuracy.

- On the other hand, not all of the acceptance criteria were met by the EpiOcular™ EIT protocol for the solid chemicals. Sensitivity was < 90% even at the 60% cut-off and of the 6 chemicals that were under-predicted with the 60% cut-off based on the mode of all predictions, one was classified *in vivo* as Category 1.

- Analysis of the EIVS data for solid chemicals indicated scope for improvement through a balanced increase in sensitivity with decrease in specificity to attain a compromise of sensitivity ≥ 90% with specificity maintained ≥ 60%. Optimisation was therefore recommended for the EpiOcular™ EIT protocol for solid chemicals.

Optimisation of the EpiOcular™ EIT solid chemicals protocol was performed at the method developer’s laboratory (MatTek Corporation) in order to increase the sensitivity of the assay to the level requested by the VMG. This optimisation led to an increase of the exposure time from 90 minutes to 6 hours. The optimisation work was performed independently of the EIVS but with guidance and scientific support from the VMG. The VMG provided 11 EIVS solid chemicals to MatTek Corporation for the optimisation of the EpiOcular™ EIT solid chemicals protocol, including the 6 solid chemicals that had been under-predicted (false negatives) by the original protocol plus 5 correctly predicted not classified (UN GHS No Cat) chemicals that had shown borderline results. MatTek Corporation was able to complete the optimisation of the solid chemicals protocol without delay, enabling follow-up validation within EIVS (post-optimisation validation), including analysis of the results by the VMG. The validation of the

EpiOcular™ EIT optimised solids protocol was conducted with the original 52 EIVS solid chemicals plus an extra 8 selected to compensate for the 11 used during the optimisation of the protocol. The post-optimisation validation of the EpiOcular™ EIT optimised solid chemicals protocol took place in a single laboratory, at Beiersdorf (i.e., the lead laboratory for EpiOcular™ EIT in the original validation study), since the main purpose of this follow-up study was to evaluate the predictive capacity of the optimised protocol. Based on the very high reproducibility (WLR and BLR) achieved in the validation study of the original EpiOcular™ EIT protocols and of SkinEthic™ HCE, using multiple exposure times and post-treatment incubation periods, the VMG considered that a simple change in exposure time in the EpiOcular™ EIT solid chemicals protocol would not affect the reproducibility of the test method. Nevertheless, the VMG decided to assess the WLR of the EpiOcular™ EIT optimised solid chemicals protocol at Beiersdorf and based on the results decide if any additional reproducibility data (e.g., BLR) generated with the new protocol would be necessary.

EpiOcular™ EIT post-optimisation validation study (solids protocol)

Based on the results for the fraction of complete test sequences (98.3% in total), it can be concluded that the post-optimisation validation of the EpiOcular™ EIT optimised solid chemicals protocol at Beiersdorf was based on high-quality data. The acceptance criterion for this characteristic was unequivocally fulfilled (≥ 85%). One chemical (chemical #98; 4,4'-(4,5,6,7-Tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide; INCI name: TETRABROMOPHENOL BLUE) was considered incompatible with the test method due to too high colour interference with the MTT assay and was therefore excluded from the statistical analysis.

The EpiOcular™ EIT optimised solid chemicals protocol was found to be at least as reproducible as the original solid chemicals protocol, with 93.2% and 96.6% concordance of classifications (based on 59 chemicals) being obtained by Beiersdorf with the optimised protocol for the 50% and 60% cut-offs analysed in this study, respectively, as compared to 92.0% and 94.0% obtained by the same laboratory with the original protocol (based on 50 chemicals). Forty nine (49) chemicals are common to the two datasets. If only these are considered in the calculations, the concordance of classifications obtained by Beiersdorf were 91.8% (50% cut-off) and 95.9% (60% cut-off) for the optimised protocol and 91.8% (50% cut-off) and 93.9% (60% cut-off) for the original protocol. The WLR of the EpiOcular™ EIT optimised solid chemicals protocol was thus significantly above the acceptance criterion set by the VMG (WLR ≥ 85%). The WLR obtained by Beiersdorf with the optimised solid chemicals protocol (as described above) was also comparable to the WLR obtained by considering the data acquired by all three laboratories that participated in the validation of the original protocol, i.e., total concordance of classifications of 92.8% (based on 50 chemicals in Beiersdorf and 51 chemicals in Harlan and IIVS) or 92.5% (based on 49 chemicals in all three laboratories) for both the 50% and 60% cut-offs.

Taking 60% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, the overall accuracy (78.0%), the specificity (60.7%) and the sensitivity (93.5%) were all 'definitely acceptable'

according to the acceptance criteria as defined by the VMG (overall accuracy ≥ 75%; specificity ≥ 60%; sensitivity ≥ 90%).

Taking 50% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, the overall accuracy (76.8%) and the specificity (64.3%) were 'definitely acceptable' according to the acceptance criteria defined by the VMG (overall accuracy ≥ 75%; specificity ≥ 60%; sensitivity ≥ 90%), whereas the sensitivity (88.2%) was between the limits of 'definitely unacceptable' (< 80%) and 'definitely acceptable' (≥ 90%), but very close to being 'definitely acceptable'.

Based on these findings the VMG concluded that:

- The validation of EpiOcular™ EIT optimised solids protocol was of high quality due to a near complete dataset with negligible re-testing performed.

- The WLR was well above the acceptance criterion set by the VMG (WLR ≥ 85%), and concordance of classifications within a single laboratory was above 90% for EpiOcular™ EIT at Beiersdorf.

- Further BLR evaluation was identified, by the core VMG, to be unnecessary given the previous good reproducibility of the EpiOcular™ EIT test method, and a similar (or even slightly better) WLR observed for the optimised solids protocol as compared to the original protocol. With the increased exposure time in the optimised solid chemicals protocol, a stronger separation between classified and not-classified chemicals in the viability scale was observed as compared to the original protocol, which is expected to improve the reproducibility of the test method. The fact that two SkinEthic™ HCE protocols with different exposure times were evaluated and showed equally high BLR provides additional evidence supporting the conclusion that further BLR assessment of the EpiOcular™ EIT optimised solid chemicals protocol is not necessary.

- The optimised EpiOcular™ EIT protocol for solid chemicals met all of the VMG acceptance criteria for sensitivity, specificity and overall accuracy using the 60% cut-off, but not with the 50% cut-off, with sensitivity being slightly lower than the 'definitely acceptable' criterion in the latter case. The overall accuracy was also higher with a 60% cut-off than with a 50% cut-off. The 60% cut-off was therefore considered to be better than the 50% cut-off with the optimised solids protocol, similarly to what had been concluded for the liquids protocol.

- The overall predictive capacity of EpiOcular™ EIT considering a combination of the data obtained for the liquid chemicals protocol with the data obtained using the optimised solid chemicals protocol, and a cut-off of 60%, consists of a sensitivity of 95.7%, a specificity of 63.0% (63.7% if chemical #37 is counted twice since it was tested both with the liquids protocol and with the optimised solids protocol) and an overall accuracy of 79.7% (79.8% if chemical #37 is counted twice). On this basis, all of the acceptance criteria defined by the VMG were met. Two out of 57 chemicals (2 solid Cat 2B chemicals) were under-predicted (false negatives) and 20 out of 54 chemicals (9 liquids and 11 solids) were over-predicted (false positives) based on the mode of all predictions.

SkinEthic™ HCE main validation study

Two naïve laboratories participating in the validation of SkinEthic™ HCE, one European, CARDAM, and one in the US, CeeTox, were trained by the lead laboratory L'Oréal to assure optimal transfer of the SE and LE test protocols into their facilities and to guarantee that the SOP did not allow for individual (different) interpretation of the experimental steps. All procedures and assay documentation were discussed and comments and suggestions for improvement and clarification of the SOP were collected and implemented by L'Oréal in a final version of the SOP that was used in the ring trial of the validation study. The laboratory technicians from all three participating laboratories assigned to the project performed the test method with 14 coded test chemicals (3 No Cat, 2 Cat 2, 6 Cat 1 and 3 undefined) at their test facility to demonstrate transferability of the test method. The variability obtained with both the SE and LE protocols at the three laboratories was very low with SD below 18% being obtained for the majority of the tested chemicals in all laboratories. Concordance between results of the three laboratories that participated on the transfer study was very good, especially considering that highly challenging chemicals (including colorants and direct MTT reducers) had been selected for the study. The WLR ranged from 86.7% (CeeTox) to 87.5% (L'Oréal and CARDAM) and the BLR between the three laboratories in particular was excellent (100% for the SE protocol and 92.3% for the LE protocol). All the participating laboratories demonstrated their proficiency in performing the SkinEthic™ HCE and readiness to enter the formal validation study.

Based on the results for the fraction of complete test sequences (100% in total for the SE protocol, 99.7% in total for the LE protocol), it can be concluded that the validation of the SkinEthic™ HCE was based on high-quality data. The acceptance criterion for this characteristic was unequivocally fulfilled (≥ 85%).

None of the 104 chemicals tested was considered incompatible with the test method by any of the three laboratories, with either the SE or the LE protocol. All chemicals were thus included in all of the statistical analyses.

The SkinEthic™ HCE test method was found to be highly reproducible. The WLR (93.9% and 95.5% concordance of classifications for the SE and LE, respectively) and the BLR (92.3% concordance of classifications for both the SE and the LE protocols) were significantly above the acceptance criteria set by the VMG (WLR ≥ 85% and BLR ≥ 80%).

The only prediction model that was evaluated used a mean viability of 50% as the threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals. The specificity of this prediction model was found to be ‘definitely acceptable’ according to the acceptance criterion defined by the VMG (≥ 60%), regardless of the protocol or strategy (SE: 88.5%; LE: 65.5%; test strategy: 77.1%). The sensitivity was on the other hand ‘definitely unacceptable’ (< 80%) according to the same acceptance criteria (SE: 42.7%; LE: 71.6%; test strategy: 54.5%). The overall accuracy was between the limits of ‘definitely unacceptable’ (< 65%) and ‘definitely acceptable’ (≥ 75%) (SE: 65.6%; LE: 68.6%; test strategy: 65.8%).

Based on these findings the VMG concluded that:

- SkinEthic™ HCE SE and LE can be easily transferred among properly equipped and staffed laboratories, including those having no prior experience in performance of similar test methods i.e., (naïve laboratories). Experienced personnel can readily be trained in the test method, and the necessary equipment and supplies can be readily obtained. The

SkinEthic™ HCE SOP is clearly written and the testing and analysis of results can be performed without difficulties.

- The validation study was of high quality due to a near complete dataset with negligible re-testing performed.

- The WLR was well above the acceptance criterion set by the VMG (WLR ≥ 85%), and concordance of classifications within a single laboratory was above 90% in the participating laboratories for both the SE and LE protocols of SkinEthic™ HCE.

- The BLR was also well above the acceptance criterion set by the VMG (BLR ≥ 80%), and the concordance of final classifications obtained between the different participating laboratories was greater than 90% for both the SE and LE protocols of SkinEthic™ HCE.

- Not all of the VMG acceptance criteria were met by either the SE or LE protocols of SkinEthic™ HCE alone. Sensitivity, in particular, was 'definitely unacceptable' being < 80% with both protocols (SE: 42.7%; LE: 71.6%). Moreover, of the 30 chemicals that were under-predicted by SE and of the 15 that were under-predicted by LE based on the mode of all predictions, 14 and 5, respectively, were classified *in vivo* as Category 1, which is also 'definitely unacceptable'.

- The use of EPRA to orient chemicals to the LE (non-reactive) or SE (reactive) protocol is also not valid due to a false negative rate of 45.5% and 10 Category 1 chemicals being under-predicted as non-irritants (based on the mode of all predictions). It was therefore decided not to conduct a reproducibility assessment of EPRA.

- Analysis of the data for the SkinEthic™ HCE indicated scope for improvement. Further optimisation has therefore been recommended for the SkinEthic™ HCE test method considering different protocols for liquid chemicals and solid chemicals, as with EpiOcular™ EIT.

1. Introduction

1.1. Background and history

The assessment of ocular toxicity, (i.e., eye irritation and serious eye damage) is important to ensure the safety of products and their components used in our daily life. In several EU legislations related to chemicals and products, the generation of information on eye irritation and serious eye damage represents a standard requirement (EC, 2006a). The traditional eye irritation test used to be the Draize eye test performed on albino rabbits (OECD TG 405; OECD, 2012a). However, ethical and scientific considerations as well as legal requirements in EU legislations have triggered the development and validation of alternative methods to the Draize eye test. In particular, the EU Cosmetics Regulation expressly forbids the use of animals in the safety evaluation of cosmetic products and ingredients (EC, 2009). Furthermore, the EU REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) legislation encourages the use of *in vitro* methods, in particular for serious eye damage/eye irritation testing (EC, 2006a).

In order to reduce and/or replace the Draize rabbit eye test, the use of testing strategies is generally recommended, due to the fact that the range of criteria for injury and inflammation covered by the Draize rabbit eye test is unlikely to be covered by a single *in vitro* test (Eskes *et al*., 2005). A testing strategy has been suggested for regulatory purposes to replace or reduce animal testing (Scott *et al.*, 2010). It proposes, based on the expected ocular toxicity profile of the test chemical, the use of one of the two following tiered testing approaches before progression of further *in vitro* testing:

- the Bottom-Up approach, which starts with using *in vitro* test methods that can accurately identify chemicals not requiring classification for eye hazards according to the UN Globally Harmonized System of Classification and Labelling of Chemicals (UN GHS) and the EU Classification, Labelling and Packaging (EU CLP) system (UN, 2013; EC, 2008); and
- the Top-Down approach, which starts with using *in vitro* test methods that can accurately identify chemicals inducing serious and/or irreversible eye damage (UN GHS / EU CLP Category 1).

These two tiered testing approaches have served as the basis for the validation efforts undertaken for eye hazard testing during the last decade in Europe and in the United States (ICCVAM, 2006, 2010; ESAC 2007, 2009), and led to the regulatory adoption of three alternative test methods by the OECD since 2009 for both the top-down and bottom-up approaches (OECD, 2012b, 2013a,b).

However, not all *in vivo* mechanisms of ocular toxicity may be covered by the test methods currently adopted. In particular, test methods using Reconstructed human Cornea-like Epithelia (RhCE), may be relevant for assessing conjunctiva epithelial responses (OECD, 2010). Furthermore, considering the small prevalence of eye irritants and chemicals inducing serious eye damage (Adriaens *et al*., 2014), RhCE test methods could be very important to reduce animal testing by identifying chemicals not requiring classification in a non-animal testing strategy.

Two test methods based on commercially available RhCE models, the EpiOcular™ OCL-200 and the SkinEthic™ Human Corneal Epithelium (HCE), were developed and underwent corporate (pre)validation studies in the early 2000's (Blazka *et al*., 2003; Van Goethem *et al*., 2006; Doucet *et al*., 2006). The EpiOcular™ OCL-200 uses non-transformed human epidermal keratinocytes cultured to form a stratified squamous, non-keratinized epithelium; whereas the SkinEthic™ HCE model uses immortalized human corneal cells which develop into a multi-layered tissue that resembles morphologically and physiologically the human corneal epithelium. In both cases, test materials can be applied neat directly on the surface of the reconstructed tissues.

The corporate validation study on the EpiOcular™ OCL-200 assay and the corporate pre-validation study on the SkinEthic™ HCE assay were submitted to the former European Centre for the Validation of Alternative Methods (ECVAM) for evaluation in December 2005. The ECVAM Eye Irritation Task Force positively reviewed the two submissions and recommended in 2006 protocol improvements prior to enter a formal validation study. The two assays have then undergone protocol optimisation and assessment in a multi-laboratory trial managed by Cosmetics Europe between 2007 and 2008 leading to the optimisation of the protocols and refinement of the prediction models of the two RhCE test methods (Harbell *et al*., 2009; Cotovio *et al*., 2010; Kaluzhny *et al*., 2011; Pfannenbecker *et al*., 2013; Alépée *et al*., 2013). In this optimisation and pre-validation study, the assays were shown to predict eye irritant properties of test substances with approximately 80% of accuracy, and the results of this optimisation study were submitted to ECVAM in 2008.

Further to the request and review for additional data, the prospective Eye Irritation Validation Study (EIVS) on the two RhCE models was then initiated in December 2008. The study which ended in 2013 (see Table 1.1), was co-sponsored by EURL ECVAM and Cosmetics Europe. The primary goal of the EIVS was to evaluate the usefulness and limitations of the two RhCE *in vitro* test methods (each having two different protocols: Liquids and Solids for EpiOcular™ Eye Irritation Test (EIT); SE and LE for SkinEthic™ HCE) and of the EPRA+SkinEthic™ HCE SE/LE Test Strategy (TS) for discriminating non-classified test substances from classified ones (Freeman *et al*., 2010). For SkinEthic™ HCE, a total of 104 coded chemicals were tested in both SE and LE in 3 runs and 3 replicate tissues per run, in 3 laboratories, for each protocol. The same 104 chemicals were also tested in EPRA in 1 run with 3 replicate measurements in 1 laboratory. For EpiOcular™ EIT, a total of 52 liquids, 51 solids and 1 chemical with borderline physical state (melting point near room temperature) were tested in the liquids and solids protocols, respectively, in 3 runs and 2 replicate tissues per run, in 3 laboratories, for each protocol.

Optimisation of the EpiOcular™ EIT solids protocol was performed at the method developer's laboratory (MatTek Corporation) in order to increase the sensitivity of the assay to the level requested by the VMG. This optimisation led to an increase of the exposure time from 90 min to 6 hours.

Fifty two of these core EIVS test substances plus an additional 8 selected test substances were tested in blind in three runs in one laboratory in a follow-up validation of an optimised EpiOcular™ EIT solids protocol.

Table 1.1: Chronology and Management of the EURL ECVAM - Cosmetics Europe Eye Irritation Validation Study (EIVS)

Year	Month / Meeting / Teleconference	Key Discussions / Decisions / Actions
2005	**December**	- **First submissions to ECVAM** of corporate pre-validation study on the SkinEthic™ HCE test method (Van Goethem *et al*., 2006) and of a corporate validation study on the EpiOcular™ ET_{50} test method for surfactants and surfactant-based formulations
2006	ECVAM Eye Irritation Task Force meeting	- Requirement for additional information on both SkinEthic™ HCE and EpiOcular™ ET_{50} test methods before initiation of a formal validation study
2008	**September**	- **Updated submission to ECVAM** including optimisation and pre-validation of the SkinEthic™ HCE model (Cotovio *et al*., 2010; Alépée *et al*., 2013) and of the EpiOcular™ Eye Irritation Test method (Kaluzhny *et al*., 2011; Pfannenbecker *et al*., 2013)
	December: 1st Validation Management Group (VMG) meeting of the Eye Irritation Validation Study (EIVS)	- Planning of the study including project plan; discussions on study design initiated; request for additional information on the EPRA test; chemicals selection initiated
2009	**February**	- **Submission of the Cyl/Lys EPRA and GSH/GSSG reactivity assays to ECVAM as an integral part of the SkinEthic™ HCE submission**
	April: 2nd EIVS VMG Meeting	- Discussion on the use of two tissue replicates (instead of three) with the EpiOcular™ EIT test method in EIVS (in accordance with what was used in pre-validation studies); conduct and management of the study; discussion on project plan and study design; discussion on study acceptance criteria initiated; discussion on the EPRA submission; **decision not to include the GSH/GSSG reactivity assay in the SkinEthic™ HCE test strategy and to withdraw it from EIVS**; discussion on chemicals selection
	June: 3rd EIVS VMG Meeting	- Conduct and management of the study; discussion on project plan and study design; **Approval of prediction model to be used with EPRA in EIVS**; planning of training and transferability of EPRA at TNO; discussion on chemicals selection; discussion on EPRA reliability study design
	June: EIVS VMG Teleconference	- Discussion on study design
	June	- **TNO training on EPRA completed**
	July: EIVS VMG Teleconference	- Discussion on study design
	July: EIVS VMG Teleconference	- **Decision on and approval of EIVS study design**
	August: EIVS VMG Meeting during WC8	- **Chemicals acquisition initiated**; discussion on chemicals selection; discussion on TNO EPRA training and transferability studies
	September: 4th EIVS VMG Meeting	- Conduct and management of the study; discussion on study acceptance criteria; planning of the quality assurance audits on the RhCE production sites; SOPs and contracts with the participating laboratories; discussion on chemicals selection
	October: EIVS VMG Teleconference	- Discussion on chemicals selection; planning of quality assurance audits on the RhCE production sites
	October	- **TNO EPRA transferability study completed**
	November: EIVS VMG Teleconference	- **Approval of the EPRA training and transferability results and report from TNO**; planning of quality assurance audits on the RhCE production sites
	November: 5th EIVS VMG Meeting	- **Approval of EPRA reliability study design**; conduct and management of the study; discussion on project plan; discussion on guidance on study conduct and study acceptance criteria; discussion on chemicals selection

	December: EIVS VMG Teleconference	- Discussion on chemicals selection
2010	**January:** EIVS VMG Teleconference	- Discussion on chemicals selection: identification of first set of 77 chemicals for EPRA testing, of which only 73 were actually tested (eligible for final selection for EIVS)
	January: EIVS VMG Teleconference	- Discussion on chemicals selection; discussion on discontinued production of MTI-001a insert membrane, its replacement by the MTI-001b insert membrane for the EpiOcular™ EIT tissue production at MatTek Corporation and the discovery of a problem with the new insert membrane, which was bursting with certain chemicals; discussion on the conduct of adapted controls for colorants and direct MTT reducers
	January: EIVS VMG Teleconference	- Follow-up on discussion on problem with insert used to produce EpiOcular™ EIT tissues at MatTek Corporation; follow-up on discussion on the conduct of adapted controls for colorants and direct MTT reducers
	February: EIVS VMG Teleconference	- Discussion on guidance on study conduct and study acceptance criteria; discussion on chemicals selection
	March: EIVS VMG Teleconference	- Discussion on guidance on study conduct and study acceptance criteria; discussion on chemicals selection
	March	- **Quality Assurance audit on the SkinEthic™ HCE tissues production site**
	March: 6th EIVS VMG Meeting	- **EPRA SOP finalised and approved**; conduct and management of the study; discussion on guidance on study conduct and study acceptance criteria; update on problem encountered with insert used to produce EpiOcular™ EIT tissues at MatTek Corporation: initiation of testing of two new insert membranes (MTI-002 and MTI-003); discussion on chemicals selection
	April	- **SkinEthic™ HCE participating laboratories training and transferability studies completed**
	May: EIVS VMG Teleconference	- Review of first set of EPRA results for 55 chemicals obtained by TNO
	May	- **Quality Assurance audit on the EpiOcular™ EIT tissues production site**
	May	- **Statistical analysis on the use of two tissue replicates with the EpiOcular™ EIT test method conducted by NICEATM**
	June: EIVS VMG Teleconference	- **Approval of the SkinEthic™ HCE training and transferability results and SOP; Selection of a first set of 34 chemicals for EIVS testing** (based on first set of EPRA results) and decision to ship them to the laboratories for testing; Identification of second set of 55 chemicals for EPRA testing, of which only 49 were actually tested (eligible for final selection for EIVS)
	June	- **Communication from MatTek Corporation to VMG on their decision to withdraw the use of MTI-002 insert membrane for EpiOcular™ EIT tissue production due to supply difficulties and to poorer performance as compared to the other inserts**
	June	- **Chemicals coding and distribution initiated**
	June	- **SkinEthic™ HCE experimental phase started**
	September: EIVS VMG Teleconference	- Review of second set of EPRA results for 53 chemicals obtained by TNO; **Selection of a second set of 46 chemicals for EIVS testing** (based on second set of EPRA results) and decision to ship them to the laboratories for testing

	September: EIVS VMG Teleconference	- Approval of comparative statistical analysis on use of old MTI-001a insert membrane (discontinued) versus bursting MTI-001b insert membrane versus new MTI-003 insert membranes with the EpiOcular™ EIT test method and **decision to use MTI-003 insert membrane in the multi-laboratory testing part of the validation study**; **Decision to evaluate two prediction models for EpiOcular™ EIT in EIVS**, one based on a cut-off at 60% viability as in the original submission and a second one based on a cut-off at 50% viability considering the results obtained with the testing of 94 chemicals with the new insert membranes
	September: 7th EIVS VMG Meeting	- **Approval of quality assurance audits of the RhCE production sites; Approval to use of two tissue replicates (instead of three) with the EpiOcular™ EIT test method in EIVS** (supported by statistical analysis performed by NICEATM); discussion on project plan and on guidance on study conduct and study acceptance criteria: general consensus reached on both documents; preparation and discussion of a Statistical Analysis and Reporting Plan; discussion on chemicals selection
	November: EIVS VMG Teleconference	- Discussion of an issue with meeting acceptance criteria with positive control for LE during initial testing performed by one of the participating laboratories of the SkinEthic™ HCE test method and planning of a strategy to solve the problem; discussion on chemicals selection
	November	- **EpiOcular™ EIT participating laboratories training and transferability studies completed**
	November: EIVS VMG Teleconference	- **Approval of the EpiOcular™ training and transferability results; Approval of the final Project Plan and of the Guidance on EIVS Conduct & Performance Criteria document;** discussion on chemicals selection
	December: EIVS VMG Teleconference	- Discussion on chemicals selection: OECD toolbox analysis of selected chemicals & decision to withdraw from the study a chemical that had been selected in the second set of 46 chemicals due to inconsistent physical state between what had been tested *in vivo* (red to brown liquid) and what was acquired for EIVS (white crystalline solid)
	December: EIVS VMG Teleconference	- Discussion on chemicals selection: identification of third and final set of 15 chemicals for EPRA testing, of which only 14 were actually tested (eligible for final selection for EIVS)
2011	**January:** EIVS VMG Teleconference	- Review of new data from SkinEthic™ HCE participating laboratory that had shown issues with the LE positive control and approval of continuation of testing at that laboratory
	February	- **Approval of the EpiOcular™ EIT SOP**
	March: EIVS VMG Teleconference	- Discussion on chemicals selection: decision to replace a strong MTT reducer that had been selected in the first set of 34 chemicals, based on results obtained by one of the SkinEthic™ HCE participating laboratories; decision to include in the final chemicals selection 2 strong colorants that produced permanent coloration of the cornea *in vivo* as extra EIVS chemicals
	March	- **EpiOcular™ EIT experimental phase started**
	April: EIVS VMG Teleconference	- Review of third set of EPRA results for 33 chemicals obtained by TNO (6 of which were re-tests); **Completion of EIVS chemicals selection: Selection of a third and final set of 28 chemicals for EIVS testing** (based on third set of EPRA results) and decision to ship them to the laboratories for testing
	April	- **Chemicals coding and distribution completed**

	June: EIVS VMG Teleconference	- **Approval of the final Statistical Analysis and Reporting Plan**; monitoring of testing progression in all participating laboratories; discussion on the inclusion of an addendum to the Guidance on EIVS Conduct & Performance Criteria document providing further instructions for the testing of direct MTT reducers and/or coloured test chemicals
	June: EIVS VMG Teleconference	- **Approval of the Addendum to the Guidance on EIVS Conduct & Performance Criteria document**
	November: 8th EIVS VMG Meeting	- **Preliminary analysis of results from main validation study** (completed for the three EpiOcular™ EIT participating laboratories and for two of the three SkinEthic™ HCE participating laboratories): **recommendations for EpiOcular™ EIT to optimise its protocol for solid materials and for SkinEthic™ HCE to optimise both its protocols**; **Decision not to conduct a multi-laboratory reliability assessment of EPRA due to the non-validity of the proposed SkinEthic™ HCE testing strategy**
	November: EIVS VMG Teleconference	- VMG communication to MatTek Corporation and Beiersdorf on the outcome obtained with the EpiOcular™ EIT test method and the need to optimised the solids protocol based on the preliminary results; VMG communication to L'Oréal on the outcome obtained with the SkinEthic™ HCE test method, the non-validity of the testing strategy, and the need to optimise the SE and LE protocols potentially for the testing of liquids and solids, respectively, based on the preliminary results
2012	**February**	- **EpiOcular™ EIT experimental phase officially completed in all three participating laboratories, including all the necessary re-testing identified by the VMG**
	February	- **First version of EpiOcular™ EIT EIVS statistics report available**
	February: EIVS VMG Teleconference	- Discussion on chemicals selection for optimisation and post- optimisation validation of EpiOcular™ EIT and SkinEthic™ HCE; revision of timelines for ESAC peer-review
	May	- **First version of SkinEthic™ HCE EIVS statistics report available**
	May: 9th EIVS VMG Meeting	- Review of the EpiOcular™ EIT and SkinEthic™ HCE statistics reports on the results from the main validation study; planning of the optimisation and possible post-optimisation validation of the EpiOcular™ EIT solids protocol and of SkinEthic™ HCE
	June	- **First version of EIVS Chemicals Selection Report available**
	June: EIVS VMG Teleconference	- Discussions with L'Oréal about optimisation of a SkinEthic™ HCE protocol for liquid chemicals; discussion on chemicals selection for post- optimisation validation of EpiOcular™ EIT and SkinEthic™ HCE
	July	- **Official communication to ESAC and the public on the outcome of the main part of EIVS**
	August	- **Statistical analyses on the use of two tissue replicates with the SkinEthic™ HCE SE and LE protocols conducted by NICEATM**
	October: EIVS VMG Teleconference	- MatTek Corporation reporting to VMG on the successful optimisation of the EpiOcular™ EIT solids protocol – request from the VMG for more information; discussion on chemicals selection for the post- optimisation validation of the EpiOcular™ EIT optimised solids protocol; decision from L'Oréal to withdraw from optimising the SkinEthic™ HCE test method within EIVS as more time will be required to get to a positive outcome

	December: EIVS VMG Teleconference	- Review of further data on the optimisation of the EpiOcular™ EIT solids protocol provided by MatTek Corportation; **approval of chemicals selection for the post- optimisation validation of the EpiOcular™ EIT optimised solids protocol**; planning of the post-optimisation validation of the EpiOcular™ EIT optimised solids protocol: decision to conduct the work at Beiersdorf
	December: EIVS VMG Teleconference	- Request to MatTek Corporation for further data on the optimisation of the EpiOcular™ EIT solids protocol to support a VMG approval of the optimised protocol; planning of the post-optimisation validation of the EpiOcular™ EIT optimised solids protocol; revised statistics report from the main validation study on the EpiOcular™ EIT test method made available and presented to the VMG
2013	**January:** EIVS VMG Teleconference	- **Approval of the EpiOcular™ EIT optimised solids protocol**; review of comments received on the revised statistics report from the main validation study on the EpiOcular™ EIT test method
	February	- **Chemicals coding and distribution for the validation of the optimised EpiOcular™ EIT solids protocol**
	March	- **Experimental work for the validation of the optimised EpiOcular™ EIT solids protocol started at Beiersdorf**
	April	- **SkinEthic™ HCE experimental phase officially completed in all three participating laboratories, including all the necessary re-testing identified by the VMG**
	April: EIVS VMG Teleconference	- Review of EIVS Chemicals Selection Report; debriefing on Cosmetics Europe HPLC project; discussion on outstanding EIVS activities
	June	- **Experimental work for the validation of the optimised EpiOcular™ EIT solids protocol completed at Beiersdorf**
	June: EIVS VMG Teleconference	- Planning of next steps: report on potential reasons for misclassifications, closing of chemicals repository at TNO, drafting of statistics report on the post-optimisation validation study on the EpiOcular™ EIT optimised solids, drafting of Validation Study Report, preparation of ESAC peer-review
	July	- **First version of the statistics report on the post-optimisation validation study of the EpiOcular™ EIT optimised solids protocol available**
	September: EIVS VMG Teleconference	- Review of reasons for misclassifications in EIVS main study; review of the statistics report on the post-optimisation validation study on the EpiOcular™ EIT optimised solids protocol; planning of next steps: drafting of the Validation Study Report and preparation of ESAC peer-review; **Approval of the results from the post-optimisation validation study on the EpiOcular™ EIT optimised solids protocol and of the overall results of the EIVS validation study**
	November: 10th and final EIVS VMG Meeting	- **Discussion on final VMG recommendations on EpiOcular™ EIT and SkinEthic™ HCE; Discussion on the Chemicals Selection Report, the Statistics Reports and the Validation Study Report; Presentation and discussion of the Cosmetics Europe study on the use of HPLC with RhCE assays to increase applicability to coloured chemicals; Preparation of OECD SPSFs on EpiOcular™ EIT and on HPLC-photometry as an alternative formazan detection system for RhCE/MTT-based test methods; Preparation of ESAC peer-review of EIVS, the post-optimisation validation of the EpiOcular™ EIT optimised solids protocol and of HPLC-photometry as an alternative formazan detection system for RhCE/MTT-based test methods**
2014	**January**	- **Final version of the Chemicals Selection Report available; Approval of final Chemicals Selection Report**

	March	- **Seventh and final version of the EpiOcular™ EIT EIVS statistics report available; Eighth and final version of the SkinEthic™ HCE EIVS statistics report available; Fifth and final version of the statistics report on the post-optimisation validation study of the EpiOcular™ EIT optimised solids protocol available** - **Approval of the final EpiOcular™ EIT and SkinEthic™ HCE statistics reports (EIVS and post-optimisation validation)** - **Approval of the final VMG conclusions on EIVS and recommendations on EpiOcular™ EIT and SkinEthic™ HCE** - **Approval of the Validation Study Report**

VMG = Validation Management Group; EIVS = Eye Irritation Validation Study; CSG = Chemicals Selection Group

1.2. Goals and objectives of the study

The objective of the EURL ECVAM – Cosmetics Europe Eye Irritation Validation Study (EIVS) was to evaluate the validity of the RhCE-based EpiOcular™ EIT and the SkinEthic™ HCE Short-time Exposure (SE), Long-time Exposure (LE) and Test Strategy (TS) through a prospective study for the regulatory hazard assessment of chemicals for serious eye damage/eye irritation according to the United Nations Globally Harmonized System of Classification and Labelling of Chemicals (UN GHS) and as implemented by the European Commission Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (EU CLP) (UN, 2013; EC, 2008). In particular, these RhCE-based test methods shall be incorporated into the Bottom-Up and Top-Down tiered test strategy schemes as defined by Scott and co-workers (2010) to identify chemicals not requiring classification and labelling for serious eye damage/eye irritation. The ultimate purpose of the Bottom-Up/Top-Down tiered test strategy is to replace the traditional *in vivo* Draize eye irritation test [Method B.5 of EC Regulation 440/2008 (EC, 2008) or OECD TG 405 (OECD, 2012a)].

For this purpose, EIVS assessed the relevance (predictive capacity) and reliability (reproducibility within and between laboratories) of the EpiOcular™ EIT and the SkinEthic™ HCE SE, LE and TS by testing a statistically significant number of coded test chemicals (substances and mixtures), supported by complete and quality assured *in vivo* Draize eye irritation data for comparative evaluation of results. Specifically, the EIVS assessed the validity of the EpiOcular™ EIT protocol for liquids, the EpiOcular™ EIT protocol for solids, an optimised EpiOcular™ EIT protocol for solids, the SkinEthic™ HCE Short-time Exposure (SE) protocol, the SkinEthic™ HCE Long-time Exposure (LE) protocol, and the SkinEthic™ HCE test strategy combining the SE and LE protocols with the Eye irritation Peptide Reactivity Assay (EPRA).

The RhCE models and protocols described above were evaluated to be used as stand-alone (independent) test methods to reliably discriminate chemicals not classified as eye irritant ("non-irritants") from classified ones (in the framework of a Bottom-Up/Top-Down test strategy, Scott *et al.*, 2010), defined according to UN GHS (No Category versus Category 1/Category 2A/Category 2B; UN, 2013) and as implemented in the EU CLP (No Category versus Category 1/Category 2; EC, 2008).

The SkinEthic™ HCE TS and the EpiOcular™ EIT were developed for maximum sensitivity (ability to detect positives, with low rate of false negatives) rather than for optimal overall accuracy with balanced sensitivity and specificity (ability to detect negatives, with low rate of false positives). Sensitivity had therefore a bigger weight than specificity and overall accuracy in their development. However, it was also sought to achieve a sufficiently high specificity and overall accuracy, in order to allow identification of the highest number of chemicals not requiring classification for serious eye damage/eye irritation. By achieving satisfactory specificity, the SkinEthic™ HCE TS and the EpiOcular™ EIT would represent stand-alone (independent) test methods for the identification of “non-irritants”. Importantly, the test methods are not intended to differentiate between UN GHS/EU CLP Category 1 (irreversible/serious eye damage) and UN GHS/EU CLP Category 2 (reversible eye irritation effects). As proposed by the ECVAM workshop of February 2005, this differentiation would be left to another tier of the Bottom-Up/Top-Down test strategy (Scott *et al.*, 2010).

The EIVS was undertaken in accordance with the principles and criteria documented in the OECD *Guidance Document on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment* (No. 34, OECD, 2005) and according to the Modular Approach to validation (Hartung *et al.*, 2004).

2. Materials and methods

2.1. Management and conduct of the validation study

2.1.1. Study management

The management structure of the EIVS on RhCE-based test methods, which took place between 2008 and 2013, is shown in Figure 2.1. The study comprised:

- a Validation Management Group (VMG) responsible for overseeing the conduct of all aspects of the study;
- a study coordinator (EURL ECVAM);
- a study logistics coordinator (TNO);
- an independent Chemicals Selection Group (CSG);
- independent biostatististical analyses;
- the lead and participating laboratories of the test methods evaluated;
- and liaisons from the USA, Japan and Canada in the framework of the International Cooperation on Alternative Test Methods (ICATM).

The VMG comprised a chair, co-chair, sponsor representatives (EURL ECVAM and Cosmetics Europe), coordinating organisation's representatives (TNO and ECVAM), independent biostatisticians (TNO and EURL ECVAM), external scientists, the chair of the Chemicals Selection Group (CSG), representatives of the lead laboratories for each test method (L'Oréal and Beiersdorf), and liaisons from the USA, Japan and Canada. Its composition is shown in Figure 2.2.

Operational decisions, including discussions regarding chemical selection, were taken by the core VMG only, i.e., did not involve the lead laboratories' representatives. The representatives of the lead laboratories were consulted on technical issues relating to the test methods and supported the core VMG in monitoring the progress of the experimental work. The ICATM liaisons were invited to advise the VMG on all aspects of the study.

The overall study coordination was conducted by EURL ECVAM. This included the organisation of all necessary VMG meetings and teleconferences, and the maintenance of a website where the EIVS documents not related to chemical selection were made available to VMG members and ICATM liaisons. EURL ECVAM was also responsible for organising the Quality Control audits on data collection, on data handling and analysis, as well as on the biostatistical reports produced by the TNO biostatistician.

TNO (Quality of Life) on the other hand coordinated the communication flow between all parties, prepared the draft minutes of the VMG meetings and telephone conferences, organized the meetings between laboratories, and organised the study conduct. TNO was also responsibility for logistics of test chemical acquisition, coding and distribution. Finally, TNO arranged Quality Assurance audits on the RhCE production sites.

Figure 2.1: Management Structure of the Eye Irritation Validation Study

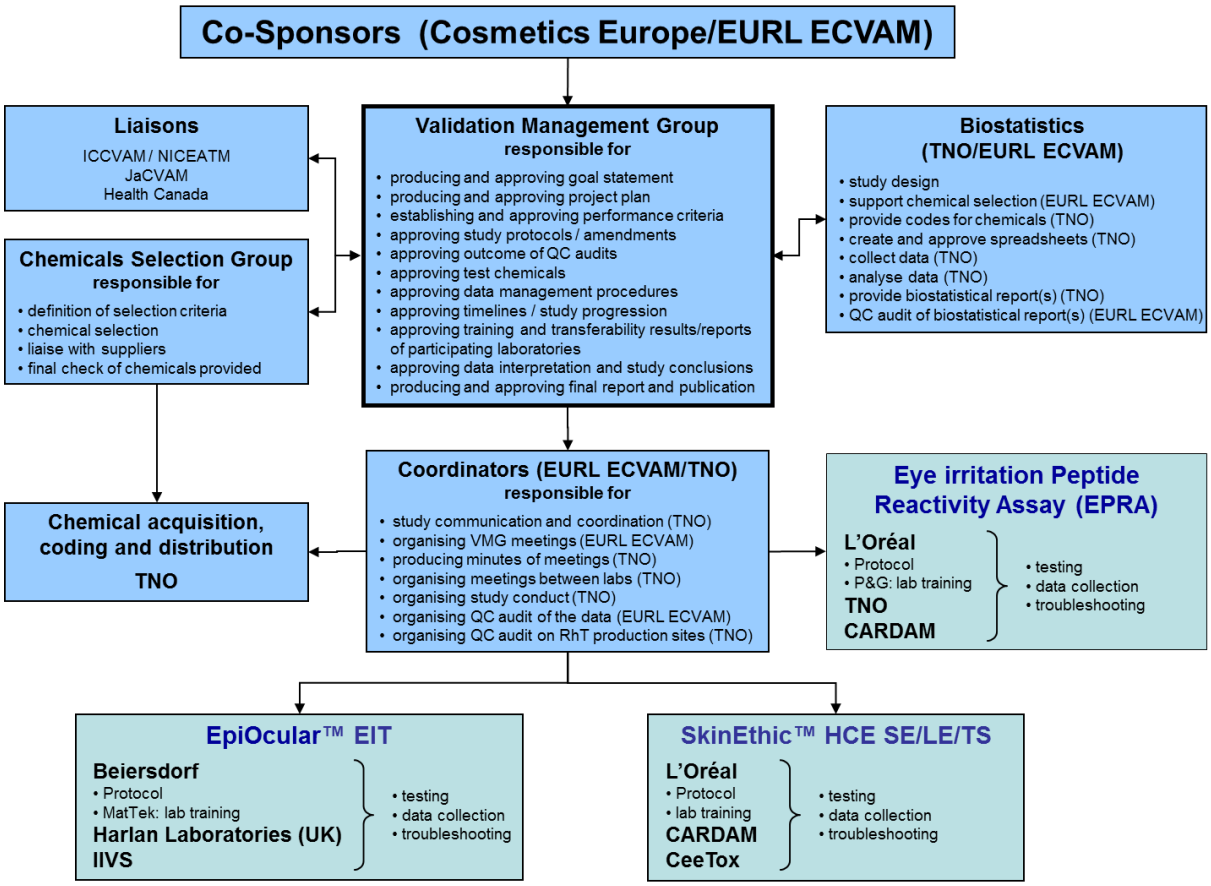

Figure 2.2. Composition of the Validation Management Group

Core VMG	Chair	Stuart John Freeman, Farino Consulting
	Co-chair	Valérie Zuang, EURL ECVAM
	EURL ECVAM sponsor	João Barroso / George Kirmizidis / Michael Wilhelm Schaeffer
	Cosmetics Europe sponsor	Pauline McNamee, Procter & Gamble
	Logistics Coordinator	Jan Lammers / Astrid Reus, TNO
	Biostatisticians	Carina de Jong-Rubingh / Rinke Klein Entink, TNO
		Anna Compagnoni / André Kleensang / Roman Liška, EURL ECVAM
	External scientists	Chantra Eskes / João Barroso, SeCAM
	Chair of CSG	Thomas Cole, EURL ECVAM
EpiOcular™ lead laboratory		Uwe Pfannenbecker, Beiersdorf
SkinEthic™ HCE lead laboratory		Nathalie Alépée, L'Oréal
NICEATM liaison		Bill Stokes / Waren Casey / David Allen / Elisabeth Lipscomb
ICCVAM liaison		Jill Merrill
JaCVAM liaison		Hajime Kojima
Health Canada liaison		Alison McLaughlin

Regarding sponsorship, EURL ECVAM and Cosmetics Europe co-sponsored the EIVS, with the main financial support being provided by Cosmetics Europe.

Cosmetics Europe financed the following activities:
- conduct of the EPRA;
- lead and participating laboratories for the two test methods;
- statistical support provided by TNO;
- financial support of the independent chair of the VMG;
- independent CRO responsible for the test chemicals purchase, coding and distribution to the laboratories (TNO);
- overall logistical coordination of the study (TNO);
- part of the independent Quality Assurance audits on the RhCE models production sites;
- purchase cost of existing chemicals;
- purchase of a proportion of the RhCE tissues;
- preparation of the validation study report.

EURL ECVAM on the other hand financed:
- management and coordination of the study, including the organisation of VMG meetings and teleconferences;
- statistical support provided by ECVAM;
- part of the independent Quality Assurance audits on the RhCE models production sites;
- independent Quality Control audit on data collection, handling and analysis;
- independent Quality Control audit of the biostatistical report(s);
- purchase of a proportion of the RhCE tissues;
- publication of the study.

2.1.2. Participating laboratories

The laboratories participating in the study were defined as shown in Figure 2.1. The specific obligations and responsibilities of the participating laboratories included, but were not limited to, the adherence to the project plan and guidance on study conduct and its addendum throughout the study, the adherence to the test method SOP, the adherence to the work program, assuring compliance with GLP-like principles, specifying and applying proper Quality Assurance procedures, and meeting the data submission deadlines. All participating laboratories had competence in performing the test method(s) and provided competent personnel, adequate facilities, equipment, supplies, and proper health and safety guidelines. The lead laboratories were further responsible for preparing detailed SOP for the EpiOcular™ EIT, SkinEthic™ HCE SE/LE and EPRA, and for providing training to the technical staff of the other testing facilities. Each participating laboratory appointed a Study Director and a Safety Officer.

The Study Directors represented the single point of study control with ultimate responsibility for the overall technical conduct of the study, the documentation and reporting of the results, as well as GLP adherence or adherence to the minimum quality requirements. The Study Director was responsible for collecting the data of his/her laboratory and to send them to the Logistics Coordinator of the study (to be forwarded to the TNO biostatistician). The Study Directors were also responsible for sending timely Study Reports to the contact person of the

VMG, i.e. the Logistics Coordinator, to allow for a proper monitoring of the progress of the study. Such reports included all relevant experimental data as well as all deviations from the Project Plan and SOP. The study directors were the primary contact point for the communications between the VMG and the testing facilities.

The Safety Officers were not involved in the actual conduct of the validation study. They were responsible for receiving the blinded (coded) test chemicals and for transferring them to the responsible person of the laboratory. A sealed Safety Package containing the Material Safety Data Sheets (MSDSs) for all test chemicals accompanied the test chemicals and was retained by the Safety Officer until the completion of EIVS. The package would be opened by the Safety Officer only in case of an accident with one of the coded test chemicals at the laboratory. At the end of the validation study, all Safety Officers returned the packages to the Logistics Coordinator of the study. None of the Safety Packages had to be opened during the validation study.

The participating laboratories were allowed to freely communicate and meet during the training and transferability phases of EIVS. Such meetings were organized by the lead laboratories and occurred without a formal approval by the VMG. However, during the testing phase, the participating laboratories and the personnel responsible for providing training on the test methods, no longer had any form of contact with each other regarding EIVS without the previous knowledge and approval by the VMG. All VMG approved meetings or other forms of communication between the participating laboratories during the testing phase were organised by the Logistics Coordinator (TNO) in collaboration with the lead laboratories.

2.1.3. Study design

The study design of the EIVS was defined prior to initiation of testing in a project plan agreed by the VMG. In addition, the VMG prepared a Guidance document on the conduct of the RhCE assays establishing pre-defined: testing procedures, criteria for re-conducting tests and runs, test acceptance criteria, biostatistical analyses procedures, study quality criterion, and the performance criteria to assess the scientific validity of the test methods.

Reconstructed human Cornea-like Epithelium models

Training of the participating laboratories in conducting the EpiOcular™ EIT or the SkinEthic™ HCE SE/LE assays were provided by the respective test method developer (MatTek Corporation for EpiOcular™ EIT and L'Oréal for SkinEthic™ HCE SE/LE). The lead laboratories (Beiersdorf for EpiOcular™ EIT and L'Oréal for the SkinEthic™ HCE), in collaboration with the test method developers, were responsible for issuing final test method Standard Operating Procedures (SOP). Upon completion of the training phase, the participating laboratories tested 5-10 chemicals to demonstrate transferability of the assay and to confirm test method protocol adequacy. The test method developers in collaboration with the participating laboratories were responsible for issuing training and transferability reports upon completion of the transferability studies.

In the testing phase of EIVS, the test chemicals in the final chemical selection set (104 test chemicals plus 2 extra strong colorants) were tested using the four protocols of the two RhCE test methods (liquids protocol of EpiOcular™ EIT, solids protocol of EpiOcular™ EIT,

SkinEthic™ HCE SE and SkinEthic™ HCE LE) in at least three independent tests (using different tissue batches and performed in separate runs) by each of three independent laboratories (all chemicals were tested in each of the SkinEthic™ HCE protocols, while only the liquids (52 plus 1 solid that was considered as a liquid by the participating laboratories) were tested in the liquids protocol of EpiOcular™ EIT and only the solids (51 + 2 strong colorants) were tested in the solids protocol of EpiOcular™ EIT). One other chemical (#27) was sent to all participating laboratories for testing but was excluded and replaced by another chemical (one of the final 104) at a very early stage of the study on request of one of the SkinEthic™ HCE participating laboratories because it was identified as a very strong MTT reducer. However, by the time this chemical was replaced, it had already been tested in a complete test sequence by all three EpiOcular™ EIT participating laboratories. Since in EpiOcular™ EIT this chemical only produced minor interference with the MTT assay, it was decided to consider it in the statistical evaluations presented in this report. Each of the EIVS chemicals was tested with the two different exposure/post-treatment periods of the SkinEthic™ HCE SE/LE protocol, and with one of the two EpiOcular™ EIT exposure procedures depending on the test chemical being solid or liquid. Importantly, the three laboratories participating in the validation of EpiOcular™ EIT were not instructed on the physical state of the test chemicals. Therefore, each laboratory participating in the validation of the EpiOcular™ EIT decided on its own on the physical state of each test chemical and the appropriate exposure procedure to use. Finally, each control and test chemical included in one run was tested in two (EpiOcular™ EIT) or three (SkinEthic™ HCE SE/LE) replicate tissues. The VMG decision to use two replicate tissues instead of three with the EpiOcular™ EIT test method in EIVS was mostly due to technical considerations, but was also based on the fact that the pre-validation studies had already been performed with only two tissue replicates and was supported by biostatistical analyses performed by the US liaisons NICEATM (see chapter 2.1.3.1 below).

The EIVS testing phase was conducted in three consecutive phases to allow for periodic opportunities to evaluate the frequency of technical errors and any other problems that might occur during testing. At the end of each testing phase the Study Directors forwarded the data acquired by their laboratories to the Logistics Coordinator after internal quality check who provided it to the TNO biostatistician for immediate preliminary analyses of Within Laboratory Reproducibility and compliance with Study Quality criteria (number of complete/incomplete test sequences as described in the Performance Criteria). Once completed, these phased statistical analyses and their conclusions were provided to the core VMG who reviewed them and determined if modifications to the protocol and/or study plan were warranted/appropriate in order to avoid future occurrences of identified issues.

Eye Irritation Peptide Reactivity assay

During the chemicals selection phase, all eligible chemicals identified by the CSG had their chemical reactivity determined based on the Cysteine/Lysine Eye Irritation Peptide Reactivity Assay (EPRA), in a blind study at TNO, with a single test consisting of three replicate measurements. Before testing with EPRA started at TNO, the EPRA developer (Procter & Gamble) trained TNO in conducting the assay. Upon completion of the training phase, TNO tested 11 test chemicals to demonstrate transferability of the assay and to confirm test method protocol adequacy. TNO was responsible for issuing training and transfer reports upon completion of the transferability study. The results of the training and transferability were reviewed and approved by the VMG before TNO progressed with testing of chemicals

eligible for selection for EIVS. TNO and the test method developer (P&G) were responsible for issuing a final SOP that was used during testing.

Since chemicals found eligible by the CSG did not all become available for EPRA testing at TNO at the same time (due to differences in the time required to gain access to *in vivo* Draize eye irritation study reports for different chemicals, and to differences in the time required to obtain commercially available and proprietary chemical samples), the selection of a final test chemical set was phased, with subsets of 28-46 test chemicals being selected by the CSG in different stages, as the data from the EPRA analysis became available, and until the final amount of 104 test chemicals was reached. These chemical subsets were as balanced as possible considering the criteria described in chapter 2.3 and, upon approval by the core VMG, they were distributed to the participating laboratories for viability assessment. The VMG had agreed that a multi-laboratory reproducibility assessment of the EPRA, using a subset of the full validation set (at least 20 chemicals), tested in three laboratories and in three independent tests (performed in separate runs) consisting of three replicate measurements each to determine the WLR and BLR of the assay, would be conducted only after finalisation of the testing of the 104 selected chemicals with SkinEthic™ HCE SE and LE, if these viability data together with EPRA data acquired by TNO during chemicals selection for all these 104 chemicals would demonstrate the validity of the SkinEthic™ HCE TS. This preliminary evaluation of the usefulness of the SkinEthic™ HCE TS upon completion of the viability assessment study demonstrated its non-validity and therefore, the VMG decide not to conduct the multi-laboratory reproducibility assessment of the EPRA. Should this have been conducted, the lead laboratory for this reproducibility study would have been L'Oréal and the other participating laboratories would have been TNO and CARDAM.

2.1.3.1. Number of tissue replicates used in EpiOcular™ EIT

The EpiOcular™ EIT was developed using two concurrently tested tissue replicates on the basis of practical considerations in the technical procedures for conduct of this test method, i.e., the washing procedure after chemical exposure is done on two replicate tissues together and therefore the use of an uneven number of tissue replicates is not technically possible. The variability between two concurrently treated tissue replicates was found to be low in the 296 pairs of replicates produced by seven laboratories for a wide set of test chemicals during the pre-validation study of the EpiOcular™ EIT. Briefly, 99%, 95%, 90% and 74% of the 296 pairs of concurrently treated tissue replicates showed a difference of viability below 20%, 15%, 10% and 5%, respectively. Two independent biostatisticians from ECVAM and NICEATM evaluated the data and their conclusions led the VMG to consider the use of two tissue replicates for EpiOcular™ EIT in EIVS as sufficiently statistically and scientifically justified.

2.1.3.2. Data submission

The Logistics Coordinator collected the data from each participating laboratory via the Study Directors at the end of each RhCE testing phase and forwarded it to the TNO biostatistician. The TNO biostatistician organised the data in specific data collection software (MS EXCEL spreadsheets). The collected data was circulated to every participating laboratory for a quality check. At the end of each RhCE testing phase a preliminary analysis of WLR and

compliance with Study Quality criteria (number of complete / incomplete test sequences as defined by the Guidance on Study Conduct & Performance Criteria VMG document) was performed without decoding the test chemicals (to avoid breaking the code before completion of the study). Upon completion of the RhCE testing phases by all participating laboratories and preliminary “blind” determination of WLR and Study Quality criteria for each laboratory, test chemicals were decoded and the TNO biostatistician conducted a complete statistical analysis of the data and provided biostatistical reports to the VMG. The VMG did a quality control of the processes of data collection, handling and analysis, as well as of the final biostatistics reports.

2.1.3.3. Data analysis and statistics

The data management procedures and statistical tools that were used for data analysis included in the final biostatistics reports were described in the Guidance document on the conduct of the EIVS and in a Statistical Analysis and Reporting Plan. The biostatistics analyses procedures reported in the Statistical Analysis and Reporting Plan were developed by the ECVAM and TNO biostatisticians before completion of the experimental phase of the study and were approved by the VMG before the biostatistics analyses began.

The reproducibility and predictive capacity of EpiOcular™ EIT were evaluated for the whole test method (liquids plus solids) because each test chemical was tested in a single protocol (as a solid or a liquid), but the two protocols were also evaluated separately in terms of their predictive capacity. For SkinEthic™ HCE, since all of the selected test chemicals were tested in both the SE and the LE protocols, these two protocols were fully independently assessed for their reproducibility and predictive capacity, considering them as independent test methods. The EPRA/SE/LE TS was evaluated for its predictive capacity only.

Two prediction models were evaluated separately for EpiOcular™ EIT, the first using 60% mean tissue viability as the threshold differentiating classified (UN GHS Cat 1 and Cat 2) chemicals (mean tissue viability ≤ 60%) from non-classified (UN GHS No Cat) chemicals (mean tissue viability > 60%) and the second using a threshold of 50% mean tissue viability. The EpiOcular™ EIT was originally developed by MatTek Corporation with the single threshold of 60% mean tissue viability in the prediction model and the submission of the test method to ECVAM for validation only mentioned this single prediction model. However, in the beginning of the EIVS and even before training and transferability took place, MatTek Corporation was faced with the necessity to replace the insert membrane used in the production of the EpiOcular™ tissues due to discontinued production of the insert membrane used until then (MTI-001a). A replacement insert membrane (MTI-003) was approved by the VMG for use in EIVS after multiple testing of 94 chemicals at MatTek Corporation and comparative statistical analysis performed by the EURL ECVAM biostatistician on the use of the old MTI-001a insert membrane (discontinued) versus the new MTI-003 insert membrane. The results showed that with the MTI-003 membrane a sensitivity higher than 90% could potentially still be achieved using a 50% cut-off instead of 60%, with a significant gain in specificity. Considering these new data, the VMG decided to evaluate two prediction models with EpiOcular™ EIT in EIVS, one based on the original cut-off at 60% mean tissue viability as in the submission to ECVAM and a second one based on a cut-off at 50% mean tissue viability. A single prediction model using 50% mean tissue viability as the threshold differentiating classified (UN GHS Cat 1 and Cat 2) chemicals (mean tissue viability ≤ 50%)

from non-classified (UN GHS No Cat) chemicals (mean tissue viability > 50%) was evaluated with the SkinEthic™ HCE SE, LE and TS.

2.1.3.3.1. Within-laboratory reproducibility

For each laboratory, concordance of classifications and overall Standard Deviation (SD) were calculated based only on qualified tests from test chemicals for which at least two qualified tests (see definitions for details) were available. In addition, the Standard Deviation associated with each laboratory was calculated using all available test sequences, i.e., including both qualified and non-qualified tests (see definitions for details).

2.1.3.3.2. Between-laboratory reproducibility

For the calculation of BLR the final classification for each test chemical in each participating laboratory was established by using the arithmetic mean value of viability over the different qualified tests performed. Concordance of classifications between laboratories and overall Standard Deviation of the study were calculated based only on qualified tests (see definitions for details) from test chemicals for which at least one qualified test per laboratory was available. In addition, the overall Standard Deviation of the study was calculated using all available test sequences, i.e., including both qualified and non-qualified tests (see definitions for details).

2.1.3.3.3. Predictive capacity

All qualified tests for each test chemical (see definitions for details) were used to calculate the predictive capacity values. The calculations were based on the individual predictions of each qualified test in each laboratory and not on the arithmetic mean values of viability over the different qualified tests performed.

2.1.3.4. Quality aspects

Laboratories

Participating laboratories that were compliant with Good Laboratory Practices (GLP) performed the studies in accordance with GLP standards (OECD, 1999). Non GLP-compliant laboratories used the OECD principles of GLP as guidelines for conducting the validation study. Any deviations from these principles were documented along with a discussion of their impact on the study results.

The following requirements were considered essential for the mutual acceptance of information produced during the validation process (Balls *et al*., 1995):

- Qualified personnel, and appropriate facilities, equipment and materials to be available for the timely and proper conduct of the study
- Records of the qualifications, training and experience, and a job description for each professional and technical individual involved in the study, to be maintained.
- For each study, an individual with appropriate qualifications, training and experience to be appointed as responsible for the study overall conduct and for any report issued (Study Director).
- Instruments used for the generation of experimental data to be inspected regularly, cleaned, maintained and calibrated according to established SOPs, if available, or to manufacturers' instructions. Records of these processes to be kept, and made available for inspection on request.

- Reagents to be labelled, as appropriate, to indicate their source, identity, concentration and stability. The labelling should include the preparation and expiry dates, and specific storage conditions.
- All data generated during a study to be recorded directly, promptly and legibly by the individual(s) responsible. These entries should be attributable and dated.
- All changes to data should be identified with the date and the identity of the individual responsible, and a reason for the change should be documented at the time.

Tissue model suppliers

According to OECD GLP Consensus Document No.5 “Compliance of Laboratory Suppliers with GLP Principles”, the responsibility for the quality and fitness for use of equipment and materials rests entirely with the management of the test facility (OECD, 1999).

The acceptability of equipment and materials in laboratories complying to GLP principles should therefore be guaranteed to any regulatory authority to whom studies are submitted. In some countries where GLP has been implemented, suppliers belong to national regulatory or voluntary accreditation schemes (for example, for laboratory animals) which can provide users with additional documentary evidence that they are using a test system of a defined quality.

The audits on the RhCE tissue production sites (MatTek Corporation and EpiSkin Laboratories), were carried out by TNO and ECVAM, and focused on the procedures established to guarantee a defined quality of the tissue models, as defined in an audit protocol previously approved by the VMG.

Records and archives

At the end of EIVS, the original raw (not applicable for GLP-compliant laboratories) and processed data or copies thereof were submitted to ECVAM and Cosmetics Europe for storing and archiving. In addition, other records relevant to EIVS (instrument logs, calibration records, facility logs, etc.) were asked to be made available for inspection upon request by the VMG.

Raw and processed data or copies thereof (depending if the laboratory is or not GLP compliant) were asked to be stored and archived at the participating laboratory for at least five years after completion of EIVS. The data which are stored electronically were asked to be periodically copied, and backup files produced and maintained.

2.1.4. Pre-defined study quality criterion

To limit the bias introduced in the calculations of reproducibility and predictive capacity due to the exclusion of the most variable tests (non-qualified tests) from some of the calculations (see chapter 2.1.3.3), and also to avoid further bias introduced by a reduction of the data used in some of the calculations (at least 104 test chemicals are needed to reach the statistical power defined for the study), the VMG decided to define a target value for the number of complete test sequences that should be available after re-testing as an objective to secure the quality of the study, i.e., to limit the amount of missing data due to the predefined test acceptance criteria (see chapters 2.2.1.4 and 2.2.2.1.4). The target value defined prior to the initiation of the validation study was as follows:

In each participating laboratory, at least 85% of the test sequences (see definitions for details) should contain three qualified tests (89 out of 104 test sequences, for 104 test chemicals).

2.1.5. Pre-defined performance criteria to assess the scientific validity of the test methods

Prior to the initiation of the validation study, the VMG defined test method performance criteria for reliability and predictive capacity, which it considered appropriate for judging the performance of the SkinEthic™ HCE SE, LE and TS and of the EpiOcular™ EIT with the test chemicals selected for EIVS.

One recommendation of a previous ESAC Peer Review Panel on cell-based assays was to receive guidance from the VMG to evaluate the performance of these cell-based assays. Therefore, within the framework of EIVS, the VMG also suggests the use of these test method performance criteria as a basis for the evaluation of the performance of the SkinEthic™ HCE LE, SE and TS and of the EpiOcular™ EIT by the ESAC Peer Review Panel after the completion of EIVS.

The test method performance criteria developed by the VMG for EIVS and described below took into account: (a) the background and specific objectives of the validation study (see chapter 1 above); (b) the requirements of regulatory authorities and industry when testing and classifying chemicals for eye irritation; (c) the within test variability in the *in vivo* Draize eye test and the manner in which Draize eye test data are currently used for classifying eye hazards according to UN GHS / EU CLP (UN, 2013; EC, 2008); (d) the standards of performance which are expected from the *in vitro* tests evaluated; (e) the way in which the *in vitro* tests are to be used (as a test within a tiered test strategy); and (f) the power of the design of the validation study.

2.1.5.1. Acceptance criteria for reproducibility

Analysis of reproducibility were not limited to the parameters described below. Other statistical tools, e.g., the overall Standard Deviation of the study calculated from all qualified tests as well as from all available tests (qualified and non-qualified), were also considered before making a final recommendation on the reproducibility of the test methods.

Within-laboratory reproducibility

The concordance of classifications (UN GHS / EU CLP not classified versus classified) for the set of chemicals tested during validation obtained in different, independent runs within a single laboratory should ideally be equal or higher (≥) than 85% for all participating laboratories[1].

[1] The within laboratory reproducibility values obtained in the pre-validation of the SkinEthic™ HCE were of 90 to 100% concordance of classifications, and for EpiOcular™ EIT of 95 to 100% concordance of classifications (considering the classification cut-off of 60% viability).

Between-laboratory reproducibility

The concordance of final classifications (UN GHS / EU CLP not classified versus classified) for the set of chemicals tested during validation obtained by the different participating laboratories should ideally be equal or higher (≥) than 80%[2].

2.1.5.2. Acceptance criteria for predictive capacity

The SkinEthic™ HCE SE, LE and TS and the EpiOcular™ EIT (liquids and solids protocols) were assessed for their usefulness as stand-alone (independent) test methods to identify chemicals not requiring classification for serious eye damage/eye irritation (UN GHS / EU CLP No Category; "non-irritants") and their reliable discrimination from all classes of classified chemicals as e.g., the initial step of a Bottom-Up approach (in the framework of a Bottom-Up/Top-Down test strategy, Scott *et al.*, 2010). As already mentioned above, the SkinEthic™ HCE and the EpiOcular™ EIT were developed for maximum sensitivity (ability to detect positives, with low rate of false negatives) rather than for optimal accuracy with balanced sensitivity and specificity (ability to detect negatives, with low rate of false positives). However, it was also sought to achieve a sufficiently high specificity in order to allow the identification of the highest number of chemicals not classified as irritant to the eye. By achievement of satisfactory specificity, the SkinEthic™ HCE and the EpiOcular™ EIT would present stand-alone (independent) test methods for identification of "non-classified" chemicals.

Based on these premises, the EIVS VMG defined "definitely acceptable" and "definitely unacceptable" rates of over-prediction and under-prediction to evaluate the scientific validity of the SkinEthic™ HCE SE, LE and TS and of the EpiOcular™ EIT, which are outlined in Table 2.1. In particular, the following points were felt to be important to recommend the test methods as being sufficiently predictive to be considered as scientifically valid:

(a) Ten percent (10%) false negatives should be "definitely acceptable" (sensitivity ≥ 90%), while more than 20% would be "definitely unacceptable"[3]. In previous validation studies for eye irritation led by ECVAM (cytotoxicity and cell-based assays) or ICCVAM (organotypic assays) the peer-review panels responsible for evaluating the validated test methods considered 0% false negatives as a test method performance criterion for acceptance of test methods to be used as an initial step in a Bottom-Up test strategy (identification of chemicals not classified as eye irritant). However, the Draize rabbit eye test shows the potential for up to 12% over classification of chemicals as UN GHS Category 2 (instead of UN GHS No Category) due solely to its within test variability (Adriaens *et al*., 2014). The actual rate of over-prediction of the Draize test may be even higher when considering other factors like between laboratory variability and predictivity. Thus, the EIVS VMG agreed that a False Negative rate up to 10% should be "definitely acceptable" for the UN GHS and EU CLP classification and labelling systems (UN, 2013; EC, 2008) for a test method to be considered useful as a stand-

[2] The between laboratory reproducibility values obtained in the pre-validation of the SkinEthic™ HCE were of 95 to 100% concordance of classifications, and for EpiOcular™ EIT 100% concordance of classifications (considering the classification cut-off of 60% viability).

[3] During pre-validation, the EpiOcular™ EIT showed a sensitivity of 100% (considering the classification cut-off of 60% viability), while the SkinEthic™ HCE test strategy showed a sensitivity of 87%.

alone test for the identification of chemicals not requiring classification for serious eye damage/eye irritation (initial step in a Bottom-up approach). Nevertheless, the nature, severity, duration, and frequency of *in vivo* eye injuries (based on the Draize eye irritation test) for chemicals that produce false negative results from *in vitro* tests were fully discussed and considered by the VMG in assessing the usefulness and limitations of the *in vitro* test methods for regulatory hazard classification and labelling purposes.

(b) Ideally, no ocular corrosives/severe eye irritants (Category 1) should be under-predicted as No Category, but more than 10% Category 1 chemicals being under-classified as No Category would be "definitely unacceptable". By using all qualified tests to calculate the predictive capacity values, the probability of obtaining 0% under-prediction of Category 1 chemicals (0 out of about 200 tests) is extremely low due to the accepted fact that reproducibility of SkinEthic™ HCE SE/LE and EpiOcular™ EIT both within and between laboratories is not 100%. Therefore, the rate of under-prediction of Category 1 chemicals as No Category (Category 1 → No Category), was calculated using the mode of the *in vitro* predictions of all qualified tests obtained in the three participating laboratories for each test chemical classified as UN GHS/EU CLP Category 1 based on *in vivo* Draize eye irritation data. This approach more closely reflects the real testing situation (post-validation). Thus, in a post-validation testing situation, a single qualified test obtained in one laboratory is usually sufficient to classify a test chemical, but if a borderline result, such as non-concordant replicate measurements and/or mean percent viability equal to 50±5%, is obtained, a second test may be considered, as well as a third one, in case of discordant results between the first two tests, in which case the mode of the three classifications is taken as the final decision.

(c) About 40% false positives should be "definitely acceptable" (specificity ≥ 60%), while more than 50% would be "definitely unacceptable"[4]. Since the purpose of the test methods will be the identification of chemicals not requiring classification for serious eye damage/eye irritation (UN GHS/EU CLP No Category) as an initial step of a Bottom-Up test strategy (Scott *et al.*, 2010), the VMG considered that it is acceptable to have a lower specificity than sensitivity (higher false positives than false negatives). Nevertheless, specificity should not be too low in order to allow for the correct identification of the majority of the non-classified chemicals.

(d) About 25% of overall misclassifications would be "definitely acceptable" (overall accuracy ≥ 75%), while more than 35% would be "definitely unacceptable". Potential reasons for misclassification were analysed in detail, including individual tissue score lesions of misclassified chemicals, which may be considered in future regulatory acceptance of the evaluated assays.

(e) Misclassification of borderline chemicals, identified from *in vivo* Draize eye irritation data and/or structure-activity relationship considerations, would be easier to justify compared to non-borderline chemicals.

The VMG also decided that if the rates of over-prediction and under-prediction achieved in EIVS would fall between the "definitely acceptable" and the "definitely unacceptable"

[4] During pre-validation, the EpiOcular™ EIT showed a specificity of 68% (considering the classification cut-off of 60% viability), while the SkinEthic™ HCE test strategy showed a specificity of 69%.

margins, a recommendation on the scientific validity of the test method would not be made before all of the validation data would have been evaluated and discussed, including a thorough discussion on the potential reasons for misclassification and limitations of the test method.

Table 2.1. Acceptance performance criteria for over-prediction and under-prediction rates in the framework of EIVS

	False Negatives[a] (%)	Cat 1 → No Cat[b] (%)	False Positives[c] (%)	Overall misclassifications[d] (%)
"Definitely acceptable" rates	≤ 10	0	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	0 < Cat 1 FN ≤ 10	40 < FP ≤ 50	25 < OM ≤ 35
"Definitely unacceptable" rates	> 20	> 10	> 50	> 35

[a] equal to (1-Sensitivity), [b] based on the mode of all qualified tests, [c] equal to (1-Specificity), [d] equal to (1-Overall accuracy)

2.2. Test Methods

The EIVS assessed the validity of the EpiOcular™ EIT protocol for liquids, the EpiOcular™ EIT protocol for solids, the SkinEthic™ HCE Short-time Exposure (SE) protocol, the SkinEthic™ HCE Long-time Exposure (LE) protocol, and the SkinEthic™ HCE test strategy (TS) combining the SE and LE protocols with the Eye irritation Peptide Reactivity Assay (EPRA). Both, the EpiOcular™ EIT and the SkinEthic™ HCE test methods use as test systems reconstructed human corne-like epethilium (RhCE), and protocols consist of a topical exposure of the neat test chemical to the epithelial surface of the tissue construct.

2.2.1. EpiOcular™ EIT

Use of the EpiOcular™ OCL-200 RhCE model for eye hazard characterization has been established for several years. The utility of the model for determining the degree of eye irritation potential of surfactants and surfactant-containing materials was initially demonstrated using a time-to-toxicity protocol which measures the time at which 50% of cultured cells (ET_{50}) remain viable, relative to negative controls (Blazka *et al.*, 2003). This ET_{50}-based test method was submitted to the former European Centre for the Validation of Alternative Methods (ECVAM) for evaluation in December 2005. ECVAM positively reviewed the submission in 2006 and recommended to MatTek Corporation (the test method developer) the development of a protocol covering a wider applicability domain to include also non-surfactant chemicals, prior to entering a formal validation study. Following ECVAM recommendations, MatTek Corporation developed the EpiOcular™ Eye Irritation Test (EIT), a test method with a wide applicability domain, which was then assessed between 2007 and 2009 in a multi-laboratory trial involving 7 laboratories and managed by Cosmetics Europe (Kaluzhny *et al.*, 2011; Pfannenbecker *et al.*, 2013). In this pre-validation study, the test method was shown to be transferable and to reproducibly discriminate chemicals not

requiring a classification for eye irritation or serious eye damage (No Category) from all classified chemicals (Category 2 and Category 1) under UN GHS with 98% concordance between laboratories (Pfannenbecker *et al*., 2013). Furthermore, the predictive capacity of the test method for liquids and solids combined (using cell viability > 60% for triggering identification of non-classified chemicals) was shown to give an overall accuracy of 85%, with a sensitivity of 98% and a specificity of 73% (Kaluzhny *et al*., 2011). The results of this study were submitted to ECVAM in 2008. The EpiOcular™ EIT protocol used in the pre-validation and the present validation study differs from the ET_{50} protocol in that it uses a single exposure time for each chemical tested.

The assessment of chemicals ocular hazards using the EpiOcular™ EIT test method is based on the depth of injury model of Maurer and Jester (Jester, 2006; Jester *et al*., 2001; Maurer *et al*., 2002), where slight to moderate irritants act on the corneal epithelium leading to cell death. In this assay, the test article is applied to the surface of the cornea epithelial construct for a fixed period, removed, and the tissue allowed to express the resulting damage. Liquids and solids are treated with different exposure and post-exposure incubations. Concurrent negative and positive control are used with each assay. Two tissue replicates are used for each treatment and control group. Relative tissue viability is determined against the negative control-treated tissues by the reduction of the vital dye MTT (3-[4,5 - dimethylthiazol-2-yl] - 2,5 - diphenyltetrazolium bromide).

2.2.1.1. Functional characteristics

The EpiOcular™ OCL-200 RhCE model uses normal human epidermal keratinocytes cultured to form a stratified squamous epithelium (Sheasgreen *et al*., 1996). The EpiOcular™ tissue construct is a non-keratinized multilayered epithelium prepared from non-transformed, human-derived epidermal keratinocytes. It is intended to model the cornea epithelium with progressively stratified but not cornified cells. These cells are not transformed or transfected with genes to induce an extended life span in culture. The “tissue” is prepared in inserts with a porous membrane (MTI-003) through which the nutrients pass to the cells. A cell suspension is seeded into the MTI-003 membrane in specialized medium. After a period of initial cell proliferation, the medium is removed from the top of the tissue so that the epithelial surface is in direct contact with the air. This allows the test chemical to be directly applied to the epithelial surface in a fashion similar to how the corneal epithelium would be exposed *in vivo*. The ability to expose the tissue topically is essential to model the same kind of progressive injury expected *in vivo*. It also allows both solid and liquid test chemicals to be applied directly to the tissue.

The key parameter involved in the EpiOcular™ functional quality control is the ET_{50}, which is the exposure time required for 0.3% (v/v) Triton X-100 to reduce the tissue viability (as measured by the MTT assay) to 50% (Kaluzhny *et al*., 2011). The ET_{50} represents an indirect measure of the tissue barrier properties, due to the fact that Triton X-100 is applied topically to the EpiOcular™ tissue and allowed to interact with the tissue for various time durations. To affect the capacity of the tissue to reduce MTT, Triton X-100 must penetrate into the tissue and permeate to the supra-basal and basal tissue layers, since the MTT assay monitors the mitochondrial activity present, primarily in the supra-basal and basal cell layers of the 3-D tissue. Reproducible ET_{50} values thus indicate that the tissue thickness and barrier properties are constant. A reproducible barrier function is important for determining the toxicities of test materials applied to the apical tissue surface, as they must penetrate across the apical cell

layers to interact with and affect the viable cells within the tissue (i.e., the basal cell layer). In the ET_{50} EpiOcular™ quality control assay, the tissues are exposed to 100µL 0.3% Triton X-100 for 5, 20, and 60 minutes (n = 2 tissues per exposure time). In addition, negative control tissues are exposed to 100µL of ultrapure water for 60 minutes. The purpose of this quality control assay is to ensure reproducible tissue properties across independent lots of the tissue produced over time (Kaluzhny *et al*., 2011).

Histological evaluation is another functional quality control of the tissues. Cultures are fixed with 10% (v/v) formalin, embedded in paraffin, and cut into 5µm cross-sections. The sections are then stained with haematoxylin and eosin (HE) by following standard procedures, and observed under a light microscope. An EpiOcular™ tissue should exhibit at least 3–4 layers of viable cells and should lack a cornified layer.

2.2.1.2. Standard operating procedures

The test protocol and prediction model of the EpiOcular™ EIT were developed by MatTek Corporation using a total of 60 chemicals (39 liquids and 21 solids) from across a range of chemical classes (Kaluzhny *et al*., 2011). Standard Operating Procedure on how to perform the EpiOcular™ EIT was available prior to initiation of the present validation study, and following training and transferability (see chapter 3.1.1.2.3), the SOP was revised to take into account any clarifications deemed necessary. The final SOP used during EIVS was approved by the VMG before initiating the practical testing phase of EIVS.

The SOP comprises a detailed description on how to perform the assay and includes negative and positive controls as well as controls for possible interfering compounds such as MTT-reducers and colorants (Kaluzhny *et al*., 2011). In particular, separate protocols are employed for liquids and solids. In the original protocols submitted to EURL ECVAM for validation tissues are exposed to liquids for 30 minutes followed by a 120-minute post-treatment incubation and to solids for 90 minutes followed by 18-hour post treatment incubation (Figure 2.3). However, during EIVS the EpiOcular™ EIT solid chemicals protocol was optimised and the exposure time was increased from 90 minutes to 6 hours, with the post-treatment incubation time being maintained at 18 hours.

Briefly for liquids, all test articles that could be pipetted at 37°C were tested with the liquids protocol. The EpiOcular™ tissues were transferred from proprietary agarose where they were package into 6-well plates containing 1 mL of medium (provided with the OCL-200 kit) and pre-incubated for one hour under standard culture conditions, which are defined as an atmosphere with 95 ± 3% relative humidity, 5 ± 0.5% (v/v) CO_2, and a temperature of 37 ± 1°C. After 1 hour, the medium was changed and the EpiOcular™ cultures were further pre-incubated overnight (16–18 hours) under standard culture conditions. On day 1 of the test, the tissues were pre-treated for 30 minutes with 20 µL of calcium and magnesium-free DPBS. If the DPBS did not spread across the tissue surface, the plate was tapped to ensure that the entire tissue surface was in contact with the liquid. Next, 50 µL of the NC (ultrapure H_2O), the positive control (methyl acetate, CAS No. 79-20-9), or liquid test articles were applied topically onto each tissue and the tissues were incubated for 30 ± 2 minutes under standard culture conditions. Each test article and control were tested with duplicate tissues (n = 2). To prepare for rinsing the tissues, three 150 mL beakers were filled with 100 mL DPBS for each test article. After a 30-minute exposure to the test articles or controls, each pair of duplicate tissues was successively rinsed by dipping, swirling, and decanting through its set

of three beakers. After the final rinse and decanting, the tissues were immersed in 5 mL of EpiOcular™ assay medium in a 12-well plate for 12 ± 2 minutes (post-soak) at room temperature. After the post-soak period, the medium was decanted from the cell culture inserts and the inserts containing the tissues were transferred to a 6-well plate containing 1mL of warm medium (37°C) and post-incubated for 120 ± 15 minutes under standard culture conditions. Finally, the tissue viability was assessed by using the MTT assay (Kaluzhny *et al*., 2011).

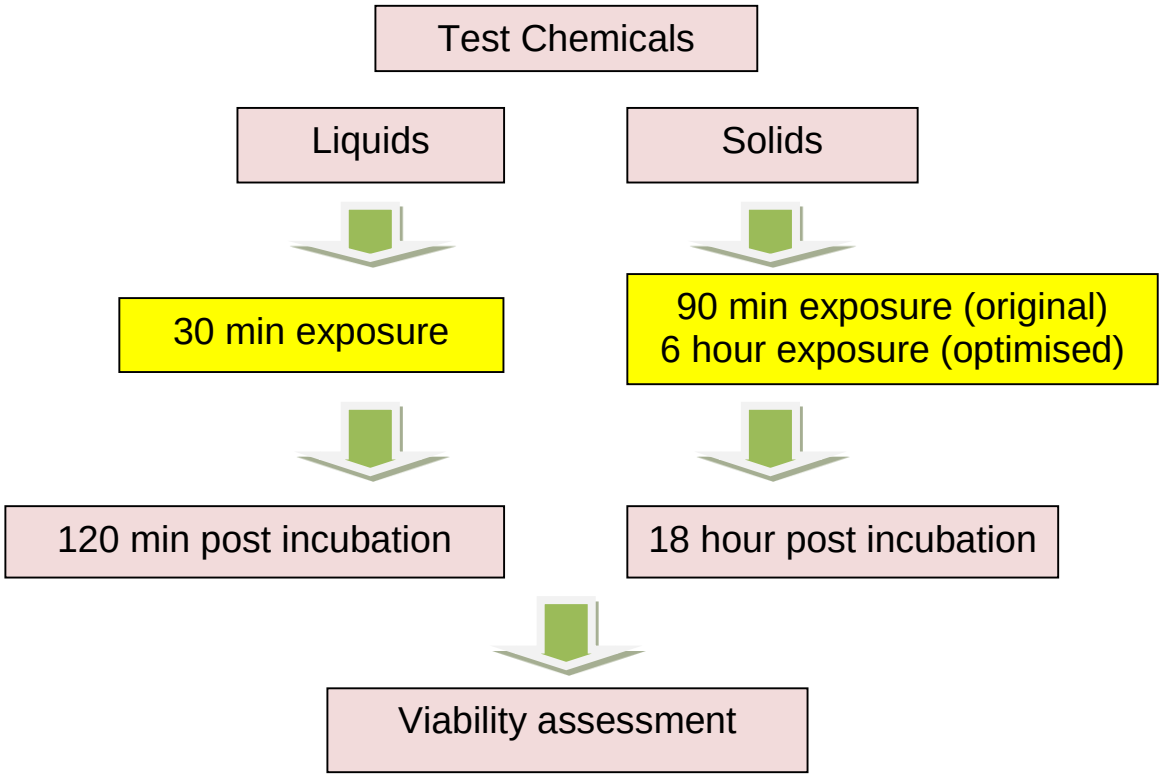

Figure 2.3. Testing strategy for MatTek EpiOcular™ Eye Irritation Test

Regarding solids, any test sample that could not be pipetted at 37°C was tested using the solids protocol. Prior to exposure of the test sample, the tissues were prepared, pre-incubated, and pre-wet with DPBS, as described previously for liquid test articles. Next, 50 µL of the control substances (H_2O and methyl acetate), or approximately 50 mg of solid test material, were applied topically to the EpiOcular™ tissues, the latter by using a calibrated tool (micro spatula, spoon, or syringe). Each test sample and control was tested in duplicate tissues, as described above. The tissues were exposed to the test chemicals for 90 ± 5 minutes (6 hours ± 15 minutes in the optimised protocol) under SCC. The rinsing and post-soak conditions were the same as those described for the liquid samples, except that the tissues exposed to solid test samples were post-incubated for 18 hours ± 15 minutes (the post soak was increased from 12 ± 2 minutes to 25 ± 2 minutes in the optimised protocol while the post-treatment incubation time was maintained at 18 hours ± 15 minutes). After the 18-hour post-incubation period, tissue viability was determined by using the MTT assay (Kaluzhny *et al*., 2011).

2.2.1.3. Endpoints and prediction model

Potential ocular hazard effects of chemicals are assessed by measuring the viability of the treated tissues following a fixed time treatment and post-incubation time as described above. The relative tissue viability (against the negative control-treated constructs) is assessed by the reduction of the vital dye MTT (3-[4,5 - dimethylthiazol-2-yl] - 2,5 - diphenyltetrazolium bromide). The chemical is predicted to be classified according to the UN GHS and EU CLP classification scheme (UN, 2013; EC, 2008), if the relative cell viability falls below a pre-determined level. The initial cut-off proposed by the test developer was 60% cell viability as shown in table 2.2 (Kaluzhny *et al*., 2011). Briefly:

- if the test article-treated tissue viability is > 60% relative to negative control-treated tissue viability, the test article is considered not to require classification according to the UN GHS / EU CLP classification schemes (UN, 2013; EC, 2008).

- if the test article-treated tissue viability is ≤ 60% relative to negative control-treated tissue viability, the test article is identified as classified according to the UN GHS / EU CLP classification schemes (UN, 2013; EC, 2008).

Table 2.2. Prediction model initially proposed for the EpiOcular™ EIT (Kaluzhny *et al*., 2011)

***In vitro* result**	***In vivo* prediction (UN GHS / EU CLP)**
mean tissue viability ≤ 60%	classified (Cat 1 and Cat 2)
mean tissue viability > 60%	non-classified (no-category)

In the beginning of the EIVS and even before training and transferability took place, MatTek Corporation was faced with the necessity to replace the insert membrane used in the production of the EpiOcular™ tissues due to discontinued production of the insert membrane used until then (MTI-001a). A replacement insert membrane (MTI-003) was approved by the Validation Management Group (VMG) for use in EIVS after multiple testing of 94 chemicals at MatTek Corporation and comparative statistical analysis performed by the EURL ECVAM biostatistician on the use of the old MTI-001a insert membrane (discontinued) versus the new MTI-003 insert membrane. The results showed that with the MTI-003 membrane a sensitivity higher than 90% could potentially still be achieved using a 50% cut-off instead of 60%, with a significant gain in specificity. Considering these new data, the VMG decided to evaluate two prediction models with EpiOcular™ EIT in EIVS, one based on the original cut-off at 60% mean tissue viability as in the submission to EURL ECVAM and a second one based on a cut-off at 50% mean tissue viability.

2.2.1.4. Run and test acceptance criteria

The run and test acceptance criteria are based on the results obtained for the negative control, positive control and test chemicals. Furthermore, if applicable, controls should be used to evaluate the non-specific colour and MTT reduction interference as described in the EpiOcular™ EIT SOP. The following run and test acceptance criteria as described in the

EpiOcular™ EIT SOP have been approved by the VMG prior to the practical testing phase of the EIVS.

1) the negative control OD > 1.0 and < 2.3,

2) the mean relative viability of the positive control is

a) 30 minute exposure: below 50% of control viability

b) 90 minute exposure (or 6 hour in the optimised protocol): below 50% of control viability

3) the difference of viability between the two tissues of a single chemical is < 20% in the same run (for positive and negative control tissues and tissues of single chemicals). This applies also to the killed controls (single chemicals and negative killed control) and the colorant controls which will be calculated as percent values related to the viability of the relating negative control.

2.2.1.5. Applicability and limitations

The EpiOcular™ EIT allows discriminating non-classified from classified materials according to the UN GHS/ EU CLP classification schemes. However, it has not been designed to differentiate between UN GHS / EU CLP Category 1 (serious eye damage) and Category 2 (eye irritation) classifications. The test method allows the hazard identification of mono and multi-component test chemicals. Gasses and aerosols cannot be evaluated with the current protocol. Other than that no further limitations are currently known regarding the spectrum chemicals to which the assay is applicable to, so that it is assumed to be applicable to the full spectrum of chemical classes and physico-chemical properties.

2.2.2. SkinEthic™ HCE SE, LE and test strategy

The SkinEthic™ HCE test method for assessing the potential ocular hazards of chemicals was originally developed by Van Goethem *et al*. (2006), which used a short exposure time (SE). Evaluation of this protocol using an enlarged set of test substances (about 100) led to the optimisation of the SkinEthic™ HCE test method to include two exposure times. The short exposure time (SE), consists of a 10-minute exposure of tissue to test substance with no post-treatment incubation, while the long exposure time (LE) exposes the tissue to test substance for 1 hour with a further post-treatment incubation of 16 hours.

In a pre-validation study involving 3 different laboratories, the SkinEthic™ HCE test method showed 95% (19/20) concordant predictions between-laboratories for the LE protocol to identify non-classified versus classified test substances (Alépée *et al*., 2013). Van Goethem *et al*. (2006) showed for the SkinEthic™ HCE SE an accuracy of 80%, a sensitivity of 100% and a specificity of 56% based on 20 test chemicals. Further optimisation by testing 435 substances showed the SkinEthic™ HCE LE protocol to have an overall accuracy of 82%, and a balanced sensitivity and specificity of 81% and 83% respectively (Cotovio *et al*., 2010).

By combining the two exposure times in a paradigm that uses the Eye irritation Peptide Reactivity Assay (EPRA) to allocate test chemicals to one or other treatment time, the overall accuracy was shown to increase to nearly 80%, with a sensitivity of 86.7% and a specificity of 68.9% (under GHS, submission reviewed by EURL ECVAM). The criterion for allocation of

test substances to either short or long exposure times is based on their intrinsic chemical reactivity, as defined by their electrophilic potential to react with cysteine- or lysine-containing peptides and measured through EPRA. The EPRA corresponds to the direct peptide reactivity assay (DPRA) developed by Gerberick and co-workers (2007), with minor differences in the protocol and prediction model.

2.2.2.1. SkinEthic™ human reconstructed corneal epithelium

The SkinEthic™ HCE model uses immortalised human corneal cells which, when cultured in defined conditions, develop into a multi-layered tissue which resembles morphologically and physiologically the human corneal epithelium (Nguyen *et al*., 2003). The test method consists of a topical exposure of the neat test substance onto the SkinEthic™ HCE, followed by cell viability assessment. Viability decrease in test substance treated tissues is expressed comparatively to negative controls (PBS treated tissues). Percent (%) viability is used to predict and classify eye irritation potential following a defined prediction model.

2.2.2.1.1. Functional characteristics

To construct SkinEthic™ HCE tissues, immortalized human corneal epithelial cells are cultured in a chemically defined medium, on a permeable synthetic membrane insert, and at the air-liquid interface. Under these culture conditions, the transformed human corneal epithelial cell line (LSU Eye Centre, New Orleans, USA) forms a corneal epithelial tissue (mucosa), resembling ultra-structurally (tissue morphology and thickness) the corneal mucosa of the human eye (Nguyen *et al*., 2003). As *in vivo* epithelium, the SkinEthic™ HCE model is characterized by the presence of intermediate filaments, mature hemi-desmosomes and desmosomes, and specific cytokeratins. The 0.5 cm² multilayered epithelium contains about 5 to 7 cell layers, including columnar cells and Wing cells.

Each lot of tissues is quality assured according to specific quality control standards including: histology (cell layers) and tissue viability (MTT mean optical density) and reproducibility (SD).

2.2.2.1.2. Standard operating procedures

The test protocol and prediction model of the SkinEthic™ HCE SE was developed by Goethem *et al*. (2006) using 20 chemicals, and the SkinEthic™ HCE LE by Cotovio *et al*. (2010) using 102 substances. Standard Operating Procedure on how to perform the SkinEthic™ HCE was available prior to initiation of the present validation study, and was revised to take into account any clarifications deemed necessary by the VMG. The final SOP used during EIVS was approved by the VMG before initiating the practical testing phase of EIVS.

The SOP comprises a detailed description on how to perform the assay and includes negative and positive controls as well as controls for possible interfering compounds such as MTT-reducers and colorants. Briefly, the SkinEthic™ HCE tissue cultures are placed in 1 mL maintenance medium (6-wells plate). The culture inserts are incubated (at least overnight) at 37°C, 5% CO2 in a humidified incubator. Following this equilibration period, the cultures are transferred into a 24-wells plate containing 300 µL SkinEthic™ maintenance medium per well. Test substances are applied topically onto the SkinEthic™ HCE for 10 minutes (short exposure time treatment) or 1 hour (long exposure time treatment). Three tissue replicates

are used per test substance, positive control and negative control. Tissues are then rinsed to remove the test substance and transferred to fresh medium. After a 10 minutes treatment (short exposure time treatment) or after a 1 hourr treatment + 16 hours post incubation period (long exposure time treatment), the MTT assay is performed by transferring the tissues to wells containing 0.3 mL MTT medium (0.5 mg/mL). After 3 hours MTT incubation at 37°C, 5% CO_2 in a humidified incubator, the blue formazan salt formed is extracted with 1.5 mL isopropanol per tissue (new 24-well plates, extraction time: from 2 hours (minimum) to overnight). After shaking, the optical density of the extracted formazan (200 µL per well of a 96 well plate, 2 aliquots) is determined using a spectrophotometer at 570 nm (filter band pass ± 30 nm). The percentage viability of each of the treated tissues is then calculated from the percentage MTT conversion in the test substances treated tissues relative to the corresponding negative controls (100% viable).

2.2.2.1.3. Endpoints and prediction model

Cell viability determination was used as the endpoint of the SkiEthic™ HCE test method and is based on cellular mitochondrial dehydrogenase activity, measured by tetrazolium salt MTT reduction [(3-4,5-dimethyl triazole 2-yl) 2,5-diphenyltetrazoliumbromide], and conversion into a blue formazan salt that is quantitatively measured after extraction from tissues (Mossman, 1983). The reduction of cell viability in treated tissues is compared to negative controls and expressed as a % value. Measurements rely on optical densities measurement at 570 nm (filter band pass ± 30 nm) by using a spectrophotometer multi-well plate reader.

Tissues treated with chemicals classified for eye hazards (UN GHS/EU CLP Category 2 and Category 1) are expected to show a decrease in viability below a certain threshold in respect to the negative control. The prediction model proposed by the test developer is shown in table 2.3, i.e., according to UN GHS and EU CLP classification:

- if the % viability is > 50%, the test substance is predicted as not requiring classification (No Category);

- if the % viability is ≤ 50%, the test substance is predicted as requiring classified for ocular hazards (Category 1 / Category 2) .

The prediction model does not discriminate UN GHS / EU CLP Cat 1 from Cat 2.

Table 2.3. Prediction model proposed for the SkinEthic™ HCE

***In vitro* result**	***In vivo* prediction (UN GHS / EU CLP)**
mean tissue viability ≤ 50%	classified (Cat 1 and Cat 2)
mean tissue viability > 50%	non-classified (no-category)

2.2.2.1.4. Run and test acceptance criteria

The run and test acceptance criteria are based on the results obtained for the negative control, positive control and test chemicals. Furthermore, if applicable, controls should be

used to evaluate the non-specific colour and MTT reduction interference as described in the SkinEthic™ HCE SOP. The following run and test acceptance criteria as described in the SkinEthic™ HCE SOP have been approved by the VMG prior to the practical testing phase of the EIVS.

1) Negative control

For both exposure times (SE and LE), a run meets the acceptance criteria if the mean Optical Density (OD_{NC}) of the three replicate tissues treated with NC is ≥ 0.7 at 570 nm (± 30nm) with an upper acceptance limit of 1.5, and if the Standard Deviation calculated for the % viability of the three treated replicate tissues (2 values from each of three tissues) is ≤ 18% (mean % viability = 100%). The absolute OD of the negative control (NC) tissues (PBS treated) in the MTT-test is an indicator of tissue viability in the testing laboratory after shipping and storage procedures and under use conditions.

2) Positive control

The % viability measured is an indicator of tissue response capacity in the testing laboratory after shipping and storage procedures, and under use conditions. For both exposure times, a run meets the acceptance criteria if the mean viability of the three replicate tissues (2 values from each of three tissues) treated with the positive control, expressed as % of the negative control, is ≤ 50% and the Standard Deviation value is ≤ 18%.

The run is qualified (qualified run) if both the negative and the positive controls data fulfil the above criteria requirements. Otherwise, the run will be considered as non-qualified. Non-qualified runs have to be documented and reported.

3) Test chemicals

For both exposure times, a test meets the acceptance criterion if the Standard Deviation calculated for the % viability of the three treated replicate tissues (2 values from each of three tissues) is ≤ 18%. For a given test chemical, if the Standard Deviation exceeds 18%, the test substance should be retested.

A qualified test for a single test substance is a “test” for which all pre-defined acceptance criteria are fulfilled (variability of replicates) within a qualified run. Otherwise, the test will be considered as not qualified.

2.2.2.1.5. Applicability and limitations

The SkinEthic™ HCE test method only discriminates test chemicals in 2 different classes: as “No Category” (No Cat) or as classified (GHS Category 1 / Category 2) according to UN GHS and EU CLP. However, it has not been designed to differentiate between UN GHS / EU CLP Category 1 (serious eye damage) and Category 2 (eye irritation) classifications. The test method allows the hazard identification of mono and multi-component test chemicals. Gasses and aerosols cannot be evaluated with the current protocols. Other

than that no further limitations are currently known regarding the spectrum chemicals to which the assay is applicable to, so that it is assumed to be applicable to the full spectrum of chemical classes and physico-chemical properties.

2.2.2.2. Test strategy with EPRA

The SkinEthic™ HCE test strategy uses three separate assays, i.e., EPRA, SkinEthic™ HCE SE, and SkinEthic™ HCE LE. In this strategy, test chemicals are tested in the short-time exposure (SkinEthic™ HCE SE: 10 min exposure without post-treatment incubation) or in the long-time exposure (SkinEthic™ HCE LE: 1 hour exposure followed by 16 hour post-treatment incubation) depending on their chemical reactivity (defined as the electrophilic potential to react with cysteine or lysine containing peptides), as measured by EPRA.

The chemical reactivity of the test chemical is reported as percent depletion of the nucleophile, which is determined as the reduction of the peptide concentration in the samples relative to the average concentration of the controls. If the percent cysteine and lysine peptide depletion relative to the control is > 5.95%, the test chemical is categorised as reactive. If the percent cysteine and lysine peptide depletion is ≤ 5.95%, the test chemical is categorised as non-reactive. Thus chemicals demonstrating an ability to bind in significant amounts to a cysteine- or lysine-containing peptide are deemed to be reactive (Gerberick *et al*., 2007), and are allocated to the short exposure (10 minutes) time treatment, while those chemicals that do not show significant binding to cysteine and lysine peptides and are considered non-reactive are allocated to the long exposure (1 hour exposure + 16 hours post-treatment incubation) time treatment (Figure 2.4). The validity of the testing strategy was determined in the post-study analysis of data.

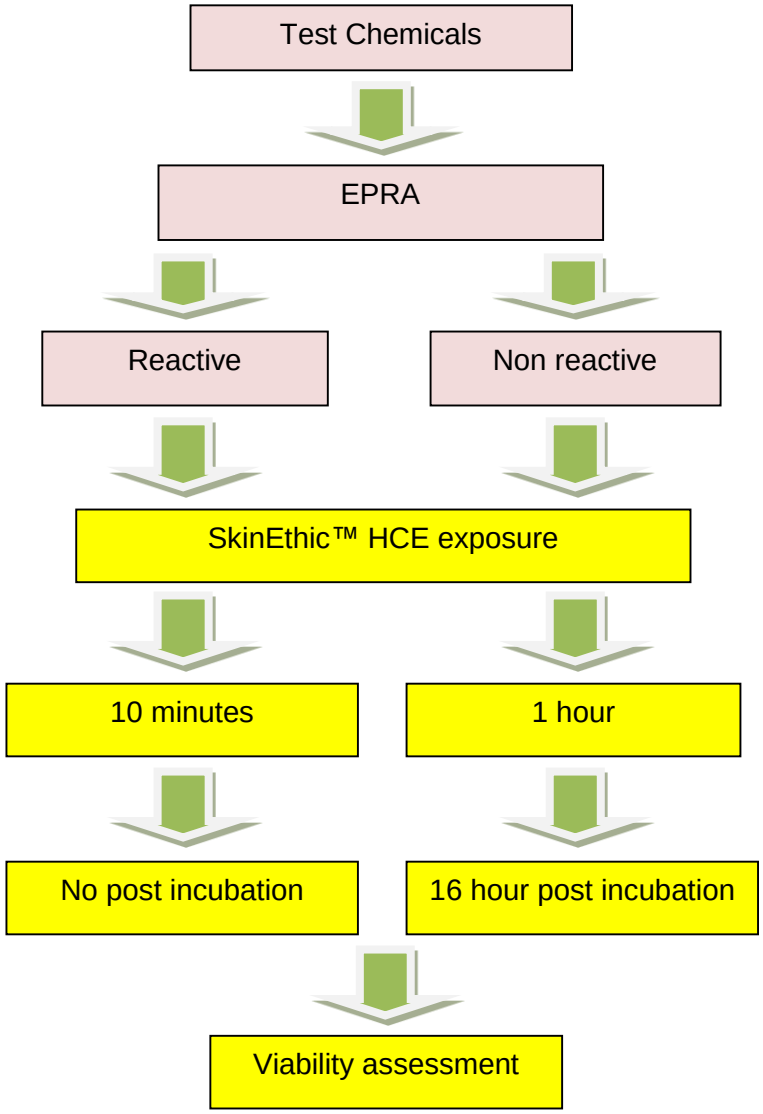

Figure 2.4. Testing strategy for SkinEthic™ HCE

2.3. Chemicals selection and distribution

Chemical selection during the EIVS was carried out by the Chemicals Selection Group (CGS) as described by Cole and co-workers (see chemicals selection report; Cole *et al.*, 2014). The CSG was composed of the following members:

Tom Cole (ECVAM; coordinator)
João Barroso (ECVAM)
Chantra Eskes (independent scientist)
William Stokes (NICEATM)
Amanda Cockshott (HSE; UK Competent Authority)
Betty Hakkert (RIVM; NL Competent Authority)

The roles and responsibilities of the CSG are shown in Figure 2.1. The members of Competent Authorities (Amanda Cockshott and Betty Hakkert) gave support in reviewing *in vivo* Draize eye irritation reports on CosIng ingredients provided by DG SANCO.

In the framework of the International Cooperation on Alternative Test Methods (ICATM), liaisons from NICEATM, ICCVAM, JaCVAM and Health Canada are invited to propose eligible test chemicals for selection, supported by quality assured *in vivo* Draize eye irritation data.

Final approval of the test chemicals proposed by the CSG was the responsibility of the core VMG. Respecting non-disclosure of chemical identities to the test facilities, the VMG lead laboratory representatives did not participate in the selection process.

A principal requirement for chemical selection was availability of complete and quality assured supporting *in vivo* data sets, for comparative evaluation of *in vitro* method predictive capacity. Systematic assignment of serious eye damage/eye irritation classifications from *in vivo* data was facilitated by computation of reported scores compiled into a customised Excel template. In cases of insufficient data for assignment of classification category, or other anomaly, the template assigns 'study criteria not met' (SCNM) effectively disqualifying the chemical from selection for EIVS, regardless of any precautionary regulatory classification.

Considering the two *in vitro* test methods included four alternative time combinations for exposure and incubation (EpiOcular™ EIT separating liquids from solids, SkinEthic™ HCE differentiating EPRA reactive from non-reactive chemicals) effectively four protocols were under evaluation, requiring a balanced chemical selection of: (i) classified versus non-classified chemicals; (ii) solids versus liquids; and (iii) EPRA reactivity versus non-reactivity. Statistical power analysis (sample size calculation) by the ECVAM biostatistician and the TNO biostatistician stipulated a minimum requirement of 26 classified chemicals and 26 non-classified chemicals per protocol, therefore totalling 104 chemicals in complement (52 classified and 52 non-classified chemicals). Acknowledging the difficulty of fulfilling all three chemicals selection conditions listed above, the VMG allowed margins for approximation. Thus, the symmetry of classified versus non-classified was set at 50±5%, with a 50/50 weighting of category 1 and category 2, and including adequate representation of sub-categories 2A and 2B. For physical state, liquids versus solids, 50±10% was admitted. Considering EPRA reactivity was only determined ad hoc to the chemical selection, the division of reactive versus non-reactive was set with a wider margin at 50±15%.

Essentially five recognised databases introduced primary sources for shortlisting eligible chemicals or formed a basis for inquiring access to original proprietary studies:

1) ECETOC database of eye irritation reference chemicals (ECETOC, 1998).
2) EC (DG-SANCO) Cosmetics Ingredients (CosIng) database (EC, 1996; 2006b; Pauwels, 2008).
3) EC New Chemicals Database (NCD) of notified substances (EC, 1967; 1979; 1992).
4) ICCVAM (NICEATM) database of eye irritation reference chemicals.
5) US EPA database of pesticide actives.

The ECETOC database is a published compilation, providing a ready source of consolidated *in vivo* data sets on established reference chemicals. The ICCVAM database, which overlaps ECETOC, and originally published as a summary version, is maintained by NICEATM with comprehensive data and additional chemicals for internal regulatory and research use. The

US EPA database is an unpublished compendium, also maintained for regulatory use. Through liaison with NICEATM, the ICCVAM and EPA databases provided quality assured *in vivo* data.

CosIng is a comprehensive inventory, but simply providing references to summary data only, available in official SCCS/P opinions which cover just a limited number of chemicals. When indicated (cited as source references in SCCS/P opinions) the original study reports containing raw *in vivo* data are generally proprietary documents, retained in confidential archive by DG-SANCO. Under bilateral arrangement, original study reports on shortlisted chemicals were provided for internal review of eligibility, where priority was given to retail rather than proprietary chemicals. Subsequently, permissions were confirmed from *in vivo* study owners allowing citation of eye irritation scores as supporting data, respective of chemicals actually selected.

NCD is also comprehensive of chemicals, but again with only summary data registered, condensed from proprietary studies fulfilled under regulatory obligation. Access to complete proprietary *in vivo* data sets required cooperation of individual sponsors to provide original study reports for review of eligibility, including agreement to release of data on relevant chemicals ultimately selected. Bilateral collaboration with individual manufacturers also secured supply of proprietary sample material for *in vitro* assay.

Logistically, the chemical selection was managed in two stages, first determining eligible and available substances for preliminary EPRA, followed by definitive selection for *in vitro* assay. In practice, a protracted period of investigation and confirmation was required to resolve selection of a balanced final set. To facilitate VMG overview and monitoring of progress, an operational master list was generated (ultimately comprising 160 potentially eligible and available chemicals).

From the VMG master list of 160 chemicals, 135 were eventually shortlisted for EPRA. Chronologically, with EPRA results on a first batch of 55 chemicals presented to the VMG in May 2010, a first set of 34 chemicals was definitively selected for *in vitro* testing. A second set of 45 chemicals was subsequently added to the definitive selection, following EPRA results on a second batch of 53, reported to the VMG in August 2010. Further development of the master list continued until the end of 2010, when a third batch of chemicals was shortlisted for EPRA testing. Following acquisition and reactivity analysis, EPRA results on 27 extra chemicals were presented to the VMG in April 2011 with addition of 28 chemicals to complete the definitive selection for EIVS ring trial *in vitro* testing, totalling 107.

The published ECETOC database contains eye irritation *in vivo* data compiled from 149 studies (132 pure chemicals). With priority given to chemicals not previously tested during pre-validation method development, 31 were selected for EIVS (11 solids, 20 liquids): 7 category 1, 4 category 2A, 3 category 2B, 17 GHS unclassified.

A documented overview of CosIng had identified 131 chemicals with supporting references (via SCCS/P opinions) to full *in vivo* study reports archived at DG-SANCO, including 72 pure chemicals (preparations, mainly aqueous dilutions, excluded). Reduced to 38, indicated as available through retail supply, 21 were determined eligible by fully compliant *in vivo* data sets. Ultimately, 14 were selected for EIVS, including 2 proprietary chemicals also found available from the original 72 shortlist (12 solids, 2 liquids): 4 category 1, 3 category 2A, 1 category 2B, 6 GHS unclassified.

Adopting a pragmatic approach to short-listing eligible chemicals from NCD, about 300 eye irritants were found among about 20 companies affiliated to the EPAA, aiming to facilitate cooperation in obtaining proprietary data and/or sample material. Eliminating chemicals with incomplete data sets (relating to animal welfare) and/or insufficient purity, provided a shortlist of 70 irritants. Similarly, about 200 eligible non-irritants were sorted from NCD. From twelve companies actually solicited, six provided *in vivo* study reports for review of eligibility, comprising 35 chemicals (18 irritants, 17 non-irritants). In addition, two companies not formally affiliated to EPAA also contributed another 30 study reports (18 irritants, 12 non-irritants) bringing the total to 65 candidates (36 irritants, 29 non-irritants). Eventually from NCD etc. (proprietary) 40 chemicals were selected for EIVS (19 solids, 21 liquids): 16 category 1, 4 category 2A, 20 GHS unclassified.

With collaborative assistance of NICEATM, about 50 chemicals from the ICCVAM database were initially proposed for consideration. Review of eligibility and selection requirement provided a shortlist of 26 (21 non-ECETOC) from which 15 were definitively selected for EIVS (8 solids, 7 liquids): 1 category 1, 2 category 2A, 8 category 2B, and 4 GHS unclassified.

Through liaison with NICEATM, 26 chemicals from the US EPA pesticide actives database were proposed. Review of eligibility and availability determined a shortlist of 10, from which 7 were selected according to requirement for EIVS (4 solids, 3 liquids): 1 category 2B, 6 GHS unclassified.

The EIVS chemical selection had achieved the principal objective of a balanced set with respect to eye irritancy, physical state and EPRA reactivity. The 107 chemicals included 3 extra to the original quota of 104. Two supplementary chemicals (chemicals # 106 and 107), of unique interest due to observed permanent coloration *in vivo*, were included for separate evaluation. The third additional chemical was introduced as a replacement for one which was reported to cause significant interference during *in vitro* assay (direct MTT reducer) (chemical # 27).

Following the ring trial *in vitro* testing of the 107 chemicals, and with statistical evaluation of results, the EpiOcular™ EIT protocol for solids was subject to further optimisation. Subsequently, the EpiOcular™ EIT protocol for solids was then subject to post-optimisation validation, with repeat testing of all EIVS solids, including 8 additional, extending the EIVS definitive set to a complement of 115 test item chemicals (Table 2.4). The supplementary solids comprised two GHS category 1, three category 2A, one category 2B and two GHS unclassified.

With reference to the GHS criteria for eye irritation classification, the scope and frequency represented in the *in vivo* data for the EIVS irritant chemicals was reviewed. For the category 1 chemicals, symptom persistence was predominant, particularly cornea opacity (CO) and conjunctiva redness (CR) although with CO severity also significant. Logically, for the category 2 chemicals, CO and CR symptoms were again prevalent compared to conjunctiva chemosis (CC) and iritis (IR).

For overview of the chemical domain represented in EIVS, the selected chemicals were each assigned a molecular class profile according to OECD QSAR Toolbox analysis. Organic molecules usually comprise combinations of chemical genre with multiple functional groups. From about 430 predefined categories, 95 were identified among the EIVS set. Three inorganic salts were additional.

Table 2.4. 115 EIVS chemicals: 55 no category, 14 category 2B, 16 category 2A, 30 category 1. Identity, Physical State, EPRA Reactivity, GHS Classification Category and Criteria, Eye Irritation (in vivo) Data Source, Substance Supply, Chemical Class Profile, and Selection Distribution.

EIVS #	Chemical Name	CAS #	Physical State	EPRA Reactivity	GHS Classification	GHS Classification Criteria (irritants only)	Data (*in vivo*) Source	Substance Supply (retail / proprietary)	Chemical Class Profile OECD ToolBox 3.1 (nested) Inorganic Salt (additional)	Main validation study selection	Optimisation selection EpiOcular solids protocol	Post-Optimisation selection EpiOcular solids protocol
Symbols: **Physical State**: L = Liquid, S = Solid; **EPRA Reactivity**: R = Reactive, NR = Non-Reactive **GHS classification category (cat) criteria**: CO = cornea opacity, CR = conjunctiva redness, CC = conjunctiva chemosis, IR = Iritis s = single score (any animal, any time), m = mean score (days 1-3, at least 2/3 or 4/6 animals), i = irreversible score (21 days, any animal) **Selection Distribution**: **+** = selected												
1	**1-bromo hexane**	111-25-1	L	R	no cat		ECETOC	retail	Alkyl halide	+		
2	**1-methyl propyl benzene**	135-98-8	L	NR	no cat		ECETOC	retail	Aryl	+		
3	**2-ethoxy ethyl meth acrylate**	2370-63-0	L	R	no cat		ECETOC	retail	Alkoxy|Ether|Methacrylate	+		
4	**iso-octyl thioglycolate** INCI name: ISOOCTYL THIOGLYCOLATE	25103-09-7	L	R	no cat		ECETOC	retail	Carboxylic acid ester|Isopropyl|Thioalcohol	+		

5	**4-(methylthio)-benzaldehyde**	3446-89-7	L	R	no cat		ECETOC	retail	Aldehyde|Aryl|Sulfide	+		
6	**dipropyl disulphide**	629-19-6	L	R	no cat		ECETOC	retail	Disulfide	+		
7	**1-bromo-4-chlorobutane**	6940-78-9	L	R	no cat		ECETOC	retail	Alkyl halide	+		
8	**1-bromo-octane**	111-83-1	L	NR	no cat		ECETOC (EpiOcular R&D)	retail	Alkyl halide	+		
9	**1,9-decadiene**	1647-16-1	L	NR	no cat		ECETOC (EpiOcular R&D)	retail	Allyl	+		
10	**2,2-dimethyl-3-pentanol**	3970-62-5	L	NR	no cat		ECETOC (EpiOcular R&D)	retail	Alcohol|Alkane branched with quaternary carbon|tert-Butyl	+		
11	**2-(2-ethoxy ethoxy) ethanol** INCI name: ETHOXY DIGLYCOL	111-90-0	L	NR	no cat		Proprietary DG-SANCO	retail	Alcohol|Alkoxy|Ether	+		
12	**bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated** (53-57%, aqueous emulsion)	68123-18-2	L	R	no cat		Proprietary NCD etc.	propri-etary	Alkyl halide|Epoxide|Phenol|Saturated heterocyclic fragment	+		

13	**bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated** (56%, aqueous emulsion)	455946-46-0	L	R	no cat		Proprietary NCD etc.	propri -etary	Alcohol|Aliphatic Amine, primary| Aliphatic Amine, secondary| Alkane branched with quaternary carbon|Alkyl halide|Epoxide| Ether|Phenol| Saturated heterocyclic fragment	+		
14	**dioctyl ether** INCI name: DICAPRYLYL ETHER	629-82-3	L	NR	no cat		Proprietary NCD etc.	retail	Ether	+		
15	**dioctyl carbonate** INCI name: DICAPRYLYL CARBONATE	1680-31-5	L	NR	no cat		Proprietary NCD etc.	retail	Carbonate	+		
16	**2-propylheptyl octanoate** INCI name: PROPYLHEPTYL CAPRYLATE	868839-23-0	L	NR	no cat		Proprietary NCD etc.	propri -etary	Alkane, branched with tertiary carbon| Carboxylic acid ester	+		
17	**polyglyceryl-3 diisoocta decanoate** INCI name: POLYGLYCERYL-3 DIISOSTEARATE	63705-03-3	L	NR	no cat		Proprietary NCD etc.	propri -etary	Alcohol| Carboxylic acid ester|Isopropyl	+		

18	**steareth-10 allyl ether/acrylates copolymer** (30%, aqueous) INCI name: STEARETH-10 ALLYL ETHER/ ACRYLATES COPOLYMER	109292-17-3	L	R	no cat		Proprietary NCD etc.	propri -etary	Acrylate|Alkoxy| Allyl|Carboxylic acid|Ether	+		
19	**dimethyl siloxane, mono dimethylvinyl siloxy- and mono trimethoxy siloxy-terminated** (95%)	471277-16-4	L	NR	no cat		Proprietary NCD etc.	propri -etary	Alkene| AlkoxySilane| Silane	+		
20	**ricinoleic acid tin salt**	71828-07-4	L	NR	no cat		Proprietary NCD etc.	propri -etary	Dihydroxyl group	+		
21	**1-ethyl-3-methyl imidazolium ethyl sulphate**	342573-75-5	L	NR	no cat		Proprietary NCD etc.	retail	Alkoxy| Ammonium salt| Aryl| Imidazole|Sulfate	+		
22	**3-phenoxy benzyl alcohol**	13826-35-2	L	NR	no cat		ICCVAM	retail	Alcohol|Benzyl| Ether	+		
23	**ethyl thioglycolate** INCI name: ETHYL THIOGLYCOLATE	623-51-8	L	NR	no cat		ECETOC	retail	Carboxylic acid ester|Thioalcohol	+		

24	**glycidyl methacrylate**	106-91-2	L	R	no cat		ECETOC	retail	Epoxide|Methacrylate|Saturated heterocyclic fragment	+		
25	**piperonyl butoxide** INCI name: PIPERONYL BUTOXIDE	51-03-6	L	NR	no cat		US-EPA pesticide	retail	Alkoxy|Benzodioxole|Benzyl|Ether	+		
26	**propiconazole**	60207-90-1	L	NR	no cat		US-EPA pesticide	retail	Aromatic heterocyclic halide|Aryl|Aryl halide|Dioxolane|Saturated heterocyclic fragment|Triazole	+		
27	**2-ethylhexyl Thioglycolate** (strong MTT reducer *in vitro*: Not tested in SkinEthic™ HCE)	7659-86-1	L	R	no cat		ECETOC	retail		+		
28	**4,4'-methylene bis-(2,6-di-tert-butylphenol)**	118-82-1	S	NR	no cat		ECETOC	retail	Benzyl|Phenol|tert-Butyl	+		+
29	**tetradecyl tetradecanoate** INCI name: MYRISTYL MYRISTATE	3234-85-3	S	NR	no cat		ECETOC	retail	Carboxylic acid ester	+		+

30	**1,1-dimethyl guanidine sulphate**	598-65-2	S	NR	no cat		ECETOC (EpiOcular R&D)	retail	Aliphatic Amine, tertiary|Amidine|Guanidine	**+**		**+**
31	**potassium tetrafluoroborate**	14075-53-7	S	R	no cat		ECETOC (EpiOcular R&D)	retail	Inorganic Salt	**+**		**+**
32	**2,6-dihydroxy-3,4-dimethyl pyridine** INCI name: 2,6-DIHYDROXY-3,4-DIMETHYL PYRIDINE	84540-47-6	S	R	no cat		Proprietary DG-SANCO	retail	Heterocyclic Phenol	**+**		**+**
33	**2,2'-[[4-[(2-methoxyethyl) amino]-3-nitrophenyl] imino]bis-ethanol** INCI name: HC BLUE NO. 11	23920-15-2	S	R	no cat		Proprietary DG-SANCO	retail	Alcohol|Aromatic amine|Ether|Nitrobenzene	**+**		**+**
34	**2,2'-[[3-methyl-4-[(4-nitro phenyl)azo] phenyl]imino] bis-ethanol** INCI name: DISPERSE RED 17	3179-89-3	S	R	no cat		Proprietary DG-SANCO	retail	Alcohol|Aromatic amine|Azo|Nitrobenzene	**+**		**+**

35	**2,5,6-triamino-4-pyrimidinol sulphate** INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	1603-02-7	S	R	no cat		Proprietary DG-SANCO	retail	Aryl|Pyrimidine|Sulfate	+	+	+
36	**1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea** INCI name: TRICLOCARBAN	101-20-2	S	NR	no cat		Proprietary DG-SANCO	retail	Aromatic heterocyclic halide| Aryl halide| Urea derivatives	+		+
37	**polyethylene glycol (PEG-40) hydrogenated castor oil** INCI name: PEG-40 HYDROGENATED CASTOR OIL	61788-85-0	S/L	R	no cat		Proprietary NCD etc.	retail	Acylal|Alcohol|Allyl|Ether	+	+	+

38	**2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethyl butyl)phenol)** INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYL BUTYLPHENOL	103597-45-1	S	NR	no cat		Proprietary NCD etc.	retail	Alkane branched with quaternary carbon|Fused carbocyclic aromatic|Fused saturated heterocycles| Precursors quinoid compounds| tert-Butyl	+		+
39	**2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol]** INCI name: BIS-ETHYLHEXYL OXYPHENOL METHOXYPHENYL TRIAZINE	187393-00-6	S	NR	no cat		Proprietary NCD etc.	retail	Alkoxy|Aryl| Ether|Phenol| Triazine	+		+
40	**acrylamidopropyl trimonium chloride/ acrylamide copolymer**	75150-29-7	S	NR	no cat		Proprietary NCD etc.	propri -etary	Acrylamide| Ammonium salt	+	+	+

41	**tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate** INCI name: ETHYLHEXYL TRIAZONE	88122-99-0	S	NR	no cat		Proprietary NCD etc.	propri-etary	Alkane, branched with tertiary carbon|Aromatic amine|Aryl|Carboxylic acid ester|Melamine	+		+
42	**trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate** INCI name: SODIUM ASCORBYL PHOSPHATE	66170-10-3	S	R	no cat		Proprietary NCD etc.	retail	Dihydroxyl group|Enol|Furanone/Furanondione|Phosphate ester	+	+	+
43	**hexyl 2-(1-(diethylamino hydroxyphenyl) methanoyl) benzoate** INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE	302776-68-7	S	R	no cat		Proprietary NCD etc.	retail	Aromatic amine|Carboxylic acid ester|Ketone|Phenol	+		+

44	**[3-chloro-4-[(3-fluorobenzyl) oxy]phenyl] (6-iodo quinazolin-4-yl)amine**	231278-20-9	S	NR	no cat		Proprietary NCD etc.	retail	Aromatic amine| Aromatic heterocyclic halide| Aryl halide| Benzyl| Ether| Quinazoline	+		+
45	**1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxy phenoxy) ethyl]amino] propan-2-ol**	72956-09-3	S	NR	no cat		Proprietary NCD etc.	retail	Alcohol| Aliphatic Amine, secondary| Carbazole|Ether	+		+
46	**cellulose, 2-(2-hydroxy-3-(trimethyl ammonium) propoxy)ethyl ether chloride** (91%) INCI name: POLY QUATERNIUM-10	68610-92-4	S	NR	no cat		Proprietary NCD etc.	retail	Alcohol| Ammonium salt| Ether	+	+	+
47	**3,4-dimethoxy benzaldehyde** INCI name: VERATRALDEHYDE	120-14-9	S	R	no cat		ICCVAM	retail	Aldehyde|Aryl| Ether	+		+
48	**sodium hydrogensulphite** INCI name: SODIUM BISULFITE	7631-90-5	S	NR	no cat		ICCVAM (SkinEthic R&D)	retail	Inorganic Salt	+		+

49	**propyl-4-hydroxybenzoate** INCI name: PROPYLPARABEN	94-13-3	S	NR	no cat		ICCVAM	retail	Carboxylic acid ester|Phenol	+		+
50	**iodosulfuron-methyl-sodium**	144550-36-7	S	R	no cat		US-EPA pesticide	retail	Aromatic heterocyclic halide|Aryl|Aryl halide|Carboxylic acid ester|Ether|Sulfonamide|Sulfonyl urea|Triazine|Urea derivatives	+		+
51	**1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene** common name: Amitraz	33089-61-1	S	R	no cat		US-EPA pesticide	retail	Amidine|Aryl	+		+
52	**2-anilino-4,6-dimethyl pyrimidine** common name: Pyrimethanil	53112-28-0	S	NR	no cat		US-EPA pesticide	retail	Aromatic amine|Aryl|Pyrimidine	+		+

53	**3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5] oxadiazinan-4-ylidene-N-nitroamine** common name: Thiamethoxam	153719-23-4	S	R	no cat		US-EPA pesticide	retail	Allyl| Aryl halide| Guanidine| Saturated heterocyclic fragment	+		+
54	**3-chloro propionitrile**	542-76-7	L	R	cat 2B	CO-m≥1	ECETOC (EpiOcular R&D)	retail	Alkyl halide| Nitrile	+		
55	**2-methylpropanal** INCI name: 2-METHYLPROPANAL	78-84-2	L	R	cat 2B	CO-m≥1, CR-m≥2	ICCVAM (SkinEthic R&D)	retail	Aldehyde| Isopropyl	+		
56	**isopropyl acetoacetate**	542-08-5	L	R	cat 2B	CR-m≥2	ICCVAM	retail	Carboxylic acid ester|Isopropyl| Ketone	+		
57	**2-methyl-1-pentanol**	105-30-6	L	NR	cat 2B	CO-m≥1	ECETOC (SkinEthic R&D)	retail	Alcohol|Alkane, branched with tertiary carbon	+		
58	**1-(1-methyl-2-propoxyethoxy) propan-2-ol** INCI name: PPG-2 PROPYL ETHER	29911-27-1	L	R	cat 2B	CO-m≥1	ICCVAM (EpiOcular R&D)	retail	Alcohol|Alkoxy| Ether	+		
59	**ethyl-2-methyl acetoacetate**	609-14-3	L	NR	cat 2B	CO-m≥1	ECETOC (EpiOcular R&D)	retail	Carboxylic acid ester|Ketone	+		

60	**diethyl toluamide** INCI name: DIETHYL TOLUAMIDE common name: DEET	134-62-3	L	NR	cat 2B	CO-m≥1	US-EPA pesticide	retail	Benzamide	+		
61	**2-hydroxy-1,4-naphthoquinone** INCI name: LAWSONE	83-72-7	S	R	cat 2B	CR-m≥2	Proprietary DG-SANCO	retail	Diketone	+		+
62	**1,4-dibutoxy benzene**	104-36-9	S	R	cat 2B	CR-m≥2, CC-m≥2	ICCVAM	retail	Alkoxy|Aryl| Ether	+	+	+
63	**4-nitrobenzoic acid**	62-23-7	S	R	cat 2B	CR-m≥2	ICCVAM	retail	Carboxylic acid| Nitrobenzene	+		+
64	**ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate**	96568-04-6	S	R	cat 2B	CO-m≥1	ICCVAM	retail	Aromatic heterocyclic halide| Aryl halide| Carboxylic acid ester|Ketone	+		+
65	**2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane** INCI name: CAMPHENE	79-92-5	S	R	cat 2B	CR-m≥2	ICCVAM (EpiOcular R&D)	retail	Alkane, branched with tertiary carbon|Alkene| Bicycloheptane| Bridged-ring carbocycles| Cycloalkane	+		+
66	**sodium chloroacetate**	3926-62-3	S	R	cat 2B	CR-m≥2	ICCVAM (SkinEthic R&D) (EpiOcular R&D)	retail	Alkyl halide| Carboxylic acid	+		+

67	**gamma-butyrolactone** INCI name: BUTYROLACTONE	96-48-0	L	NR	cat 2A	CO-m≥1, CR-m≥2, CC-m≥2, IR-m≥1	ECETOC	retail	Lactone| Oxolane| Saturated heterocyclic fragment	+		
68	**cyclopentanol**	96-41-3	L	NR	cat 2A	CO-m≥1, CR-m≥2, CC-m≥2	ECETOC (EpiOcular R&D)	retail	Alcohol| Cycloalkane	+		
69	**alkyl (C10-16) glucoside sodium carboxylate** (~ 30%, aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	383178-66-3	L	R	cat 2A	CR-m≥2, IR-m≥1	Proprietary NCD etc.	propri -etary	Dihydroxyl group	+		
70	**methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-oxobicyclo [2.2.1]hept-2-ylidene)methyl] anilinium sulphate** (30%, aqueous) INCI name: CAMPHOR BENZALKONIUM METHOSULFATE	52793-97-2	L	R	cat 2A	CO-m≥1, CR-m≥2, CC-m≥2, IR-m≥1	Proprietary DG-SANCO	propri -etary	Alkene| Aromatic amine| Bicycloheptane| Bridged-ring carbocycles| Cycloalkane| Cycloketone| Sulfate	+		

71	**1-propoxy-2-propanol** INCI name: PROPYLENE GLYCOL PROPYL ETHER	1569-01-3	L	NR	cat 2A	CO-m≥1	ICCVAM	retail	Alcohol|Alkoxy| Ether	**+**		
72	**2,4,11,13-tetra azatetradecane diimidamide, N,N''-bis (4-chlorophenyl)-3,12-diimino-, di-D-gluconate** (20%, aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE	18472-51-0	L	R	cat 2A	CO-m≥1	ICCVAM	retail	Aromatic heterocyclic halide| Aryl halide| Dihydroxyl group| Guanidine	**+**		
73	**3,3'-dithiopropionic acid**	1119-62-6	S	R	cat 2A	CO-m≥1	ECETOC	retail	Carboxylic acid| Disulfide	**+**	**+**	**+**
74	**2-amino-3-hydroxy pyridine** INCI name: 2-AMINO-3-HYDROXYPYRIDINE	16867-03-1	S	R	cat 2A	CR-m≥2	Proprietary DG-SANCO	retail	Heterocyclic Phenol	**+**	**+**	**+**
75	**sodium benzoate** INCI name: SODIUM BENZOATE	532-32-1	S	NR	cat 2A	CR-m≥2	Proprietary DG-SANCO	retail	Aryl| Carboxylic acid	**+**		**+**

76	**6,7-dihydro-2,3-dimethyl-imidazo[1,2-a] pyridin-8(5H)-one**	362525-73-3	S	NR	cat 2A	CO-m≥1, CR-m≥2, CC-m≥2, IR-m≥1	Proprietary NCD etc.	propri-etary	Aryl|Cycloketone| Fused saturated heterocycles| Fused unsaturated heterocycles| Imidazole| Piperidine| Saturated heterocyclic amine| Saturated heterocyclic fragment	+		+
77	**methyl (2E)-[2-(chloromethyl) phenyl] (methoxyimino) acetate**	189813-45-4	S	R	cat 2A	CO-m≥1, CR-m≥2, CC-m≥2	Proprietary NCD etc.	propri-etary	Alkyl halide|Benzyl| Carboxylic acid ester|Ketoxime derivatives	+	+	+
78	**(2R,3R)-3-((R)-1-(tert-butyl dimethyl siloxy)ethyl)-4-oxoazetidin-2-yl acetate**	76855-69-1	S	R	cat 2A	CO-m≥1, CR-m≥2, CC-m≥2, IR-m≥1	Proprietary NCD etc.	retail	Acetoxy| AlkoxySilane| Lactam|tert-Butyl	+	+	+
79	**ammonium nitrate** INCI name: AMMONIUM NITRATE	6484-52-2	S	NR	cat 2A	CR-m≥2	ECETOC	retail	Inorganic Salt	+		+

80	**methyl thioglycolate** INCI name: METHYL THIOGLYCOLATE	2365-48-2	L	R	cat 1	CO-s=4	ECETOC	retail	Carboxylic acid ester|Thioalcohol	+		
81	**3-diethylamino propionitrile**	5351-04-2	L	R	cat 1	CO-s=4, CO-m≥3	ECETOC	retail	Aliphatic Amine, tertiary| Nitrile	+		
82	**coco alkyl dimethyl betaine** (~ 30%, aqueous) INCI name: COCO-BETAINE	68424-94-2	L	NR	cat 1	CO-i>21, CR-i>21	Proprietary NCD etc.	retail	Ammonium salt| Carboxylic acid	+		
83	**coco amidopropyl betaine** (~ 30%, aqueous) INCI name: COCAMIDOPROPYL BETAINE	61789-40-0	L	NR	cat 1	CO-i>21, CR-i>21	Proprietary NCD etc.	retail	Ammonium salt| Carboxamide| Carboxylic acid	+		
84	**sodium coco amphoacetate** (~ 30%, aqueous)	61791-32-0	L	NR	cat 1	CO-i>21, CR-i>21	Proprietary NCD etc.	propri -etary	Alcohol| Aliphatic Amine, tertiary| Carboxamide| Carboxylic acid	+		
85	**triethanol ammonium alkyl sulphate** (~ 40%, aqueous) INCI name: TEA-C12-14 ALKYL SULFATE	90583-18-9	L	R	cat 1	CO-i>21, CR-i>21	Proprietary NCD etc.	propri -etary	Alcohol| Aliphatic Amine, tertiary| Alkoxy|Sulfate	+		

86	**di-sodium alkyl ether sulfosuccinate** (~ 30%, aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE	68815-56-5	L	R	cat 1	CO-i>21, CR-i>21	Proprietary NCD etc.	propri -etary	Alkoxy| Carboxylic acid| Carboxylic acid ester|Ether| Sulfonic acid	+		
87	**sodium alkyl ether sulphate** (~ 30%, aqueous) INCI name: SODIUM LAURETH SULFATE	68891-38-3	L	R	cat 1	CO-i>21, CR-i>21	Proprietary NCD etc.	retail	Alkoxy|Ether| Sulfate	+		
88	**bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer** (60%, aqueous)	118569-52-1	L	NR	cat 1	CO-i>21, CC-i>21, IR-i>21	Proprietary NCD etc.	propri -etary	Aliphatic Amine, primary| Aliphatic Amine, secondary| Alkyl halide| Epoxide| Ether|Phenol| Saturated heterocyclic fragment	+		
89	**ethoxylated (5 EO) alkyl (C10-14) alcohol**	66455-15-0	L	NR	cat 1	CO-i>21	Proprietary NCD etc.	propri -etary	Alcohol|Alkoxy| Ether	+		

90	**alkyl (C10-16) glucoside** (~ 50%, aqueous) INCI name: LAURYL GLUCOSIDE	110615-47-9	L	NR	cat 1	CO-i>21, CR-i>21, CC-i>21	Proprietary NCD etc.	retail	Dihydroxyl group	+		
91	**(ethylenediamine propyl)trimethoxy silane**	1760-24-3	L	NR	cat 1	CO-i>21, CR-i>21, CC-i>21	Proprietary NCD etc.	retail	Aliphatic Amine, primary| Aliphatic Amine, secondary| AlkoxySilane	+		
92	**tetraethylene glycol diacrylate**	17831-71-9	L	R	cat 1	CO-s=4, IR-m>1.5	ICCVAM	retail	Acrylate|Ether	+		
93	**2,5-dimethyl-2,5-hexanediol**	110-03-2	S	NR	cat 1	CR-i>21, CC-i>21, IR-i>21	ECETOC	retail	Alcohol	+		+
94	**dodecanoic acid** INCI name: LAURIC ACID	143-07-7	S	NR	cat 1	CO-i>21, CR-i>21	ECETOC	retail	Carboxylic acid	+		+
95	**1,2,4-triazole sodium salt**	41253-21-8	S	NR	cat 1	CO-s=4	ECETOC	retail	Aryl|Triazole	+		+
96	**1-naphthalene acetic acid** INCI name: 1-NAPHTHALENE ACETIC ACID	86-87-3	S	R	cat 1	CO-s=4, CO-i>21, CR-i>21, CC-i>21, IR-i>21	ECETOC	retail	Benzyl| Carboxylic acid| Fused carbocyclic aromatic| Naphthalene	+		+

97	**sodium oxalate** INCI name: SODIUM OXALATE	62-76-0	S	NR	cat 1	CO-s=4, CO-i>21	ECETOC	retail	Oxocarboxylic acid	+		+
98	**4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide** INCI name: TETRABROMO PHENOL BLUE	4430-25-5	S	R	cat 1	CO-s=4, CO-m≥3	Proprietary DG-SANCO	retail	Aromatic heterocyclic halide| Aromatic perhalogen carbons| Aryl halide| Benzoxathiole S-oxide| Phenol|Sulfonate ester	+		+
99	**1,2-benzisothiazol-3(2H)-one** INCI name: BENZISO THIAZOLINONE	2634-33-5	S	R	cat 1	CO-s=4, IR-m>1.5	Proprietary DG-SANCO	retail	Benzthiazolinone/ Benzo isothiazolinone	+		+
100	**ethyl lauroyl arginate HCl** INCI name: ETHYL LAUROYL ARGINATE HCL	60372-77-2	S	NR	cat 1	CO-s=4, CO-m≥3, CO-i>21, CR-i>21, CC-i>21, IR-i>21	Proprietary DG-SANCO	propri-etary	Aliphatic Amine, primary|Amidin| Carboxamide| Carboxylic acid ester| Guanidine	+		+

101	**2-[(4-aminophenyl) azo]-1,3-dimethyl-1H-imidazolium chloride** INCI name: BASIC ORANGE 31	97404-02-9	S	NR	cat 1	CR-i>21	Proprietary NCD etc.	retail	Ammonium salt| Aniline|Aryl|Azo| Guanidine| Imidazole	+		+
102	**disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene) bis(benzene sulphonate)** INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	27344-41-8	S	NR	cat 1	CR-i>21	Proprietary NCD etc.	retail	Alkene|Biphenyl| Sulfonic acid	+	+	+
103	**3,4-dimethyl-1H-pyrazole**	2820-37-3	S	NR	cat 1	CO-i>21, CR-i>21, IR-i>21	Proprietary NCD etc.	retail	Allyl|Aryl| Pyrazole	+		+
104	**N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide**	171887-03-9	S	R	cat 1	CO-i>21	Proprietary NCD etc.	retail	Aromatic heterocyclic halide|Aryl halide| Formylamino	+		+
105	**1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate**	54424-29-2	S	R	cat 1	CO-i>21, IR-i>21	Proprietary NCD etc.	propri -etary	Aliphatic Amine, tertiary|Allyl| Unsaturated heterocyclic amine| Unsaturated heterocyclic fragment	+		+

106	**4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methyl benzenamine hydrochloride** INCI name: BASIC VIOLET 2 (permanent coloration *in vivo*: evaluated separately)	3248-91-7	S	R	cat 1	perman-ent color-ation	Proprietary DG-SANCO	retail		**+**		
107	**xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxy carbonyl)phenyl]-tetrafluoroborate** (permanent coloration *in vivo*: evaluated separately)	134429-57-5	S	R	cat 1	perman-ent color-ation	Proprietary NCD etc.	propri-etary		**+**		

108	**2',6',8-trifluoro-5-methoxy [1,2,4]triazolo [1,5-c]pyrimidine-2-sulfonanilide** common name: florasulam	145701-23-1	S	NR	no cat		US-EPA pesticide	retail	Alkenyl halide| Aromatic heterocyclic halide|Aryl| Aryl halide| Ether| Fused ring triazol pyrimidine| Fused unsaturated heterocycles| Sulfonamide			+
109	**2-(diphenylacetyl)-1,3-indandione** common name: diphacinone	82-66-6	S	NR	no cat		US-EPA pesticide	retail	Indandione			+
110	**2-methyl-1,1'-biphenyl-3-ylmethyl (Z) -3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethyl cyclopropane carboxylate** common name: bifenthrin	82657-04-3	S	R	cat 2B	CO-m≥1	US-EPA pesticide	retail	Alkenyl halide| Biphenyl| Carboxylic acid ester| Cycloalkane| Perhalogenated carbons derivatives			+
111	**4-carboxy benzaldehyde**	619-66-9	S	R	cat 2A	CO-m≥1, CR-m≥2, IR-m≥1	ECETOC (EpiOcular R&D)	retail	Aldehyde|Aryl| Carboxylic acid			+

112	**1,5-naphthalenediol** INCI name: 1,5-NAPHTHALENE DIOL	83-56-7	S	R	cat 2A	CR-m≥2	Proprietary DG-SANCO	retail	Fused carbocyclic aromatic|Naphthalene|Phenol			**+**
113	**1,3-bis-(2,4-diaminophenoxy) propane tetrachloride** INCI name: 1,3-BIS-(2,4-DIAMINO PHENOXY) PROPANE HCL	74918-21-1	S	R	cat 2A	CR-m≥2	Proprietary DG-SANCO	retail	Aminoaniline, meta|Ether			**+**
114	**(-)-trans-4-(4'-fluorophenyl)-3-hydroxymethyl-1-methyl piperidine**	105812-81-5	S	NR	cat 1	CO-s=4	Proprietary NCD etc.	retail	Alcohol|Alkane, branched with tertiary carbon|Aromatic heterocyclic halide|Aryl halide|Piperidine|Saturated heterocyclic amine|Saturated heterocyclic fragment			**+**

115	**benzoic acid** INCI name: BENZOIC ACID	65-85-0	S	NR	cat 1	CO-i>21, CR-i>21, CC-i>21	Proprietary DG-SANCO	retail	Aryl| Carboxylic acid			**+**

The majority of the EIVS chemicals are pure single constituent substances, each represented by a discrete molecular structure. However, the selection included 8 polymers (3 homopolymers, 5 copolymers) 4 occurring in aqueous medium. The EIVS set also included 10 quasi polymers (8 occurring as aqueous liquids) characterised by limited molecular weight distributions corresponding to serial analogues differentiated by incremental chain lengths (e.g., alkyl C10-C16) but predominantly of specific molecular weight in overall composition (e.g., alkyl C12: lauryl / dodecyl). The range included alkyl, acyl and ethoxy analogue compositions. Another 2 chemicals (discrete compositions) produced as aqueous liquids brought the total number of aqueous chemicals to 14 selected.

Overall distributions of GHS classification with physical state and EPRA reactivity have been compiled (Tables 2.5 and 2.6). In addition, proportions of published versus proprietary *in vivo* data sources, and retail versus proprietary substance supply, have been summed. While *in vivo* data sources were equal between published and proprietary, over 80% of the chemicals were indicated as available for laboratory supply through regular commercial retail. The EIVS set therefore provides ample option for sub-set selection of performance standard reference chemicals, relevant to future validation projects on eye irritation.

Independent coding and distribution of test chemicals was conducted by TNO. TNO is certified according to ISO 9001 and GLP, and has proven experience of reliable services. TNO purchased, coded and supplied commercially available chemicals, including cosmetic ingredients from the CosIng inventory. Non-commercially available chemicals were sent directly to TNO for coding and distribution. All test chemicals were randomly coded. Each test chemical had a code that was unique for each laboratory. The same code was used for the SkinEthic™ HCE SE and for the SkinEthic™ HCE LE protocols. The codes were generated and provided by the TNO biostatistician. Expiry dates were provided for all test chemicals.

Table 2.5. Distribution of UN GHS classification and physical state of the EIVS chemicals. Numbers in brackets are for the extra chemicals used in the validation of the optimised EpiOcular™ EIT solid chemicals protocol.

	GHS Classification (category) Liquid (Liq) / Solid (Sol)							
	Cat 1		Cat 2A		Cat 2B		No Cat	
	Liq	Sol	Liq	Sol	Liq	Sol	Liq	Sol
Totals: Liquids & Solids	13	13[a] (+2)	6	7 (+3)	7	6 (+1)	26[b]	26 (+2)
Totals: GHS Categories	26[a] (+2)		13 (+3)		13 (+1)		52[b] (+2)	
Totals: Classified / Not-Classified	52[a] (+6)						52[b] (+2)	
Grand Total	104[a,b] (+8)							

[a] excluding the two extra chemicals that produced permanent coloration *in vivo* (chemicals 106 and 107 in Table 2.4)

[b] excluding the chemical that was replaced due to very strong direct MTT reduction (chemical 27 in Table 2.4)

Table 2.6. Distribution of UN GHS classification and EPRA reactivity of the EIVS chemicals. Numbers in brackets are for the extra chemicals used in the validation of the optimised EpiOcular™ EIT solid chemicals protocol.

	GHS Classification (category) EPRA Reactive (R) / Non-Reactive (NR)							
	Cat 1		Cat 2A		Cat 2B		No Cat	
	R	NR	R	NR	R	NR	R	NR
Totals: Reactive & Non-Reactive	11[a]	15 (+2)	7 (+3)	6	10 (+1)	3	22[b]	30 (+2)
Totals: GHS Categories	26[a] (+2)		13 (+3)		13 (+1)		52[b] (+2)	
Totals: Classified / Not-Classified	52[a] (+6)						52[b] (+2)	
Grand Total	104[a,b] (+8)							

[a] excluding the two extra chemicals that produced permanent coloration *in vivo* (chemicals 106 and 107 in Table 2.4)

[b] excluding the chemical that was replaced due to very strong direct MTT reduction (chemical 27 in Table 2.4)

3. Results

3.1. EpiOcular™ EIT

3.1.1. Main validation study

In the following, a summary of the results obtained in the main validation study of the EpiOcular™ EIT and the conclusions of the VMG based on those results are given. Please refer to Annex 1 containing the "EIVS Statistical Analysis and Reporting on the EpiOcular™ EIT" by Carina Rubingh (EIVS biostatistician from TNO) for more detailed statistical analysis of the study.

The three laboratories participating in the validation of EpiOcular™ EIT, two European, Beiersdorf (the lead laboratory) and Harlan UK (naïve laboratory), and one in the US, IIVS, were trained by MatTek Corporation to assure optimal transfer of the test protocol into their facilities and to guarantee that the Standard Operating Procedure (SOP) did not allow for individual (different) interpretation of the experimental steps. All procedures and assay documentation were discussed and comments and suggestions for improvement and clarification of the SOP were collected and implemented by MatTek Corporation in a final version of the SOP that was used in the ring trial of the validation study. The nine laboratory technicians assigned to the project (three per laboratory) performed the test method with 8 coded test chemicals (2 liquid No Cat, 2 solid No Cat, 2 liquid Cat 2, 1 solid Cat 2, 1 liquid Cat 1 and 2 solid Cat 1) at their test facility to demonstrate transferability of the test method. The variability of the particular experiments performed by single operators was very low, as judged by the difference in viability between tissue replicates (only 1 out of 108 results showed a difference > 20%). All test chemicals were consistently predicted by the three laboratories and nine operators using 50% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, while, using a 60% cut-off in the prediction model, 1 liquid chemical was predicted differently by one operator in one laboratory. Highly reproducible results were therefore obtained between operators and laboratories in the EpiOcular™ EIT transfer study. All the participating laboratories demonstrated their proficiency in performing the EpiOcular™ EIT and readiness to enter the formal validation study.

Tables 3.1 and 3.2 on pages 86 and 87 show the final corrected viabilities and corresponding predictions for the 60% viability cut-off obtained for the liquid chemicals tested in the main validation study. Tables 3.3 and 3.4 on pages 88 and 89 show the final corrected viabilities and corresponding predictions for the 60% viability cut-off obtained for the solid chemicals tested in the main validation study. Based on the results for the fraction of complete test sequences (99.7% in total), it can be concluded that the validation of the EpiOcular™ EIT was based on high-quality data. The acceptance criterion for this characteristic was unequivocally fulfilled (≥ 85%). One chemical (chemical #33; 2,2'-[[4-[(2-Methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol; INCI name: HC BLUE NO. 11) was considered incompatible with the test method at Beiersdorf due to too high colour interference with the MTT assay and was therefore excluded from the statistical analysis for that laboratory.

The EpiOcular™ EIT test method was found to be highly reproducible. The WLR (93.6% and 95.2% concordance of classifications for the 50% and 60% cut-offs analysed in this study, respectively) and the BLR (91.3% and 93.3% concordance of classifications for the 50% and

60% cut-offs analysed in this study, respectively) were significantly above the acceptance criteria set by the VMG (WLR ≥ 85% and BLR ≥ 80%).

Taking 60% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, the overall accuracy (79.0%) and specificity (70.5%) were 'definitely acceptable' according to the acceptance criteria as defined by the VMG (overall accuracy ≥ 75%; specificity ≥ 60%), whereas the sensitivity (87.6%) was between the limits of 'definitely unacceptable' (< 80%) and 'definitely acceptable' (≥ 90%). Considering only the liquid chemicals, the test method fulfilled all of the 'definitely acceptable' criteria (overall accuracy of 81.9%; sensitivity of 98.3%; specificity of 66.7%). For the solid chemicals both the overall accuracy (75.9%) and the specificity (74.8%) were 'definitely acceptable', whereas the sensitivity (76.9%) was 'definitely unacceptable'. Of note, the solid chemicals protocol showed balanced predictive capacity values with the 60% cut-off.

Taking 50% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, the overall accuracy (77.9%) and specificity (74.5%) were 'definitely acceptable' according to the acceptance criteria defined by the VMG (overall accuracy ≥ 75%; specificity ≥ 60%), whereas the sensitivity (81.4%) was still between the limits of 'definitely unacceptable' (< 80%) and 'definitely acceptable' (≥ 90%). Again, considering only the liquid chemicals, the test method fulfilled all of the 'definitely acceptable' criteria (overall accuracy of 82.5%; sensitivity of 96.2%; specificity of 69.8%), while for the solid chemicals only the specificity (79.7%) was 'definitely acceptable'. The overall accuracy (73.0%) fell short of 'definitely acceptable' (≥ 75%) but surpassed 'definitely unacceptable' (< 65%), while the sensitivity (66.7%) was 'definitely unacceptable'.

Based on these findings the VMG concluded that:

- EpiOcular™ EIT can be easily transferred among properly equipped and staffed laboratories, including those having no prior experience in performance of similar test methods i.e., naïve laboratories. Experienced personnel can readily be trained in the test method, and the necessary equipment and supplies can be readily obtained. The EpiOcular™ EIT SOP is clearly written and the testing and analysis of results can be performed without difficulties.

- The validation study was of high quality due to a near complete dataset with negligible re-testing performed.

- The WLR was well above the acceptance criterion set by the VMG (WLR ≥ 85%), and concordance of classifications within a single laboratory was above 90% for EpiOcular™ EIT in the participating laboratories.

- The BLR was also well above the acceptance criterion set by the VMG (BLR ≥ 80%), and the concordance of final classifications obtained between the different participating laboratories was greater than 90% for EpiOcular™ EIT.

- The EpiOcular™ EIT protocol for liquid chemicals met all of the VMG acceptance criteria for sensitivity, specificity and overall accuracy. The 60% cut-off was considered to be better than the 50% cut-off because it resulted in a better sensitivity and generated no false negatives

based on the mode of all predictions (the 50% cut-off generated one false negative for a Category 2B chemical), with similar overall accuracy.

- On the other hand, not all of the acceptance criteria were met by the EpiOcular™ EIT protocol for the solid chemicals. Sensitivity was < 90% even at the 60% cut-off and of the 6 chemicals that were under-predicted with the 60% cut-off based on the mode of all predictions, one was classified *in vivo* as Category 1.

- Analysis of the EIVS data for solid chemicals indicated scope for improvement through a balanced increase in sensitivity with decrease in specificity to attain a compromise of sensitivity ≥ 90% with specificity maintained ≥ 60%. Optimisation was therefore recommended for the EpiOcular™ EIT protocol for solid chemicals.

Optimisation of the EpiOcular™ EIT solid chemicals protocol was performed at the method developer's laboratory (MatTek Corporation) in order to increase the sensitivity of the assay to the level requested by the VMG. This optimisation led to an increase of the exposure time from 90 minutes to 6 hours. The optimisation work was performed independently of the EIVS but with guidance and scientific support from the VMG. The VMG provided 11 EIVS solid chemicals to MatTek Corporation for the optimisation of the EpiOcular™ EIT solid chemicals protocol, including the 6 solid chemicals that had been under-predicted (false negatives) by the original protocol plus 5 correctly predicted not classified (UN GHS No Cat) chemicals that had shown borderline results. MatTek Corporation was able to complete the optimisation of the solid chemicals protocol without delay, enabling follow-up validation within EIVS (post-optimisation validation), including analysis of the results by the VMG. The validation of the EpiOcular™ EIT optimised solids protocol was conducted with the original 52 EIVS solid chemicals plus an extra 8 selected to compensate for the 11 used during the optimisation of the protocol. The post-optimisation validation of the EpiOcular™ EIT optimised solid chemicals protocol took place in a single laboratory, at Beiersdorf (i.e., the lead laboratory for EpiOcular™ EIT in the original validation study), since the main purpose of this follow-up study was to evaluate the predictive capacity of the optimised protocol. Based on the very high reproducibility (WLR and BLR) achieved in the validation study of the original EpiOcular™ EIT protocols and of SkinEthic™ HCE, using multiple exposure times and post-treatment incubation periods, the VMG considered that a simple change in exposure time in the EpiOcular™ EIT solid chemicals protocol would not affect the reproducibility of the test method. Nevertheless, the VMG decided to assess the WLR of the EpiOcular™ EIT optimised solid chemicals protocol at Beiersdorf and based on the results decide if any additional reproducibility data (e.g., BLR) generated with the new protocol would be necessary.

3.1.2. Post-optimisation validation of the optimised EpiOcular™ EIT solid chemicals protocol

In the following, a summary of the results obtained in the post-optimisation validation study of the optimised EpiOcular™ EIT solid chemicals protocol and the conclusions of the VMG based on those results are given. Please refer to Annex 2 containing the "EIVS Statistical Analysis of the Data Generated under SOP Ver 8.0 of EpiOcular™ EIT" by Roman Liška (EIVS biostatistician from EURL ECVAM) for more detailed statistical analysis of the study.

Tables 3.3 and 3.4 on pages 88 and 89 show the final corrected viabilities and corresponding predictions for the 60% viability cut-off obtained for the solid chemicals tested in the post-optimisation validation of the optimised EpiOcular™ EIT solid chemicals protocol. Based on

the results for the fraction of complete test sequences (98.3% in total), it can be concluded that the post-optimisation validation of the EpiOcular™ EIT optimised solid chemicals protocol at Beiersdorf was based on high-quality data. The acceptance criterion for this characteristic was unequivocally fulfilled (≥ 85%). One chemical (chemical #98; 4,4'-(4,5,6,7-Tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide; INCI name: TETRABROMOPHENOL BLUE) was considered incompatible with the test method due to too high colour interference with the MTT assay and was therefore excluded from the statistical analysis.

The EpiOcular™ EIT optimised solid chemicals protocol was found to be at least as reproducible as the original solid chemicals protocol, with 93.2% and 96.6% concordance of classifications (based on 59 chemicals) being obtained by Beiersdorf with the optimised protocol for the 50% and 60% cut-offs analysed in this study, respectively, as compared to 92.0% and 94.0% obtained by the same laboratory with the original protocol (based on 50 chemicals). Forty nine (49) chemicals are common to the two datasets. If only these are considered in the calculations, the concordance of classifications obtained by Beiersdorf were 91.8% (50% cut-off) and 95.9% (60% cut-off) for the optimised protocol and 91.8% (50% cut-off) and 93.9% (60% cut-off) for the original protocol. The WLR of the EpiOcular™ EIT optimised solid chemicals protocol was thus significantly above the acceptance criterion set by the VMG (WLR ≥ 85%). The WLR obtained by Beiersdorf with the optimised solid chemicals protocol (as described above) was also comparable to the WLR obtained by considering the data acquired by all three laboratories that participated in the validation of the original protocol, i.e., total concordance of classifications of 92.8% (based on 50 chemicals in Beiersdorf and 51 chemicals in Harlan and IIVS) or 92.5% (based on 49 chemicals in all three laboratories) for both the 50% and 60% cut-offs.

Taking 60% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, the overall accuracy (78.0%), the specificity (60.7%) and the sensitivity (93.5%) were all 'definitely acceptable' according to the acceptance criteria as defined by the VMG (overall accuracy ≥ 75%; specificity ≥ 60%; sensitivity ≥ 90%).

Taking 50% mean viability as the prediction model threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals, the overall accuracy (76.8%) and the specificity (64.3%) were 'definitely acceptable' according to the acceptance criteria defined by the VMG (overall accuracy ≥ 75%; specificity ≥ 60%; sensitivity ≥ 90%), whereas the sensitivity (88.2%) was between the limits of 'definitely unacceptable' (< 80%) and 'definitely acceptable' (≥ 90%), but very close to being 'definitely acceptable'.

Based on these findings the VMG concluded that:

- The validation of EpiOcular™ EIT optimised solids protocol was of high quality due to a near complete dataset with negligible re-testing performed.

- The WLR was well above the acceptance criterion set by the VMG (WLR ≥ 85%), and concordance of classifications within a single laboratory was above 90% for EpiOcular™ EIT at Beiersdorf.

- Further BLR evaluation was identified, by the core VMG, to be unnecessary given the previous good reproducibility of the EpiOcular™ EIT test method, and a similar (or even

slightly better) WLR observed for the optimised solids protocol as compared to the original protocol. With the increased exposure time in the optimised solid chemicals protocol, a stronger separation between classified and not-classified chemicals in the viability scale was observed as compared to the original protocol, which is expected to improve the reproducibility of the test method. The fact that two SkinEthic™ HCE protocols with different exposure times were evaluated and showed equally high BLR provides additional evidence supporting the conclusion that further BLR assessment of the EpiOcular™ EIT optimised solid chemicals protocol is not necessary.

- The optimised EpiOcular™ EIT protocol for solid chemicals met all of the VMG acceptance criteria for sensitivity, specificity and overall accuracy using the 60% cut-off, but not with the 50% cut-off, with sensitivity being slightly lower than the 'definitely acceptable' criterion in the latter case. The overall accuracy was also higher with a 60% cut-off than with a 50% cut-off. The 60% cut-off was therefore considered to be better than the 50% cut-off with the optimised solids protocol, similarly to what had been concluded for the liquids protocol.

- The overall predictive capacity of EpiOcular™ EIT considering a combination of the data obtained for the liquid chemicals protocol with the data obtained using the optimised solid chemicals protocol, and a cut-off of 60%, consists of a sensitivity of 95.7%, a specificity of 63.0% (63.7% if chemical #37 is counted twice since it was tested both with the liquids protocol and with the optimised solids protocol) and an overall accuracy of 79.7% (79.8% if chemical #37 is counted twice). On this basis, all of the acceptance criteria defined by the VMG are met. Two out of 57 chemicals (2 solid Cat 2B chemicals) were under-predicted (false negatives) and 20 out of 54 chemicals (9 liquids and 11 solids) were over predicted (false positives) based on the mode of all predictions.

TABLE 3.1. EpiOcular™ EIT final corrected viabities for liquid test chemicals

Chem. #	CAS RN	GHS Cat.	% Viability (final corrected)								
			Beiersdorf			Harlan			IIVS		
			Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
1	111-25-1	No Cat	67.8	68.8	71.3	66.7	62.5	70.4	75.3	68.2	62.7
2	135-98-8	No Cat	83.0	80.1	77.3	74.6	79.8	78.9	84.2	79.3	80.4
3	2370-63-0	No Cat	55.4	63.0	64.2	37.2	38.1	38.6	51.4	49.0	47.5
4	25103-09-7	No Cat	106.9	104.6	115.5	60.8	57.9	64.3	100.9	93.0	94.8
5	3446-89-7	No Cat	83.5	72.2	86.4	56.7	41.4	40.3	71.8	65.4	50.3
6	629-19-6	No Cat	81.2	83.7	90.9	73.2	71.1	84.7	88.6	80.7	81.3
7	6940-78-9	No Cat	34.6	42.3	38.7	31.0	36.8	36.6	40.5	43.4	32.1
8	111-83-1	No Cat	101.4	97.3	102.8	89.6	94.7	94.8	101.2	99.6	95.2
9	1647-16-1	No Cat	95.4	101.9	98.0	91.9	82.6	96.5	106.0	100.5	98.3
10	3970-62-5	No Cat	33.0	31.1	35.3	14.4	9.8	13.2	16.6	23.8	16.8
11	111-90-0	No Cat	29.8	27.5	29.8	21.2	19.0	16.4	31.6	33.7	28.9
12	68123-18-2	No Cat	94.1	91.5	91.6	92.7	91.9	96.7	96.4	92.5	94.6
13	455946-46-0	No Cat	107.9	87.8	105.4	88.8	97.5	85.1	84.0	81.4	85.8
14	629-82-3	No Cat	98.3	98.7	104.9	90.6	97.9	103.0	94.6	95.7	96.9
15	1680-31-5	No Cat	97.2	101.7	109.5	104.9	93.0	106.3	102.4	93.9	95.3
16	868839-23-0	No Cat	100.4	110.9	103.3	103.8	102.1	94.0	95.7	105.5	102.9
17	63705-03-3	No Cat	102.5	98.1	91.9	86.9	100.6	103.9	96.6	98.1	95.3
18	109292-17-3	No Cat	112.3	69.6	109.5	101.5	91.0	96.8	94.1	95.3	95.0
19	471277-16-4	No Cat	106.4	106.4	111.8	108.8	105.3	113.1	95.6	98.4	98.9
20	71828-07-4	No Cat	31.1	57.2	49.8	9.1	0.0	19.1	48.1	33.2	41.5
21	342573-75-5	No Cat	82.8	82.9	83.2	71.8	67.4	77.6	86.2	81.5	85.4
22	13826-35-2	No Cat	51.6	39.3	45.1	24.0	23.3	13.0	37.7	35.5	39.0
23	623-51-8	No Cat	40.8	46.0	39.5	17.5	22.4	4.9	18.9	8.6	10.4
24	106-91-2	No Cat	48.4	45.6	43.5	28.0	19.4	21.3	53.0	33.9	32.6
25	51-03-6	No Cat	107.6	105.0	101.3	104.8	108.9	104.9	95.0	103.2	107.3
26	60207-90-1	No Cat	22.7	19.4	22.4	30.6	40.7	35.6	31.6	35.6	35.3
27	7659-86-1	No Cat	100.3	107.5	98.1	115.1	85.6	95.0	99.8	101.5	99.4
37	61788-85-0	No Cat	80.4	75.0	79.7	74.2	66.5	78.3	86.3	80.1	78.0
54	542-76-7	Cat 2B	48.8	47.8	45.2	17.1	25.2	19.9	51.8	43.1	30.1
55	78-84-2	Cat 2B	2.3	2.1	2.1	2.2	1.8	2.6	2.5	2.6	2.5
56	542-08-5	Cat 2B	46.4	54.5	60.3	20.8	26.5	27.3	47.5	34.8	29.6
57	105-30-6	Cat 2B	24.4	19.8	19.1	5.0	7.7	6.5	20.4	20.3	12.6
58	29911-27-1	Cat 2B	22.0	22.7	22.2	6.8	2.1	2.6	14.4	13.4	13.0
59	609-14-3	Cat 2B	62.6	67.5	78.3	46.6	36.3	47.0	56.6	52.8	43.6
60	134-62-3	Cat 2B	20.5	13.6	12.6	6.7	16.0	9.3	26.8	13.8	21.2
67	96-48-0	Cat 2A	15.0	10.8	10.7	4.1	4.3	4.9	13.6	15.3	14.6
68	96-41-3	Cat 2A	3.5	2.4	4.3	4.0	2.8	3.3	2.7	7.0	3.0
69	383178-66-3	Cat 2A	13.2	15.0	13.9	10.5	14.0	16.9	13.6	14.4	14.1
70	52793-97-2	Cat 2A	12.5	17.9	15.4	9.9	10.3	12.9	14.3	12.3	12.2
71	1569-01-3	Cat 2A	5.2	6.2	4.7	7.9	7.4	4.0	7.7	9.1	7.4
72	18472-51-0	Cat 2A	4.7	2.2	4.9	5.4	3.7	3.8	5.4	3.2	3.1
80	2365-48-2	Cat 1	18.1	16.6	17.7	6.3	0.0	15.3	9.3	5.0	9.7
81	5351-04-2	Cat 1	2.5	1.8	3.1	3.6	3.2	3.4	5.6	3.9	3.1
82	68424-94-2	Cat 1	4.5	1.6	5.4	1.5	2.1	1.7	5.3	6.9	2.6
83	61789-40-0	Cat 1	5.5	6.1	5.3	4.6	3.6	7.6	5.4	6.8	4.0
84	61791-32-0	Cat 1	12.6	5.6	22.1	6.7	7.0	4.2	17.8	18.7	9.3
85	90583-18-9	Cat 1	15.9	18.1	26.7	5.6	9.2	12.5	14.0	13.1	17.8
86	68815-56-5	Cat 1	25.3	20.7	27.2	41.8	23.4	24.8	31.8	32.7	20.5
87	68891-38-3	Cat 1	26.3	26.3	33.6	20.0	14.4	22.2	30.8	17.4	24.4
88	118569-52-1	Cat 1	4.5	5.3	7.4	5.2	7.8	5.4	3.9	7.0	3.5
89	66455-15-0	Cat 1	10.7	7.2	10.6	5.8	7.8	8.1	9.0	12.6	9.7
90	110615-47-9	Cat 1	40.4	28.5	25.6	25.4	32.6	14.4	35.5	34.7	30.8
91	1760-24-3	Cat 1	20.0	35.0	38.3	17.6	12.4	20.4	21.1	19.6	19.5
92	17831-71-9	Cat 1	47.5	41.0	49.8	18.2	14.8	13.1	39.6	39.3	51.2

TABLE 3.2. EpiOcular™ EIT final predictions for liquid test chemicals

Chem. #	CAS RN	GHS Cat.	Predictions (60% viability cut-off)								
			Beiersdorf			Harlan			IIVS		
			Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
1	111-25-1	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
2	135-98-8	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
3	2370-63-0	No Cat	I	NI	NI	I	I	I	I	I	I
4	25103-09-7	No Cat	NI	NI	NI	NI	I	NI	NI	NI	NI
5	3446-89-7	No Cat	NI	NI	NI	I	I	I	NI	NI	I
6	629-19-6	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
7	6940-78-9	No Cat	I	I	I	I	I	I	I	I	I
8	111-83-1	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
9	1647-16-1	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
10	3970-62-5	No Cat	I	I	I	I	I	I	I	I	I
11	111-90-0	No Cat	I	I	I	I	I	I	I	I	I
12	68123-18-2	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
13	455946-46-0	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
14	629-82-3	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
15	1680-31-5	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
16	868839-23-0	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
17	63705-03-3	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
18	109292-17-3	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
19	471277-16-4	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
20	71828-07-4	No Cat	I	I	I	I	I	I	I	I	I
21	342573-75-5	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
22	13826-35-2	No Cat	I	I	I	I	I	I	I	I	I
23	623-51-8	No Cat	I	I	I	I	I	I	I	I	I
24	106-91-2	No Cat	I	I	I	I	I	I	I	I	I
25	51-03-6	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
26	60207-90-1	No Cat	I	I	I	I	I	I	I	I	I
27	7659-86-1	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
37	61788-85-0	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
54	542-76-7	Cat 2B	I	I	I	I	I	I	I	I	I
55	78-84-2	Cat 2B	I	I	I	I	I	I	I	I	I
56	542-08-5	Cat 2B	I	I	NI	I	I	I	I	I	I
57	105-30-6	Cat 2B	I	I	I	I	I	I	I	I	I
58	29911-27-1	Cat 2B	I	I	I	I	I	I	I	I	I
59	609-14-3	Cat 2B	NI	NI	NI	I	I	I	I	I	I
60	134-62-3	Cat 2B	I	I	I	I	I	I	I	I	I
67	96-48-0	Cat 2A	I	I	I	I	I	I	I	I	I
68	96-41-3	Cat 2A	I	I	I	I	I	I	I	I	I
69	383178-66-3	Cat 2A	I	I	I	I	I	I	I	I	I
70	52793-97-2	Cat 2A	I	I	I	I	I	I	I	I	I
71	1569-01-3	Cat 2A	I	I	I	I	I	I	I	I	I
72	18472-51-0	Cat 2A	I	I	I	I	I	I	I	I	I
80	2365-48-2	Cat 1	I	I	I	I	I	I	I	I	I
81	5351-04-2	Cat 1	I	I	I	I	I	I	I	I	I
82	68424-94-2	Cat 1	I	I	I	I	I	I	I	I	I
83	61789-40-0	Cat 1	I	I	I	I	I	I	I	I	I
84	61791-32-0	Cat 1	I	I	I	I	I	I	I	I	I
85	90583-18-9	Cat 1	I	I	I	I	I	I	I	I	I
86	68815-56-5	Cat 1	I	I	I	I	I	I	I	I	I
87	68891-38-3	Cat 1	I	I	I	I	I	I	I	I	I
88	118569-52-1	Cat 1	I	I	I	I	I	I	I	I	I
89	66455-15-0	Cat 1	I	I	I	I	I	I	I	I	I
90	110615-47-9	Cat 1	I	I	I	I	I	I	I	I	I
91	1760-24-3	Cat 1	I	I	I	I	I	I	I	I	I
92	17831-71-9	Cat 1	I	I	I	I	I	I	I	I	I

TABLE 3.3. EpiOcular™ EIT final corrected viabities for solid test chemicals

Chem. #	CAS RN	GHS Cat.	% Viability (final corrected)											
			Beiersdorf (original)			Harlan (original)			IIVS (original)			Beiersdorf (optimised)		
			Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
28	118-82-1	No Cat	*99.4*	*99.6*	*95.8*	*94.9*	*94.5*	*90.9*	*105.4*	*112.9*	*100.6*	119.0	91.9	109.3
29	3234-85-3	No Cat	*82.9*	*91.8*	*88.2*	*57.4*	*112.0*	*83.0*	*102.5*	*105.7*	*101.4*	136.5	105.6	98.6
30	598-65-2	No Cat	*55.6*	*39.0*	*46.8*	*35.0*	*25.2*	*14.2*	*55.4*	*51.8*	*69.2*	3.1	3.1	2.3
31	14075-53-7	No Cat	*82.1*	*90.3*	*62.3*	*96.6*	*77.4*	*96.3*	*98.2*	*97.8*	*103.9*	91.8	88.6	85.3
32	84540-47-6	No Cat	*0.0*	*0.9*	*0.2*	*1.1*	*0.9*	*0.9*	*2.5*	*2.8*	*2.1*	2.6	2.3	2.2
33	23920-15-2	No Cat	-	-	-	*44.1*	*48.3*	*40.3*	*88.9*	*89.2*	*83.2*	4.9	2.0	4.1
34	3179-89-3	No Cat	*111.1*	*111.5*	*116.5*	*81.4*	*54.1*	*63.2*	*95.6*	*107.1*	*80.9*	12.3	14.5	-1.9
35	1603-02-7	No Cat	*73.7*	*72.0*	*77.0*	*62.3*	*69.3*	*77.4*	*99.9*	*95.2*	*99.4*	32.5	40.6	55.9
36	101-20-2	No Cat	*110.9*	*102.8*	*107.5*	*103.1*	*88.2*	*98.5*	*110.7*	*110.8*	*105.6*	100.5	110.0	109.5
37	61788-85-0	No Cat	*80.4*	*75.0*	*79.7*	*74.2*	*66.5*	*78.3*	*86.3*	*80.1*	*78.0*	89.2	65.2	68.1
38	103597-45-1	No Cat	*102.8*	*100.9*	*119.7*	*99.7*	*113.0*	*95.8*	*101.1*	*101.9*	*108.0*	118.2	94.7	95.2
39	187393-00-6	No Cat	*101.9*	*99.5*	*117.3*	*100.9*	*114.7*	*88.4*	*102.5*	*101.7*	*104.8*	116.3	108.6	99.4
40	75150-29-7	No Cat	*49.4*	*59.5*	*62.1*	*72.9*	*56.2*	*60.2*	*62.3*	*63.0*	*60.2*	64.0	44.9	58.3
41	88122-99-0	No Cat	*101.2*	*98.8*	*90.4*	*98.2*	*86.4*	*88.8*	*99.3*	*102.5*	*94.0*	102.6	111.3	117.2
42	66170-10-3	No Cat	*64.7*	*85.0*	*58.7*	*53.4*	*66.0*	*60.1*	*85.3*	*81.8*	*70.5*	3.2	4.2	2.7
43	302776-68-7	No Cat	*93.9*	*112.1*	*102.6*	*125.3*	*91.6*	*163.7*	*99.8*	*102.0*	*103.4*	123.6	126.8	92.9
44	231278-20-9	No Cat	*104.5*	*98.7*	*97.3*	*101.6*	*95.0*	*103.9*	*98.1*	*94.2*	*102.9*	114.8	106.2	115.2
45	72956-09-3	No Cat	*110.6*	*101.4*	*118.8*	*112.5*	*97.9*	*112.6*	*98.6*	*98.4*	*94.8*	98.4	102.2	86.4
46	68610-92-4	No Cat	*68.4*	*68.9*	*72.6*	*73.1*	*58.9*	*80.0*	*65.2*	*60.8*	*57.8*	66.0	59.8	62.0
47	120-14-9	No Cat	*4.4*	*5.0*	*4.6*	*3.4*	*2.0*	*3.2*	*3.2*	*2.9*	*2.6*	1.9	2.0	2.5
48	7631-90-5	No Cat	*2.7*	*3.6*	*3.0*	*2.8*	*3.1*	*2.5*	*2.7*	*2.5*	*2.4*	2.4	2.4	2.4
49	94-13-3	No Cat	*0.0*	*0.0*	*0.0*	*11.7*	*5.5*	*3.8*	*11.9*	*15.8*	*15.6*	5.6	3.2	3.1
50	144550-36-7	No Cat	*89.7*	*89.6*	*83.5*	*99.1*	*97.1*	*96.7*	*95.6*	*92.7*	*97.4*	86.5	99.6	99.5
51	33089-61-1	No Cat	*99.1*	*91.5*	*101.1*	*93.3*	*100.1*	*84.8*	*95.4*	*98.7*	*106.0*	23.4	40.0	43.7
52	53112-28-0	No Cat	*104.8*	*103.1*	*130.8*	*106.5*	*105.7*	*93.4*	*101.3*	*95.1*	*105.7*	138.5	110.8	105.9
53	153719-23-4	No Cat	*93.0*	*105.7*	*119.4*	*108.2*	*123.4*	*104.0*	*106.3*	*101.7*	*107.2*	110.8	117.4	104.2
108	145701-23-1	No Cat	-	-	-	-	-	-	-	-	-	102.0	111.0	89.8
109	82-66-6	No Cat	-	-	-	-	-	-	-	-	-	83.1	89.5	100.0
61	83-72-7	Cat 2B	*16.0*	*15.9*	*22.9*	*17.0*	*11.3*	*9.4*	*16.3*	*16.4*	*21.4*	2.5	3.5	3.0
62	104-36-9	Cat 2B	*115.2*	*110.1*	*101.7*	*101.7*	*104.7*	*105.9*	*109.8*	*105.2*	*97.1*	106.5	116.5	98.0
63	62-23-7	Cat 2B	*40.6*	*34.3*	*27.0*	*56.8*	*41.0*	*50.2*	*49.6*	*38.9*	*43.7*	6.0	4.7	5.8
64	96568-04-6	Cat 2B	*36.9*	*22.8*	*30.0*	*16.0*	*20.7*	*35.1*	*39.6*	*29.7*	*28.2*	1.9	2.1	1.9
65	79-92-5	Cat 2B	*50.5*	*52.1*	*51.7*	*20.3*	*16.2*	*51.8*	*63.8*	*41.6*	*53.9*	6.2	4.8	3.2
66	3926-62-3	Cat 2B	*6.0*	*8.0*	*6.4*	*4.8*	*2.7*	*3.0*	*2.7*	*6.6*	*2.0*	2.3	2.7	2.1
110	82657-04-3	Cat 2B	-	-	-	-	-	-	-	-	-	105.1	114.1	111.4
73	1119-62-6	Cat 2A	*73.9*	*88.1*	*89.0*	*78.4*	*86.0*	*87.8*	*102.5*	*105.8*	*82.9*	4.1	2.9	20.4
74	16867-03-1	Cat 2A	*72.5*	*65.9*	*88.8*	*76.7*	*74.5*	*81.6*	*87.2*	*99.3*	*88.8*	51.5	23.0	18.3
75	532-32-1	Cat 2A	*74.8*	*81.1*	*83.9*	*17.4*	*2.0*	*2.7*	*5.0*	*5.8*	*4.4*	1.9	2.0	6.5
76	362525-73-3	Cat 2A	*54.8*	*53.5*	*53.4*	*59.0*	*32.3*	*52.8*	*26.9*	*26.3*	*28.7*	2.5	3.1	2.4
77	189813-45-4	Cat 2A	*103.6*	*94.1*	*92.8*	*94.7*	*61.8*	*65.2*	*98.2*	*107.3*	*103.6*	55.0	59.8	56.5
78	76855-69-1	Cat 2A	*79.9*	*80.9*	*88.9*	*65.8*	*62.0*	*63.4*	*87.8*	*86.9*	*85.9*	52.8	46.4	48.4
79	6484-52-2	Cat 2A	*2.4*	*3.3*	*2.2*	*2.7*	*2.8*	*2.2*	*2.9*	*2.3*	*3.2*	2.2	2.1	2.1
111	619-66-9	Cat 2A	-	-	-	-	-	-	-	-	-	3.9	3.9	3.4
112	83-56-7	Cat 2A	-	-	-	-	-	-	-	-	-	29.1	19.3	14.7
113	74918-21-1	Cat 2A	-	-	-	-	-	-	-	-	-	5.9	6.7	4.7
93	110-03-2	Cat 1	*11.5*	*9.5*	*5.7*	*6.2*	*9.3*	*8.5*	*10.3*	*21.3*	*18.0*	2.3	2.5	2.1
94	143-07-7	Cat 1	*2.1*	*2.3*	*2.6*	*5.7*	*3.0*	*2.6*	*5.2*	*5.8*	*4.3*	1.3	2.6	1.2
95	41253-21-8	Cat 1	*2.4*	*2.5*	*2.2*	*2.5*	*2.7*	*2.7*	*1.6*	*2.3*	*2.1*	2.4	2.4	2.0
96	86-87-3	Cat 1	*28.9*	*41.1*	*36.1*	*35.5*	*35.3*	*30.9*	*33.2*	*38.9*	*54.1*	12.3	9.5	6.0
97	62-76-0	Cat 1	*56.2*	*47.2*	*55.5*	*55.3*	*51.7*	*51.0*	*59.0*	*55.1*	*51.1*	27.6	29.8	29.6
98	4430-25-5	Cat 1	*0.0*	*0.0*	*0.0*	*0.0*	*0.0*	*0.0*	*0.0*	*0.0*	*0.0*	-	-	-
99	2634-33-5	Cat 1	*2.6*	*2.8*	*3.1*	*3.3*	*2.3*	*2.4*	*1.9*	*2.0*	*1.7*	2.1	2.2	2.7
100	60372-77-2	Cat 1	*9.8*	*3.6*	*2.4*	*10.0*	*14.9*	*8.5*	*10.5*	*8.2*	*8.9*	18.0	15.0	20.1
101	97404-02-9	Cat 1	*34.1*	*33.2*	*34.3*	*26.2*	*50.6*	*42.0*	*19.9*	*21.6*	*13.8*	2.3	2.5	2.2
102	27344-41-8	Cat 1	*10.1*	*110.2*	*124.3*	*38.0*	*55.0*	*52.1*	*76.7*	*87.8*	*108.2*	14.3	14.6	19.8
103	2820-37-3	Cat 1	*2.0*	*3.5*	*2.0*	*1.9*	*1.9*	*1.6*	*1.7*	*2.1*	*2.1*	1.3	1.4	1.4
104	171887-03-9	Cat 1	*37.4*	*38.9*	*42.9*	*40.3*	*36.3*	*48.4*	*47.1*	*34.8*	*24.4*	25.7	22.7	17.1
105	54424-29-2	Cat 1	*2.5*	*2.8*	*2.4*	*3.9*	*2.6*	*1.9*	*2.1*	*2.4*	*2.4*	2.4	2.4	2.1
114	105812-81-5	Cat 1	-	-	-	-	-	-	-	-	-	5.7	7.6	2.9
115	65-85-0	Cat 1	-	-	-	-	-	-	-	-	-	2.3	2.1	2.1

TABLE 3.4. EpiOcular™ EIT final predictions for solid test chemicals

Chem. #	CAS RN	GHS Cat.	Predictions (60% viability cut-off)											
			Beiersdorf (original)			Harlan (original)			IIVS (original)			Beiersdorf (optimised)		
			Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
28	118-82-1	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
29	3234-85-3	No Cat	*NI*	*NI*	*NI*	*I*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
30	598-65-2	No Cat	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*NI*	I	I	I
31	14075-53-7	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
32	84540-47-6	No Cat	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
33	23920-15-2	No Cat	-	-	-	*I*	*I*	*I*	*NI*	*NI*	*NI*	I	I	I
34	3179-89-3	No Cat	*NI*	*NI*	*NI*	*NI*	*I*	*NI*	*NI*	*NI*	*NI*	I	I	I
35	1603-02-7	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	I	I	I
36	101-20-2	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
37	61788-85-0	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
38	103597-45-1	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
39	187393-00-6	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
40	75150-29-7	No Cat	*I*	*I*	*NI*	*NI*	*I*	*NI*	*NI*	*NI*	*NI*	NI	I	I
41	88122-99-0	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
42	66170-10-3	No Cat	*NI*	*NI*	*I*	*I*	*NI*	*NI*	*NI*	*NI*	*NI*	I	I	I
43	302776-68-7	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
44	231278-20-9	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
45	72956-09-3	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
46	68610-92-4	No Cat	*NI*	*NI*	*NI*	*NI*	*I*	*NI*	*NI*	*NI*	*I*	NI	I	NI
47	120-14-9	No Cat	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
48	7631-90-5	No Cat	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
49	94-13-3	No Cat	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
50	144550-36-7	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
51	33089-61-1	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	I	I	I
52	53112-28-0	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
53	153719-23-4	No Cat	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
108	145701-23-1	No Cat	-	-	-	-	-	-	-	-	-	NI	NI	NI
109	82-66-6	No Cat	-	-	-	-	-	-	-	-	-	NI	NI	NI
61	83-72-7	Cat 2B	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
62	104-36-9	Cat 2B	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	NI	NI	NI
63	62-23-7	Cat 2B	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
64	96568-04-6	Cat 2B	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
65	79-92-5	Cat 2B	*I*	*I*	*I*	*I*	*I*	*I*	*NI*	*I*	*I*	I	I	I
66	3926-62-3	Cat 2B	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
110	82657-04-3	Cat 2B	-	-	-	-	-	-	-	-	-	NI	NI	NI
73	1119-62-6	Cat 2A	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	I	I	I
74	16867-03-1	Cat 2A	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	I	I	I
75	532-32-1	Cat 2A	*NI*	*NI*	*NI*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
76	362525-73-3	Cat 2A	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
77	189813-45-4	Cat 2A	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	I	I	I
78	76855-69-1	Cat 2A	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	*NI*	I	I	I
79	6484-52-2	Cat 2A	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
111	619-66-9	Cat 2A	-	-	-	-	-	-	-	-	-	I	I	I
112	83-56-7	Cat 2A	-	-	-	-	-	-	-	-	-	I	I	I
113	74918-21-1	Cat 2A	-	-	-	-	-	-	-	-	-	I	I	I
93	110-03-2	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
94	143-07-7	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
95	41253-21-8	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
96	86-87-3	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
97	62-76-0	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
98	4430-25-5	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	-	-	-
99	2634-33-5	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
100	60372-77-2	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
101	97404-02-9	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
102	27344-41-8	Cat 1	*I*	*NI*	*NI*	*I*	*I*	*I*	*NI*	*NI*	*NI*	I	I	I
103	2820-37-3	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
104	171887-03-9	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
105	54424-29-2	Cat 1	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	*I*	I	I	I
114	105812-81-5	Cat 1	-	-	-	-	-	-	-	-	-	I	I	I
115	65-85-0	Cat 1	-	-	-	-	-	-	-	-	-	I	I	I

3.2. SkinEthic™ HCE SE, LE and test strategy (TS)

3.2.1. Main validation study

In the following, a summary of the results obtained in the main validation study of the SkinEthic™ HCE and the conclusions of the VMG based on those results are given. Please refer to Annex 3 containing the "EIVS Statistical Analysis and Reporting on the SkinEthic™ HCE" by Carina Rubingh (EIVS biostatistician from TNO) for more detailed statistical analysis of the study.

Two naïve laboratories participating in the validation of SkinEthic™ HCE, one European, CARDAM, and one in the US, CeeTox, were trained by the lead laboratory L'Oréal to assure optimal transfer of the SE and LE test protocols into their facilities and to guarantee that the SOP did not allow for individual (different) interpretation of the experimental steps. All procedures and assay documentation were discussed and comments and suggestions for improvement and clarification of the SOP were collected and implemented by L'Oréal in a final version of the SOP that was used in the ring trial of the validation study. The laboratory technicians from all three participating laboratories assigned to the project performed the test method with 14 coded test chemicals (3 No Cat, 2 Cat 2, 6 Cat 1 and 3 undefined) at their test facility to demonstrate transferability of the test method. The variability obtained with both the SE and LE protocols at the three laboratories was very low with SD below 18% being obtained for the majority of the tested chemicals in all laboratories. Concordance between results of the three laboratories that participated on the transfer study was very good, especially considering that highly challenging chemicals (including colorants and direct MTT reducers) had been selected for the study. The WLR ranged from 86.7% (CeeTox) to 87.5% (L'Oréal and CARDAM) and the BLR between the three laboratories in particular was excellent (100% for the SE protocol and 92.3% for the LE protocol). All the participating laboratories demonstrated their proficiency in performing the SkinEthic™ HCE and readiness to enter the formal validation study.

Tables 3.5 and 3.6 on pages 92 and 93 show the final predictions obtained with SkinEthic™ HCE SE (50% viability cut-off) in the main validation study. Tables 3.7 and 3.8 on pages 94 and 95 show the final predictions obtained with SkinEthic™ HCE LE (50% viability cut-off) in the main validation study. Tables 3.9 and 3.10 on pages 96 and 97 show the final predictions obtained with SkinEthic™ HCE TS (SE or LE predictions depending on EPRA results and based on a 50% viability cut-off) in the main validation study. Based on the results for the fraction of complete test sequences (100% in total for the SE protocol, 99.7% in total for the LE protocol), it can be concluded that the validation of the SkinEthic™ HCE was based on high-quality data. The acceptance criterion for this characteristic was unequivocally fulfilled (≥ 85%).

None of the 104 chemicals tested was considered incompatible with the test method by any of the three laboratories, with either the SE or the LE protocol. All chemicals were thus included in all of the statistical analyses.

The SkinEthic™ HCE test method was found to be highly reproducible. The WLR (93.9% and 95.5% concordance of classifications for the SE and LE, respectively) and the BLR (92.3% concordance of classifications for both the SE and LE protocols) were significantly above the acceptance criteria set by the VMG (WLR ≥ 85% and BLR ≥ 80%).

The only prediction model that was evaluated used a mean viability of 50% as the threshold differentiating classified (UN GHS Cat 1 and Cat 2) from non-classified (UN GHS No Cat) chemicals. The specificity of this prediction model was found to be 'definitely acceptable' according to the acceptance criterion defined by the VMG (≥ 60%), regardless of the protocol or strategy (SE: 88.5%; LE: 65.5%; test strategy: 77.1%). The sensitivity was on the other hand 'definitely unacceptable' (< 80%) according to the same acceptance criteria (SE: 42.7%; LE: 71.6%; test strategy: 54.5%). The overall accuracy was between the limits of 'definitely unacceptable' (< 65%) and 'definitely acceptable' (≥ 75%) (SE: 65.6%; LE: 68.6%; test strategy: 65.8%).

Based on these findings the VMG concluded that:

- SkinEthic™ HCE SE and LE can be easily transferred among properly equipped and staffed laboratories, including those having no prior experience in performance of similar test methods i.e., (naïve laboratories). Experienced personnel can readily be trained in the test method, and the necessary equipment and supplies can be readily obtained. The SkinEthic™ HCE SOP is clearly written and the testing and analysis of results can be performed without difficulties.

- The validation study was of high quality due to a near complete dataset with negligible re-testing performed.

- The WLR was well above the acceptance criterion set by the VMG (WLR ≥ 85%), and concordance of classifications within a single laboratory was above 90% in the participating laboratories for both the SE and LE protocols of SkinEthic™ HCE.

- The BLR was also well above the acceptance criterion set by the VMG (BLR ≥ 80%), and the concordance of final classifications obtained between the different participating laboratories was greater than 90% for both the SE and LE protocols of SkinEthic™ HCE.

- Not all of the VMG acceptance criteria were met by either the SE or LE protocols of SkinEthic™ HCE alone. Sensitivity, in particular, was 'definitely unacceptable' being < 80% with both protocols (SE: 42.7%; LE: 71.6%). Moreover, of the 30 chemicals that were underpredicted by SE and of the 15 that were underpredicted by LE based on the mode of all predictions, 14 and 5, respectively, were classified *in vivo* as Category 1, which is also 'definitely unacceptable'.

- The use of EPRA to orient chemicals to the LE (non-reactive) or SE (reactive) protocol is also not valid due to a false negative rate of 45.5% and 10 Category 1 chemicals being underpredicted as non-irritants (based on the mode of all predictions). It was therefore decided not to conduct a reproducibility assessment of EPRA.

- Analysis of the data for the SkinEthic™ HCE indicated scope for improvement. Further optimisation has therefore been recommended for the SkinEthic™ HCE test method considering different protocols for liquid chemicals and solid chemicals, as with EpiOcular™ EIT.

TABLE 3.5. SkinEthic™ HCE SE final predictions for No Cat test chemicals

Chem. #	CAS RN	Phys. State	GHS Cat.	Predictions (50% viability cut-off)								
				CARDAM			CeeTox			L'Oréal		
				Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
1	111-25-1	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
2	135-98-8	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
3	2370-63-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
4	25103-09-7	L	No Cat	I	I	I	I	I	I	I	I	I
5	3446-89-7	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
6	629-19-6	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
7	6940-78-9	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
8	111-83-1	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
9	1647-16-1	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
10	3970-62-5	L	No Cat	I	I	I	I	I	I	I	I	I
11	111-90-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
12	68123-18-2	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
13	455946-46-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
14	629-82-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
15	1680-31-5	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
16	868839-23-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
17	63705-03-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
18	109292-17-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
19	471277-16-4	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
20	71828-07-4	L	No Cat	I	I	NI	NI	NI	NI	NI	I	I
21	342573-75-5	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
22	13826-35-2	L	No Cat	NI	NI	NI	NI	I	I	NI	NI	NI
23	623-51-8	L	No Cat	I	I	I	I	I	I	I	I	I
24	106-91-2	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
25	51-03-6	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
26	60207-90-1	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
28	118-82-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
29	3234-85-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
30	598-65-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
31	14075-53-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
32	84540-47-6	S	No Cat	NI	NI	NI	I	I	I	I	I	I
33	23920-15-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
34	3179-89-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
35	1603-02-7	S	No Cat	I	NI	I	I	NI	I	I	I	I
36	101-20-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
37	61788-85-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
38	103597-45-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
39	187393-00-6	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
40	75150-29-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
41	88122-99-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
42	66170-10-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
43	302776-68-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
44	231278-20-9	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
45	72956-09-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
46	68610-92-4	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
47	120-14-9	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
48	7631-90-5	S	No Cat	I	I	NI	I	I	I	I	I	I
49	94-13-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
50	144550-36-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
51	33089-61-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
52	53112-28-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
53	153719-23-4	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI

TABLE 3.6. SkinEthic™ HCE SE final predictions for Cat 2B, Cat 2A and Cat 1 test chemicals

Chem. #	CAS RN	Phys. State	GHS Cat.	Predictions (50% viability cut-off)								
				CARDAM			CeeTox			L'Oréal		
				Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
54	542-76-7	L	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	I
55	78-84-2	L	Cat 2B	I	I	I	I	I	I	I	I	I
56	542-08-5	L	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
57	105-30-6	L	Cat 2B	I	I	I	I	I	I	I	I	I
58	29911-27-1	L	Cat 2B	I	I	I	I	I	I	I	I	I
59	609-14-3	L	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
60	134-62-3	L	Cat 2B	I	I	I	I	I	I	I	I	I
61	83-72-7	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
62	104-36-9	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
63	62-23-7	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
64	96568-04-6	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
65	79-92-5	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
66	3926-62-3	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
67	96-48-0	L	Cat 2A	I	I	I	I	I	I	I	I	I
68	96-41-3	L	Cat 2A	I	I	I	I	I	I	I	I	I
69	383178-66-3	L	Cat 2A	NI	I	NI	NI	NI	NI	NI	NI	NI
70	52793-97-2	L	Cat 2A	I	I	I	I	I	I	I	I	I
71	1569-01-3	L	Cat 2A	I	I	I	I	I	I	I	I	I
72	18472-51-0	L	Cat 2A	I	I	I	I	I	I	I	I	I
73	1119-62-6	S	Cat 2A	NI	NI	NI	NI	I	I	NI	NI	NI
74	16867-03-1	S	Cat 2A	NI	NI	NI	NI	NI	I	NI	NI	NI
75	532-32-1	S	Cat 2A	NI	I	I	NI	NI	NI	I	I	I
76	362525-73-3	S	Cat 2A	NI	NI	NI	I	NI	NI	NI	NI	NI
77	189813-45-4	S	Cat 2A	NI	NI	NI	I	NI	NI	NI	NI	NI
78	76855-69-1	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
79	6484-52-2	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
80	2365-48-2	L	Cat 1	I	I	I	I	I	I	I	I	I
81	5351-04-2	L	Cat 1	I	I	I	I	I	I	I	I	I
82	68424-94-2	L	Cat 1	I	I	I	I	I	I	I	I	I
83	61789-40-0	L	Cat 1	I	I	I	I	I	I	I	I	I
84	61791-32-0	L	Cat 1	I	I	I	I	I	I	I	I	I
85	90583-18-9	L	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
86	68815-56-5	L	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
87	68891-38-3	L	Cat 1	NI	NI	NI	NI	NI	I	NI	NI	NI
88	118569-52-1	L	Cat 1	I	I	I	I	I	I	I	I	I
89	66455-15-0	L	Cat 1	NI	NI	NI	NI	NI	I	NI	NI	NI
90	110615-47-9	L	Cat 1	NI	NI	NI	NI	NI	NI	NI	I	I
91	1760-24-3	L	Cat 1	NI	I	NI	I	I	I	I	I	I
92	17831-71-9	L	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
93	110-03-2	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
94	143-07-7	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
95	41253-21-8	S	Cat 1	I	I	I	I	I	I	I	I	I
96	86-87-3	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
97	62-76-0	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
98	4430-25-5	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
99	2634-33-5	S	Cat 1	I	I	I	I	I	I	I	I	I
100	60372-77-2	S	Cat 1	I	NI	I	I	I	I	I	NI	NI
101	97404-02-9	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
102	27344-41-8	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
103	2820-37-3	S	Cat 1	I	I	I	I	I	I	I	I	I
104	171887-03-9	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
105	54424-29-2	S	Cat 1	I	I	I	I	I	I	I	I	I

TABLE 3.7. SkinEthic™ HCE LE final predictions for No Cat test chemicals

Chem. #	CAS RN	Phys. State	GHS Cat.	Predictions (50% viability cut-off)								
				CARDAM			CeeTox			L'Oréal		
				Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
1	111-25-1	L	No Cat	I	I	I	I	I	I	I	I	I
2	135-98-8	L	No Cat	I	I	I	I	I	I	I	I	I
3	2370-63-0	L	No Cat	I	I	I	I	I	I	I	I	I
4	25103-09-7	L	No Cat	I	I	I	I	I	I	I	I	I
5	3446-89-7	L	No Cat	I	I	I	I	I	I	I	I	I
6	629-19-6	L	No Cat	I	I	I	I	I	I	I	I	I
7	6940-78-9	L	No Cat	I	I	I	I	I	I	I	I	I
8	111-83-1	L	No Cat	I	I	I	I	I	I	I	I	I
9	1647-16-1	L	No Cat	NI	I	NI	I	I	I	I	I	I
10	3970-62-5	L	No Cat	I	I	I	I	I	I	I	I	I
11	111-90-0	L	No Cat	I	I	I	NI	NI	NI	NI	NI	I
12	68123-18-2	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
13	455946-46-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
14	629-82-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
15	1680-31-5	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
16	868839-23-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
17	63705-03-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
18	109292-17-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
19	471277-16-4	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
20	71828-07-4	L	No Cat	I	I	I	I	I	.	I	I	I
21	342573-75-5	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
22	13826-35-2	L	No Cat	I	I	I	I	I	I	I	I	I
23	623-51-8	L	No Cat	I	I	I	I	I	I	I	I	I
24	106-91-2	L	No Cat	I	I	I	I	I	I	I	I	I
25	51-03-6	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
26	60207-90-1	L	No Cat	I	I	I	I	I	I	I	I	I
28	118-82-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
29	3234-85-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
30	598-65-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
31	14075-53-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
32	84540-47-6	S	No Cat	I	I	I	I	I	I	I	I	I
33	23920-15-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
34	3179-89-3	S	No Cat	I	I	NI	NI	NI	NI	NI	NI	NI
35	1603-02-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
36	101-20-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
37	61788-85-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
38	103597-45-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
39	187393-00-6	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
40	75150-29-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
41	88122-99-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
42	66170-10-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
43	302776-68-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
44	231278-20-9	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
45	72956-09-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
46	68610-92-4	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
47	120-14-9	S	No Cat	NI	NI	NI	I	I	NI	I	I	I
48	7631-90-5	S	No Cat	I	I	I	I	I	I	I	I	I
49	94-13-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
50	144550-36-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
51	33089-61-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
52	53112-28-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
53	153719-23-4	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI

TABLE 3.8. SkinEthic™ HCE LE final predictions for Cat 2B, Cat 2A and Cat 1 test chemicals

Chem. #	CAS RN	Phys. State	GHS Cat.	Predictions (50% viability cut-off)								
				CARDAM			CeeTox			L'Oréal		
				Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
54	542-76-7	L	Cat 2B	I	I	I	I	I	I	I	I	I
55	78-84-2	L	Cat 2B	I	I	I	I	I	I	I	I	I
56	542-08-5	L	Cat 2B	I	I	I	I	I	I	I	I	I
57	105-30-6	L	Cat 2B	I	I	I	I	I	I	I	I	I
58	29911-27-1	L	Cat 2B	I	I	I	I	I	I	I	I	I
59	609-14-3	L	Cat 2B	I	I	I	I	I	I	I	I	I
60	134-62-3	L	Cat 2B	I	I	I	I	I	I	I	I	I
61	83-72-7	S	Cat 2B	NI	NI	NI	I	I	I	NI	NI	NI
62	104-36-9	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
63	62-23-7	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
64	96568-04-6	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
65	79-92-5	S	Cat 2B	NI	I	I	NI	NI	NI	I	NI	NI
66	3926-62-3	S	Cat 2B	I	I	I	I	I	I	NI	I	I
67	96-48-0	L	Cat 2A	I	I	I	I	I	I	I	I	I
68	96-41-3	L	Cat 2A	I	I	I	I	I	I	I	I	I
69	383178-66-3	L	Cat 2A	I	I	I	I	I	I	I	I	I
70	52793-97-2	L	Cat 2A	I	I	I	I	I	I	I	I	I
71	1569-01-3	L	Cat 2A	I	I	I	I	I	I	I	I	I
72	18472-51-0	L	Cat 2A	I	I	I	I	I	I	I	I	I
73	1119-62-6	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
74	16867-03-1	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
75	532-32-1	S	Cat 2A	I	I	I	I	I	I	I	I	I
76	362525-73-3	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
77	189813-45-4	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
78	76855-69-1	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
79	6484-52-2	S	Cat 2A	NI	NI	NI	I	I	I	I	NI	I
80	2365-48-2	L	Cat 1	I	I	I	I	I	I	I	I	I
81	5351-04-2	L	Cat 1	I	I	I	I	I	I	I	I	I
82	68424-94-2	L	Cat 1	I	I	I	I	I	I	I	I	I
83	61789-40-0	L	Cat 1	I	I	I	I	I	I	I	I	I
84	61791-32-0	L	Cat 1	I	I	I	I	I	I	I	I	I
85	90583-18-9	L	Cat 1	I	I	I	I	I	I	I	I	I
86	68815-56-5	L	Cat 1	I	I	I	I	I	I	I	I	I
87	68891-38-3	L	Cat 1	I	I	I	I	I	I	I	I	I
88	118569-52-1	L	Cat 1	I	I	I	I	I	I	I	I	I
89	66455-15-0	L	Cat 1	I	I	I	I	I	I	I	I	I
90	110615-47-9	L	Cat 1	I	I	I	I	I	I	I	I	I
91	1760-24-3	L	Cat 1	I	I	I	I	I	I	I	I	I
92	17831-71-9	L	Cat 1	I	I	I	I	I	I	I	I	I
93	110-03-2	S	Cat 1	I	I	I	I	NI	NI	I	I	I
94	143-07-7	S	Cat 1	I	I	I	I	I	I	I	I	I
95	41253-21-8	S	Cat 1	I	I	I	I	I	I	I	I	I
96	86-87-3	S	Cat 1	I	NI	NI	I	I	NI	I	I	I
97	62-76-0	S	Cat 1	NI	I	NI	NI	NI	NI	NI	NI	NI
98	4430-25-5	S	Cat 1	NI	NI	NI	NI	NI	I	I	I	I
99	2634-33-5	S	Cat 1	I	I	I	I	I	I	I	I	I
100	60372-77-2	S	Cat 1	I	I	I	I	I	I	I	I	I
101	97404-02-9	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	I
102	27344-41-8	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
103	2820-37-3	S	Cat 1	I	I	I	I	I	I	I	I	I
104	171887-03-9	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
105	54424-29-2	S	Cat 1	I	I	I	I	I	I	I	I	I

TABLE 3.9. SkinEthic™ HCE TS final predictions for No Cat test chemicals

Chem. #	CAS RN	Phys. State	GHS Cat.	Predictions (50% viability cut-off)								
				CARDAM			CeeTox			L'Oréal		
				Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
1	111-25-1	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
2	135-98-8	L	No Cat	I	I	I	I	I	I	I	I	I
3	2370-63-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
4	25103-09-7	L	No Cat	I	I	I	I	I	I	I	I	I
5	3446-89-7	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
6	629-19-6	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
7	6940-78-9	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
8	111-83-1	L	No Cat	I	I	I	I	I	I	I	I	I
9	1647-16-1	L	No Cat	NI	I	NI	I	I	I	I	I	I
10	3970-62-5	L	No Cat	I	I	I	I	I	I	I	I	I
11	111-90-0	L	No Cat	I	I	I	NI	NI	NI	NI	NI	I
12	68123-18-2	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
13	455946-46-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
14	629-82-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
15	1680-31-5	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
16	868839-23-0	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
17	63705-03-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
18	109292-17-3	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
19	471277-16-4	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
20	71828-07-4	L	No Cat	I	I	I	I	I	.	I	I	I
21	342573-75-5	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
22	13826-35-2	L	No Cat	I	I	I	I	I	I	I	I	I
23	623-51-8	L	No Cat	I	I	I	I	I	I	I	I	I
24	106-91-2	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
25	51-03-6	L	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
26	60207-90-1	L	No Cat	I	I	I	I	I	I	I	I	I
28	118-82-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
29	3234-85-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
30	598-65-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
31	14075-53-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
32	84540-47-6	S	No Cat	NI	NI	NI	I	I	I	I	I	I
33	23920-15-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
34	3179-89-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
35	1603-02-7	S	No Cat	I	NI	I	I	NI	I	I	I	I
36	101-20-2	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
37	61788-85-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
38	103597-45-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
39	187393-00-6	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
40	75150-29-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
41	88122-99-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
42	66170-10-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
43	302776-68-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
44	231278-20-9	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
45	72956-09-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
46	68610-92-4	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
47	120-14-9	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
48	7631-90-5	S	No Cat	I	I	I	I	I	I	I	I	I
49	94-13-3	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
50	144550-36-7	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
51	33089-61-1	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
52	53112-28-0	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI
53	153719-23-4	S	No Cat	NI	NI	NI	NI	NI	NI	NI	NI	NI

TABLE 3.10. SkinEthic™ HCE TS final predictions for Cat 2B, Cat 2A and Cat 1 test chemicals

Chem. #	CAS RN	Phys. State	GHS Cat.	Predictions (50% viability cut-off)								
				CARDAM			CeeTox			L'Oréal		
				Test 1	Test 2	Test 3	Test 1	Test 2	Test 3	Test 1	Test 2	Test 3
54	542-76-7	L	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	I
55	78-84-2	L	Cat 2B	I	I	I	I	I	I	I	I	I
56	542-08-5	L	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
57	105-30-6	L	Cat 2B	I	I	I	I	I	I	I	I	I
58	29911-27-1	L	Cat 2B	I	I	I	I	I	I	I	I	I
59	609-14-3	L	Cat 2B	I	I	I	I	I	I	I	I	I
60	134-62-3	L	Cat 2B	I	I	I	I	I	I	I	I	I
61	83-72-7	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
62	104-36-9	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
63	62-23-7	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
64	96568-04-6	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
65	79-92-5	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
66	3926-62-3	S	Cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI
67	96-48-0	L	Cat 2A	I	I	I	I	I	I	I	I	I
68	96-41-3	L	Cat 2A	I	I	I	I	I	I	I	I	I
69	383178-66-3	L	Cat 2A	NI	I	NI	NI	NI	NI	NI	NI	NI
70	52793-97-2	L	Cat 2A	I	I	I	I	I	I	I	I	I
71	1569-01-3	L	Cat 2A	I	I	I	I	I	I	I	I	I
72	18472-51-0	L	Cat 2A	I	I	I	I	I	I	I	I	I
73	1119-62-6	S	Cat 2A	NI	NI	NI	NI	I	I	NI	NI	NI
74	16867-03-1	S	Cat 2A	NI	NI	NI	NI	NI	I	NI	NI	NI
75	532-32-1	S	Cat 2A	I	I	I	I	I	I	I	I	I
76	362525-73-3	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
77	189813-45-4	S	Cat 2A	NI	NI	NI	I	NI	NI	NI	NI	NI
78	76855-69-1	S	Cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI
79	6484-52-2	S	Cat 2A	NI	NI	NI	I	I	I	I	NI	I
80	2365-48-2	L	Cat 1	I	I	I	I	I	I	I	I	I
81	5351-04-2	L	Cat 1	I	I	I	I	I	I	I	I	I
82	68424-94-2	L	Cat 1	I	I	I	I	I	I	I	I	I
83	61789-40-0	L	Cat 1	I	I	I	I	I	I	I	I	I
84	61791-32-0	L	Cat 1	I	I	I	I	I	I	I	I	I
85	90583-18-9	L	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
86	68815-56-5	L	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
87	68891-38-3	L	Cat 1	NI	NI	NI	NI	NI	I	NI	NI	NI
88	118569-52-1	L	Cat 1	I	I	I	I	I	I	I	I	I
89	66455-15-0	L	Cat 1	I	I	I	I	I	I	I	I	I
90	110615-47-9	L	Cat 1	I	I	I	I	I	I	I	I	I
91	1760-24-3	L	Cat 1	I	I	I	I	I	I	I	I	I
92	17831-71-9	L	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
93	110-03-2	S	Cat 1	I	I	I	I	NI	NI	I	I	I
94	143-07-7	S	Cat 1	I	I	I	I	I	I	I	I	I
95	41253-21-8	S	Cat 1	I	I	I	I	I	I	I	I	I
96	86-87-3	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
97	62-76-0	S	Cat 1	NI	I	NI	NI	NI	NI	NI	NI	NI
98	4430-25-5	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
99	2634-33-5	S	Cat 1	I	I	I	I	I	I	I	I	I
100	60372-77-2	S	Cat 1	I	I	I	I	I	I	I	I	I
101	97404-02-9	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	I
102	27344-41-8	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
103	2820-37-3	S	Cat 1	I	I	I	I	I	I	I	I	I
104	171887-03-9	S	Cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI
105	54424-29-2	S	Cat 1	I	I	I	I	I	I	I	I	I

4. Discussion

4.1. Overall study conclusions

Considering the findings of the main validation of the EpiOcular™ EIT original liquids and solids protocols the VMG concluded that:

- EpiOcular™ EIT can be easily transferred among properly equipped and staffed laboratories, including those having no prior experience in similar test methods i.e., naïve laboratories. Experienced personnel can readily be trained in the test method, and the necessary equipment and supplies can be readily obtained. The EpiOcular™ EIT SOP is clearly written and the testing and analysis of results can be performed without difficulties.

- Based on the predefined study quality criterion, the main validation study was of high quality due to a near complete dataset with negligible re-testing performed (99.7% complete test sequences in total which is higher than the predefined acceptance cut-off of 85%).

- The 60% cut-off was considered to be better than the 50% cut-off because it resulted in a better sensitivity with very similar overall accuracy.

- The overall WLR based on concordance of classifications within each laboratory for the 60% cut-off was 95.2%, which was well above the acceptance criterion set by the VMG (≥ 85%).

- The BLR based on the concordance of final classifications obtained between the different participating laboratories for the 60% cut-off was 93.3%, also well above the acceptance criterion set by the VMG (≥ 80%).

- The EpiOcular™ EIT protocol for liquid chemicals using the 60% cut-off had sensitivity of 98.3%, specificity of 66.7% and overall accuracy of 81.9%, thus meeting all of the acceptance criteria defined by the VMG (≥ 90%, ≥ 60% and ≥ 75%, respectively).

- On the other hand, not all of the acceptance criteria were met by the EpiOcular™ EIT protocol for the solid chemicals. Sensitivity was < 90% even at the 60% cut-off and of the 6 chemicals that were under-predicted with the 60% cut-off based on the mode of all predictions, one was classified *in vivo* as Category 1.

- Analysis of the EIVS data for solid chemicals indicated scope for improvement through a balanced increase in sensitivity with decrease in specificity to attain a compromise of sensitivity ≥ 90% with specificity maintained ≥ 60%. Further optimisation was therefore recommended for the EpiOcular™ EIT protocol for solid chemicals.

Optimisation of the EpiOcular™ EIT solids protocol was performed at the method developer's laboratory (MatTek Corporation) in order to increase the sensitivity of the assay to the level requested by the VMG. This optimisation led to an increase of the exposure time from 90 min to 6 hours. MatTek Corporation was able to complete the optimisation of the solid chemicals protocol without delay, enabling follow-up validation within EIVS (post-optimisation validation), including analysis of the results by the VMG. The post-optimisation validation of the EpiOcular™ EIT optimised solid chemicals protocol took place in a single laboratory, at Beiersdorf (i.e., the lead laboratory for EpiOcular™ EIT in the original validation study).

- Based on the predefined study quality criterion, the post-optimisation validation study was of high quality due to a near complete dataset with negligible re-testing performed (98.3% complete test sequences in total, which is higher than the predefined acceptance cut-off of 85%).

-The WLR of the optimised EpiOcular™ EIT solids protocol was 96.6%, which was well above the acceptance criterion set by the VMG (≥ 85%).

-Given the previous good reproducibility of the EpiOcular™ EIT test method, and a similar (or even slightly better) WLR observed for the optimised solids protocol as compared to the original protocol, the VMG considered that it is unnecessary to perform further BLR evaluation of EpiOcular™ EIT. With the increased exposure time in the optimised solid chemicals protocol, a stronger separation between irritants and non-irritants in the viability scale was observed as compared to the original protocol, which is expected to improve the reproducibility of the test method. The fact that two SkinEthic™ HCE protocols with different exposure times were evaluated and showed equally high BLR provides additional evidence supporting the conclusion that further BLR assessment of the EpiOcular™ EIT optimised solid chemicals protocol is not necessary.

- The optimised EpiOcular™ EIT protocol for solid chemicals showed a sensitivity of 93.5%, specificity of 60.7% and overall accuracy of 78.0% using the 60% cut-off, thus meeting all of the acceptance criteria defined by the VMG (≥ 90%, ≥ 60% and ≥ 75%, respectively).

- The overall predictive capacity of EpiOcular™ EIT considering a combination of the data obtained with the liquid chemicals protocol with the data obtained with the optimised solid chemicals protocol, and a cut-off of 60%, consists of a sensitivity of 95.7%, a specificity of 63.0% (63.7% if chemical #37 is counted twice since it was tested both with the liquids protocol and with the optimised solids protocol) and an overall accuracy of 79.7% (79.8% if chemical #37 is counted twice), thus meeting all of the acceptance criteria defined by the VMG. Two out of 57 chemicals (2 solid Cat 2B chemicals) were under-predicted (false negatives) and 20 out of 54 chemicals (9 liquids and 11 solids) were over-predicted (false positives) based on the mode of all predictions.

Considering the findings of the validation of the SkinEthic™ HCE the VMG concluded that:

- SkinEthic™ HCE SE and LE can be easily transferred among properly equipped and staffed laboratories, including those having no prior experience in similar test methods i.e., (naïve laboratories). Experienced personnel can readily be trained in the test method, and the necessary equipment and supplies can be readily obtained. The SkinEthic™ HCE SOP is clearly written and the testing and analysis of results can be performed without difficulties.

- Based on the predefined study quality criterion, the validation study was of high quality due to a near complete datasets with negligible re-testing performed (100% and 99.7% complete test sequences in total for the SE and LE, respectively, which is higher than the predefined acceptance cut-off of 85%).

- The overall WLR based on concordance of classifications within each laboratory was 93.9% and 95.5% for the SE and LE, respectively, which was well above the acceptance criterion set by the VMG (≥ 85%).

- The BLR based on the concordance of final classifications obtained between the different participating laboratories was 92.3% for both the SE and LE, also well above the acceptance criterion set by the VMG (≥ 80%).

- The specificity of SkinEthic™ HCE was found to be 'definitely acceptable' according to the acceptance criterion defined by the VMG (≥ 60%), regardless of the protocol or strategy (SE: 88.5%; LE: 65.5%; test strategy: 77.1%). The sensitivity was on the other hand 'definitely unacceptable' (< 80%) according to the same acceptance criteria (SE: 42.7%; LE: 71.6%; test strategy: 54.5%). The overall accuracy was between the limits of 'definitely unacceptable' (< 65%) and 'definitely acceptable' (≥ 75%) (SE: 65.6%; LE: 68.6%; test strategy: 65.8%).

- Analysis of the data for the SkinEthic™ HCE indicated scope for improvement. Further optimisation has therefore been recommended for the SkinEthic™ HCE test method considering different protocols for liquid chemicals and solid chemicals, as with EpiOcular™ EIT.

4.2. VMG recommendations

The VMG acknowledges that due to the variability of individual animal responses within the same test in the *in vivo* Draize eye test (animal-to-animal within-test variability) there is an overall probability of about 12% that chemicals classified as UN GHS Cat 2 by the *in vivo* Draize eye test could be equally identified as UN GHS No Cat (Adriaens *et al.*, 2014). This probability would most likely significantly increase if the variability of the *in vivo* responses between repeated tests and between laboratories would also be considered (Weil & Scala, 1971; Marzulli and Ruggles, 1973; Cormier *et al.*, 1996). These estimates should therefore be acknowledged when considering the validity of alternative methods and testing strategies for serious eye damage/eye irritation.

Considering the above and based on the datasets acquired in this study the VMG considers the EpiOcular™ EIT original liquid chemicals protocol and the optimised solid chemicals protocol as scientifically valid (reproducible and accurate) to identify chemicals not requiring classification for serious eye damage/eye irritation according to the UN GHS classification system and thus recommends to proceed to peer-review. The VMG recommends that the 60% cut-off is used rather than the 50% cut-off because (i) for the liquid chemicals protocol the 60% cut-off resulted in a better sensitivity, with very similar overall accuracy, and generated no false negatives based on the mode of all predictions as compared to the 50% cut-off, which generated one false negative for a Category 2B chemical, and (ii) for the optimised solids protocol the 60% cut-off met all of the acceptance criteria defined by the VMG and resulted in better sensitivity and overall accuracy than the 50% cut-off, which failed to meet the 'definitely acceptable' criterion for sensitivity.

Considering the 60% cut-off, the EpiOcular™ EIT has an overall accuracy of 80% (82% based on 53 liquid chemicals and 78% based on 59 solid chemicals), sensitivity of 96% (98% based on 26 liquid chemicals and 94% based on 31 solid chemicals), false negative rate of 4% (2% based on 26 liquid chemicals and 6% based on 31 solid chemicals), specificity of 63% (65% based on 27 liquid chemicals and 61% based on 28 solid chemicals) and false

positive rate of 37% (35% based on 27 liquid chemicals and 39% based on 28 solid chemicals), when compared to *in vivo* rabbit eye test data classified according to the UN GHS classification system. The false positive rate obtained (i.e., *in vivo* UN GHS No Category chemicals producing a mean percent tissue viability ≤ 60%, which are therefore predicted by EpiOcular™ EIT as requiring classification and labelling) is not critical in the since all test chemicals that produce a tissue viability ≤ 60% will require further testing with other adequately valid *in vitro* test methods, or as a last option in rabbits, using a sequential testing strategy in a weight-of-evidence approach.

The EpiOcular™ EIT should be used within a testing strategy such as the Bottom-Up/Top-Down approach suggested by Scott *et al.* (2010) e.g., as an initial step in a Bottom-Up approach or as one of the last steps in a Top-Down approach to identify chemicals not requiring classification and labelling according to UN GHS. A chemical identified as not requiring classification and labelling for serious eye damage/eye irritation by EpiOcular™ EIT should not require any further testing in other test methods within the testing strategy. However, the EpiOcular™ EIT is not intended to differentiate between UN GHS Category 1 (serious eye damage) and UN GHS Category 2 (eye irritation). This differentiation will need to be addressed by another tier of the testing strategy (Scott *et al.*, 2010). A chemical that is identified as requiring classification for eye irritation/serious eye damage with EpiOcular™ EIT will thus require additional testing (*in vitro* and/or *in vivo*) to establish a definitive classification. The EpiOcular™ EIT is therefore not considered valid as a stand-alone replacement for the *in vivo* Draize rabbit eye test.

The validation study demonstrated that EpiOcular™ EIT is able to detect all types of ocular effects observed *in vivo* (i.e., corneal, iridal and conjunctival injuries). In this respect, it should be noted that effects on the iris are of lesser importance for classification of chemicals according to UN GHS, since iritis on its own rarely drives the UN GHS classification of chemicals *in vivo* (both Category 1 and Category 2) (1.8-3.1% of the chemicals). In fact, test chemical that cause classifiable effects to the iris also almost always cause classifiable corneal opacity (Adriaens *et al.*, 2014).

A wide range of chemical types, including polymers, NLPs (no-longer polymers), liquids, solids, waxes, viscous materials, gel-like chemicals, coloured chemicals, non-coloured chemicals, oxidisers, reducers, inert chemicals, cosmetics ingredients (including dyes, preservatives and UV filters), industrial chemicals, pesticides, chemical intermediates, pharmaceuticals, a wide range of chemical classes (as identified by OECD Toolbox analysis), a wide range of molecular weights, a wide range of chemical structures, etc., have been included in the EIVS. Based on this comprehensive chemical set, no clear limitations of applicability could be identified. In particular, neither false positive nor false negative results could be associated to a particular chemical type. The VMG therefore recommends that EpiOcular™ EIT is considered applicable to the testing of all types of substances and mixtures, until proven contrary. However, more detailed analysis of the data have revealed that liquid test chemicals that are positive in EpiOcular™ EIT (i.e., that produce a tissue viability ≤ 60%) and have LogP > 2.5 may correspond to false positive predictions. For such test chemicals, additional testing should be considered using another *in vitro* test method able to identify chemicals that do not require classification for eye irritation or serious eye damage (UN GHS No Category) rather than using an *in vitro* test method able to identify chemicals inducing serious eye damage (UN GHS Category 1) as is normally suggested in a Bottom-Up approach (Scott *et al.*, 2010).

Chemical #37 was tested as a liquid in the EpiOcular™ EIT during validation of the original liquid and solid chemicals protocols (main part of EIVS) and as a solid during the validation of the EpiOcular™ EIT optimised solid chemicals protocol, based on independent decisions of the participating laboratories, considering the instructions provided in the validated SOP. Given this, the VMG recommends that section B.5.6 of the EpiOcular™ EIT SOP is amended to further clarify the procedure for identifying the protocol to be used for test chemicals with unclear physical state. It is recommended that all viscous, waxy and gel-like chemicals are placed in a water bath for 15 minutes at 37°C before deciding if they should be tested with the liquids or the solids protocol. Moreover, the test chemical should not be brought to room temperature before testing and should be applied directly from the water bath.

Based on the data acquired in EIVS, the VMG concluded that the test and run acceptance criteria for EpiOcular™ EIT ($1.0 < OD_{NC} < 2.3$; PC mean viability < 50%; Viability range between tissue replicates < 20%) and SkinEthic™ HCE ($0.7 \leq OD_{NC} \leq 1.5$; PC mean viability ≤ 50%; SD between tissue replicates ≤ 18%) are adequate. It should however be noted that, as indicated in the last version of the EpiOcular™ EIT SOP, recent experience has shown that under certain circumstances like extended shipping time (e.g., > 4 days to Japan) the negative control OD can be < 1.0 in particular with the test protocol for solids. In such cases a lower acceptance limit for the negative control OD of > 0.8 may be more appropriate. Moreover, the VMG recognises that, based on the EIVS data, a stricter acceptance criterion for the positive control of the SkinEthic™ HCE SE protocol, like PC mean viability ≤ 30%, would probably have been more appropriate than the 50% cut-off used in EIVS. The VMG therefore recommends that any future similar or modified RhCE/MTT-based test method aiming at identifying chemicals not requiring classification for serious eye damage/eye irritation (using tissues modelling the corneal epithelium), including an optimised SkinEthic™ HCE test method, use positive control(s) and associated acceptance criteria that are strict enough to allow easy detection of inappropriate conduct of the assay. Such a strict combination of positive control and associated acceptance criterion were already used with the liquid and solid chemicals protocols of EpiOcular™ EIT and with the LE protocol of SkinEthic™ HCE in EIVS. This allowed for early detection and correction of an issue in the conduct of the SkinEthic™ HCE LE assay at the CeeTox laboratory, thus demonstrating the high value of having such strict criteria for the positive control in place.

The core VMG does not recommend the use of EPRA to orient chemicals to the LE (non-reactive) or SE (reactive) protocols as proposed in the SkinEthic™ HCE TS. The LE and the SE protocols alone are also not considered suitable to identify chemicals not requiring classification for serious eye damage/eye irritation. The VMG therefore recommends optimisation of the SkinEthic™ HCE test method considering different protocols for liquid chemicals and solid chemicals. Nevertheless, the VMG acknowledges the high reproducibility of the SkinEthic™ HCE regardless of the protocol used (SE or LE).

Based on the highly reproducible data acquired with both EpiOcular™ EIT and SkinEthic™ HCE in EIVS using multiple exposure times and post-treatment incubation periods, it is reasonable to conclude that the reproducibility of this type of test methods is not affected by varying the exposure or the post-treatment incubation times.

An independent statistical analysis of the data acquired in EIVS with SkinEthic™ HCE SE and LE protocols using three replicate tissues per test demonstrated that reducing the number of replicates from 3 to 2 will have almost no impact on the classification decision for a given test. The probability is less than 1% that such a reduction would change the

classification for a given test. Based on this and on similar findings obtained with EpiOcular™ EIT, the VMG concludes that the use of two tissue replicates in any similar or modified RhCE/MTT-based test method aiming at identifying chemicals not requiring classification for serious eye damage/eye irritation (using tissues modelling the corneal epithelium) is statistically and scientifically justified.

The VMG considers that the current endpoint detection system using standard absorbance (OD) measurement with a spectrophotometer is appropriate to assess direct MTT-reducers and colour interfering test chemicals, when the observed interference with the measurement of MTT formazan is not too strong (i.e., the ODs of the tissue extracts obtained with the test chemical without any correction for direct MTT reduction and/or colour interference are within the linear range of the spectrophotometer) (e.g., below 140% of the negative control) or when the uncorrected percent viability obtained with the test chemical is ≤ 60%, thus already identifying the test chemical as requiring classification and labelling. Nevertheless, results for test chemicals producing non-specific MTT reduction and/or colour interference ≥ 60% of the negative control should be taken with caution. Standard absorbance (OD) can however not be measured when the interference with the measurement of MTT formazan is too strong (i.e., leading to uncorrected ODs falling outside of the linear range of the spectrophotometer) and the uncorrected percent viability obtained with the test chemical is > 60%. For coloured test chemicals or test chemicals that become coloured in contact with water or isopropanol that interfere too strongly with the MTT-reduction assay an alternative endpoint detection system like HPLC/UPLC-photometry may be required. This is because the HPLC/UPLC system allows for the separation of the MTT formazan from the chemical before its quantification.

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Annex 1

Statistical analysis on the EpiOcular™ EIT main validation study

TNO report

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Eye Irritation Validation Study on Human Tissue Models: Statistical Analysis and Reporting on the EpiOcular™ EIT

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Summary

The goal of the Eye Irritation Validation Study (EIVS) was to assess the relevance (predictive capacity) and reliability (reproducibility within and between laboratories) of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT, by testing a statistically significant number of coded test chemicals (substances and mixtures), supported by complete and quality assured in vivo Draize eye irritation data for comparative evaluation of results. In this report a complete, objective and transparent analysis of within-laboratory and between-laboratory reproducibility as well as predictive capacity based on the submitted test data for EpiOcular™ EIT is presented.

Based on the results for the fraction of complete test sequences (99.7% in total), the within-laboratory variability (93.6% and 95.2% concordance in total, using a 50% cut-off and a 60% cut-off value, respectively) and the between laboratory variability (91.3% and 93.2% concordance in total, using a 50% cut-off and a 60% cut-off value, respectively), the validation of the EpiOcular™ EIT was based on high-quality data. The acceptance criteria for these three characteristics were easily fulfilled.

One chemical (chemical 33; *2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11*) for Beiersdorf was excluded from the statistical analysis, since it was not compatible with the test method.

The EpiOcular™ EIT test method is highly reproducible. The within-laboratory reproducibility (WLR) and between-laboratory reproducibility (BLR) was well above the acceptance criteria set by the VMG (i.e. WLR ≥ 85% and BLR ≥ 80%).

Using a 50% cut-off value, meaning that a chemical for which the mean viabililty was below 50% is classified as irritant, the accuracy (0.777) and the specificity (0.740) are ‘definitely acceptable’ according to the acceptance criteria as defined by the VMG, whereas some further evaluation is recommended for the sensitivity (0.814). It is seen that the test method fulfils the acceptance criteria if only liquids are taken into account (accuracy=0.822; sensitivity=0.962; specificity=0.687). On the other hand, not all of the acceptance criteria were met by the protocol for the solid chemicals (accuracy=0.730; sensitivity=0.667; specificity=0.797).

Using a 60% cut-off value, meaning that a chemical for which the mean viabililty was below 60% is classified as irritant, the accuracy (0.788) and the specificity (0.699) are ‘definitely acceptable’ according to the acceptance criteria as defined by the VMG, whereas some further evaluation is recommended for the sensitivity (0.876). It is seen that the test method fulfils the acceptance criteria if only liquids are taken into account (accuracy=0.816; sensitivity=0.983; specificity=0.654). On the other hand, not all of the acceptance criteria were met by the protocol for the solid chemicals (accuracy=0.759; sensitivity=0.769; specificity=0.748).

Contents

1 Introduction

The goal of the Eye Irritation Validation Study (EIVS) was to assess the relevance (predictive capacity) and reliability (reproducibility within and between laboratories) of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT, by testing a statistically significant number of coded test chemicals (substances and mixtures), supported by complete and quality assured in vivo Draize eye irritation data for comparative evaluation of results.

Specifically, EIVS assessed the validity of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT as stand-alone (independent) test methods to reliably discriminate chemicals not classified as eye irritant ("non-irritants") from all classes of eye irritant chemicals (in the framework of a Bottom-Up/Top-Down test strategy, Scott L. et al., 2010), defined according to the United Nations Globally Harmonized System (GHS) of Classification and Labelling of Chemicals (UN GHS: No Category versus Category 1/Category 2A/Category 2B; UN, 2007) and as implemented in the European Commission Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (EU CLP: No Category versus Category 1/Category 2).

The SkinEthic™ HCE test strategy and the EpiOcular™ EIT were developed for maximum sensitivity (ability to detect positives, with low rate of false negatives) rather than for optimal overall accuracy with balanced sensitivity and specificity (ability to detect negatives, with low rate of false positives). Sensitivity had therefore a bigger weight than specificity and overall accuracy in their development. However, it was also sought to achieve a sufficiently high specificity and overall accuracy, in order to allow identification of the highest number of chemicals not classified as irritant to the eye. By achieving satisfactory specificity, the SkinEthic™ HCE test strategy and the EpiOcular™ EIT would represent stand-alone (independent) test methods for the identification of "non-irritants". Importantly, the test methods were not intended to differentiate between UN GHS/EU CLP Category 1 (irreversible effects) and UN GHS/EU CLP Category 2 (reversible effects). As proposed by the ECVAM workshop of February 2005, this differentiation would be left to another tier of the Bottom-Up/Top-Down test strategy (Scott L. et al., 2010).

The EIVS was undertaken in accordance with the principles and criteria documented in the OECD Guidance Document on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment (No. 34, OECD, 2005) and according to the Modular Approach to validation (Hartung T. et al., 2004).

The objective of this report is to summarize and present a complete, objective and transparent analysis of within-laboratory and between-laboratory reproducibility as well as predictive capacity based on the submitted test data for EpiOcular™ EIT. The results for the SkinEthic™ HCE test strategy will be reported in a separate report.

2 Material and Methods

2.1 Study Design

The EpiOcular™ EIT was tested in three laboratories.

Lead Laboratory	Beiersdorf (Germany)
Additional Laboratory 1	Harlan (UK)
Additional Laboratory 2	IIVS (USA)

Each laboratory tested the same 106 chemicals in three runs each, in two tissues. These chemicals were coded and distributed by TNO (The Netherlands). The chemicals were tested blinded. Contact between the laboratories during the testing was not allowed in order to safeguard the blinding. More details regarding the study design can be found in the project plan (appendix VIII).

The chemicals that were used in the validation study are listed in Table 2.1.1.

Table 2.1.1 List of tested chemicals in EIVS validation study

Chemical	Substance name	State	CAS #	GHS Class
1	1-bromohexane	Liquid	111-25-1	no cat
2	1-methylpropyl benzene	Liquid	135-98-8	no cat
3	2-ethoxyethyl methacrylate	Liquid	2370-63-0	no cat
4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	Liquid	25103-09-7	no cat
5	4-(methylthio)-benzaldehyde	Liquid	3446-89-7	no cat
6	dipropyl disulphide	Liquid	629-19-6	no cat
7	1-bromo-4-chlorobutane	Liquid	6940-78-9	no cat
8	1-bromo-octane	Liquid	111-83-1	no cat
9	1,9-decadiene	Liquid	1647-16-1	no cat
10	2,2-dimethyl-3-pentanol	Liquid	3970-62-5	no cat
11	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	Liquid	111-90-0	no cat
12	bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated (53-57% aqueous emulsion)	Liquid	68123-18-2	no cat
13	bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated (56% aqueous emulsion)	Liquid	455946-46-0	no cat
14	dioctyl ether INCI name: DICAPRYLYL ETHER	Liquid	629-82-3	no cat
15	dioctyl carbonate INCI name: DICAPRYLYL CARBONATE	Liquid	1680-31-5	no cat
16	2-propylheptyl octanoate INCI name: PROPYLHEPTYL CAPRYLATE	Liquid	868839-23-0	no cat
17	polyglyceryl-3 diisooctadecanoate INCI name: POLYGLYCERYL-3 DIISOSTEARATE	Liquid	63705-03-3	no cat
18	steareth-10 allyl ether/acrylates copolymer (30% aqueous) INCI name: STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	Liquid	109292-17-3	no cat
19	dimethyl siloxane, mono dimethylvinylsiloxy- and mono trimethoxysiloxy-terminated (95%)	Liquid	471277-16-4	no cat
20	ricinoleic acid tin salt	Liquid	71828-07-4	no cat
21	1-ethyl-3-methylimidazolium ethylsulphate	Liquid	342573-75-5	no cat
22	3-phenoxybenzyl alcohol	Liquid	13826-35-2	no cat
23	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE	Liquid	623-51-8	no cat
24	glycidyl methacrylate	Liquid	106-91-2	no cat
25	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE	Liquid	51-03-6	no cat
26	propiconazole	Liquid	60207-90-1	no cat
27[1]	2-ethylhexylthioglycolate	Liquid	7659-86-1	no cat
28	4,4'-methylene bis-(2,6-di-tert-butylphenol)	Solid	118-82-1	no cat
29	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE	Solid	3234-85-3	no cat

Chemical	Substance name	State	CAS #	GHS Class
30	1,1-dimethylguanidine sulphate	Solid	598-65-2	no cat
31	potassium tetrafluoroborate	Solid	14075-53-7	no cat
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	Solid	84540-47-6	no cat
33	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11	Solid	23920-15-2	no cat
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	Solid	3179-89-3	no cat
35	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	Solid	1603-02-7	no cat
36	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN	Solid	101-20-2	no cat
37[3]	polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL	Solid	61788-85-0	no cat
38	2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYLBUTYLPHENOL	Solid	103597-45-1	no cat
39	2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol] INCI name: BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE	Solid	187393-00-6	no cat
40	acrylamidopropyltrimonium chloride/acrylamide copolymer	Solid	75150-29-7	no cat
41	tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate INCI name: ETHYLHEXYL TRIAZONE	Solid	88122-99-0	no cat
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	Solid	66170-10-3	no cat
43	hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE	Solid	302776-68-7	no cat
44	[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine	Solid	231278-20-9	no cat
45	1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol	Solid	72956-09-3	no cat
46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	Solid	68610-92-4	no cat
47	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE	Solid	120-14-9	no cat
48	sodium hydrogensulphite INCI name: SODIUM BISULFITE	Solid	7631-90-5	no cat
49	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN	Solid	94-13-3	no cat
50	iodosulfuron-methyl-sodium	Solid	144550-36-7	no cat
51	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz	Solid	33089-61-1	no cat
52	2-anilino-4,6-dimethylpyrimidine common name: Pyrimethanil	Solid	53112-28-0	no cat
53	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam	Solid	153719-23-4	no cat
54	3-chloropropionitrile	Liquid	542-76-7	cat 2B
55	2-methylpropanal INCI name: 2-METHYLPROPANAL	Liquid	78-84-2	cat 2B
56	isopropyl acetoacetate	Liquid	542-08-5	cat 2B
57	2-methyl-1-pentanol	Liquid	105-30-6	cat 2B
58	1-(1-methyl-2-propoxyethoxy)propan-2-ol INCI name: PPG-2 PROPYL ETHER	Liquid	29911-27-1	cat 2B
59	ethyl-2-methyl acetoacetate	Liquid	609-14-3	cat 2B
60	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET	Liquid	134-62-3	cat 2B
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	Solid	83-72-7	cat 2B
62	1,4-dibutoxy benzene	Solid	104-36-9	cat 2B
63	4-nitrobenzoic acid	Solid	62-23-7	cat 2B
64	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate	Solid	96568-04-6	cat 2B
65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	Solid	79-92-5	cat 2B
66	sodium chloroacetate	Solid	3926-62-3	cat 2B
67	gamma-butyrolactone INCI name: BUTYROLACTONE	Liquid	96-48-0	cat 2A
68	cyclopentanol	Liquid	96-41-3	cat 2A (ICCVAM: cat 2B)
69	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	Liquid	383178-66-3	cat 2A (ICCVAM: cat 2B)

Chemical	Substance name	State	CAS #	GHS Class
70	methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-oxobicyclo[2.2.1]hept-2-ylidene)methyl]anilinium sulphate (30% aqueous) INCI name: CAMPHOR BENZALKONIUM METHOSULFATE	Liquid	52793-97-2	cat 2A
71	1-propoxy-2-propanol INCI name: PROPYLENE GLYCOL PROPYL ETHER	Liquid	1569-01-3	cat 2A (ICCVAM: cat 2B)
72	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE	Liquid	18472-51-0	cat 2A (ICCVAM: cat 2B)
73	3,3'-dithiopropionic acid	Solid	1119-62-6	cat 2A (ICCVAM: cat 2B)
74	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	Solid	16867-03-1	cat 2A
75	sodium benzoate INCI name: SODIUM BENZOATE	Solid	532-32-1	cat 2A
76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	Solid	362525-73-3	cat 2A
77	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate	Solid	189813-45-4	cat 2A
78	(2R,3R)-3-((R)-1-(tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate	Solid	76855-69-1	cat 2A
79	ammonium nitrate INCI name: AMMONIUM NITRATE	Solid	6484-52-2	cat 2A (ICCVAM: cat 2B)
80	methylthioglycolate INCI name: METHYL THIOGLYCOLATE	Liquid	2365-48-2	cat 1
81	3-diethylaminopropionitrile	Liquid	02/04/5351	cat 1
82	coco alkyl dimethyl betaine (~ 30% aqueous) INCI name: COCO-BETAINE	Liquid	68424-94-2	cat 1
83	coco amidopropyl betaine (~ 30% aqueous) INCI name: COCAMIDOPROPYL BETAINE	Liquid	61789-40-0	cat 1
84	sodium coco amphoacetate (~ 30% aqueous)	Liquid	61791-32-0	cat 1
85	triethanol ammonium alkyl sulphate (~ 40% aqueous) INCI name: TEA-C12-14 ALKYL SULFATE	Liquid	90583-18-9	cat 1
86	di-sodium alkyl ether sulfosuccinate (~ 30% aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE	Liquid	68815-56-5	cat 1
87	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE	Liquid	68891-38-3	cat 1
88	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)	Liquid	118569-52-1	cat 1
89	ethoxylated (5 EO) alkyl (C10-14) alcohol	Liquid	66455-15-0	cat 1
90	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	Liquid	110615-47-9	cat 1
91	(ethylenediaminepropyl)trimethoxysilane	Liquid	1760-24-3	cat 1
92	tetraethylene glycol diacrylate	Liquid	17831-71-9	cat 1
93	2,5-dimethyl-2,5-hexanediol	Solid	110-03-2	cat 1
94	dodecanoic acid INCI name: LAURIC ACID	Solid	143-07-7	cat 1
95	1,2,4-triazole sodium salt	Solid	41253-21-8	cat 1
96	1-naphthalene acetic acid	Solid	86-87-3	cat 1
97	sodium oxalate INCI name: SODIUM OXALATE	Solid	62-76-0	cat 1
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	Solid	4430-25-5	cat 1
99	1,2-benzisothiazol-3(2H)-one INCI name: BENZISOTHIAZOLINONE	Solid	2634-33-5	cat 1
100	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	Solid	60372-77-2	cat 1
101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31	Solid	97404-02-9	cat 1
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	Solid	27344-41-8	cat 1
103	3,4-dimethyl-1H-pyrazole	Solid	2820-37-3	cat 1
104	N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide	Solid	171887-03-9	cat 1
105	1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate	Solid	54424-29-2	cat 1
106[2]	4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methylbenzenamine hydrochloride INCI name: BASIC VIOLET 2	Solid	3248-91-7	cat 1
107[2]	xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxycarbonyl)phenyl]-tetrafluoroborate	Solid	134429-57-5	cat 1

[1] sent to all participating laboratories for testing but excluded at a very early stage of the study on request of one of the participating laboratories because it was identified as a very strong MTT reducer

[2] extra chemicals not for statistics but for a later purpose of evaluation using an HPLC based detection system.

[3] Chemical 37 (polyethylene glycol (PEG-40) hydrogenated castor oil, INCI name: PEG-40 HYDROGENATED CASTOR OIL) was originally selected by the EIVS VMG as being a solid. However, all three laboratories participating in the validation of the EpiOcular™ EIT independently considered the chemical as being liquid due to its low melting point and tested it using the liquid protocol of EpiOcular™ EIT (see statistical report on EpiOcular™ EIT). Hence, chemical 37 was reclassified as liquid by the VMG and was statistically analysed as such.

Chemical 106 (*4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methylbenzenamine hydrochloride INCI name: BASIC VIOLET 2*) and chemical 107 (*xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxycarbonyl)phenyl]-tetrafluoroborate*) were sent to all participating laboratories for testing but excluded at a very early stage of the study on request of one of the participating laboratories because it was identified as a very strong MTT reducer. These two chemicals are excluded from any statistical analysis. Hence, the statistical analysis is based on 104 chemicals.

In Table 2.1.2, the decoding of the chemicals is given.

Table 2.1.2 Decoding of chemicals

Chemical	Substance name	BDF	Harlan	IIVS
1	1-bromohexane	B56	H47	V95
2	1-methylpropyl benzene	B63	H26	V92
3	2-ethoxyethyl methacrylate	B3	H9	V29
4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	B16	H6	V20
5	4-(methylthio)-benzaldehyde	B11	H48	V96
6	dipropyl disulphide	B9	H67	V90
7	1-bromo-4-chlorobutane	B10	H21	V81
8	1-bromo-octane	B25	H35	V48
9	1,9-decadiene	B6	H68	V38
10	2,2-dimethyl-3-pentanol	B24	H25	V40
11	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	B39	H42	V49
12	bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated (53-57% aqueous emulsion)	B57	H73	V94
13	bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated (56% aqueous emulsion)	B48	H66	V61
14	dioctyl ether INCI name: DICAPRYLYL ETHER	B61	H52	V33
15	dioctyl carbonate INCI name: DICAPRYLYL CARBONATE	B85	H28	V55
16	2-propylheptyl octanoate INCI name: PROPYLHEPTYL CAPRYLATE	B18	H59	V10
17	polyglyceryl-3 diisooctadecanoate INCI name: POLYGLYCERYL-3 DIISOSTEARATE	B84	H87	V75
18	steareth-10 allyl ether/acrylates copolymer (30% aqueous) INCI name: STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	B35	H30	V41
19	dimethyl siloxane, mono dimethylvinylsiloxy- and mono trimethoxysiloxy-terminated (95%)	B106	H115	V114
20	ricinoleic acid tin salt	B20	H46	V8
21	1-ethyl-3-methylimidazolium ethylsulphate	B38	H24	V103
22	3-phenoxybenzyl alcohol	B54	H98	V47
23	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE	B129	H128	V127
24	glycidyl methacrylate	B133	H117	V126
25	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE	B191	H186	V150

Chemical	Substance name	BDF	Harlan	IIVS
26	propiconazole	B155	H159	V170
27	2-ethylhexylthioglycolate	B60	H71	V11
28	4,4'-methylene bis-(2,6-di-tert-butylphenol)	B43	H86	V30
29	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE	B128	H116	V136
30	1,1-dimethylguanidine sulphate	B124	H133	V130
31	potassium tetrafluoroborate	B135	H134	V140
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	B101	H76	V80
33	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11	B87	H20	V58
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	B80	H54	V37
35	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	B71	H10	V66
36	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN	B46	H14	V72
37	polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL	B113	H107	V115
38	2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYLBUTYLPHENOL	B92	H88	V59
39	2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol] INCI name: BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE	B79	H53	V1
40	acrylamidopropyltrimonium chloride/acrylamide copolymer	B26	H58	V54
41	tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate INCI name: ETHYLHEXYL TRIAZONE	B115	H111	V109
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	B109	H105	V111
43	hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE	B110	H106	V107
44	[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine	B107	H109	V105
45	1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol	B112	H112	V108
46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	B108	H108	V113
47	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE	B105	H110	V106
48	sodium hydrogensulphite INCI name: SODIUM BISULFITE	B136	H131	V123
49	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN	B178	H155	V197
50	iodosulfuron-methyl-sodium	B168	H167	V146
51	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz	B169	H161	V156
52	2-anilino-4,6-dimethylpyrimidine common name: Pyrimethanil	B145	H188	V166
53	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam	B177	H176	V164
54	3-chloropropionitrile	B58	H79	V104
55	2-methylpropanal INCI name: 2-METHYLPROPANAL	B121	H130	V133
56	isopropyl acetoacetate	B118	H124	V134
57	2-methyl-1-pentanol	B30	H34	V50
58	1-(1-methyl-2-propoxyethoxy)propan-2-ol INCI name: PPG-2 PROPYL ETHER	B134	H136	V128
59	ethyl-2-methyl acetoacetate	B130	H138	V132
60	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET	B125	H126	V131
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	B59	H4	V69
62	1,4-dibutoxy benzene	B122	H135	V139
63	4-nitrobenzoic acid	B132	H123	V137
64	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate	B34	H33	V101
65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	B117	H121	V117
66	sodium chloroacetate	B119	H139	V129
67	gamma-butyrolactone INCI name: BUTYROLACTONE	B22	H96	V15
68	cyclopentanol	B78	H22	V52
69	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	B8	H56	V36
70	methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-oxobicyclo[2.2.1]hept-2-ylidene)methyl]anilinium sulphate (30% aqueous) INCI name: CAMPHOR	B138	H127	V118

Chemical	Substance name	BDF	Harlan	IIVS
	BENZALKONIUM METHOSULFATE			
71	1-propoxy-2-propanol INCI name: PROPYLENE GLYCOL PROPYL ETHER	B28	H104	V3
72	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE	B137	H122	V120
73	3,3'-dithiopropionic acid	B15	H3	V27
74	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	B99	H39	V39
75	sodium benzoate INCI name: SODIUM BENZOATE	B23	H85	V28
76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	B81	H74	V87
77	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate	B2	H44	V34
78	(2R,3R)-3-((R)-1-(tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate	B40	H19	V85
79	ammonium nitrate INCI name: AMMONIUM NITRATE	B131	H125	V119
80	methylthioglycolate INCI name: METHYL THIOGLYCOLATE	B45	H78	V93
81	3-diethylaminopropionitrile	B27	H15	V2
82	coco alkyl dimethyl betaine (~ 30% aqueous) INCI name: COCO-BETAINE	B67	H102	V71
83	coco amidopropyl betaine (~ 30% aqueous) INCI name: COCAMIDOPROPYL BETAINE	B53	H65	V88
84	sodium coco amphoacetate (~ 30% aqueous)	B100	H82	V26
85	triethanol ammonium alkyl sulphate (~ 40% aqueous) INCI name: TEA-C12-14 ALKYL SULFATE	B7	H77	V42
86	di-sodium alkyl ether sulfosuccinate (~ 30% aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE	B31	H103	V6
87	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE	B64	H27	V19
88	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)	B17	H89	V25
89	ethoxylated (5 EO) alkyl (C10-14) alcohol	B73	H16	V98
90	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	B14	H70	V83
91	(ethylenediaminepropyl)trimethoxysilane	B44	H72	V84
92	tetraethylene glycol diacrylate	B174	H175	V191
93	2,5-dimethyl-2,5-hexanediol	B21	H41	V16
94	dodecanoic acid INCI name: LAURIC ACID	B104	H90	V32
95	1,2,4-triazole sodium salt	B13	H60	V5
96	1-naphthalene acetic acid	B52	H95	V53
97	sodium oxalate INCI name: SODIUM OXALATE	B70	H62	V22
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	B102	H83	V9
99	1,2-benzisothiazol-3(2H)-one INCI name: BENZISOTHIAZOLINONE	B29	H92	V18
100	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	B199	H163	V154
101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31	B37	H51	V65
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	B47	H50	V68
103	3,4-dimethyl-1H-pyrazole	B76	H91	V56
104	N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide	B88	H12	V45
105	1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate	B33	H61	V86
106	4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methylbenzenamine hydrochloride INCI name: BASIC VIOLET 2	B74	H23	V13
107	xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxycarbonyl)phenyl]-tetrafluoroborate	B55	H36	V14

2.2 Archiving

A data file in a flat file format will be provided which includes all quality checked test-results from all three laboratories for possible later use. A readme-file will be provided which explains each variable in the data set.

The SAS code which was used for statistical analysis is provided in Appendix II.

2.3 Receipt of data

The study results were received by the statistician from the Trial coordinator. The receipt of data was reported in an excel file. The report on the receipt of data can be found in Appendix III.

2.4 Acceptance criteria

2.4.1 Test acceptance criteria

The test acceptance criteria are described in detail in the EpiOcular™ SOP..

In short, the following test acceptance criteria are applied.

Subject	Criteria	Remark
NC response	1.0 < OD < 2.3	
PC mean viability	< 50%	
Tissue variability	Range < 20%	Between replicates, for chemicals, PC and NC

2.4.2 Study acceptance criteria

The study acceptance criteria are described in detail in the Guidance on eye irritation validation study (EIVS) conduct for the reconstructed human tissue (RhT) assays and performance criteria to assess the scientific validity of SkinEthic™ HCE and EpiOcular™ EIT and its addendum (see appendix VII and VIII).

In short, the following study acceptance criteria are applied.

Subject	Criteria	Remark
Complete test sequences	>= 85%	In each laboratory
Within laboratory variability (concordance of classification)	>= 85%	Using test chemicals for which at least two qualified tests are available
Between laboratory variability (concordance of classification)	>= 80%	Using test chemicals for which at least one qualified test per laboratory is available
Sensitivity	>=90%	Based on all qualified tests
Specificity	>=60%	Based on all qualified tests
Accuracy	>=75%	Based on all qualified tests

A test sequence is considered complete if it contains three qualified tests. Otherwise, the test sequence is considered as incomplete.

If the test method fulfils the above stated acceptance criteria, the performance of the method is considered to be ‘definitely acceptable’. For sensitivity, specificity and accuracy, some additional criteria are defined to be able to distinguish between a definitely unacceptable performance and a performance which might need some further evaluation. These criteria are defined as follows:

	False Negatives[a] (%)	False Positives[b] (%)	Overall misclassifications[c] (%)
"Definitely acceptable" rates	≤ 10	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	40 < FP ≤ 50	25 < OM ≤ 35
"Definitely unacceptable" rates	> 20	> 50	> 35

[a] equal to (1-Sensitivity), [b] equal to (1-Specificity), [c] equal to (1-Overall accuracy)

2.5 Statistical methods

The statistical analyses are performed according to the Statistical Analysis and Reporting Plan for the ECVAM/COLIPA Eye Irritation Validation Study on Reconstructed Human Tissue Models (final version May 3, 2011). The statistical analysis is based on the performance criteria document Guidance on eye irritation validation study (EIVS) conduct for the reconstructed human tissue (RhT) assays and performance criteria to assess the scientific validity of SkinEthic™ HCE and EpiOcular™ EIT and its addendum (see appendix VII and VIII).

2.5.1 Quality checks

Before starting the statistical analyses, the following quality checks were done:

- Is the information complete?
- Are the test acceptance criteria always met?
- Are there any deviations from the study plan?
- Are there any remarks and special observations as given in the reporting sheet by the study personal?

Some chemicals might be incompatible with the test method. Evaluation of compatibility was evaluated for colouring or MTT-reducing chemicals by the following criteria:

RULE 1 – IF the mean of %NSC or %NSMTT of all qualified tests obtained for a chemical in one laboratory is less than or equal to (≤) 50%, THEN this chemical is considered to be compatible with the test method. The chemical should be included in the overview tables, and included in all statistical calculations of reproducibility and predictive capacity.

RULE 2 – IF the mean of %NSC or %NSMTT of all qualified tests obtained for a chemical in one laboratory is greater than (>) 50% AND their classification (I or NI) remains the same upon correction, THEN this chemical is considered to be compatible with the test method. The chemical should be included in the overview tables, and included in all statistical calculations of reproducibility and predictive capacity.

RULE 3 – IF the mean of %NSC or %NSMTT of all qualified tests obtained for a chemical in one laboratory is greater than (>) 50% AND the classification of at least one of the qualified tests changes upon correction, THEN this chemical is considered to be incompatible with the test method. The chemical should be included in the overview tables, but excluded from all statistical calculations of reproducibility and predictive capacity.

2.5.2 Descriptive statistics

The descriptive statistics contain summary tables on the chemical selection set (e.g. cross tables with solids/liquids), the number of qualified tests, the number of complete test sequences, *etcetera*.

2.5.3 Within Laboratory Reproducibility (WLR)

For each laboratory, concordance of classifications and overall Standard Deviation were calculated based on qualified tests from test chemicals for which at least two qualified tests are available. For each laboratory, concordance of classifications and overall Standard Deviation were also calculated based on all tests performed, including both qualified and non-qualified tests. The WLR is calculated using a 50% and a 60% cut-off.

2.5.4 Between laboratory Reproducibility (BLR)

For the calculation of BLR the final classification for each test chemical in each participating laboratory should be obtained by using the arithmetic mean value of viability over the different qualified tests performed. Concordance of classifications between laboratories and overall Standard Deviation of the study were calculated based only on qualified tests from test chemicals for which at least one qualified test per laboratory is available. The overall Standard Deviation of the study is also calculated based on all tests performed, including both qualified and non-qualified tests. The BLR is calculated using a 50% and a 60% cut-off.

2.5.5 Predictive capacity (accuracy)

All qualified tests for each test chemical were used to calculate the predictive capacity values. The calculations were based on the individual predictions of each qualified test in each laboratory and not on the arithmetic mean values of viability over the different qualified tests performed. The predictive capacity is calculated using a 50% and a 60% cut-off.

3 Results

3.1 Quality checks

Data were imported from the original spread sheets into a SAS data base. All test results in the data base are checked by the laboratories and their approval was given for completeness and correctness before the statistical analysis was started.

The remarks and special observations as given by the study personal in the reporting sheets are listed in Appendix IV.

In Table 3.1.1, the number of non-qualified and qualified runs are given, based on the acceptance criteria for NC and PC.

Table 3.1.1 Number of non-qualified and qualified runs, based on the acceptance criteria for NC and PC, subdivided into laboratories

laboratory		No. Qualified	%	No .Non-Qualified	%
Beiersdorf	NC	42	100.0	0	0.0
	PC	41	97.6	1	2.4
Harlan	NC	42	97.7	1	2.3
	PC	43	100.0	0	0.0
IIVS	NC	44	100.0	0	0.0
	PC	44	100.0	0	0.0

There were no major deviations from the study plan (see appendix IV for detailed remarks).

3.2 Descriptive statistics

3.2.1 Distribution of test chemicals

In Table 3.2.1 the distribution of test chemicals is given. The 104 chemicals were equally distributed among irritants (50%) and non-irritants (50%) and among liquids (50%) and solids (50%).

Table 3.2.1 Distribution of test chemicals (upper: frequencies, lower: percentages)

Classification	Liquid[1]	Solid	Total
I	26 25.0	26 25.0	52 50.0
NI	26 25.0	26 25.0	52 25.0
Total	52 50.0	52 50.0	104 100.00

[1] Chemical 37 (*polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL*) was listed as solid. However, all three laboratories used the liquid protocol to test this chemical. Hence, chemical 37 is statistically analysed as a liquid.

Corrections on total viability were made for MTT-reducing and/or colouring chemicals. Whether this correction had to be made was decided by the laboratory. For some chemicals, the judgement whether it regards an MTT-reducer or a colorant differed between laboratories as is shown in Table 3.2.2. In appendix I, a list is given of all MTT-reducing and/or colouring chemicals. If a chemical is treated

as an MTT-reducer or a colorant in at least one of the laboratories, it is listed in appendix I.

Table 3.2.2 Colouring or MTT-reducing chemicals which are treated differently between laboratories are indicated by #.

		MTT				Colouring			
Chemical	**name**	**Beiersdorf**	**Harlan**	**IIVS**		**Beiersdorf**	**Harlan**	**IIVS**	
1	1-bromohexane	No	No	No		No	No	No	
2	1-methylpropyl benzene	No	No	No		No	No	No	
3	2-ethoxyethyl methacrylate	No	No	No		No	No	No	
4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	Yes	Yes	Yes		No	No	No	
5	4-(methylthio)-benzaldehyde	Yes	Yes	Yes		No	No	No	
6	dipropyl disulphide	No	No	No		No	No	No	
7	1-bromo-4-chlorobutane	No	No	No		No	No	No	
8	1-bromo-octane	No	No	No		No	No	No	
9	1,9-decadiene	No	No	Yes	#	No	No	No	
10	2,2-dimethyl-3-pentanol	No	No	Yes	#	No	No	No	
11	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	No	No	No		No	No	No	
12	bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated (53-57% aqueous emulsion)	No	No	No		No	No	Yes	#
13	bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated (56% aqueous emulsion)	No	No	No		No	No	Yes	#
14	dioctyl ether INCI name: DICAPRYLYL ETHER	No	No	No		No	No	No	
15	dioctyl carbonate INCI name: DICAPRYLYL CARBONATE	No	No	No		No	No	No	
16	2-propylheptyl octanoate INCI name: PROPYLHEPTYL CAPRYLATE	No	No	No		No	No	No	
17	polyglyceryl-3 diisooctadecanoate INCI name: POLYGLYCERYL-3 DIISOSTEARATE	No	No	No		No	No	No	
18	steareth-10 allyl ether/acrylates copolymer (30% aqueous) INCI name: STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	No	No	No		No	No	No	
19	dimethyl siloxane, mono dimethylvinylsiloxy- and mono trimethoxysiloxy-terminated (95%)	No	No	No		No	No	No	
20	ricinoleic acid tin salt	Yes	Yes	Yes		No	No	No	
21	1-ethyl-3-methylimidazolium ethylsulphate	No	No	No		No	No	No	
22	3-phenoxybenzyl alcohol	Yes	Yes	Yes		No	No	No	
23	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE	Yes	Yes	Yes		No	No	No	
24	glycidyl methacrylate	No	No	Yes	#	No	No	No	
25	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE	Yes	Yes	Yes		No	No	No	
26	propiconazole	Yes	No	No	#	No	No	No	
28	4,4'-methylene bis-(2,6-di-tert-butylphenol)	No	No	No		No	No	No	
29	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE	Yes	No	No	#	No	No	No	
30	1,1-dimethylguanidine sulphate	Yes	No	No	#	No	No	No	
31	potassium tetrafluoroborate	No	No	No		No	No	No	
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	Yes	Yes	Yes		No	Yes	No	#
33	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11	Yes	Yes	Yes		Yes	Yes	Yes	
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	Yes	Yes	Yes		Yes	Yes	Yes	
35	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	Yes	Yes	Yes		No	No	No	
36	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN	Yes	No	No	#	No	No	No	
37	polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL	No	No	No		No	No	No	
38	2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYLBUTYLPHENOL	No	No	No		No	No	No	
39	2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol] INCI name: BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE	No	No	No		No	No	No	
40	acrylamidopropyltrimonium chloride/acrylamide copolymer	No	No	No		No	No	No	
41	tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino)	No	No	No		No	No	No	

		MTT				Colouring			
Chemical	**name**	**Beiersdorf**	**Harlan**	**IIVS**		**Beiersdorf**	**Harlan**	**IIVS**	
	tribenzoate INCI name: ETHYLHEXYL TRIAZONE								
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	Yes	Yes	Yes		No	No	No	
43	hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE	No	No	No		No	No	No	
44	[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine	No	No	No		No	No	No	
45	1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol	No	No	No		No	No	No	
46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	No	No	No		No	No	No	
47	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE	No	Yes	No	#	No	No	No	
48	sodium hydrogensulphite INCI name: SODIUM BISULFITE	Yes	No	No	#	No	No	No	
49	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN	Yes	Yes	Yes		No	No	No	
50	iodosulfuron-methyl-sodium	Yes	No	Yes	#	No	No	No	
51	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz	Yes	No	No	#	No	No	No	
52	2-anilino-4,6-dimethylpyrimidine common name: Pyrimethanil	No	No	No		No	No	No	
53	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam	Yes	No	No	#	No	No	No	
54	3-chloropropionitrile	No	No	No		No	No	No	
55	2-methylpropanal INCI name: 2-METHYLPROPANAL	No	No	No		No	No	No	
56	isopropyl acetoacetate	Yes	Yes	Yes		No	No	No	
57	2-methyl-1-pentanol	No	No	Yes	#	No	No	No	
58	1-(1-methyl-2-propoxyethoxy)propan-2-ol INCI name: PPG-2 PROPYL ETHER	No	No	Yes	#	No	No	No	
59	ethyl-2-methyl acetoacetate	No	No	No		No	No	No	
60	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET	Yes	No	No	#	No	No	No	
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	No	No	No		No	No	No	
62	1,4-dibutoxy benzene	Yes	No	No	#	No	No	No	
63	4-nitrobenzoic acid	No	No	No		No	No	No	
64	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate	No	No	No		No	No	No	
65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	No	No	No		No	No	No	
66	sodium chloroacetate	No	No	Yes	#	No	No	No	
67	gamma-butyrolactone INCI name: BUTYROLACTONE	No	No	Yes	#	No	No	No	
68	cyclopentanol	No	No	No		No	No	No	
69	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	No	No	No		No	No	No	
70	methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-oxobicyclo[2.2.1]hept-2-ylidene)methyl]anilinium sulphate (30% aqueous) INCI name: CAMPHOR BENZALKONIUM METHOSULFATE	No	No	No		No	No	No	
71	1-propoxy-2-propanol INCI name: PROPYLENE GLYCOL PROPYL ETHER	No	No	No		No	No	No	
72	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE	No	Yes	Yes	#	Yes	No	No	#
73	3,3'-dithiopropionic acid	No	No	No		No	No	No	
74	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	Yes	Yes	Yes		No	Yes	Yes	#
75	sodium benzoate INCI name: SODIUM BENZOATE	No	No	No		No	No	No	
76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	No	No	No		No	No	No	
77	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate	No	No	No		No	No	No	
78	(2R,3R)-3-((R)-1-(tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate	No	No	No		No	No	No	
79	ammonium nitrate INCI name: AMMONIUM NITRATE	No	No	No		No	No	No	
80	methylthioglycolate INCI name: METHYL THIOGLYCOLATE	Yes	Yes	Yes		No	No	No	

		MTT				Colouring			
Chemical	**name**	**Beiersdorf**	**Harlan**	**IIVS**		**Beiersdorf**	**Harlan**	**IIVS**	
81	3-diethylaminopropionitrile	Yes	Yes	Yes		No	No	No	
82	coco alkyl dimethyl betaine (~ 30% aqueous) INCI name: COCO-BETAINE	No	No	No		No	No	No	
83	coco amidopropyl betaine (~ 30% aqueous) INCI name: COCAMIDOPROPYL BETAINE	No	No	No		No	No	No	
84	sodium coco amphoacetate (~ 30% aqueous)	Yes	No	Yes	#	No	No	No	
85	triethanol ammonium alkyl sulphate (~ 40% aqueous) INCI name: TEA-C12-14 ALKYL SULFATE	No	No	No		No	No	No	
86	di-sodium alkyl ether sulfosuccinate (~ 30% aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE	No	No	No		No	No	No	
87	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE	No	No	No		No	No	No	
88	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)	Yes	Yes	Yes		No	No	Yes	#
89	ethoxylated (5 EO) alkyl (C10-14) alcohol	No	No	No		No	No	No	
90	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	No	Yes	No	#	No	No	No	
91	(ethylenediaminepropyl)trimethoxysilane	Yes	Yes	Yes		No	No	No	
92	tetraethylene glycol diacrylate	Yes	Yes	Yes		No	No	No	
93	2,5-dimethyl-2,5-hexanediol	No	No	No		No	No	No	
94	dodecanoic acid INCI name: LAURIC ACID	No	No	No		No	No	No	
95	1,2,4-triazole sodium salt	Yes	Yes	Yes		No	No	No	
96	1-naphthalene acetic acid	No	No	No		No	No	No	
97	sodium oxalate INCI name: SODIUM OXALATE	No	No	No		No	No	No	
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	Yes	Yes	Yes		Yes	Yes	Yes	
99	1,2-benzisothiazol-3(2H)-one INCI name: BENZISOTHIAZOLINONE	No	No	Yes	#	No	No	No	
100	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	Yes	No	No	#	No	No	No	
101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31	No	No	No		Yes	No	No	#
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	No	No	No		No	No	No	
103	3,4-dimethyl-1H-pyrazole	Yes	No	No	#	No	No	No	
104	N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide	No	No	No		No	No	No	
105	1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate	No	No	No		No	No	No	

3.2.2 Number and fraction of qualified and non-qualified tests

If the difference in viability between the two tested tissues was above 20%, the test was considered to be non-qualified. This could concern the tests for the NC, the PC and the chemicals. The number and fraction of qualified and non-qualified tests are presented in Table 3.2.3, subdivided into laboratories and total. Some chemicals were not compatible with the test method, as is also shown in Table 3.2.3. These chemicals were excluded for statistical analysis ('Excluded' in Table 3.2.3). The reasons for the non-qualification of a test or the exclusion of a chemical is presented in Appendix V.

Table 3.2.3 Number and fraction of qualified and non-qualified tests

laboratory	Call	No.	Fraction (%)
Beiersdorf	Qualified and included	309	93.9
	Non-Qualified	15	4.6
	Excluded	5	1.5
Harlan	Qualified and included	312	99.0

laboratory	Call	No.	Fraction (%)
	Non-Qualified	3	1.0
IIVS	Qualified and included	312	97.5
	Non-Qualified	8	2.5
Total	Qualified and included	933	96.8
	Non-Qualified	26	2.7
	Excluded	5	0.5

3.2.3 Chemicals within a run

Table 3.2.4 shows the chemicals within each run subdivided into laboratories. The chemicals are tested in each run with a test with NC and a test with PC.

Table 3.2.4 Chemicals within each run subdivided into laboratories (chemicals with test numbers between brackets)

laboratory	run										
Beiersdorf	EIVS_BDF_liquids_14219F_08_01	3(1)	6(1)	7(1)	8(1)	9(1)	16(1)	69(1)	70(1)	83(1)	87(1)
	EIVS_BDF_liquids_14222B_09_04	3(2)	6(2)	7(2)	8(2)	9(2)	16(2)	69(2)	70(2)	83(2)	87(2)
	EIVS_BDF_liquids_14225D_10_07	3(3)	6(3)	7(3)	8(3)	9(3)	16(3)	69(3)	70(3)	83(3)	87(3)
	EIVS_BDF_liquids_14225E_10_06	1(1)	2(1)	5(1)	11(1)	54(1)	67(1)	68(1)	80(1)	85(1)	
	EIVS_BDF_liquids_14234C_11_09	1(2)	2(2)	5(2)	11(2)	54(2)	67(2)	68(2)	80(2)	85(2)	
	EIVS_BDF_liquids_14241C_12_13	1(3)	2(3)	5(3)	11(3)	54(3)	67(3)	68(3)	80(3)	85(3)	
	EIVS_BDF_liquids_14248A_13_17	4(1)	14(1)	22(1)	23(1)	56(1)	57(1)	71(1)	81(1)	89(1)	91(1)
	EIVS_BDF_liquids_14256A_14_19	4(2)	14(2)	22(2)	23(2)	56(2)	57(2)	71(2)	81(2)	89(2)	91(2)
	EIVS_BDF_liquids_14256C_14_21	10(1)	17(1)	21(1)	24(1)	37(1)	55(1)	58(1)	59(1)	90(1)	
	EIVS_BDF_liquids_14263A_15_22	4(3)	14(3)	22(3)	23(3)	56(3)	57(3)	71(3)	81(3)	89(3)	91(3)
	EIVS_BDF_liquids_14263B_15_24	10(2)	17(2)	21(2)	24(2)	55(2)	58(2)	59(2)	72(2)	90(2)	
	EIVS_BDF_liquids_14277E_17_27	10(3)	17(3)	21(3)	24(3)	55(3)	58(3)	59(3)	72(3)	90(3)	
	EIVS_BDF_liquids_14283A_18_29	12(1)	13(1)	15(1)	18(1)	19(1)	20(1)	82(1)	84(1)	86(1)	88(1)
	EIVS_BDF_liquids_14289D_19_32	12(2)	13(2)	15(2)	18(2)	19(2)	20(2)	82(2)	84(2)	86(2)	88(2)
	EIVS_BDF_liquids_14296A_20_34	12(3)	13(3)	15(3)	18(3)	19(3)	20(3)	82(3)	84(3)	86(3)	88(3)
	EIVS_BDF_liquids_15003B_21_38	25(1)	26(1)	37(2)	60(1)	92(1)					
	EIVS_BDF_liquids_15007B_23_40	25(2)	26(2)	37(3)	60(2)	72(4)	92(2)				
	EIVS_BDF_liquids_15013A_24_42	25(3)	26(3)	37(4)	60(3)	92(3)					
	EIVS_BDF_solids_14219D_08_02	28(1)	35(1)	36(1)	73(1)	74(1)	93(1)	95(1)	96(1)	97(1)	
	EIVS_BDF_solids_14222A_09_05	28(2)	35(2)	36(2)	73(2)	74(2)	93(2)	95(2)	96(2)	97(2)	
	EIVS_BDF_solids_14225C_10_08	28(3)	35(3)	36(3)	73(3)	74(3)	93(3)	95(3)	96(3)	97(3)	
	EIVS_BDF_solids_14234A_11_10	30(1)	41(1)	42(1)	48(1)	62(1)	76(1)	77(1)	94(1)	103(1)	105(1)
	EIVS_BDF_solids_14234B_11_11	32(1)	34(1)	47(1)	61(1)	64(1)	79(1)				
	EIVS_BDF_solids_14241A_12_15	32(2)	34(2)	47(2)	61(2)	64(2)	74(4)	79(2)			
	EIVS_BDF_solids_14241B_12_14	30(2)	41(2)	42(2)	48(2)	62(2)	76(2)	77(2)	94(2)	103(2)	105(2)
	EIVS_BDF_solids_14248B_13_16	30(3)	41(3)	42(3)	48(3)	62(3)	76(3)	77(3)	94(3)	103(3)	105(3)
	EIVS_BDF_solids_14248C_13_18	32(3)	34(3)	47(3)	61(3)	64(3)	79(3)				
	EIVS_BDF_solids_14256B_14_20	31(1)	43(1)	44(1)	46(1)	63(1)	65(1)	66(1)	75(1)	78(1)	104(1)
	EIVS_BDF_solids_14263C_15_23	31(2)	43(2)	44(2)	46(2)	63(2)	65(2)	66(2)	75(2)	78(2)	104(2)
	EIVS_BDF_solids_14277D_17_26	31(3)	43(3)	44(3)	46(3)	63(3)	65(3)	66(3)	75(3)	78(3)	104(3)
	EIVS_BDF_solids_14283B_18_30	29(1)	50(1)	98(1)	101(1)	107(1)					
	EIVS_BDF_solids_14283C_18_28	31(3)	43(3)	44(3)	46(3)	63(3)	65(3)	66(3)	75(3)	78(3)	104(3)
	EIVS_BDF_solids_14289C_19_31	38(1)	39(1)	40(1)	45(1)	49(1)	51(1)	52(1)	53(1)	99(1)	102(1)
	EIVS_BDF_solids_14289E_19_33	29(2)	50(2)	98(2)	101(2)	107(2)					
	EIVS_BDF_solids_14296B_20_36	38(2)	39(2)	40(2)	45(2)	49(2)	51(2)	52(2)	53(2)	99(2)	102(2)
	EIVS_BDF_solids_14296C_20_35	29(3)	50(3)	98(3)	101(3)	107(3)					
	EIVS_BDF_solids_15003A_21_37	38(3)	39(3)	40(3)	45(3)	49(3)	51(3)	52(3)	53(3)	99(3)	102(3)
	EIVS_BDF_solids_15003B_21_39	100(1)	107(4)								
	EIVS_BDF_solids_15007B_23_41	100(2)									
	EIVS_BDF_solids_15013A_24_43	75(5)	100(3)								
	EIVS_BDF_solids_15019A_25_44	29(4)	50(4)								
	EIVS_BDF_solids_15025A_26_50	33(5)	107(5)								
Harlan	EIVS_HARLAN_LIQUIDS_14296D_20_10	5(1)	22(1)	80(1)							
	EIVS_HARLAN_LIQUIDS_15003C_21_11	5(2)	22(2)	80(2)							
	EIVS_HARLAN_LIQUIDS_15007C_23_12	5(3)	22(3)	80(3)							
	EIVS_HARLAN_LIQUIDS_15029A_27_14	4(1)	23(1)	56(1)	72(1)	81(1)	90(1)	91(1)			
	EIVS_HARLAN_LIQUIDS_15030A_28_15	4(2)	23(2)	56(2)	72(2)	81(2)	90(2)	91(2)			
	EIVS_HARLAN_LIQUIDS_15033A_31_16	4(3)	23(3)	56(3)	72(3)	81(3)	90(3)	91(3)			
	EIVS_HARLAN_LIQUIDS_15033B_31_16	12(1)	13(1)	15(1)	18(1)	19(1)	26(1)	60(1)	82(1)	84(1)	86(1)
	EIVS_HARLAN_LIQUIDS_15034A_32_17	12(2)	13(2)	15(2)	18(2)	19(2)	26(2)	60(2)	82(2)	84(2)	86(2)
	EIVS_HARLAN_LIQUIDS_15035A_33_18	12(3)	13(3)	15(3)	18(3)	19(3)	26(3)	60(3)	82(3)	84(3)	86(3)
	EIVS_HARLAN_LIQUIDS_15037A_34_19	20(1)	25(1)	88(1)	92(1)						
	EIVS_HARLAN_LIQUIDS_15040B_38_20	20(2)	25(2)	88(2)	92(2)						
	EIVS_HARLAN_LIQUIDS_15046B_41_21	20(3)	25(3)	88(3)	92(3)						
	EIVS_HARLAN_SOLIDS_14296E_20_10	35(1)	42(1)	47(1)	95(1)						
	EIVS_HARLAN_SOLIDS_15003C_21_11	35(2)	42(2)	47(2)	95(2)						
	EIVS_HARLAN_SOLIDS_15007A_23_12	35(3)	42(3)	47(3)	95(3)						
	EIVS_HARLAN_SOLIDS_15013B_24_13	32(1)	34(1)	74(1)							
	EIVS_HARLAN_SOLIDS_15029B_27_14	32(2)	33(2)	34(2)	74(2)						
	EIVS_HARLAN_SOLIDS_15030B_28_15	32(3)	33(3)	34(3)	74(3)						
	EIVS_HARLAN_SOLIDS_15037B_34_19	33(4)	40(1)	49(1)	98(1)	106(1)	107(1)				
	EIVS_HARLAN_SOLIDS_15040A_38_20	40(2)	49(2)	98(2)	106(2)	107(2)					
	EIVS_HARLAN_Solids_15033C_31_16	29(1)	38(1)	39(1)	50(1)	51(1)	52(1)	53(1)	100(1)	101(1)	102(1)
	EIVS_HARLAN_Solids_15034B_32_17	29(2)	38(2)	39(2)	50(2)	51(2)	52(2)	53(2)	100(2)	101(2)	102(2)
	EIVS_HARLAN_Solids_15035B_33_18	29(3)	38(3)	39(3)	50(3)	51(3)	52(3)	53(3)	100(3)	101(3)	102(3)
	EIVS_Harlan_Solids_15046A_41_21	40(3)	49(3)	98(3)	106(3)	107(3)					
	EIVS_Harlan_Solids_15048A_42_22	40(4)	49(4)	98(4)	106(4)	107(4)					

laboratory	run										
	EIVS_Harlan_liquids_14225A_10_01	2(1)	3(1)	7(1)	8(1)	16(1)	68(1)	69(1)	70(1)	83(1)	87(1)
	EIVS_Harlan_liquids_14234D_11_02	2(2)	3(2)	7(2)	8(2)	16(2)	68(2)	69(2)	70(2)	83(2)	87(2)
	EIVS_Harlan_liquids_14241E_12_03	2(3)	3(3)	7(3)	8(3)	16(3)	68(3)	69(3)	70(3)	83(3)	87(3)
	EIVS_Harlan_liquids_14248E_13_04	1(1)	6(1)	9(1)	11(1)	14(1)	54(1)	57(1)	67(1)	85(1)	89(1)
	EIVS_Harlan_liquids_14263D_15_05	1(2)	6(2)	9(2)	11(2)	14(2)	54(2)	57(2)	67(2)	85(2)	89(2)
	EIVS_Harlan_liquids_14270A_16_06	1(3)	6(3)	9(3)	11(3)	14(3)	54(3)	57(3)	67(3)	85(3)	89(3)
	EIVS_Harlan_liquids_14277B_17_07	10(1)	17(1)	21(1)	24(1)	37(1)	55(1)	58(1)	59(1)	71(1)	
	EIVS_Harlan_liquids_14283D_18_08	10(2)	17(2)	21(2)	24(2)	37(2)	55(2)	58(2)	59(2)	71(2)	
	EIVS_Harlan_liquids_14289A_19_09	10(3)	17(3)	21(3)	24(3)	37(3)	55(3)	58(3)	59(3)	71(3)	
	EIVS_Harlan_solids_14225B_10_01	28(1)	36(1)	41(1)	61(1)	73(1)	77(1)	93(1)	96(1)	97(1)	105(1)
	EIVS_Harlan_solids_14234E_11_02	28(2)	36(2)	41(2)	61(2)	73(2)	77(2)	93(2)	96(2)	97(2)	105(2)
	EIVS_Harlan_solids_14241D_12_03	28(3)	36(3)	41(3)	61(3)	73(3)	77(3)	93(3)	96(3)	97(3)	105(3)
	EIVS_Harlan_solids_14248F_13_04	48(1)	62(1)	63(1)	64(1)	76(1)	78(1)	79(1)	94(1)	103(1)	104(1)
	EIVS_Harlan_solids_14263E_15_05	48(2)	62(2)	63(2)	64(2)	76(2)	78(2)	79(2)	94(2)	103(2)	104(2)
	EIVS_Harlan_solids_14270B_16_06	48(3)	62(3)	63(3)	64(3)	76(3)	78(3)	79(3)	94(3)	103(3)	104(3)
	EIVS_Harlan_solids_14277C_17_07	30(1)	31(1)	43(1)	44(1)	45(1)	46(1)	65(1)	66(1)	75(1)	99(1)
	EIVS_Harlan_solids_14283E_18_08	30(2)	31(2)	43(2)	44(2)	45(2)	46(2)	65(2)	66(2)	75(2)	99(2)
	EIVS_Harlan_solids_14289B_19_09	30(3)	31(3)	43(3)	44(3)	45(3)	46(3)	65(3)	66(3)	75(3)	99(3)
IIVS	EIVS_IIVS_liquids_14219_week1_number1_AH	1(1)	2(1)	5(1)	6(1)	7(1)	8(1)	11(1)	54(1)	68(1)	80(1)
	EIVS_IIVS_liquids_14219_week1_number1_HI	3(1)	9(1)	16(1)	67(1)	69(1)	70(1)	83(1)	85(1)	87(1)	
	EIVS_IIVS_liquids_14222_week2_number2_AH	1(2)	2(2)	5(2)	6(2)	7(2)	8(2)	11(2)	54(2)	68(2)	80(2)
	EIVS_IIVS_liquids_14222_week2_number2_HI	3(2)	9(2)	16(2)	67(2)	69(2)	70(2)	83(2)	85(2)	87(2)	
	EIVS_IIVS_liquids_14225_week3_number3_AH	1(3)	2(3)	5(3)	6(3)	7(3)	8(3)	11(3)	54(3)	68(3)	80(3)
	EIVS_IIVS_liquids_14225_week3_number3_HI	3(3)	9(3)	16(3)	67(3)	69(3)	70(3)	83(3)	85(3)	87(3)	
	EIVS_IIVS_liquids_14234_week4_number4_HI	4(1)	14(1)	17(1)	22(1)	57(1)	71(1)	81(1)	89(1)	90(1)	91(1)
	EIVS_IIVS_liquids_14241_week5_number6_HI	4(2)	14(2)	17(2)	22(2)	57(2)	71(2)	81(2)	89(2)	90(2)	91(2)
	EIVS_IIVS_liquids_14248_week6_number5_AH	10(1)	21(1)	23(1)	24(1)	37(1)	55(1)	56(1)	58(1)	59(1)	72(1)
	EIVS_IIVS_liquids_14248_week6_number7_HI	4(3)	14(3)	17(3)	22(3)	57(3)	71(3)	81(3)	89(3)	90(3)	91(3)
	EIVS_IIVS_liquids_14256_week7_number6_AH	10(2)	21(2)	24(2)	37(2)	55(2)	56(2)	58(2)	59(2)	72(2)	
	EIVS_IIVS_liquids_14263_week8_number8_AH	10(3)	21(3)	23(2)	24(3)	37(3)	55(3)	56(3)	58(3)	59(3)	72(3)
	EIVS_IIVS_liquids_14270_week9_number10_AH	10(4)	15(1)	18(1)	19(1)	20(1)	23(3)	60(1)	82(1)	84(1)	86(1)
	EIVS_IIVS_liquids_14277_week10_number12_AH	15(2)	18(2)	19(2)	20(2)	25(1)	26(1)	60(2)	82(2)	84(2)	86(2)
	EIVS_IIVS_liquids_14283_week11_number13_AH	15(3)	18(3)	19(3)	20(3)	25(2)	26(2)	60(3)	82(3)	84(3)	86(3)
	EIVS_IIVS_liquids_14289_week12_number14_AH	12(1)	13(1)	88(1)							
	EIVS_IIVS_liquids_14289_week12_number15_AH	20(4)	92(1)								
	EIVS_IIVS_liquids_14296_week13_number17_AH	12(2)	13(2)	88(2)							
	EIVS_IIVS_liquids_14296_week13_number18_AH	26(3)	92(2)								
	EIVS_IIVS_liquids_15003_week14_number19_AH	12(3)	13(3)	88(3)							
	EIVS_IIVS_liquids_15003_week14_number20_AH	26(4)	92(3)								
	EIVS_IIVS_liquids_15007_week16_number22_AH	25(3)	90(4)								
	EIVS_IIVS_solids_14219_week1_number1_MK	28(1)	61(1)	73(1)	74(1)	93(1)	95(1)	96(1)	97(1)		
	EIVS_IIVS_solids_14222_week2_number2_MK	28(2)	61(2)	73(2)	74(2)	93(2)	95(2)	96(2)	97(2)		
	EIVS_IIVS_solids_14225_week3_number3_MK	28(3)	61(3)	73(3)	74(3)	93(3)	95(3)	96(3)	97(3)		
	EIVS_IIVS_solids_14234_week4_number4_MK	32(1)	34(1)	35(1)	36(1)	41(1)	42(1)	45(1)	75(1)	99(1)	
	EIVS_IIVS_solids_14241_week5_number5_MK	32(2)	34(2)	35(2)	36(2)	41(2)	42(2)	45(2)	75(2)	99(2)	
	EIVS_IIVS_solids_14248_week6_number6_MK	32(3)	34(3)	35(3)	36(3)	41(3)	42(3)	45(3)	75(3)	99(3)	
	EIVS_IIVS_solids_14256_week7_number7_AH	43(1)	44(1)	46(1)	47(1)	65(1)	79(1)				
	EIVS_IIVS_solids_14256_week7_number7_MK	33(1)	64(1)	76(1)	77(1)	78(1)	94(1)	103(1)	104(1)	105(1)	
	EIVS_IIVS_solids_14263_week8_number8_MK	34(4)	64(2)	76(2)	77(2)	78(2)	94(2)	103(2)	104(2)	105(2)	
	EIVS_IIVS_solids_14263_week8_number9_AH	43(2)	44(2)	46(2)	47(2)	65(2)	79(2)				
	EIVS_IIVS_solids_14270_week9_number10_MK	33(2)	64(3)	76(3)	77(3)	78(3)	94(3)	103(3)	104(3)	105(3)	
	EIVS_IIVS_solids_14270_week9_number11_AH	43(3)	44(3)	46(3)	47(3)	51(1)	52(1)	53(1)	65(3)	79(3)	100(1)
	EIVS_IIVS_solids_14277_week10_number11_MK	30(1)	31(1)	34(5)	63(1)	98(1)	106(1)				
	EIVS_IIVS_solids_14283_week11_number12_MK	30(2)	31(2)	48(1)	62(1)	63(2)	66(1)	98(2)	106(2)		
	EIVS_IIVS_solids_14289_week12_number13_MK	30(3)	31(3)	48(2)	62(2)	63(3)	66(2)	98(3)	106(3)		
	EIVS_IIVS_solids_14296_week13_number14_MK	29(1)	38(1)	39(1)	40(1)	49(1)	50(1)	101(1)	102(1)	107(1)	
	EIVS_IIVS_solids_15003_week14_number15_MK	29(2)	38(2)	39(2)	40(2)	49(2)	50(2)	101(2)	102(2)	107(2)	
	EIVS_IIVS_solids_15007_week15_number16_MK	29(3)	38(3)	39(3)	40(3)	49(3)	50(3)	101(3)	102(3)	107(3)	
	EIVS_IIVS_solids_15007_week16_number23_AH	51(2)	52(2)	53(2)	100(2)						
	EIVS_IIVS_solids_15013_week16_number17_MK	33(3)	48(3)	62(3)	66(3)	104(4)	107(4)				
	EIVS_IIVS_solids_15013_week17_number24_AH	51(3)	52(3)	53(3)	100(3)						
	EIVS_IIVS_solids_15030_week18_number19_MK	33(4)	107(5)								

3.2.4 Number of tests within each test sequence

In Table 3.2.5, the number of tests within each test sequence is given, subdivided into laboratories and chemicals.

Table 3.2.5 Number of tests within each test sequence

	laboratory				laboratory		
Chemical	**Beiersdorf**	**Harlan**	**IIVS**	**Chemical**	**Beiersdorf**	**Harlan**	**IIVS**
1	3	3	3	55	3	3	3
2	3	3	3	56	3	3	3
3	3	3	3	57	3	3	3
4	3	3	3	58	3	3	3
5	3	3	3	59	3	3	3
6	3	3	3	60	3	3	3
7	3	3	3	61	3	3	3
8	3	3	3	62	3	3	3
9	3	3	3	63	4	3	3
10	3	3	4	64	3	3	3

11	3	3	3	65	4	3	3
12	3	3	3	66	4	3	3
13	3	3	3	67	3	3	3
14	3	3	3	68	3	3	3
15	3	3	3	69	3	3	3
16	3	3	3	70	3	3	3
17	3	3	3	71	3	3	3
18	3	3	3	72	3	3	3
19	3	3	3	73	3	3	3
20	3	3	4	74	4	3	3
21	3	3	3	75	5	3	3
22	3	3	3	76	3	3	3
23	3	3	3	77	3	3	3
24	3	3	3	78	4	3	3
25	3	3	3	79	3	3	3
26	3	3	4	80	3	3	3
28	3	3	3	81	3	3	3
29	4	3	3	82	3	3	3
30	3	3	3	83	3	3	3
31	4	3	3	84	3	3	3
32	3	3	3	85	3	3	3
33	5	3	4	86	3	3	3
34	3	3	5	87	3	3	3
35	3	3	3	88	3	3	3
36	3	3	3	89	3	3	3
37	4	3	3	90	3	3	4
38	3	3	3	91	3	3	3
39	3	3	3	92	3	3	3
40	3	4	3	93	3	3	3
41	3	3	3	94	3	3	3
42	3	3	3	95	3	3	3
43	4	3	3	96	3	3	3
44	4	3	3	97	3	3	3
45	3	3	3	98	3	4	3
46	4	3	3	99	3	3	3
47	3	3	3	100	3	3	3
48	3	3	3	101	3	3	3
49	3	4	3	102	3	3	3
50	4	3	3	103	3	3	3
51	3	3	3	104	4	3	4
52	3	3	3	105	3	3	3
53	3	3	3	106[1]	5	4	3
54	3	3	3	107[1]	5	4	5

[1] extra chemicals not for statistics but for a later purpose of evaluation using an HPLC based detection system.

3.2.5 Non-qualified and excluded chemicals

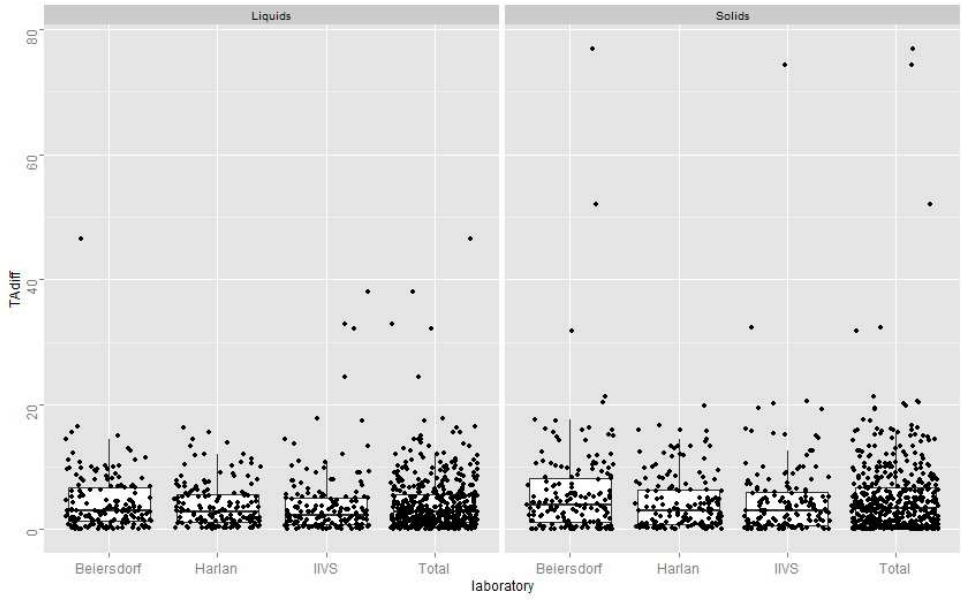
A listing of the number and fraction of non-qualified or excluded chemicals is given in Table 3.2.6.

Table 3.2.6 List, number and fraction of non-qualified or excluded chemicals, subdivided into laboratories and chemicals

laboratory	Chemical	Reason	No.	Fraction (%)
Beiersdorf	29	Non-Qualified	1	25
	31	Non-Qualified	1	25
	33	Excluded	5	100
	37	Non-Qualified	1	25
	43	Non-Qualified	1	25
	44	Non-Qualified	1	25
	46	Non-Qualified	1	25
	50	Non-Qualified	1	25
	63	Non-Qualified	1	25
	65	Non-Qualified	1	25
	66	Non-Qualified	1	25
	74	Non-Qualified	1	25
	75	Non-Qualified	2	40
	78	Non-Qualified	1	25
	104	Non-Qualified	1	25
Harlan	40	Non-Qualified	1	25
	49	Non-Qualified	1	25
	98	Non-Qualified	1	25
IIVS	10	Non-Qualified	1	25
	20	Non-Qualified	1	25
	26	Non-Qualified	1	25
	33	Non-Qualified	1	25
	34	Non-Qualified	2	40
	90	Non-Qualified	1	25
	104	Non-Qualified	1	25

In Figure 3.2.1, a boxplot is given of the differences between uncorrected viabilities for every pair of tissue replicates used for each chemical, including both qualified and unqualified tests, for each independent laboratory and for all laboraties together.

Figure 3.2.1 Differences between uncorrected viabilities for every pair of tissue replicates, per laboratory and total, including both qualified and unqualified tests.



3.2.6 Chemicals with complete test sequences

A total of three qualified tests is considered as a complete test sequence. A list of chemicals with a complete test sequence is given in Table 3.2.7. Each of the laboratory had a fraction of more than 96% complete test sequences, as is shown in Table 3.2.8. Overall, 96.5% of the 106 tested chemicals had a complete test sequence in three laboratories.

Table 3.2.7 A list of chemicals with a complete test sequence

Chemical	Beiersdorf	Harlan	IIVS	Chemical	Beiersdorf	Harlan	IIVS
1	3	3	3	55	3	3	3
2	3	3	3	56	3	3	3
3	3	3	3	57	3	3	3
4	3	3	3	58	3	3	3
5	3	3	3	59	3	3	3
6	3	3	3	60	3	3	3
7	3	3	3	61	3	3	3
8	3	3	3	62	3	3	3
9	3	3	3	63	3	3	3
10	3	3	3	64	3	3	3
11	3	3	3	65	3	3	3
12	3	3	3	66	3	3	3
13	3	3	3	67	3	3	3
14	3	3	3	68	3	3	3
15	3	3	3	69	3	3	3
16	3	3	3	70	3	3	3
17	3	3	3	71	3	3	3
18	3	3	3	72	3	3	3
19	3	3	3	73	3	3	3
20	3	3	3	74	3	3	3
21	3	3	3	75	3	3	3
22	3	3	3	76	3	3	3
23	3	3	3[1]	77	3	3	3
24	3	3	3	78	3	3	3
25	3	3	3	79	3	3	3
26	3	3	3	80	3[1]	3[1]	3[1]
28	3	3	3	81	3	3	3
29	3	3	3	82	3	3	3

Chemical	Beiersdorf	Harlan	IIVS	Chemical	Beiersdorf	Harlan	IIVS
30	3	3	3	83	3	3	3
31	3	3	3	84	3	3	3
32	3	3	3	85	3	3	3
33	excluded	3	3	86	3	3	3
34	3	3	3	87	3	3	3
35	3	3	3	88	3	3	3
36	3	3	3	89	3	3	3
37	3	3	3	90	3	3	3
38	3	3	3	91	3	3	3
39	3	3	3	92	3	3	3
40	3	3	3	93	3	3	3
41	3	3	3	94	3	3	3
42	3	3	3	95	3	3	3
43	3	3	3	96	3	3	3
44	3	3	3	97	3	3	3
45	3	3	3	98	3	3	3
46	3	3	3	99	3	3	3
47	3	3	3	100	3	3	3
48	3	3	3	101	3	3	3
49	3	3	3	102	3	3	3
50	3	3	3	103	3	3	3
51	3	3	3	104	3	3	3
52	3	3	3	105	3	3	3
53	3	3	3				
54	3	3	3				

[1] On May 10th 2012, after an evaluation of the first draft of the statistics report, the core VMG overrode the rule identifying 50% NSMTT as a cut-off to consider a chemical compatible with the test system as described in Chapter 2.5.1. of this report. In all these cases, rule 3 in Chapter 2.5.1. is fulfilled since the mean %NSC of all qualified tests is greater than (>) 50% and the classification of these qualified tests changes upon correction (from non-irritant to irritant). However, the viability values obtained in the qualified tests are definitely within the linear range of the OD measurements (within the 100% scale) and therefore, even though there is a strong MTT reduction occurring this is not interfering with the analytical capacity to measure formazan production. Moreover, the variability obtained between the different tests and controls is low. As such, these chemicals were considered compatible with the test method and their data were therefore included in all of the statistical analyses.

Table 3.2.8 Fraction of chemicals with a complete test sequence, subdivided into laboratories and total

laboratory	Fraction (%)
Beiersdorf	99.0
Harlan	100.0
IIVS	100.0
Total	99.7

Logically, less than 1% of the chemicals had an incomplete test sequence. These chemicals are presented in Table 3.2.9. The fraction of incomplete test sequences per laboratory as well as in total is given in Table 3.2.10. Only for Beiersdorf, one chemical with an incomplete test sequence was found. This chemical (*2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11*) was incompatible with the test method for Beiersdorf.

Table 3.2.9 Chemicals with incomplete test sequences

laboratory	order	Excluded	Non-qualified
Beiersdorf	33	5	0

Table 3.2.10 Fraction of incomplete test sequences per laboratory and total

laboratory	Fraction(%)
Beiersdorf	1
Harlan	0

laboratory	Fraction(%)
IIVS	0
Total	0.3

Given Table 3.2.8 and Table 3.2.10, the criteria of at least 85% complete test sequences in each laboratory was met, as is also summarized in Table 3.2.11.

Table 3.2.11 Statement whether the test method has fulfilled the performance criteria (at least 85% complete test sequences) concerning the fraction of complete test sequences.

laboratory	Fraction	Statement: criteria is
Beiersdorf	99.0	fulfilled
Harlan	100.0	fulfilled
IIVS	100.0	fulfilled
Total	99.7	fulfilled

3.2.7 Negative and Positive controls

The results for the negative and positive controls are presented in summarizing figures (see Figure 3.2.2, Figure 3.2.3, Figure 3.2.4 and Figure 3.2.5) as well as in Table 3.2.12.

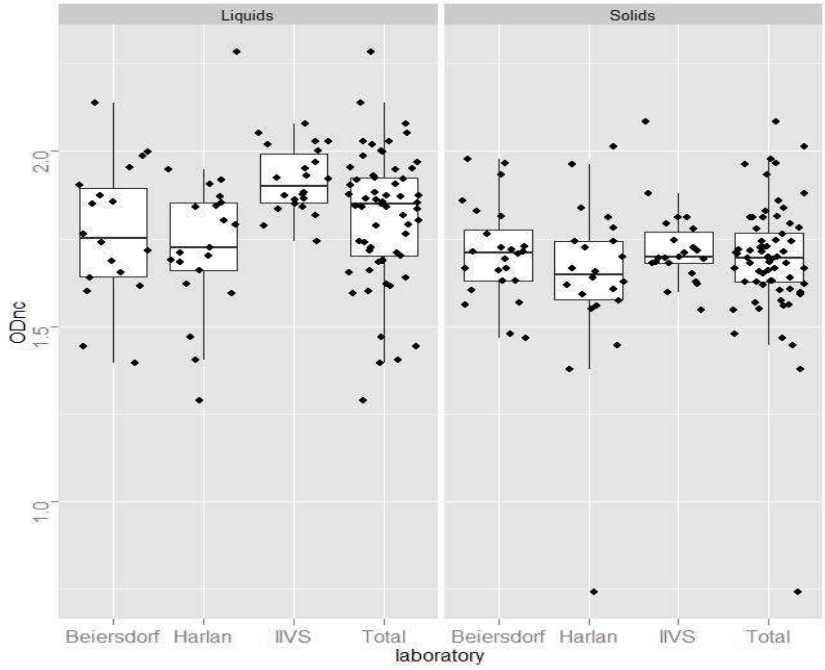


Figure 3.2.2 Mean OD-values for the Negative controls (Performance criteria: 1.0 < mean ODnc < 2.3), per laboratory and total

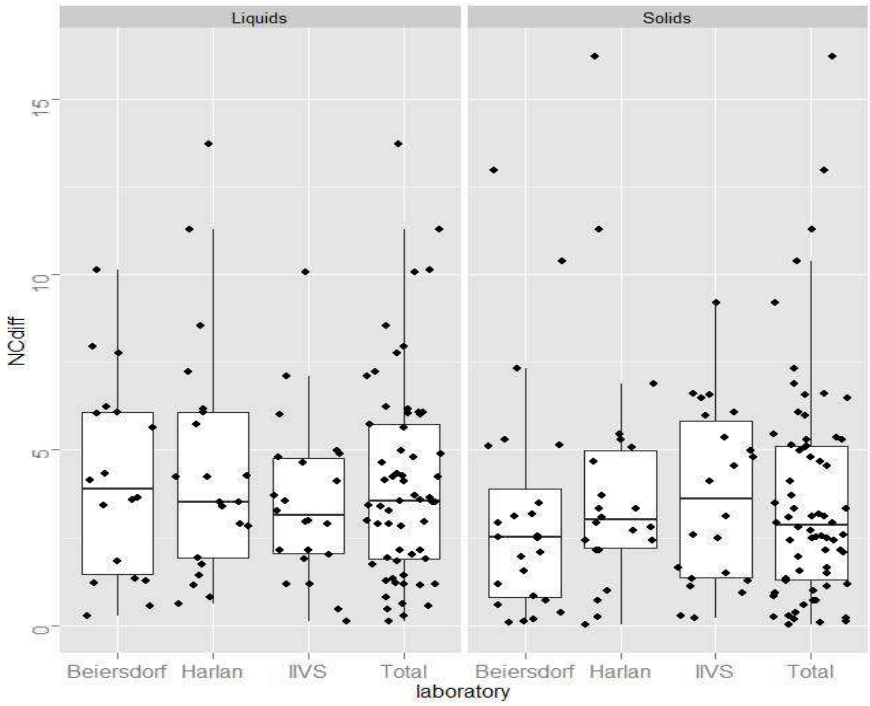


Figure 3.2.3 Differences in viabilities for the Negative controls (Performance criteria: difference <= 20%), per laboratory and total

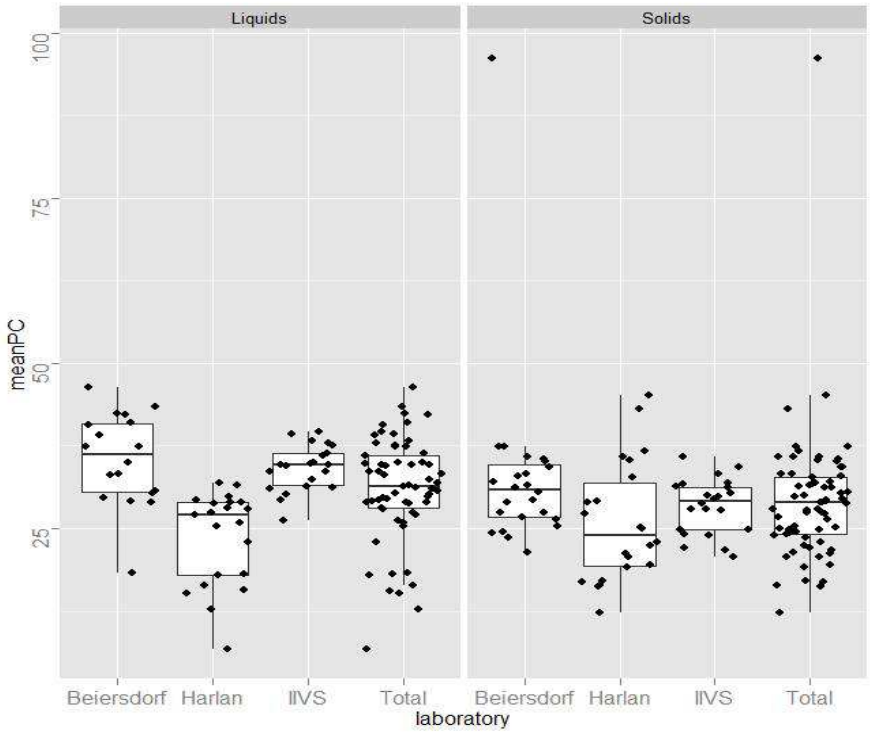


Figure 3.2.4 Mean viabilities for the Positive controls (Performance criteria: mean viability <= 50%)

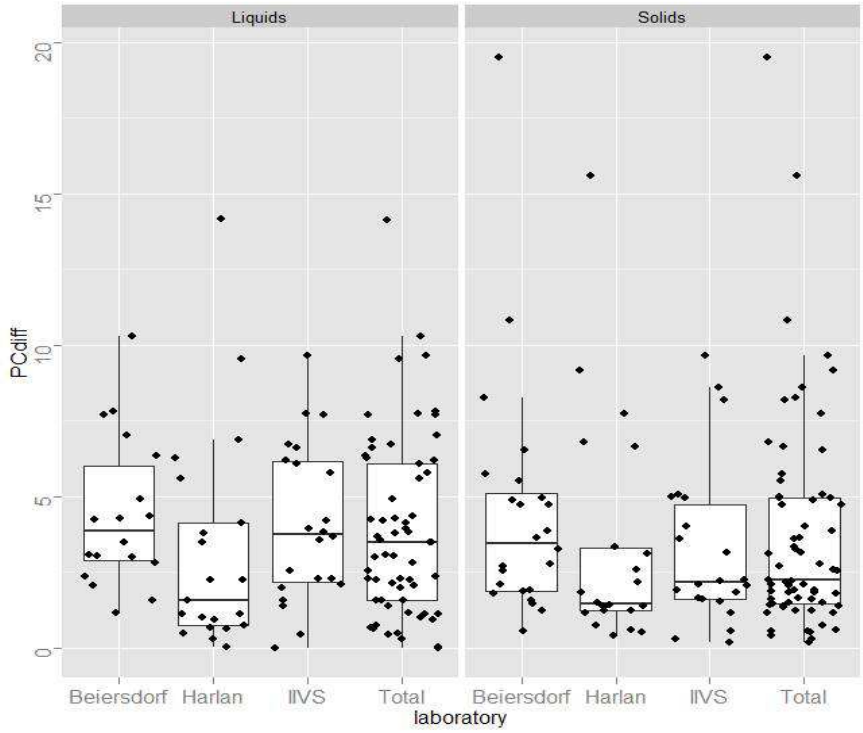


Figure 3.2.5 Differences in viabilities for the Positive controls (Performance criteria: difference <= 20%), per laboratory and total

Table 3.2.12 Numerical statistical values for the Negative and Positive Control (lower: 25th percentile – 1.5*IQR, p25: 25th percentile, median: 50th percentile, p75: 75th percentile, upper: 75th percentile + 1.5*IQR, with IQR = 75th percentile – 25th percentile).

		Liquids					Solids				
Variable[1]	**laboratory**	**lower**	**p25**	**median**	**p75**	**upper**	**lower**	**p25**	**median**	**p75**	**upper**
ODnc	Beiersdorf	1.40	1.64	1.75	1.90	2.14	1.47	1.63	1.71	1.79	1.98
	Harlan	1.40	1.66	1.73	1.85	1.95	1.38	1.57	1.65	1.74	1.96
	IIVS	1.74	1.85	1.90	2.00	2.08	1.55	1.68	1.70	1.78	1.88
	Total	1.40	1.70	1.85	1.92	2.14	1.45	1.62	1.70	1.77	1.98
NCdiff	Beiersdorf	0.28	1.34	3.89	6.07	10.12	0.10	0.77	2.51	4.30	7.32
	Harlan	0.61	1.93	3.52	6.08	11.28	0.03	2.15	3.01	5.07	6.88
	IIVS	0.13	2.04	3.13	4.81	7.12	0.21	1.33	3.61	5.97	9.19
	Total	0.13	1.90	3.54	5.72	11.28	0.03	1.29	2.86	5.13	10.38
meanPC	Beiersdorf	18.27	30.34	36.17	40.97	46.41	21.47	26.61	30.86	34.76	37.41
	Harlan	6.76	17.90	27.06	28.97	31.81	12.31	19.21	23.93	32.81	45.10
	IIVS	26.23	31.30	34.63	36.45	39.63	20.63	24.83	29.16	31.31	35.84
	Total	16.38	28.09	31.30	36.07	46.41	12.31	24.09	28.90	32.87	45.10
PCdiff	Beiersdorf	1.17	2.83	3.86	6.35	10.30	0.57	1.88	3.45	5.25	8.28
	Harlan	0.04	0.76	1.57	4.13	6.88	0.40	1.22	1.46	3.36	3.36
	IIVS	0.00	2.12	3.76	6.19	9.66	0.18	1.62	2.16	4.95	9.67
	Total	0.00	1.57	3.48	6.08	10.30	0.18	1.45	2.24	4.96	9.67

[1] ODnc = optical density for negative control, NCdiff = difference between replicates of the negative control, meanPC = viability for positive control, PCdiff = difference between replicates of the positive control (all in % viability, except for ODnc).

3.2.8 Summary of all tests results

Finally, a summary of all tests results (including the non-qualified and excluded test results) are presented in Appendix VI.

3.3 Reproducibility and accuracy using a 50% cut-off

In this section, a 50% cut-off was applied to determine the irritancy of the chemical. If the viability is above 50%, the chemical is considered to be non-irritant. If the viability is 50% or below, the chemical is considered to be irritant.

3.3.1 Within-laboratory variability

For each laboratory, concordance of classification was calculated based on qualified test from test chemicals for which at least two qualified tests were available. In Table 3.3.1 the concordance within each laboratory as well as in total is given.

Table 3.3.1 Concordance within laboratories and total

laboratory	WLV concordant	No.	Fraction(%)
Beiersdorf	NO	7	6.8
	YES	96	93.2
Harlan	NO	6	5.8
	YES	98	94.2
IIVS	NO	7	6.7
	YES	97	93.3
Total	NO	20	6.4
	YES	291	93.6

Additional descriptive statistics can identify possible reasons for non-concordant results. These are presented in Table 3.3.2. For each non-concordant result the state (liquid/solid), the GHS classification, whether it is colouring or MTTreducer and the test results are given.

Table 3.3.2 Additional descriptive statistics on non-concordant results within laboratories

							Test		
laboratory	chemical	name	LS	colouring	MTT	GHS class	1	2	3
Beiersdorf	20	ricinoleic acid tin salt	Liquid	No	Yes	no cat	31.1	57.2	49.8
	22	3-phenoxybenzyl alcohol	Liquid	No	Yes	no cat	51.6	39.3	45.1
	30	1,1-dimethylguanidine sulphate	Solid	No	Yes	no cat	55.6	39.0	46.8
	40	acrylamidopropyltrimonium chloride/acrylamide copolymer	Solid	No	No	no cat	49.4	59.5	62.1
	56	isopropyl acetoacetate	Liquid	No	Yes	cat 2B	46.4	54.5	60.3
	97	sodium oxalate INCI name: SODIUM OXALATE	Solid	No	No	cat 1	56.2	47.2	55.5
	102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	Solid	No	No	cat 1	10.1	110.2	124.3
Harlan	5	4-(methylthio)-benzaldehyde	Liquid	No	Yes	no cat	56.7	41.4	40.3
	63	4-nitrobenzoic acid	Solid	No	No	cat 2B	56.8	41.0	50.2
	65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	Solid	No	No	cat 2B	20.3	16.2	51.8
	76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	Solid	No	No	cat 2A	59.0	32.3	52.8
	101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride	Solid	No	No	cat 1	26.2	50.6	42.0

		INCI name: BASIC ORANGE 31							
	102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	Solid	No	No	cat 1	38.0	55.0	52.1
IIVS	3	2-ethoxyethyl methacrylate	Liquid	No	No	no cat	51.4	49.0	47.5
	24	glycidyl methacrylate	Liquid	No	Yes	no cat	53.0	33.9	32.6
	54	3-chloropropionitrile	Liquid	No	No	cat 2B	51.8	43.1	30.1
	59	ethyl-2-methyl acetoacetate	Liquid	No	No	cat 2B	56.6	52.8	43.6
	65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	Solid	No	No	cat 2B	63.8	41.6	53.9
	92	tetraethylene glycol diacrylate	Liquid	No	Yes	cat 1	39.6	39.3	51.2
	96	1-naphthalene acetic acid	Solid	No	No	cat 1	33.2	38.9	54.1

The concordance of classifications (irritant/non-irritant) for the set of chemicals tested during validation obtained in different, independent runs within a single laboratory should ideally be equal or higher than 85% for all participating laboratories. As summarized in Table 3.3.3, this criteria was met for each laboratory as well as in total.

Table 3.3.3 Statement whether the test method has fulfilled the performance criteria concerning the concordance of classifications within one laboratory.

laboratory	Fraction(%)	Statement: criteria is
Beiersdorf	93.2	fulfilled
Harlan	94.2	fulfilled
IIVS	93.3	fulfilled
Total	93.6	fulfilled

The within-laboratory variability is described by the concordance of classifications. Correlation coefficients between viability measurements give also information on this variability. Since the Pearson correlation coefficient is sensitive for outlying test results and high leverages, both the Pearson and the Spearman correlation coefficients (using ranks instead of the original test results) were calculated. These coefficients are presented in Table 3.3.4.

Table 3.3.4 Pearson and Spearman correlation coefficients between tests results within each laboratory as well as in total.

Correlation Coefficient	laboratory	Qual1 - Qual2	Qual1 - Qual3	Qual2 - Qual3
Pearson	Beiersdorf	0.945	0.942	0.977
	Harlan	0.958	0.970	0.955
	IIVS	0.988	0.978	0.984
	Mean	0.964	0.963	0.972
Spearman	Beiersdorf	0.933	0.942	0.974
	Harlan	0.951	0.966	0.951
	IIVS	0.973	0.959	0.960
	Mean	0.952	0.955	0.962

The arithmetic mean, standard deviation and coefficient of variation from the three valid tests are given per laboratory (see Table 3.3.5). The overall standard deviation and coefficient of variation is also using all available tests results, hence qualified and non-qualified. The results are presented in Table 3.3.6.Note that the coefficient of variation is not a useful measure if the mean is close to zero.

Table 3.3.5 Arithmetic mean, standard deviation (std) and coefficient of variation (cv) from the three valid tests are given per laboratory (n = number of qualified tests that was used for the calculation of the mean, std and cv)

	laboratory											
	Beiersdorf				Harlan				IIVS			
Chemical	mean	std	cv	n	mean	std	cv	n	mean	std	cv	n
1	69.3	1.8	2.6	3	66.6	4.0	6.0	3	68.7	6.3	9.2	3
2	80.1	2.8	3.5	3	77.8	2.8	3.5	3	81.3	2.6	3.1	3
3	60.9	4.8	7.8	3	38.0	0.7	1.9	3	49.3	1.9	3.9	3
4	109.0	5.8	5.3	3	61.0	3.2	5.3	3	96.2	4.1	4.3	3
5	80.7	7.5	9.3	3	46.1	9.2	19.9	3	62.5	11.0	17.6	3
6	85.3	5.0	5.9	3	76.3	7.3	9.6	3	83.6	4.4	5.3	3
7	38.5	3.8	9.9	3	34.8	3.3	9.5	3	38.6	5.9	15.2	3
8	100.5	2.9	2.8	3	93.0	3.0	3.2	3	98.7	3.1	3.2	3
9	98.4	3.3	3.3	3	90.4	7.1	7.9	3	101.6	4.0	3.9	3
10	33.1	2.1	6.4	3	12.5	2.4	19.5	3	19.1	4.1	21.5	3
11	29.1	1.3	4.6	3	18.9	2.4	12.9	3	31.4	2.4	7.7	3
12	92.4	1.4	1.6	3	93.7	2.6	2.7	3	94.5	2.0	2.1	3
13	100.4	11.0	10.9	3	90.5	6.4	7.0	3	83.8	2.2	2.6	3
14	100.6	3.7	3.7	3	97.2	6.3	6.4	3	95.7	1.1	1.2	3
15	102.8	6.2	6.1	3	101.4	7.3	7.2	3	97.2	4.6	4.7	3
16	104.9	5.4	5.2	3	100.0	5.2	5.2	3	101.4	5.1	5.0	3
17	97.5	5.3	5.5	3	97.1	9.0	9.3	3	96.7	1.4	1.4	3
18	97.1	23.9	24.6	3	96.4	5.2	5.4	3	94.8	0.6	0.6	3
19	108.2	3.1	2.8	3	109.1	3.9	3.6	3	97.6	1.8	1.8	3
20	46.0	13.4	29.1	3	9.4	9.5	101.4	3	40.9	7.5	18.3	3
21	83.0	0.2	0.2	3	72.3	5.1	7.1	3	84.4	2.5	3.0	3
22	45.3	6.1	13.5	3	20.1	6.1	30.6	3	37.4	1.8	4.7	3
23	42.1	3.4	8.1	3	14.9	9.0	60.5	3	12.6	5.5	43.9	3
24	45.8	2.5	5.4	3	22.9	4.5	19.7	3	39.8	11.4	28.7	3
25	104.6	3.2	3.1	3	106.2	2.3	2.2	3	101.9	6.3	6.2	3
26	21.5	1.8	8.5	3	35.6	5.1	14.2	3	34.2	2.2	6.5	3
28	98.3	2.2	2.2	3	93.5	2.2	2.4	3	106.3	6.2	5.8	3
29	87.6	4.5	5.1	3	84.1	27.3	32.5	3	103.2	2.3	2.2	3
30	47.1	8.3	17.6	3	24.8	10.4	42.0	3	58.8	9.2	15.7	3
31	78.2	14.4	18.4	3	90.1	11.0	12.2	3	100.0	3.4	3.4	3
32	0.4	0.5	132.4	3	1.0	0.2	15.6	3	2.5	0.3	12.8	3
33	excluded				44.3	4.0	9.1	3	87.1	3.4	3.9	3
34	113.0	3.0	2.7	3	66.2	13.9	21.0	3	94.6	13.1	13.9	3
35	74.2	2.5	3.4	3	69.7	7.5	10.8	3	98.2	2.6	2.6	3
36	107.1	4.1	3.8	3	96.6	7.6	7.9	3	109.0	3.0	2.7	3
37	78.4	2.9	3.7	3	73.0	6.0	8.2	3	81.5	4.3	5.3	3
38	107.8	10.3	9.6	3	102.8	9.0	8.8	3	103.7	3.8	3.6	3
39	106.2	9.6	9.1	3	101.3	13.2	13.0	3	103.0	1.6	1.6	3
40	57.0	6.7	11.8	3	63.1	8.7	13.8	3	61.8	1.5	2.4	3
41	96.8	5.7	5.9	3	91.1	6.2	6.8	3	98.6	4.3	4.4	3
42	69.5	13.8	19.9	3	59.8	6.3	10.5	3	79.2	7.8	9.8	3
43	102.8	9.1	8.9	3	126.9	36.0	28.4	3	101.8	1.8	1.8	3
44	100.2	3.8	3.8	3	100.1	4.6	4.6	3	98.4	4.4	4.5	3
45	110.3	8.7	7.9	3	107.7	8.5	7.9	3	97.3	2.2	2.2	3
46	70.0	2.3	3.2	3	70.7	10.7	15.2	3	61.3	3.7	6.1	3
47	4.7	0.3	7.0	3	2.9	0.8	26.8	3	2.9	0.3	11.2	3
48	3.1	0.5	15.2	3	2.8	0.3	10.4	3	2.5	0.2	6.6	3
49	0.0	0.0	.	3	7.0	4.2	59.4	3	14.4	2.2	15.4	3
50	87.6	3.5	4.0	3	97.6	1.3	1.3	3	95.3	2.4	2.5	3
51	97.3	5.1	5.2	3	92.7	7.7	8.3	3	100.0	5.4	5.4	3
52	112.9	15.5	13.7	3	101.9	7.3	7.2	3	100.7	5.3	5.3	3
53	106.0	13.2	12.5	3	111.9	10.2	9.1	3	105.1	2.9	2.8	3
54	47.3	1.9	3.9	3	20.7	4.1	19.9	3	41.7	10.9	26.3	3
55	2.2	0.1	3.9	3	2.2	0.4	18.6	3	2.5	0.1	2.7	3
56	53.7	7.0	13.0	3	24.9	3.5	14.1	3	37.3	9.2	24.7	3
57	21.1	2.9	13.5	3	6.4	1.3	21.2	3	17.8	4.5	25.3	3
58	22.3	0.4	1.6	3	3.8	2.6	67.6	3	13.6	0.7	5.3	3
59	69.5	8.1	11.6	3	43.3	6.1	14.0	3	51.0	6.7	13.2	3
60	15.6	4.3	27.7	3	10.6	4.8	44.9	3	20.6	6.5	31.7	3
61	18.3	4.0	22.1	3	12.6	4.0	31.5	3	18.0	2.9	16.3	3

	laboratory											
	Beiersdorf				Harlan				IIVS			
Chemical	mean	std	cv	n	mean	std	cv	n	mean	std	cv	n
62	109.0	6.8	6.2	3	104.1	2.1	2.1	3	104.0	6.4	6.2	3
63	34.0	6.8	20.0	3	49.3	7.9	16.1	3	44.1	5.4	12.2	3
64	29.9	7.1	23.6	3	23.9	10.0	41.6	3	32.5	6.2	19.1	3
65	51.4	0.8	1.7	3	29.4	19.5	66.1	3	53.1	11.1	20.9	3
66	6.8	1.1	15.9	3	3.5	1.2	33.0	3	3.8	2.4	65.0	3
67	12.2	2.5	20.4	3	4.5	0.4	8.9	3	14.5	0.8	5.6	3
68	3.4	1.0	28.6	3	3.4	0.6	17.8	3	4.2	2.4	57.9	3
69	14.0	0.9	6.6	3	13.8	3.2	23.2	3	14.1	0.4	2.9	3
70	15.2	2.7	17.6	3	11.0	1.6	14.7	3	12.9	1.2	8.9	3
71	5.4	0.8	14.2	3	6.5	2.1	32.6	3	8.0	0.9	11.3	3
72	3.9	1.5	38.8	3	4.3	1.0	22.4	3	3.9	1.3	33.7	3
73	83.7	8.5	10.1	3	84.1	5.0	5.9	3	97.1	12.3	12.7	3
74	75.7	11.8	15.6	3	77.6	3.6	4.7	3	91.8	6.5	7.1	3
75	79.9	4.7	5.8	3	7.3	8.7	118.3	3	5.1	0.7	13.5	3
76	53.9	0.8	1.4	3	48.1	14.0	29.2	3	27.3	1.3	4.6	3
77	96.8	5.9	6.1	3	73.9	18.1	24.5	3	103.0	4.6	4.4	3
78	83.2	4.9	5.9	3	63.7	1.9	3.0	3	86.9	1.0	1.1	3
79	2.6	0.5	20.7	3	2.6	0.3	13.5	3	2.8	0.5	16.4	3
80	17.5	0.8	4.6	3	7.2	7.7	107.0	3	8.0	2.6	32.3	3
81	2.5	0.7	26.8	3	3.4	0.2	5.3	3	4.2	1.3	29.8	3
82	3.8	2.0	52.4	3	1.8	0.3	17.7	3	4.9	2.2	43.8	3
83	5.6	0.4	7.7	3	5.3	2.1	39.1	3	5.4	1.4	25.8	3
84	13.5	8.3	61.5	3	6.0	1.6	26.1	3	15.3	5.2	34.0	3
85	20.2	5.7	28.3	3	9.1	3.5	38.2	3	15.0	2.5	16.6	3
86	24.4	3.3	13.6	3	30.0	10.2	34.0	3	28.3	6.8	24.0	3
87	28.7	4.2	14.6	3	18.9	4.0	21.3	3	24.2	6.7	27.8	3
88	5.8	1.5	26.5	3	6.1	1.5	24.0	3	4.8	1.9	39.3	3
89	9.5	2.0	21.2	3	7.2	1.2	17.3	3	10.4	1.9	18.2	3
90	31.5	7.8	24.8	3	24.2	9.2	37.9	3	33.7	2.5	7.4	3
91	31.1	9.8	31.4	3	16.8	4.0	24.0	3	20.1	0.9	4.4	3
92	46.1	4.5	9.9	3	15.4	2.6	16.8	3	43.4	6.8	15.6	3
93	8.9	3.0	33.2	3	8.0	1.6	19.9	3	16.5	5.7	34.3	3
94	2.3	0.3	11.6	3	3.8	1.7	44.9	3	5.1	0.7	14.5	3
95	2.4	0.2	6.5	3	2.7	0.1	4.4	3	2.0	0.3	16.9	3
96	35.4	6.2	17.4	3	33.9	2.6	7.7	3	42.1	10.8	25.7	3
97	53.0	5.0	9.5	3	52.7	2.3	4.3	3	55.0	4.0	7.2	3
98	0.0	0.0	.	3	0.0	0.0	.	3	0.0	0.0	.	3
99	2.8	0.3	10.0	3	2.7	0.5	20.2	3	1.9	0.2	8.3	3
100	5.3	4.0	75.5	3	11.1	3.3	29.8	3	9.2	1.2	12.9	3
101	33.9	0.6	1.7	3	39.6	12.4	31.3	3	18.4	4.1	22.4	3
102	81.6	62.3	76.4	3	48.4	9.1	18.8	3	90.9	16.0	17.5	3
103	2.5	0.9	35.9	3	1.8	0.2	11.3	3	2.0	0.2	12.7	3
104	39.7	2.8	7.1	3	41.6	6.2	14.8	3	35.5	11.3	32.0	3
105	2.6	0.2	8.3	3	2.8	1.0	36.3	3	2.3	0.2	8.4	3

Table 3.3.6 Standard deviation (std) and coefficient of variation (cv) from all available tests results (Q=qualified and NQ=non-qualified) per laboratory (n = number of tests that was used for the calculations)

	laboratory																	
	Beiersdorf						Harlan						IIVS					
	Q			Q+NQ			Q			Q+NQ			Q			Q+NQ		
Chemical	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n
1	1.8	2.6	3	1.8	2.6	3	4.0	6.0	3	4.0	6.0	3	6.3	9.2	3	6.3	9.2	3
2	2.8	3.5	3	2.8	3.5	3	2.8	3.5	3	2.8	3.5	3	2.6	3.1	3	2.6	3.1	3
3	4.8	7.8	3	4.8	7.8	3	0.7	1.9	3	0.7	1.9	3	1.9	3.9	3	1.9	3.9	3
4	5.8	5.3	3	5.8	5.3	3	3.2	5.3	3	3.2	5.3	3	4.1	4.3	3	4.1	4.3	3
5	7.5	9.3	3	7.5	9.3	3	9.2	19.9	3	9.2	19.9	3	11.0	17.6	3	11.0	17.6	3
6	5.0	5.9	3	5.0	5.9	3	7.3	9.6	3	7.3	9.6	3	4.4	5.3	3	4.4	5.3	3
7	3.8	9.9	3	3.8	9.9	3	3.3	9.5	3	3.3	9.5	3	5.9	15.2	3	5.9	15.2	3
8	2.9	2.8	3	2.9	2.8	3	3.0	3.2	3	3.0	3.2	3	3.1	3.2	3	3.1	3.2	3
9	3.3	3.3	3	3.3	3.3	3	7.1	7.9	3	7.1	7.9	3	4.0	3.9	3	4.0	3.9	3
10	2.1	6.4	3	2.1	6.4	3	2.4	19.5	3	2.4	19.5	3	4.1	21.5	3	15.3	57.5	4

	laboratory																	
	Beiersdorf						Harlan						IIVS					
	Q			Q+NQ			Q			Q+NQ			Q			Q+NQ		
Chemical	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n
11	1.3	4.6	3	1.3	4.6	3	2.4	12.9	3	2.4	12.9	3	2.4	7.7	3	2.4	7.7	3
12	1.4	1.6	3	1.4	1.6	3	2.6	2.7	3	2.6	2.7	3	2.0	2.1	3	2.0	2.1	3
13	11.0	10.9	3	11.0	10.9	3	6.4	7.0	3	6.4	7.0	3	2.2	2.6	3	2.2	2.6	3
14	3.7	3.7	3	3.7	3.7	3	6.3	6.4	3	6.3	6.4	3	1.1	1.2	3	1.1	1.2	3
15	6.2	6.1	3	6.2	6.1	3	7.3	7.2	3	7.3	7.2	3	4.6	4.7	3	4.6	4.7	3
16	5.4	5.2	3	5.4	5.2	3	5.2	5.2	3	5.2	5.2	3	5.1	5.0	3	5.1	5.0	3
17	5.3	5.5	3	5.3	5.5	3	9.0	9.3	3	9.0	9.3	3	1.4	1.4	3	1.4	1.4	3
18	23.9	24.6	3	23.9	24.6	3	5.2	5.4	3	5.2	5.4	3	0.6	0.6	3	0.6	0.6	3
19	3.1	2.8	3	3.1	2.8	3	3.9	3.6	3	3.9	3.6	3	1.8	1.8	3	1.8	1.8	3
20	13.4	29.1	3	13.4	29.1	3	9.5	101.4	3	9.5	101.4	3	7.5	18.3	3	9.4	25.1	4
21	0.2	0.2	3	0.2	0.2	3	5.1	7.1	3	5.1	7.1	3	2.5	3.0	3	2.5	3.0	3
22	6.1	13.5	3	6.1	13.5	3	6.1	30.6	3	6.1	30.6	3	1.8	4.7	3	1.8	4.7	3
23	3.4	8.1	3	3.4	8.1	3	9.0	60.5	3	9.0	60.5	3	5.5	43.9	3	5.5	43.9	3
24	2.5	5.4	3	2.5	5.4	3	4.5	19.7	3	4.5	19.7	3	11.4	28.7	3	11.4	28.7	3
25	3.2	3.1	3	3.2	3.1	3	2.3	2.2	3	2.3	2.2	3	6.3	6.2	3	6.3	6.2	3
26	1.8	8.5	3	1.8	8.5	3	5.1	14.2	3	5.1	14.2	3	2.2	6.5	3	2.4	7.0	4
28	2.2	2.2	3	2.2	2.2	3	2.2	2.4	3	2.2	2.4	3	6.2	5.8	3	6.2	5.8	3
29	4.5	5.1	3	4.1	4.7	4	27.3	32.5	3	27.3	32.5	3	2.3	2.2	3	2.3	2.2	3
30	8.3	17.6	3	8.3	17.6	3	10.4	42.0	3	10.4	42.0	3	9.2	15.7	3	9.2	15.7	3
31	14.4	18.4	3	11.9	15.5	4	11.0	12.2	3	11.0	12.2	3	3.4	3.4	3	3.4	3.4	3
32	0.5	132.4	3	0.5	132.4	3	0.2	15.6	3	0.2	15.6	3	0.3	12.8	3	0.3	12.8	3
33	.	.	.	.	.	.	4.0	9.1	3	4.0	9.1	3	3.4	3.9	3	43.6	66.8	4
34	3.0	2.7	3	3.0	2.7	3	13.9	21.0	3	13.9	21.0	3	13.1	13.9	3	11.3	12.3	5
35	2.5	3.4	3	2.5	3.4	3	7.5	10.8	3	7.5	10.8	3	2.6	2.6	3	2.6	2.6	3
36	4.1	3.8	3	4.1	3.8	3	7.6	7.9	3	7.6	7.9	3	3.0	2.7	3	3.0	2.7	3
37	2.9	3.7	3	8.1	10.9	4	6.0	8.2	3	6.0	8.2	3	4.3	5.3	3	4.3	5.3	3
38	10.3	9.6	3	10.3	9.6	3	9.0	8.8	3	9.0	8.8	3	3.8	3.6	3	3.8	3.6	3
39	9.6	9.1	3	9.6	9.1	3	13.2	13.0	3	13.2	13.0	3	1.6	1.6	3	1.6	1.6	3
40	6.7	11.8	3	6.7	11.8	3	8.7	13.8	3	8.8	14.5	4	1.5	2.4	3	1.5	2.4	3
41	5.7	5.9	3	5.7	5.9	3	6.2	6.8	3	6.2	6.8	3	4.3	4.4	3	4.3	4.4	3
42	13.8	19.9	3	13.8	19.9	3	6.3	10.5	3	6.3	10.5	3	7.8	9.8	3	7.8	9.8	3
43	9.1	8.9	3	7.6	7.4	4	36.0	28.4	3	36.0	28.4	3	1.8	1.8	3	1.8	1.8	3
44	3.8	3.8	3	3.7	3.6	4	4.6	4.6	3	4.6	4.6	3	4.4	4.5	3	4.4	4.5	3
45	8.7	7.9	3	8.7	7.9	3	8.5	7.9	3	8.5	7.9	3	2.2	2.2	3	2.2	2.2	3
46	2.3	3.2	3	6.4	9.6	4	10.7	15.2	3	10.7	15.2	3	3.7	6.1	3	3.7	6.1	3
47	0.3	7.0	3	0.3	7.0	3	0.8	26.8	3	0.8	26.8	3	0.3	11.2	3	0.3	11.2	3
48	0.5	15.2	3	0.5	15.2	3	0.3	10.4	3	0.3	10.4	3	0.2	6.6	3	0.2	6.6	3
49	0.0	.	3	0.0	.	3	4.2	59.4	3	3.4	50.0	4	2.2	15.4	3	2.2	15.4	3
50	3.5	4.0	3	3.2	3.6	4	1.3	1.3	3	1.3	1.3	3	2.4	2.5	3	2.4	2.5	3
51	5.1	5.2	3	5.1	5.2	3	7.7	8.3	3	7.7	8.3	3	5.4	5.4	3	5.4	5.4	3
52	15.5	13.7	3	15.5	13.7	3	7.3	7.2	3	7.3	7.2	3	5.3	5.3	3	5.3	5.3	3
53	13.2	12.5	3	13.2	12.5	3	10.2	9.1	3	10.2	9.1	3	2.9	2.8	3	2.9	2.8	3
54	1.9	3.9	3	1.9	3.9	3	4.1	19.9	3	4.1	19.9	3	10.9	26.3	3	10.9	26.3	3
55	0.1	3.9	3	0.1	3.9	3	0.4	18.6	3	0.4	18.6	3	0.1	2.7	3	0.1	2.7	3
56	7.0	13.0	3	7.0	13.0	3	3.5	14.1	3	3.5	14.1	3	9.2	24.7	3	9.2	24.7	3
57	2.9	13.5	3	2.9	13.5	3	1.3	21.2	3	1.3	21.2	3	4.5	25.3	3	4.5	25.3	3
58	0.4	1.6	3	0.4	1.6	3	2.6	67.6	3	2.6	67.6	3	0.7	5.3	3	0.7	5.3	3
59	8.1	11.6	3	8.1	11.6	3	6.1	14.0	3	6.1	14.0	3	6.7	13.2	3	6.7	13.2	3
60	4.3	27.7	3	4.3	27.7	3	4.8	44.9	3	4.8	44.9	3	6.5	31.7	3	6.5	31.7	3
61	4.0	22.1	3	4.0	22.1	3	4.0	31.5	3	4.0	31.5	3	2.9	16.3	3	2.9	16.3	3
62	6.8	6.2	3	6.8	6.2	3	2.1	2.1	3	2.1	2.1	3	6.4	6.2	3	6.4	6.2	3
63	6.8	20.0	3	5.6	16.4	4	7.9	16.1	3	7.9	16.1	3	5.4	12.2	3	5.4	12.2	3
64	7.1	23.6	3	7.1	23.6	3	10.0	41.6	3	10.0	41.6	3	6.2	19.1	3	6.2	19.1	3
65	0.8	1.7	3	4.1	7.7	4	19.5	66.1	3	19.5	66.1	3	11.1	20.9	3	11.1	20.9	3
66	1.1	15.9	3	1.1	16.6	4	1.2	33.0	3	1.2	33.0	3	2.4	65.0	3	2.4	65.0	3
67	2.5	20.4	3	2.5	20.4	3	0.4	8.9	3	0.4	8.9	3	0.8	5.6	3	0.8	5.6	3
68	1.0	28.6	3	1.0	28.6	3	0.6	17.8	3	0.6	17.8	3	2.4	57.9	3	2.4	57.9	3
69	0.9	6.6	3	0.9	6.6	3	3.2	23.2	3	3.2	23.2	3	0.4	2.9	3	0.4	2.9	3
70	2.7	17.6	3	2.7	17.6	3	1.6	14.7	3	1.6	14.7	3	1.2	8.9	3	1.2	8.9	3
71	0.8	14.2	3	0.8	14.2	3	2.1	32.6	3	2.1	32.6	3	0.9	11.3	3	0.9	11.3	3
72	1.5	38.8	3	1.5	38.8	3	1.0	22.4	3	1.0	22.4	3	1.3	33.7	3	1.3	33.7	3
73	8.5	10.1	3	8.5	10.1	3	5.0	5.9	3	5.0	5.9	3	12.3	12.7	3	12.3	12.7	3
74	11.8	15.6	3	9.7	12.9	4	3.6	4.7	3	3.6	4.7	3	6.5	7.1	3	6.5	7.1	3

	laboratory																	
	Beiersdorf						Harlan						IIVS					
	Q			Q+NQ			Q			Q+NQ			Q			Q+NQ		
Chemical	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n
75	4.7	5.8	3	25.1	40.5	5	8.7	118.3	3	8.7	118.3	3	0.7	13.5	3	0.7	13.5	3
76	0.8	1.4	3	0.8	1.4	3	14.0	29.2	3	14.0	29.2	3	1.3	4.6	3	1.3	4.6	3
77	5.9	6.1	3	5.9	6.1	3	18.1	24.5	3	18.1	24.5	3	4.6	4.4	3	4.6	4.4	3
78	4.9	5.9	3	4.1	4.9	4	1.9	3.0	3	1.9	3.0	3	1.0	1.1	3	1.0	1.1	3
79	0.5	20.7	3	0.5	20.7	3	0.3	13.5	3	0.3	13.5	3	0.5	16.4	3	0.5	16.4	3
80	0.8	4.6	3	0.8	4.6	3	7.7	107.0	3	7.7	107.0	3	2.6	32.3	3	2.6	32.3	3
81	0.7	26.8	3	0.7	26.8	3	0.2	5.3	3	0.2	5.3	3	1.3	29.8	3	1.3	29.8	3
82	2.0	52.4	3	2.0	52.4	3	0.3	17.7	3	0.3	17.7	3	2.2	43.8	3	2.2	43.8	3
83	0.4	7.7	3	0.4	7.7	3	2.1	39.1	3	2.1	39.1	3	1.4	25.8	3	1.4	25.8	3
84	8.3	61.5	3	8.3	61.5	3	1.6	26.1	3	1.6	26.1	3	5.2	34.0	3	5.2	34.0	3
85	5.7	28.3	3	5.7	28.3	3	3.5	38.2	3	3.5	38.2	3	2.5	16.6	3	2.5	16.6	3
86	3.3	13.6	3	3.3	13.6	3	10.2	34.0	3	10.2	34.0	3	6.8	24.0	3	6.8	24.0	3
87	4.2	14.6	3	4.2	14.6	3	4.0	21.3	3	4.0	21.3	3	6.7	27.8	3	6.7	27.8	3
88	1.5	26.5	3	1.5	26.5	3	1.5	24.0	3	1.5	24.0	3	1.9	39.3	3	1.9	39.3	3
89	2.0	21.2	3	2.0	21.2	3	1.2	17.3	3	1.2	17.3	3	1.9	18.2	3	1.9	18.2	3
90	7.8	24.8	3	7.8	24.8	3	9.2	37.9	3	9.2	37.9	3	2.5	7.4	3	2.1	6.1	4
91	9.8	31.4	3	9.8	31.4	3	4.0	24.0	3	4.0	24.0	3	0.9	4.4	3	0.9	4.4	3
92	4.5	9.9	3	4.5	9.9	3	2.6	16.8	3	2.6	16.8	3	6.8	15.6	3	6.8	15.6	3
93	3.0	33.2	3	3.0	33.2	3	1.6	19.9	3	1.6	19.9	3	5.7	34.3	3	5.7	34.3	3
94	0.3	11.6	3	0.3	11.6	3	1.7	44.9	3	1.7	44.9	3	0.7	14.5	3	0.7	14.5	3
95	0.2	6.5	3	0.2	6.5	3	0.1	4.4	3	0.1	4.4	3	0.3	16.9	3	0.3	16.9	3
96	6.2	17.4	3	6.2	17.4	3	2.6	7.7	3	2.6	7.7	3	10.8	25.7	3	10.8	25.7	3
97	5.0	9.5	3	5.0	9.5	3	2.3	4.3	3	2.3	4.3	3	4.0	7.2	3	4.0	7.2	3
98	0.0	.	3	0.0	.	3	0.0	.	3	0.0	.	4	0.0	.	3	0.0	.	3
99	0.3	10.0	3	0.3	10.0	3	0.5	20.2	3	0.5	20.2	3	0.2	8.3	3	0.2	8.3	3
100	4.0	75.5	3	4.0	75.5	3	3.3	29.8	3	3.3	29.8	3	1.2	12.9	3	1.2	12.9	3
101	0.6	1.7	3	0.6	1.7	3	12.4	31.3	3	12.4	31.3	3	4.1	22.4	3	4.1	22.4	3
102	62.3	76.4	3	62.3	76.4	3	9.1	18.8	3	9.1	18.8	3	16.0	17.5	3	16.0	17.5	3
103	0.9	35.9	3	0.9	35.9	3	0.2	11.3	3	0.2	11.3	3	0.2	12.7	3	0.2	12.7	3
104	2.8	7.1	3	4.0	10.6	4	6.2	14.8	3	6.2	14.8	3	11.3	32.0	3	19.0	43.4	4
105	0.2	8.3	3	0.2	8.3	3	1.0	36.3	3	1.0	36.3	3	0.2	8.4	3	0.2	8.4	3
Overall																		
Mean	5.0			5.3			5.5			5.5			3.9			4.5		
SD	7.0			7.2			5.5			5.5			3.3			5.4		

3.3.2 Between-laboratory variability

The arithmetic mean value of viability over the different qualified tests per laboratory was used to calculate the inter-laboratory variability. For calculation on the between-laboratory variability, only those chemicals are included for which at least one qualified test per laboratory was available. Table 3.3.7 gives the mean standard deviation as well as the standard deviation of the standard deviations

Table 3.3.7 Mean standard deviation and standard deviation per chemical considering the standard deviations as reported for each participating laboratory (Q=qualified and NQ=non-qualified).

	Q		**Q+NQ**	
Chemical	**mean SD**	**std SD**	**mean SD**	**std SD**
1	4.0	2.2	4.0	2.2
2	2.7	0.1	2.7	0.1
3	2.5	2.1	2.5	2.1
4	4.4	1.3	4.4	1.3
5	9.2	1.8	9.2	1.8
6	5.6	1.5	5.6	1.5
7	4.3	1.4	4.3	1.4
8	3.0	0.1	3.0	0.1
9	4.8	2	4.8	2.0
10	2.9	1.1	6.6	7.5
11	2.1	0.6	2.1	0.6
12	2.0	0.6	2.0	0.6

	Q		Q+NQ	
Chemical	**mean SD**	**std SD**	**mean SD**	**std SD**
13	6.5	4.4	6.5	4.4
14	3.7	2.6	3.7	2.6
15	6.0	1.4	6.0	1.4
16	5.2	0.2	5.2	0.2
17	5.2	3.8	5.2	3.8
18	9.9	12.3	9.9	12.3
19	2.9	1.1	2.9	1.1
20	10.1	3	10.8	2.3
21	2.6	2.5	2.6	2.5
22	4.7	2.5	4.7	2.5
23	6.0	2.8	6.0	2.8
24	6.1	4.7	6.1	4.7
25	3.9	2.1	3.9	2.1
26	3.0	1.8	3.1	1.7
28	3.5	2.3	3.5	2.3
29	11.4	13.9	11.2	14.0
30	9.3	1.1	9.3	1.1
31	9.6	5.6	8.8	4.7
32	0.3	0.2	0.3	0.2
34	10.0	6.1	9.4	5.7
35	4.2	2.9	4.2	2.9
36	4.9	2.4	4.9	2.4
37	4.4	1.5	6.2	1.9
38	7.7	3.5	7.7	3.5
39	8.1	5.9	8.1	5.9
40	5.6	3.7	5.7	3.7
41	5.4	1	5.4	1.0
42	9.3	4	9.3	4.0
43	15.7	18	15.1	18.3
44	4.3	0.4	4.2	0.5
45	6.4	3.7	6.4	3.7
46	5.6	4.5	7.0	3.5
47	0.5	0.3	0.5	0.3
48	0.3	0.2	0.3	0.2
49	2.1	2.1	1.9	1.7
50	2.4	1.1	2.3	0.9
51	6.1	1.4	6.1	1.4
52	9.4	5.4	9.4	5.4
53	8.8	5.3	8.8	5.3
54	5.6	4.7	5.6	4.7
55	0.2	0.2	0.2	0.2
56	6.6	2.9	6.6	2.9
57	2.9	1.6	2.9	1.6
58	1.2	1.2	1.2	1.2
59	6.9	1	6.9	1.0
60	5.2	1.2	5.2	1.2
61	3.6	0.6	3.6	0.6
62	5.1	2.6	5.1	2.6
63	6.7	1.3	6.3	1.4
64	7.7	2	7.7	2.0
65	10.5	9.3	11.6	7.7
66	1.6	0.8	1.6	0.8
67	1.2	1.1	1.2	1.1
68	1.3	1	1.3	1.0
69	1.5	1.5	1.5	1.5
70	1.8	0.8	1.8	0.8
71	1.3	0.7	1.3	0.7
72	1.3	0.3	1.3	0.3
73	8.6	3.7	8.6	3.7
74	7.3	4.1	6.6	3.0
75	4.7	4	11.5	12.5
76	5.3	7.5	5.3	7.5
77	9.5	7.4	9.5	7.4

	Q		Q+NQ	
Chemical	**mean SD**	**std SD**	**mean SD**	**std SD**
78	2.6	2.1	2.3	1.6
79	0.5	0.1	0.5	0.1
80	3.7	3.6	3.7	3.6
81	0.7	0.5	0.7	0.5
82	1.5	1.0	1.5	1.0
83	1.3	0.8	1.3	0.8
84	5.0	3.4	5.0	3.4
85	3.9	1.7	3.9	1.7
86	6.8	3.4	6.8	3.4
87	5.0	1.5	5.0	1.5
88	1.6	0.2	1.6	0.2
89	1.7	0.4	1.7	0.4
90	6.5	3.5	6.3	3.8
91	4.9	4.5	4.9	4.5
92	4.6	2.1	4.6	2.1
93	3.4	2.1	3.4	2.1
94	0.9	0.7	0.9	0.7
95	0.2	0.1	0.2	0.1
96	6.5	4.1	6.5	4.1
97	3.8	1.4	3.8	1.4
98	0.0	0.0	0.0	0.0
99	0.3	0.2	0.3	0.2
100	2.8	1.5	2.8	1.5
101	5.7	6.1	5.7	6.1
102	29.1	28.9	29.1	28.9
103	0.4	0.4	0.4	0.4
104	6.8	4.3	9.7	8.1
105	0.5	0.5	0.5	0.5
Overall				
Mean	4.8		5.0	
SD	3.9		4.0	

Concordance of classification between laboratories was calculated based on qualified test from test chemicals for which at least one qualified test was available. In Table 3.3.8 the concordance between laboratories is given.

Table 3.3.8 Concordance between laboratories

BLV concordant	No.	Fraction(%)
NO	9	8.7
YES	94	91.3

Additional descriptive statistics can identify possible reasons for non-concordant results. These are presented in Table 3.3.9. For each non-concordant result the state (liquid/solid), the GHS classification, whether it is colouring or MTTreducer and the test results are given.

Table 3.3.9 Additional descriptive statistics on non-concordant results between laboratories

Chemical	name	LS	coloring	MTT	GHS classification	Beiersdorf	Harlan	IIVS
3	2-ethoxyethyl methacrylate	Liquid	No	No	no cat	60.9	38.0	49.3
5	4-(methylthio)-benzaldehyde	Liquid	No	Yes	no cat	80.7	46.1	62.5
30	1,1-dimethylguanidine sulphate	Solid	No	No	no cat	.	24.8	58.8
30	1,1-dimethylguanidine sulphate	Solid	No	Yes	no cat	47.1	.	.
56	isopropyl acetoacetate	Liquid	No	Yes	cat 2B	53.7	24.9	37.3
59	ethyl-2-methyl acetoacetate	Liquid	No	No	cat 2B	69.5	43.3	51.0
65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	Solid	No	No	cat 2B	51.4	29.4	53.1

75	sodium benzoate INCI name: SODIUM BENZOATE	Solid	No	No	cat 2A	79.9	7.3	5.1
76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	Solid	No	No	cat 2A	53.9	48.1	27.3
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	Solid	No	No	cat 1	81.6	48.4	90.9

The concordance for the set of chemicals tested during validation obtained by the different participating laboratories should ideally be equal or higher than 80%. As summarized in Table 3.3.10, this criteria was met.

Table 3.3.10 Statement whether the test method has fulfilled the performance criteria concerning the concordance of classifications between laboratories.

Fraction (%)	Statement: criteria is
91.3	fulfilled

A two-way ANOVA was applied to test for differences in mean viabilities between laboratories and chemicals. Due to higher variation for higher mean viabilities, data were analysed after log-transformation. Since it is not possible to take the LOG of zero, four observations were excluded for analysis (all three means for *4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE* (chemical 98) and the mean for *propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN* (chemical 49) from Beiersdorf). After log-transformation, three outlying observations (*2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE* (chemical 32) and *sodium benzoate INCI name: SODIUM BENZOATE* (chemical 75) from Beiersdorf; *sodium benzoate INCI name: SODIUM BENZOATE* (chemical 75) from IIVS) were removed before analysis in order to fulfil the ANOVA-requirements. An outlier was defined as an observation with a residual > 3* residual error. The results from the two-way ANOVA are presented in Table 3.3.11. The null hypothesis of no difference was rejected at the 0.01 level of probability (α=0.01).

Table 3.3.11 Two-way ANOVA with factors laboratory and chemical, applied to the arithmetic mean value of the included test results (based on log-transformation)

Effect	NumDF	DenDF	FValue	pvalue
laboratory	2	198	24.66	<.0001
chemical	101	198	69.33	<.0001

Both factors were statistically significant. A Tukey post-hoc test was performed to test the differences between the three laboratories. The results of this post-hoc test are given in Table 3.3.12. Significant differences were found between Beiersdorf and Harlan (p<0.0001) and between Harlan and IIVS (p<0.0001). The mean viability over all chemicals was statistically significant lower for Harlan compared to Beiersdorf and IIVS.

Table 3.3.12 Results of the Tukey post-hoc test on differences between laboratories (after log-transformation)

laboratory	vs	Estimate	Standard Error	DF	Tukey-corrected p-value
Beiersdorf	Harlan	0.2369	0.03684	198	<.0001
Beiersdorf	IIVS	0.03057	0.03684	198	0.6850
Harlan	IIVS	-0.2063	0.03656	198	<.0001

The between-laboratory variability is described by the concordance of classifications between laboratories. Correlations coefficients between viability measurements give also information on this variability. Since the Pearson correlation coefficient is sensitive for outlying test results and high leverages, both the Pearson and the Spearman correlation coefficients (using ranks instead of the original test results) were calculated. These coefficients are presented in Table 3.3.13.

Table 3.3.13 Pearson and Spearman correlation coefficients between test results of the three participating laboratories.

laboratories	Pearson	Spearman
Beiersdorf-Harlan	0.936	0.942
Beiersdorf-IIVS	0.957	0.941
Harlan-IIVS	0.957	0.955
Mean correlation	0.950	0.946

3.3.3 Predictive capacity (accuracy)

All qualified tests for each test chemical was used to calculate the predictive capacity values. The calculations were based on the individual predictions of each qualified test in each laboratory.

For each statistic of the prediction model, an acceptance rate was set by the VMG. These criteria are presented in Table 3.3.14. The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria are fulfilled are presented in Table 3.3.15 (for solids and liquids, separately) and Table 3.3.16 (liquids and solids together).

Table 3.3.14 Acceptance criteria for the prediction model

	False Negatives[a] (%)	False Positives[b] (%)	Overall misclassifications[c] (%)
“Definitely acceptable” rates	≤ 10	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	40 < FP ≤ 50	25 < OM ≤ 35
“Definitely unacceptable” rates	> 20	> 50	> 35

[a] equal to (1-Sensitivity), [b] equal to (1-Specificity), [c] equal to (1-Overall accuracy)

Table 3.3.15 The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria for the prediction model are fulfilled, calculated for the protocol for liquids (a) and solids (b), separately.

(a) Liquids

laboratory	Characteristic	No.	Value	95% lower limit	95% upper limit	Statement
Beiersdorf	Accuracy	132/159	0.830	0.763	0.885	definitely acceptable
	Sensitivity	73/78	0.936	0.857	0.979	definitely acceptable
	Specificity	59/81	0.728	0.618	0.821	definitely acceptable
Harlan	Accuracy	130/159	0.818	0.749	0.874	definitely acceptable
	Sensitivity	78/78	1.000	0.954	1.000	definitely acceptable
	Specificity	52/81	0.642	0.528	0.746	definitely acceptable
IIVS	Accuracy	130/159	0.818	0.749	0.874	definitely acceptable
	Sensitivity	74/78	0.949	0.874	0.986	definitely acceptable
	Specificity	56/81	0.691	0.579	0.789	definitely acceptable
Total	Accuracy	392/477	0.822	0.784	0.855	definitely acceptable
	Sensitivity	225/234	0.962	0.928	0.982	definitely acceptable
	Specificity	167/243	0.687	0.625	0.745	definitely acceptable

(b) Solids

laboratory	Characteristic	No.	Value	95% lower limit	95% upper limit	Statement
Beiersdorf	Accuracy	107/150	0.713	0.634	0.784	Further evaluation
	Sensitivity	50/78	0.641	0.524	0.747	definitely unacceptable
	Specificity	57/72	0.792	0.680	0.878	definitely acceptable
Harlan	Accuracy	109/153	0.712	0.634	0.783	Further evaluation
	Sensitivity	52/78	0.667	0.551	0.769	definitely unacceptable
	Specificity	57/75	0.760	0.647	0.851	definitely acceptable
IIVS	Accuracy	117/153	0.765	0.689	0.829	definitely acceptable
	Sensitivity	54/78	0.692	0.578	0.792	definitely unacceptable
	Specificity	63/75	0.840	0.737	0.914	definitely acceptable
Total	Accuracy	333/456	0.730	0.687	0.770	Further evaluation
	Sensitivity	156/234	0.667	0.602	0.727	definitely unacceptable
	Specificity	177/222	0.797	0.738	0.848	definitely acceptable

Table 3.3.16 The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria for the prediction model are fulfilled

laboratory	Characteristic	No.	Value	95% lower limit	95% upper limit	Statement
Beiersdorf	Accuracy	239/309	0.773	0.723	0.819	definitely acceptable
	Sensitivity	123/156	0.788	0.716	0.850	definitely unacceptable
	Specificity	116/153	0.758	0.682	0.824	definitely acceptable
Harlan	Accuracy	239/312	0.766	0.715	0.812	definitely acceptable
	Sensitivity	130/156	0.833	0.765	0.888	further evaluation
	Specificity	109/156	0.699	0.620	0.769	definitely acceptable
IIVS	Accuracy	247/312	0.792	0.742	0.835	definitely acceptable
	Sensitivity	128/156	0.821	0.751	0.877	further evaluation
	Specificity	119/156	0.763	0.688	0.827	definitely acceptable
Total	Accuracy	725/933	0.777	0.749	0.803	definitely acceptable
	Sensitivity	381/468	0.814	0.776	0.848	further evaluation
	Specificity	344/465	0.740	0.697	0.779	definitely acceptable

In Table 3.3.17, the prediction for each qualified test result is given for liquids and solids separately, as well as the final classification based on the median of predictions.

Table 3.3.17 Final classification based on the median of all classifications for each chemicals, listed for (a) liquids and (b) solids

(a) Liquids

		Beiersdorf			Harlan			IIVS			Final classification based on median	Mispredicted tests/Total
Chemical	GHS classification	1	2	3	1	2	3	1	2	3		
1	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
2	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
3	no cat	NI	NI	NI	I	I	I	NI	I	I	I	5/9
4	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
5	no cat	NI	NI	NI	NI	I	I	NI	NI	NI	NI	2/9
6	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
7	no cat	I	I	I	I	I	I	I	I	I	I	9/9
8	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
9	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
10	no cat	I	I	I	I	I	I	I	I	I	I	9/9
11	no cat	I	I	I	I	I	I	I	I	I	I	9/9
12	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
13	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
14	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
15	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
16	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
17	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
18	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
19	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
20	no cat	I	NI	I	I	I	I	I	I	I	I	8/9
21	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
22	no cat	NI	I	I	I	I	I	I	I	I	I	8/9
23	no cat	I	I	I	I	I	I	I	I	I	I	9/9
24	no cat	I	I	I	I	I	I	NI	I	I	I	8/9
25	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
26	no cat	I	I	I	I	I	I	I	I	I	I	9/9
37	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
54	cat 2B	I	I	I	I	I	I	NI	I	I	I	1/9
55	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
56	cat 2B	I	NI	NI	I	I	I	I	I	I	I	2/9
57	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
58	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
59	cat 2B	NI	NI	NI	I	I	I	NI	NI	I	NI	5/9
60	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
67	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
68	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
69	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
70	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
71	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
72	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
80	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
81	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
82	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
83	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
84	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
85	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
86	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
87	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
88	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
89	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

		Beiersdorf			Harlan			IIVS			Final classification based on median	Mispredicted tests/Total
Chemical	GHS classification	1	2	3	1	2	3	1	2	3		
90	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
91	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
92	cat 1	I	I	I	I	I	I	I	I	NI	I	1/9

(b) Solids

		Beiersdorf			Harlan			IIVS			Final classification based on median	Mispredicted tests/Total
Chemical	GHS classification	1	2	3	1	2	3	1	2	3		
28	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
29	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
30	no cat	NI	I	I	I	I	I	NI	NI	NI	I	5/9
31	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
32	no cat	I	I	I	I	I	I	I	I	I	I	9/9
33	no cat	.	.	.	I	I	I	NI	NI	NI	undecided	3/6
34	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
35	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
36	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
38	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
39	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
40	no cat	I	NI	NI	NI	NI	NI	NI	NI	NI	NI	1/9
41	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
42	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
43	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
44	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
45	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
46	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
47	no cat	I	I	I	I	I	I	I	I	I	I	9/9
48	no cat	I	I	I	I	I	I	I	I	I	I	9/9
49	no cat	I	I	I	I	I	I	I	I	I	I	9/9
50	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
51	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
52	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
53	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
61	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
62	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
63	cat 2B	I	I	I	NI	I	NI	I	I	I	I	2/9
64	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
65	cat 2B	NI	NI	NI	I	I	NI	NI	I	NI	NI	6/9
66	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
73	cat 2A (ICCVAM: cat 2B)	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
74	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
75	cat 2A	NI	NI	NI	I	I	I	I	I	I	I	3/9
76	cat 2A	NI	NI	NI	NI	I	NI	I	I	I	NI	5/9
77	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
78	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
79	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
93	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
94	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
95	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
96	cat 1	I	I	I	I	I	I	I	I	NI	I	1/9
97	cat 1	NI	I	NI	NI	NI	NI	NI	NI	NI	NI	8/9
98	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

		Beiersdorf			Harlan			IIVS			Final classification based on median	Mispredicted tests/Total
Chemical	GHS classification	1	2	3	1	2	3	1	2	3		
99	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
100	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
101	cat 1	I	I	I	I	NI	I	I	I	I	I	1/9
102	cat 1	I	NI	NI	I	NI	NI	NI	NI	NI	NI	7/9
103	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
104	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
105	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

3.4 Reproducibility and accuracy using a 60% cut-off

In this section, a 60% cut-off was applied to determine the irritancy of the chemical. If the viability is above 60%, the chemical is considered to be non-irritant. If the viability is 60% or below, the chemical is considered to be irritant. Statistics which are independent of the cut-off value, like correlation coefficients and ANOVA results, are reported in section 3.3 for the 50% cut-off and are not repeated in this section.

3.4.1 Within-laboratory variability

For each laboratory, concordance of classification was calculated based on qualified test from test chemicals for which at least two qualified tests were available. In Table 3.4.1 the concordance within each laboratory as well as in total is given.

Table 3.4.1 Concordance within laboratories and total

laboratory	WLV concordant	No.	Fraction(%)
Beiersdorf	NO	5	4.9
	YES	98	95.1
Harlan	NO	6	5.8
	YES	98	94.2
IIVS	NO	4	3.8
	YES	100	96.2
Total	NO	15	4.8
	YES	296	95.2

Additional descriptive statistics can identify possible reasons for non-concordant results. These are presented in Table 3.4.2. For each non-concordant result the state (liquid/solid), the GHS classification, whether it is colouring or MTTreducer and the test results are given.

Table 3.4.2 Additional descriptive statistics on non-concordant results within laboratories

							Test		
laboratory	chemical	name	LS	colouring	MTT	GHS classification	1	2	3
Beiersdorf	3	2-ethoxyethyl methacrylate	liquid	No	No	no cat	55.4	63.0	64.2
Beiersdorf	40	acrylamidopropyltrimonium chloride/acrylamide copolymer	solid	No	No	no cat	49.4	59.5	62.1
Beiersdorf	42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL	solid	No	Yes	no cat	64.7	85.0	58.7

		PHOSPHATE							
Beiersdorf	56	isopropyl acetoacetate	liquid	No	Yes	cat 2B	46.4	54.5	60.3
Beiersdorf	102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	solid	No	No	cat 1	10.1	110.2	124.3
Harlan	4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	liquid	No	Yes	no cat	60.8	57.9	64.3
Harlan	29	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE	solid	No	No	no cat	57.4	112.0	83.0
Harlan	34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	solid	Yes	Yes	no cat	81.4	54.1	63.2
Harlan	40	acrylamidopropyltrimonium chloride/acrylamide copolymer	solid	No	No	no cat	72.9	56.2	60.2
Harlan	42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	solid	No	Yes	no cat	53.4	66.0	60.0
Harlan	46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	solid	No	No	no cat	73.1	58.9	80.0
IIVS	5	4-(methylthio)-benzaldehyde	liquid	No	Yes	no cat	71.8	65.4	50.3
IIVS	30	1,1-dimethylguanidine sulphate	solid	No	No	no cat	55.4	51.8	69.2
IIVS	46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	solid	No	No	no cat	65.2	60.8	57.8
IIVS	65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	solid	No	No	cat 2B	63.8	41.6	53.9

The concordance of classifications (irritant/non-irritant) for the set of chemicals tested during validation obtained in different, independent runs within a single laboratory should ideally be equal or higher than 85% for all participating laboratories. As summarized in Table 3.4.3, this criteria was met for each laboratory as well as in total.

Table 3.4.3 Statement whether the test method has fulfilled the performance criteria concerning the concordance of classifications within one laboratory.

laboratory	Fraction(%)	Statement: criteria is
Beiersdorf	95.1	fulfilled
Harlan	94.2	fulfilled
IIVS	96.2	fulfilled
Total	95.2	fulfilled

3.4.2 Between-laboratory variability

Concordance of classification between laboratories was calculated based on qualified test from test chemicals for which at least one qualified test was available for each laboratory. In Table 3.4.4 the concordance between laboratories is given.

Table 3.4.4 Concordance between laboratories

BLV concordant	No.	Fraction(%)
NO	7	6.8
YES	96	93.2

Additional descriptive statistics can identify possible reasons for non-concordant results. These are presented in Table 3.4.5. For each non-concordant result the state (liquid/solid), the GHS classification, whether it is colouring or MTT-reducer and the test results are given.

Table 3.4.5 Additional descriptive statistics on non-concordant results between laboratories

Chemical	name	LS	colouring	MTT	GHS classification	Beiersdorf	Harlan	IIVS
3	2-ethoxyethyl methacrylate	liquid	No	No	no cat	60.9	38.0	49.3
5	4-(methylthio)-benzaldehyde	liquid	No	Yes	no cat	80.7	46.1	62.5
40	acrylamidopropyltrimonium chloride/acrylamide copolymer	solid	No	No	no cat	57.0	63.1	61.8
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	solid	No	Yes	no cat	69.5	59.8	79.2
59	ethyl-2-methyl acetoacetate	liquid	No	No	cat 2B	69.5	43.3	51.0
75	sodium benzoate INCI name: SODIUM BENZOATE	solid	No	No	cat 2A	79.9	7.3	5.1
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	solid	No	No	cat 1	81.6	48.4	90.9

The concordance for the set of chemicals tested during validation obtained by the different participating laboratories should ideally be equal or higher than 80%. As summarized in Table 3.4.6, this criteria was met.

Table 3.4.6 Statement whether the test method has fulfilled the performance criteria concerning the concordance of classifications between laboratories.

Fraction (%)	Statement: criteria is
93.2	fulfilled

3.4.3 Predictive capacity (accuracy)

All qualified tests for each test chemical was used to calculate the predictive capacity values. The calculations were based on the individual predictions of each qualified test in each laboratory.

For each statistic of the prediction model, an acceptance rate was set by the VMG. These criteria are presented in Table 3.3.14. The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria are fulfilled are presented in Table 3.4.7 (for solids and liquids, separately) and Table 3.4.8 (liquids and solids together).

Table 3.4.7 The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria for the prediction model are fulfilled, calculated for the protocol for liquids (a) and solids (b), separately.

(a) Liquids

laboratory	Characteristic	No.	Value	95% lower limit	95% upper limit	Statement
Beiersdorf	Accuracy	130/159	0.818	0.749	0.874	definitely acceptable
	Sensitivity	74/78	0.949	0.874	0.986	definitely acceptable
	Specificity	56/81	0.691	0.579	0.789	definitely acceptable
Harlan	Accuracy	128/159	0.805	0.735	0.864	definitely acceptable
	Sensitivity	78/78	1.000	0.954	1.000	definitely acceptable
	Specificity	50/81	0.617	0.503	0.723	definitely acceptable
IIVS	Accuracy	131/159	0.824	0.756	0.880	definitely acceptable
	Sensitivity	78/78	1.000	0.954	1.000	definitely acceptable
	Specificity	53/81	0.654	0.540	0.757	definitely acceptable
Total	Accuracy	389/477	0.816	0.778	0.849	definitely acceptable
	Sensitivity	230/234	0.983	0.957	0.995	definitely acceptable
	Specificity	159/243	0.654	0.591	0.714	definitely acceptable

(b) Solids

laboratory	Characteristic	No.	Value	95% lower limit	95% upper limit	Statement
Beiersdorf	Accuracy	112/150	0.747	0.669	0.814	further evaluation
	Sensitivity	58/78	0.744	0.632	0.836	definitely unacceptable
	Specificity	54/72	0.750	0.634	0.845	definitely acceptable
Harlan	Accuracy	115/153	0.752	0.675	0.818	definitely acceptable
	Sensitivity	63/78	0.808	0.703	0.888	further evaluation
	Specificity	52/75	0.693	0.576	0.795	definitely acceptable
IIVS	Accuracy	119/153	0.778	0.704	0.841	definitely acceptable
	Sensitivity	59/78	0.756	0.646	0.847	definitely unacceptable
	Specificity	60/75	0.800	0.692	0.884	definitely acceptable
Total	Accuracy	346/456	0.759	0.717	0.797	definitely acceptable
	Sensitivity	180/234	0.769	0.710	0.822	definitely unacceptable
	Specificity	166/222	0.748	0.685	0.803	definitely acceptable

Table 3.4.8 The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria for the prediction model are fulfilled

laboratory	Characteristic	No.	Value	95% lower limit	95% upper limit	Statement
Beiersdorf	Accuracy	242/309	0.783	0.733	0.828	definitely acceptable
	Sensitivity	132/156	0.846	0.780	0.899	further evaluation
	Specificity	110/153	0.719	0.641	0.789	definitely acceptable
Harlan	Accuracy	243/312	0.779	0.729	0.824	definitely acceptable
	Sensitivity	141/156	0.904	0.846	0.945	definitely acceptable
	Specificity	102/156	0.654	0.574	0.728	definitely acceptable
IIVS	Accuracy	250/312	0.801	0.753	0.844	definitely acceptable
	Sensitivity	137/156	0.878	0.816	0.925	further evaluation
	Specificity	113/156	0.724	0.647	0.793	definitely acceptable
Total	Accuracy	735/933	0.788	0.760	0.814	definitely acceptable
	Sensitivity	410/468	0.876	0.843	0.905	further evaluation
	Specificity	325/465	0.699	0.655	0.740	definitely acceptable

In Table 3.4.9, the prediction for each qualified test result is given for liquids and solids separately, as well as the final classification based on the median of predictions

Table 3.4.9. Final classification based on the median of all classifications for each chemicals, listed for (a) liquids and (b) solids

(a) Liquids

		Beiersdorf			Harlan			IIVS			Final classification based on median	Mispredicted tests/Total
Chemical	GHS classification	1	2	3	1	2	3	1	2	3		
1	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
2	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
3	no cat	I	NI	NI	I	I	I	I	I	I	I	7/9
4	no cat	NI	NI	NI	NI	I	NI	NI	NI	NI	NI	1/9
5	no cat	NI	NI	NI	I	I	I	NI	NI	I	NI	4/9
6	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
7	no cat	I	I	I	I	I	I	I	I	I	I	9/9
8	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
9	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
10	no cat	I	I	I	I	I	I	I	I	I	I	9/9
11	no cat	I	I	I	I	I	I	I	I	I	I	9/9
12	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
13	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
14	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
15	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
16	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
17	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
18	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
19	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
20	no cat	I	I	I	I	I	I	I	I	I	I	9/9
21	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
22	no cat	I	I	I	I	I	I	I	I	I	I	9/9
23	no cat	I	I	I	I	I	I	I	I	I	I	9/9
24	no cat	I	I	I	I	I	I	I	I	I	I	9/9
25	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
26	no cat	I	I	I	I	I	I	I	I	I	I	9/9
37	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
54	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
55	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
56	cat 2B	I	I	NI	I	I	I	I	I	I	I	1/9
57	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
58	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
59	cat 2B	NI	NI	NI	I	I	I	I	I	I	I	3/9
60	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
67	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
68	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
69	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
70	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
71	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
72	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
80	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
81	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
82	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
83	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
84	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
85	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
86	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
87	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
88	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
89	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

Chemical	GHS classification	Beiersdorf			Harlan			IIVS			Final classification based on median	Mispredicted tests/Total
		1	2	3	1	2	3	1	2	3		
90	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
91	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
92	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

(b) Solids

Chemical	GHS classification	Beiersdorf			Harlan			IIVS			Final classification based on median	Mispredicted tests/Total
		1	2	3	1	2	3	1	2	3		
28	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
29	no cat	NI	NI	NI	I	NI	NI	NI	NI	NI	NI	1/9
30	no cat	I	I	I	I	I	I	I	I	NI	I	8/9
31	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
32	no cat	I	I	I	I	I	I	I	I	I	I	9/9
33	no cat	.	.	.	I	I	I	NI	NI	NI	0.5	3/6
34	no cat	NI	NI	NI	NI	I	NI	NI	NI	NI	NI	1/9
35	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
36	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
38	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
39	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
40	no cat	I	I	NI	NI	I	NI	NI	NI	NI	NI	3/9
41	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
42	no cat	NI	NI	I	I	NI	NI	NI	NI	NI	NI	2/9
43	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
44	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
45	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
46	no cat	NI	NI	NI	NI	I	NI	NI	NI	I	NI	2/9
47	no cat	I	I	I	I	I	I	I	I	I	I	9/9
48	no cat	I	I	I	I	I	I	I	I	I	I	9/9
49	no cat	I	I	I	I	I	I	I	I	I	I	9/9
50	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
51	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
52	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
53	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
61	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
62	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
63	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
64	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
65	cat 2B	I	I	I	I	I	I	NI	I	I	I	1/9
66	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
73	cat 2A (ICCVAM: cat 2B)	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
74	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
75	cat 2A	NI	NI	NI	I	I	I	I	I	I	I	3/9
76	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
77	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
78	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
79	cat 2A (ICCVAM: cat 2B)	I	I	I	I	I	I	I	I	I	I	0/9
93	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
94	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
95	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
96	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
97	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
98	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

		Beiersdorf			Harlan			IIVS			Final classification based on median	Mispredicted tests/Total
Chemical	GHS classification	1	2	3	1	2	3	1	2	3		
99	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
100	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
101	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
102	cat 1	I	NI	NI	I	I	I	NI	NI	NI	NI	5/9
103	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
104	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
105	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

4 Study Outcome

The validation study is considered of high quality due to a very complete dataset with very little retesting needed. The test method is highly reproducible. The within-laboratory reproducibility (WLR) and between-laboratory reproducibility (BLR) was well above the acceptance criteria set by the VMG (i.e. WLR ≥ 85% and BLR ≥ 80%).

The concordance of classifications within a single laboratory was above 90% for all participating laboratories. The concordance of final classifications obtained between the different participating laboratories was greater than 90%.

The protocol for the liquid chemicals met all the acceptance criteria of the VMG for sensitivity, specificity and overall accuracy: the number of false negatives was below 10% (overall sensitivity was 0.962 and 0.983, using a cutoff of 50% and 60%, respectively), the number of false positives was below 40% (overall specificity was 0.687 and 0.654, using a cutoff of 50% and 60%, respectively) and the overall misclassification was below 25% (overall accuracy was 0.822 and 0.816, using a cutoff of 50% and 60%, respectively).

On the other hand, not all of the acceptance criteria were met by the protocol for the solid chemicals. An overall specificity of 0.797 (50% cutoff) and 0.748 (60% cutoff) met the criteria of less than 40% false positives, but the percentage of false negatives was above the acceptable rate of 10% (overall sensitivity 0.667 and 0.769, using a cutoff of 50% and 60%, respectively). Having an overall accuracy of 0.730 using a cutoff of 50%, the solid protocol needs further evaluation before a recommendation can be made. The overall accuracy based on a 60% cutoff met the acceptance criteria (overall accuracy 0.759).

5 Signature

Zeist, March 3, 2014

Placeholder

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Appendix I MTT reducers and colourants

Note that some chemicals are treated differently by the three laboratories, as is mentioned in section 3.2.1. If a chemical is treated as an MTT-reducer or a colorant in at least one of the laboratories, it is listed in appendix I.

Chemical	MTT	colouring	protocol	name
4	Yes	No	Liquids	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE
5	Yes	No	Liquids	4-(methylthio)-benzaldehyde
20	Yes	No	Liquids	ricinoleic acid tin salt
22	Yes	No	Liquids	3-phenoxybenzyl alcohol
23	Yes	No	Liquids	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE
25	Yes	No	Liquids	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE
26	Yes	No	Liquids	propiconazole
29	Yes	No	Solids	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE
30	Yes	No	Solids	1,1-dimethylguanidine sulphate
32	Yes	No	Solids	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE
33	Yes	Yes	Solids	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11
34	Yes	Yes	Solids	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17
35	Yes	No	Solids	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE
36	Yes	No	Solids	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN
42	Yes	No	Solids	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE
48	Yes	No	Solids	sodium hydrogensulphite INCI name: SODIUM BISULFITE
49	Yes	No	Solids	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN
50	Yes	No	Solids	iodosulfuron-methyl-sodium
51	Yes	No	Solids	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz
53	Yes	No	Solids	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam
56	Yes	No	Liquids	isopropyl acetoacetate
60	Yes	No	Liquids	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET
62	Yes	No	Solids	1,4-dibutoxy benzene
72	No	Yes	Liquids	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE
74	Yes	No	Solids	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE
80	Yes	No	Liquids	methylthioglycolate INCI name: METHYL THIOGLYCOLATE
81	Yes	No	Liquids	3-diethylaminopropionitrile
84	Yes	No	Liquids	sodium coco amphoacetate (~ 30% aqueous)
88	Yes	No	Liquids	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)
91	Yes	No	Liquids	(ethylenediaminepropyl)trimethoxysilane
92	Yes	No	Liquids	tetraethylene glycol diacrylate
95	Yes	No	Solids	1,2,4-triazole sodium salt
98	Yes	Yes	Solids	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE

Chemical	MTT	colouring	protocol	name
100	Yes	No	Solids	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL
101	No	Yes	Solids	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31
103	Yes	No	Solids	3,4-dimethyl-1H-pyrazole
106[1]	Yes	Yes	Solids	4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methylbenzenamine hydrochloride INCI name: BASIC VIOLET 2
107[1]	Yes	Yes	Solids	xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxycarbonyl)phenyl]-tetrafluoroborate

[1] extra chemicals not for statistics but for a later purpose of evaluation using an HPLC based detection system.

Appendix II SAS-code for statistical analysis

```
/* ================================= */
/* STEP5_EpiOcular_SAP - Revision.sas    */
/*                                                                    */
/* Data analysis according to SAP                    */
/* 10-01-2012 Intial CdJ                                    */
/* 19-10-2012 final CdJ                                     */
/* ================================= */

LIBNAME RhT '\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis';
OPTIONS fmtsearch=(RhT.formats work.formats) NOCENTER;

PROC FORMAT;
  VALUE fmtconcl 0 = 'Qualified and included'
              1 = 'Non-Qualified'
                    2 = 'Excluded';
  VALUE fmtc 0 = 'NQ'
           1 = 'Ex'
           . = ' ';
  VALUE FMTINI 0 = 'NI'
            1 = 'I';
RUN;

/* Merge locked data with chemical information */
DATA chemorder;
  INFILE '\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\chemorder_epiocular.txt'
        DSD DELIMITER='09'x MISSOVER FIRSTOBS=2 lrecl=100000;
  INFORMAT name $200. tnocode state predGHS CAS predEPA $30. EPRAfull LYS CYS  $100.;
  FORMAT name $200. tnocode state predGHS  CAS predEPA EPRAfull $30. EPRAfull LYS CYS $100.;
  INPUT order (tnocode name CAS state predGHS predEPA LYS CYS EPRAfull EPRA BDF harlan IIVS) ($);
  IF order = . THEN DELETE;
  LS = SCAN(state,1);
  /* one chemical is treated by the laboratories as 'liquid' but stated as 'solid' */
  /* Hardened castor oil with approx. 40 mol EO (INCI name: PEG-40 Hydrogenated Castor Oil) (order 37) is listed as solid but analysed
(statistically) as a liquid (based on VMG decision Nov10 2011) */
  IF order = 37 THEN LS = 'liquid';
  /* remove deselected chemical */
  IF order = 27 THEN DELETE; * other deselected chemicals are not in the list;
  IF order < 54 THEN trueINI = "NI";
  ELSE trueINI = "I";
RUN;
DATA chemorder2;
  SET chemorder(keep = name order LS predGHS BDF rename=(BDF = chemical_code))
     chemorder(keep = name order LS predGHS harlan rename=(harlan = chemical  code))
     chemorder(keep = name order LS predGHS iivs rename=(iivs = chemical_code));
RUN;
PROC SORT data= RhT.EpiOcular_locked; BY chemical_code; RUN;
PROC SORT data= chemorder2; BY chemical_code; RUN;
DATA pre_all;
  MERGE RhT.EpiOcular_locked(in=ok2) chemorder2 (in=ok);
  BY chemical_code;
  IF ok and ok2;
  *IF test >3 then delete;
  IF order < 54 THEN trueINI = "NI";
  ELSE trueINI = "I";
  runN = INPUT(run,best12.);
  IF MTT = '' THEN MTT = 'No';
  IF coloring = '' THEN coloring = 'No';
  IF UPCASE(MTT)='YES' THEN MTT = 'Yes';
  IF UPCASE(MTT)='NO' THEN MTT = 'No';
  IF UPCASE(coloring)='YES' THEN coloring = 'Yes';
  IF UPCASE(coloring)='NO' THEN coloring = 'No';
  RETAIN test 0;
  test = test+1;
  IF first.chemical_code THEN test=1;
RUN;
PROC SORT data=pre_all; BY laboratory tmp2; RUN;

data tmp;
set pre_all;
where order IN (27 106 107);
run;
/* 09082012 CdJ Revision */
/* 16082012 CdJ Revision: addapted rules */
PROC SORT data=pre_all; BY chemical_code; RUN;
DATA rules/* (where=(order = 29))*/;
  SET pre_all;
  BY chemical_code;
  if conclusion = 1 /* non-qual */ then delete;
  IF viability >50 THEN pred50=0;
  ELSE pred50 = 1;
  IF viability >60 THEN pred60=0;
  ELSE pred60 = 1;
  IF meanTA >50 THEN pred50raw=0;
  ELSE pred50raw = 1;
  IF meanTA >60 THEN pred60raw=0;
  ELSE pred60raw = 1;
  FORMAT pred50 pred60 pred50raw pred60raw fmtpred.;
RUN;
DATA rules2;
   SET rules;
     BY chemical_code;
```

```
  RETAIN t 0;
  t = t+1;
  IF first.chemical_code THEN t=1;
  IF t>3 then delete;
RUN;
PROC SORT data=rules2; BY order  laboratory protocol ; RUN;
PROC TRANSPOSE data=rules2 out=allT1 prefix=p50_;
  VAR pred50;
  BY order  laboratory protocol ;
  ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT2 prefix=p60_;
  VAR pred60;
  BY order  laboratory protocol ;
  ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT1raw prefix=p50r_;
  VAR pred50raw;
  BY order  laboratory protocol ;
  ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT2raw prefix=p60r_;
  VAR pred60raw;
  BY order  laboratory protocol ;
  ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT3 prefix=v_;
  VAR viability;
  BY order  laboratory protocol ;
  ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT4 prefix=TA_;
  VAR meanTA;
  BY order  laboratory protocol ;
  ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT5 prefix=CC_;
  VAR meanCC;
  BY order  laboratory protocol ;
  ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT6 prefix=KC_;
  VAR meanKC;
  BY order  laboratory protocol ;
  ID t;
RUN;
DATA overall (drop=_name_);
  MERGE allT1 allT2  allT1raw allT2raw allT3 allT4 allT5 allT6;
  BY order  laboratory protocol ;
RUN;
PROC SORT data=overall; BY laboratory order; RUN;
DATA rules3_no rules3_yes;
  SET overall;
  mean_nsc=mean(CC_1,CC_2,CC_3);
  mean_mtt=mean(KC_1,KC_2,KC_3);
  * rule 1 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory is less than or equal to (=) 50%,
  THEN this chemical is considered to be compatible with the test method. The chemical should be included in the overview tables,
  and included in all statistical calculations of reproducibility and predictive capacity.;
  IF mean_nsc <= 50 THEN DO; inclusion50_nsc = 'yes'; inclusion60_nsc = 'yes'; END;
  IF mean_mtt<=50 THEN DO; inclusion50_mtt = 'yes'; inclusion60_mtt = 'yes'; END;
  * rule 2 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory is greater than (>) 50% AND
  their classification (I or NI) remains the same upon correction, THEN this chemical is considered to be compatible with the test
  method. The chemical should be included in the overview tables, and included in all statistical calculations of reproducibility and
  predictive capacity.;
  IF mean_nsc > 50 AND p50_1=p50r_1 AND  p50_2=p50r_2 AND p50_3=p50r_3 THEN inclusion50_nsc = 'yes';
  IF mean  nsc > 50 AND p60  1=p60r  1 AND  p60  2=p60r  2 AND p60  3=p60r  3 THEN inclusion60  nsc = 'yes';
  IF mean_mtt > 50 AND p50_1=p50r_1 AND  p50_2=p50r_2 AND p50_3=p50r_3 THEN inclusion50_mtt = 'yes';
  IF mean_mtt > 50 AND p60_1=p60r_1 AND  p60_2=p60r_2 AND p60_3=p60r_3 THEN inclusion60_mtt = 'yes';
* rule 3 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory is greater than (>) 50% AND
  the classification of at least one of the qualified tests changes upon correction, THEN this chemical is considered to be
  incompatible with the test method. The chemical should be included in the overview tables, but excluded from all statistical
  calculations of reproducibility and predictive capacity.;
  IF mean_nsc > 50 AND (p50_1 NE p50r_1 OR  p50_2 NE p50r_2 OR p50_3 NE p50r_3) THEN inclusion50_nsc = 'no';
  IF mean_nsc > 50 AND (p60_1 NE p60r_1 OR  p60_2 NE p60r_2 OR p60_3 NE p60r_3) THEN inclusion60_nsc = 'no';
  IF mean_mtt > 50 AND (p50_1 NE p50r_1 OR  p50_2 NE p50r_2 OR p50_3 NE p50r_3) THEN inclusion50_mtt = 'no';
  IF mean_mtt > 50 AND (p60_1 NE p60r_1 OR  p60_2 NE p60r_2 OR p60_3 NE p60r_3) THEN inclusion60_mtt = 'no';
  * output;
  IF inclusion50_nsc = 'no' OR inclusion50_mtt = 'no' OR inclusion60_nsc = 'no' OR inclusion60_mtt = 'no' THEN OUTPUT rules3_no;
  ELSE OUTPUT rules3_yes;
RUN;
/* CONCLUSION */
/* new rules give same selection : chemical 33 (BDF only), 80 and 23 */
/* exclusion of 80 and 23 is overruled in VMG */
/* chemical 33 is excluded for BDF */

DATA pre  all;
  SET pre_all;

  /* remove chemical 106 and 107 for statistical analysis */
  IF chemical_code IN ('B74' 'H23' 'V13') THEN DELETE; * 106;
  IF chemical_code IN ('B55' 'H36' 'V14') THEN DELETE; * 107;
  /* for chemical 80 and 23 the VMG overrode the 50% rule regarding NSMTT */
  IF chemical_code IN ('B129' 'H128' 'V127') then conclusion = 0; * 23;
  IF chemical_code IN ('B45' 'H78' 'V93') then conclusion = 0; * 80;
  /* for chemical 33: non-compatible for Beiersdorf */
  IF chemical_code = 'B87' THEN conclusion = 2;
RUN;
```

```
proc freq data=pre_all;
  tables laboratory *conclusion;
run;
data tmp;
  set pre_all;
*  IF    chemical_code IN ('B87' 'H20' 'V58')  then output; * chemical 33;
  IF    chemical_code IN ('V83' 'V45' )  then output;
run;



 /* ---------------------------------------- */
/* Section 4 of SAP: Quality check */
/* ---------------------------------------- */

/* 4.1.1 Quality check: is the information complete */

* quality check performed by laboratories;

/* 4.1.2 acceptance criteria always met */
PROC SORT data=pre_all out=pre412 nodupkey; BY filename; RUN;
PROC FREQ data=pre412 ;
  TABLE laboratory*NCqual/out=table412_NC NOCOL NOPERCENT;
  TABLE laboratory*PCqual/out=table412_PC NOCOL NOPERCENT;
RUN;
PROC TRANSPOSE data=table412_NC out=table412NCt;
  VAR count;
  ID NCqual;
  BY laboratory;
RUN;
PROC TRANSPOSE data=table412_PC out=table412PCt;
  VAR count;
  ID PCqual;
  BY laboratory;
RUN;
DATA table412;
  SET table412NCt(in=nc) table412PCt(in=pc);
  BY laboratory;
  IF nc THEN var = 'NC';
  IF pc THEN var = 'PC';
  IF non_qualified = . THEN non_qualified = 0;
  fraction_nq = 100* non_qualified/(non_qualified+qualified);
  fraction_q = 100*qualified/(non_qualified+qualified);
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table412.doc'
notoc_data;
PROC REPORT data = table412 NOWINDOWS HEADLINE HEADSKIP;
  COLUMN laboratory var qualified fraction_q non_qualified fraction_nq;
  DEFINE laboratory/GROUP;
  DEFINE var/DISPLAY ' ';
  DEFINE qualified/DISPLAY 'No.Qualified' width = 12 CENTER;
  DEFINE fraction_q/DISPLAY '%' width = 5 format=8.1 CENTER;
  DEFINE non_qualified/DISPLAY 'No.Non-Qualified' width = 16 CENTER;
  DEFINE fraction_nq/DISPLAY '%' width = 5 format=8.1 CENTER;
RUN; QUIT;
ODS rtf close;

/* 4.1.3 deviations from protocol */

* no major deviations;

/* 4.1.4 remarks and special observations */
PROC SORT data=RhT.epiocular_remarks out=remarks; BY chemical_code; RUN;
DATA table414;
  MERGE chemorder2 remarks(in=ok);
  BY chemical_code;
  IF ok;
RUN;
PROC SORT data=table414; BY laboratory filename rr; RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table414.doc'
notoc_data;
PROC REPORT data = table414 NOWINDOWS HEADLINE HEADSKIP;
 COLUMN filename order remark;
 DEFINE filename/ GROUP width = 50 FLOW;
 DEFINE order/ DISPLAY 'Chemical';
 DEFINE remark/ DISPLAY FLOW WIDTH = 50;
RUN; QUIT;
ODS RTF close;



/* ---------------------------------------- */
/* Section 5 of SAP: Descriptive statistics */
/* ---------------------------------------- */

/* 5.1 chemical selection set: distribution of test chemicals */
ods listing close;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_1.doc'
notoc_data;
PROC FREQ data=chemorder;
  TABLES trueINI * LS/norow nocol;
  /* 10082012 CdJ Revision */
  WHERE order NOT IN (106 107);
RUN;
ODS RTF close;
ods listing;
```

```
/* 5.2 Table with number and fraction of qualified and non_qualified runs */
PROC FREQ data=pre  all noprint;
  TABLES conclusion/out=table5_2LAB;
  BY laboratory;
RUN;
PROC FREQ data=pre_all noprint;
  TABLES conclusion/out=table5_2TOTAL;
RUN;
DATA table5_2;
  SET table5_2LAB table5_2TOTAL (in=ok);
  IF ok THEN laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_2.doc'
notoc_data;
PROC REPORT data = table5_2 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS laboratory conclusion count percent;
  DEFINE laboratory/GROUP;
  DEFINE conclusion /DISPLAY 'Call';
  DEFINE count/ DISPLAY 'No.';
  DEFINE percent/DISPLAY width = 15 format=8.1 'Fraction (%)';
RUN;QUIT;
ODS RTF close;

OPTIONS PS=42 LS=120;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_2LIST.doc'
notoc_data;
PROC REPORT data=pre_all (where=(conclusion IN (1 2)) keep = run order conclusion laboratory name TAqual PCqual NCqual color_call
MTT_call)
        NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS conclusion laboratory order run NCqual PCqual TAqual color_call MTT_call;
  DEFINE conclusion / GROUP width = 15;
  DEFINE laboratory / GROUP width = 15;
  DEFINE order/DISPLAY width = 4 'Chemical';
  DEFINE color  call/DISPLAY width = 12;
  BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;


/* 5.3 Table of chemicals within each run */
DATA pre5_3;
  SET pre_all;
  newvar = trim(left(put(order,3.)))||'('||trim(left(run))||')';
RUN;
PROC SORT data=pre5_3; BY filename; RUN;
PROC TRANSPOSE data=pre5_3 out=pre5_3t;
  VAR newvar;
  BY filename;
RUN;
DATA table5_3(drop=_name_);
  SET pre5_3t;
  IF _N_ < 51 THEN laboratory = 'Beiersdorf';
  ELSE IF _N_ > 93 THEN laboratory = 'IIVS';
  ELSE laboratory = 'Harlan';
RUN;
OPTIONS PS=42 LS=150;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_3.doc'
notoc_data;
PROC REPORT data = table5_3 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS laboratory filename col1 col2 col3 col4 col5 col6 col7 col8 col9 col10;
  DEFINE laboratory/GROUP;
  DEFINE filename/ GROUP width = 25 FLOW;
  DEFINE col1 / DISPLAY " " width=8;
  DEFINE col2 / DISPLAY " " width=8;
  DEFINE col3 / DISPLAY " " width=8;
  DEFINE col4 / DISPLAY " " width=8;
  DEFINE col5 / DISPLAY " " width=8;
  DEFINE col6 / DISPLAY " " width=8;
  DEFINE col7 / DISPLAY " " width=8;
  DEFINE col8 / DISPLAY " " width=8;
  DEFINE col9 / DISPLAY " " width=8;
  DEFINE col10 / DISPLAY " " width=8;
RUN;QUIT;
ODS RTF close;

/* 5.4 Table with number of tests within each test sequence */
OPTIONS PS=55 LS=80;
PROC SORT data=pre_all; BY laboratory tmp2 run; RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_4.doc'
notoc_data;
PROC FREQ data=pre_all ;
  TABLES order*laboratory/out=table5_4 NOROW NOCOL NOPERCENT;
RUN;
ODS RTF close;

/* 5.5 Table with list, no and fraction of NQ tests */
PROC SORT data=pre_all;
BY laboratory order;
RUN;
PROC FREQ data=pre_all NOPRINT;
  TABLES conclusion/out=table5_5;
  BY laboratory order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_5.doc'
notoc_data;
PROC PRINT data=table5_5(WHERE=(CONCLUSION IN (1 2)));
RUN;
```

```
ODS RTF close;

/* 5.6 Table with list and fraction of complete test sequences */
DATA pre5_6;
  SET pre_all;
  IF conclusion IN (1 2) THEN DELETE;
RUN;
PROC FREQ data=pre5_6 noprint;
  TABLES laboratory * order/out=pre5_6b;
RUN;
DATA table5_6LIST;
  SET pre5  6b;
  IF count >=3 THEN OUTPUT;
RUN;
PROC SORT data=pre5_6b; BY order; RUN;
PROC TRANSPOSE data=pre5_6b out=table5_6LIST;
  VAR COUNT;
  ID laboratory;
  BY order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\EpiOcular_Table5_6LIST_TESTRINKE.doc' notoc_data;
PROC PRINT data=table5_6LIST; RUN;
ODS RTF close;
PROC FREQ data=pre5_6b (rename=(count=aantal));
  TABLES aantal* laboratory/out=table5_6B;
RUN;
/* Above proc Freq statement doesn't work! adaption below gives desired results, it seems. */
/*adaption by rinke to test*/

/*PROC FREQ data=pre5_6b noprint;*/
/*   TABLES laboratory/out=table5_6B;*/
/*RUN;*/
 /* end adaption by rinke to test*/

DATA table5_6LAB;
  SET table5_6B;
  fraction_complete = 100*count/104;
  test_sequence_criteria = 'not fulfilled';
  IF fraction_complete > 85 THEN test_sequence_criteria = 'fulfilled';
RUN;
PROC MEANS data=table5_6LAB NOPRINT;
  VAR count;
  OUTPUT out=table5_6D sum=sumcount;
RUN;
DATA table5_6OVERALL;
  SET table5_6D;
  fraction_complete = 100*sumcount/(3*104);
  test_sequence_criteria = 'not fulfilled';
  IF fraction_complete >= 85 THEN test_sequence_criteria = 'fulfilled';
RUN;
DATA table5_6;
  SET table5_6LAB table5_6OVERALL(in=ok);
  IF ok then laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\EpiOcular_Table5_6_TESTRINKE.doc' notoc_data;
PROC REPORT data = table5_6 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS laboratory fraction_complete;
  DEFINE laboratory/DISPLAY;
  DEFINE fraction_complete/DISPLAY format=8.1 'Fraction';
RUN; QUIT;
ODS rtf close;
PROC DATASETS library = work;
  DELETE pre5_6 pre5_6b table5_6B table5_6D;
RUN;QUIT;

/* 5.7 Table with list and fraction of incomplete test sequences */

DATA pre5_7a pre5_7b;
  SET pre_all;
  IF conclusion IN (1 2) THEN output pre5_7a;
  IF conclusion NOT IN (1 2) THEN output pre5_7b;
RUN;
PROC FREQ data=pre5_7a noprint;
  TABLES laboratory * order/out=pre5_7a2;
RUN;
PROC FREQ data=pre5_7b noprint;
  TABLES laboratory * order/out=pre5_7b2;
RUN;
DATA pre5_7;
  MERGE pre5_7a2(rename=(count=OUT)) pre5_7b2(rename=(count=IN));
  BY laboratory order;
  IF IN NOT IN (. 0 1 2) THEN complete = 'Yes';
  IF IN IN (. 0 1 2) THEN complete = 'No';
RUN;
DATA table5_7LIST;
  SET pre5_7;
  IF IN = . THEN IN = 0;
  IF complete = 'No' THEN OUTPUT;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_7LIST.doc'
notoc_data;
PROC REPORT data = table5_7LIST NOWINDOWS HEADLINE HEADSKIP;
  COLUMN laboratory order IN OUT;
  DEFINE laboratory/GROUP;
  DEFINE order /DISPLAY ;
```

```
  DEFINE IN/DISPLAY 'Qualified' width = 10 CENTER;
  DEFINE OUT/DISPLAY 'Non-Qual or Excluded' width = 20 CENTER;
RUN; QUIT;
ODS RTF close;
PROC FREQ data=table5_7LIST noprint;
  TABLES laboratory/out=table5_7b;
RUN;
DATA table5_7LAB;
  SET table5_7B;
  fraction_incomplete = 100*count/104;
  test_sequence_criteria = 'fulfilled';
  IF fraction_incomplete > 15 THEN test_sequence_criteria = 'not fulfilled';
RUN;
PROC MEANS data=table5_7LAB NOPRINT;
  VAR count;
  OUTPUT out=table5_7D sum=sumcount;
RUN;
DATA table5_7OVERALL;
  SET table5_7D;
  fraction_incomplete = 100*sumcount/(3*104);
  test_sequence_criteria = 'fulfilled';
  IF fraction_incomplete > 15 THEN test_sequence_criteria = 'not fulfilled';
RUN;
DATA table5_7;
  SET table5_7LAB table5_7OVERALL(in=ok);
  IF ok then laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_7.doc'
notoc_data;
PROC REPORT data = table5_7 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS laboratory fraction_incomplete;
  DEFINE laboratory/DISPLAY;
  DEFINE fraction_incomplete/DISPLAY format=8.1 'Fraction';
RUN; QUIT;
ODS rtf close;
PROC DATASETS library = work;
  DELETE pre5_7 pre5_7b table5_7B table5_7D;
RUN;QUIT;

/* 5.8 statement whether test method has fulfilled the performance criteria */
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_8.doc'
notoc_data;
PROC REPORT data = table5_6 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS laboratory fraction_complete test_sequence_criteria;
  DEFINE laboratory/DISPLAY;
  DEFINE fraction_complete/DISPLAY format=8.1 'Fraction';
  DEFINE test_sequence_criteria/DISPLAY 'Statement: criteria is ' CENTER;
RUN; QUIT;
ODS rtf close;

/* 5.9 Summarise results for  NC and PC */

PROC SORT data=pre_all out=pre5_9(keep = laboratory protocol ODnc NCdiff meanPC PCdiff)  nodupkey;
  BY laboratory filename;
RUN;
DATA pre5_9b;
  SET pre5_9 pre5_9(in=set2);
  IF set2 THEN laboratory = 'Total';
RUN;
DATA pre5_9c;
  RETAIN labstate ODnc NCdiff meanPC PCdiff;
  SET pre5_9b;
  IF protocol = 'Liquids' THEN labstate = TRIM(LEFT(laboratory)) || TRIM(LEFT('(L)'));
  IF protocol = 'Solids' THEN labstate = TRIM(LEFT(laboratory)) ||  TRIM(LEFT('(S)'));
RUN;
PROC SORT data=pre5_9c out=pre5_9d; BY protocol labstate; RUN;
* Plots and statistics in R;

* TAdiff for qualified and non-qualified tests in figure like above;
PROC SORT data=pre_all out=pre5_9(keep = laboratory protocol TAdiff conclusion)  nodupkey;
  BY laboratory filename order run;
RUN;
DATA pre5_9b;
  SET pre5_9 pre5_9(in=set2);
  IF set2 THEN laboratory = 'Total';
  IF conclusion NOT IN (0 1) THEN DELETE;
RUN;
DATA pre5_9c;
  RETAIN labstate TAdiff;
  SET pre5_9b;
  IF protocol = 'Liquids' THEN labstate = TRIM(LEFT(laboratory)) || TRIM(LEFT('(L)'));
  IF protocol = 'Solids' THEN labstate = TRIM(LEFT(laboratory)) ||  TRIM(LEFT('(S)'));
RUN;
PROC SORT data=pre5_9c out=pre5_9d; BY protocol labstate; RUN;

/* 5.10 summarise results of all tests (including NQ and excl) */
PROC SORT data=pre_all; BY laboratory name; RUN;
DATA pre5_10;
  SET pre_all(drop=test);
  BY laboratory name;
  RETAIN test 0;
  test = test+1;
  IF first.name THEN test=1;
  IF conclusion = 1 THEN c = 0;
  IF conclusion = 2 THEN c = 1;
RUN;
OPTIONS PS=42 LS=120;
```

```
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table5_10.doc'
notoc  data;
PROC REPORT data=pre5_10 NOWINDOWS HEADLINE HEADSKIP ;
  COLUMNS laboratory order trueINI test, (viability TAdiff c);
  DEFINE laboratory / GROUP width = 10;
  DEFINE order / GROUP width=5 'Chemical';
  DEFINE trueINI / "GHS" GROUP width=5;
  DEFINE test / ACROSS "test";
  DEFINE viability / ANALYSIS format=8.1 'Mean';
  DEFINE TAdiff / ANALYSIS format=8.1 'Diff';
  DEFINE c / "  " ANALYSIS width = 2 format=fmtc.;
  BREAK after laboratory/SKIP;
RUN;
ODS RTF close;

/* ---------------------------------------------- */
/* Section 6 of SAP: Intralaboratory variability */
/* ---------------------------------------------- */

/* at least two qualified tests */
PROC SORT data=pre_all; BY laboratory name; RUN;
PROC FREQ data=pre_all noprint;
  TABLES conclusion/out=pre_WLV;
  BY laboratory name;
RUN;
DATA pre_WLV2;
  SET pre_WLV (where=(conclusion = 0 AND count >=2));
RUN;
DATA pre_WLV3;
  MERGE pre_all(drop=test where=(conclusion NOT IN (1 2))) pre_WLV2 (in=ok);
  BY laboratory name;
  IF ok;
  IF viability > 50 THEN predINI = 'NI';
  ELSE predINI = 'I';
  IF viability > 60 THEN predINI60 = 'NI';
  ELSE predINI60 = 'I';
RUN;
DATA WLV;
  SET pre_WLV3;
  BY laboratory name;
  RETAIN test 0;
  test = test+1;
  IF first.name THEN test=1;
  IF test > 3 THEN DELETE;
RUN;

/* 6.1 Table with concordance of classifications */
PROC SORT data=WLV; BY laboratory name; RUN;
PROC TRANSPOSE data=WLV out=pre6_1;
  BY laboratory name order;
  ID test;
  VAR predINI;
RUN;
PROC FREQ data=WLV noprint;
  TABLES predINI/out=pre6_1;
  BY laboratory name order;
RUN;
DATA pre6_1b;
  SET pre6_1;
  IF percent NE 100 THEN WLV_concordant = 'NO ';
  ELSE WLV_concordant = 'YES';
RUN;
PROC SORT data=pre6_1b out=pre6_1c nodupkey;
  BY laboratory name order;
RUN;
PROC FREQ data=pre6  1c noprint;
  TABLES WLV_concordant/out=table6_1LAB;
  BY laboratory;
RUN;
PROC FREQ data=pre6_1c noprint;
  TABLES WLV_concordant/out=table6_1TOTAL;
RUN;
DATA table6_1;
  SET table6_1LAB table6_1TOTAL(in=ok);
  IF ok THEN laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table6_1.doc'
notoc_data;
PROC REPORT data=table6_1 NOWINDOWS HEADLINE HEADSKIP ;
  COLUMNS laboratory WLV_concordant count percent;
  DEFINE laboratory / GROUP width = 10;
  DEFINE WLV_concordant / DISPLAY width=15 'WLV concordant';
  DEFINE count / DISPLAY FLOW 'No.';
  DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
  BREAK after laboratory/SKIP;
RUN;
ODS RTF close;

/* 6.2 Additional descriptives of non-concordant results */
DATA pre6_2;
  MERGE WLV pre6_1c(keep = laboratory name order WLV_concordant);
  BY laboratory name order;
RUN;
/* 16082012 CdJ revision */
DATA pre6_2b;
  SET pre6_2(where=(WLV_concordant = 'NO '));
  KEEP laboratory order name LS coloring MTT predGHS viability test;
```

```
RUN;
PROC SORT data=pre6_2b; BY laboratory order name test;
PROC TRANSPOSE data=pre6_2b out=pre6_2t(drop=_name_);
  BY laboratory order name LS coloring mTT predGHS;
  VAR viability;
  ID test;
RUN;
DATA table6_2;
  RETAIN laboratory order name LS coloring mtt predGHS _1 _2 _3;
  SET pre6_2t;
RUN;
* view in excel to create table for report;

/* 6.3 Statement per laboratory regarding WLV */
DATA table6_3 ;
  SET table6_1LAB table6_1TOTAL(in=total);
  IF total THEN laboratory = 'Total';
  WHERE WLV_concordant = 'YES';
  WLV_criteria = 'not fulfilled';
  IF percent >= 85 THEN WLV_criteria = 'fulfilled';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table6_3.doc'
notoc_data;
PROC REPORT data=table6_3 NOWINDOWS HEADLINE HEADSKIP ;
  COLUMNS laboratory percent WLV_criteria;
  DEFINE laboratory / GROUP width = 10;
  DEFINE WLV_criteria / DISPLAY width=15 'Statement: criteria is ';
  DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
RUN;
ODS RTF close;

/* 6.4 Pearson Correlations */
PROC SORT data=WLV; BY laboratory name; RUN;
PROC TRANSPOSE data=WLV out=WLVt;
  BY laboratory name;
  ID test;
  VAR viability;
RUN;
PROC CORR data=WLVt noprint outp=pearson outs=spearman;
  VAR _1 _2 _3;
  BY laboratory;
RUN;
/*PROC GPLOT data=WLVt; */
/*   PLOT   1 *   2   1 * _3 _2 * _3;*/
/*   BY laboratory;*/
/*RUN; QUIT;*/
DATA set1 (keep=laboratory _name_ _1 where=(_name_ NE '_1'))
    set2 (keep=laboratory _name_ _2 where=(_name_ NE '_2'))  ;
  SET pearson;
  WHERE _TYPE_ = 'CORR';
RUN;
PROC TRANSPOSE data=set1 out=set1T(drop=_name_) prefix = _1;
  VAR _1;
  BY laboratory;
  ID _name_;
RUN;
PROC TRANSPOSE data=set2 out=set2T(drop=_name_) prefix = _2;
  VAR _2;
  BY laboratory;
  ID _name_;
RUN;
DATA pre_pearson(drop=_2_1);
  MERGE set1T set2T;
  BY laboratory;
  FORMAT _1_2 _1_3 _2_3 8.3;
RUN;

DATA set1 (keep=laboratory _name_ _1 where=(_name_ NE '_1'))
    set2 (keep=laboratory _name_ _2 where=(_name_ NE '_2'))  ;
  SET spearman;
  WHERE _TYPE_ = 'CORR';
RUN;
PROC TRANSPOSE data=set1 out=set1T(drop=_name_) prefix = _1;
  VAR _1;
  BY laboratory;
  ID  _name_;
RUN;
PROC TRANSPOSE data=set2 out=set2T(drop=_name_) prefix = _2;
  VAR _2;
  BY laboratory;
  ID _name_;
RUN;
DATA pre_spearman(drop=_2_1);
  MERGE set1T set2T;
  BY laboratory;
  FORMAT _1_2 _1_3 _2_3 8.3;
RUN;

DATA pre6_4;
  SET pre_pearson (in=p) pre_spearman (in=s);
  BY laboratory;
  IF s THEN corr = 'spearman';
  IF p THEN corr = 'pearson';
RUN;
PROC SORT data=pre6_4; BY corr; RUN;
PROC MEANS data=pre6_4 noprint;
  VAR _1_2 _1_3 _2_3;
```

```
  BY corr;
  OUTPUT out=pre6_4b mean = _1_2 _1_3 _2_3;
RUN;

DATA pretable6_4;
  SET pre6_4 pre6_4b(in=m);
  IF m THEN laboratory = 'Mean';
  IF laboratory = 'Beiersdorf' THEN tmp1 = 1;
  IF laboratory = 'Harlan' THEN tmp1 = 2;
  IF laboratory = 'IIVS' THEN tmp1 = 3;
  IF laboratory = 'Mean' THEN tmp1 = 4;
RUN;
PROC SORT data=pretable6_4 out=table6_4(drop=tmp1 _type_ _freq_); BY corr tmp1; RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table6_4.doc'
notoc_data;
PROC REPORT data=table6_4 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS corr laboratory _1_2 _1_3 _2_3;
  DEFINE corr / GROUP;
  DEFINE laboratory/DISPLAY width = 15;
  DEFINE _1_2/ DISPLAY 'Qual1 - Qual2' format=8.3 width = 15 CENTER;
  DEFINE _1_3/ DISPLAY 'Qual1 - Qual3' format=8.3 width = 15 CENTER;
  DEFINE _2_3/ DISPLAY 'Qual2 - Qual3' format=8.3 width = 15 CENTER;
  BREAK after corr/SKIP;
RUN; QUIT;
ODS RTF close;

/* 6.5 mean and mean diff */
PROC MEANS data=WLV noprint;
  VAR viability;
  CLASS laboratory name order;
  OUTPUT out=table6_5(where=(_type_=7)) mean=means std=stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table6_5.doc'
notoc  data;
PROC REPORT data=table6_5 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS order laboratory,(means stds cvs ns);
  DEFINE order / GROUP width = 5 'Chemical';
  DEFINE laboratory/ACROSS "_laboratory_";
  DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean';
  DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std';
  DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv';
  DEFINE ns/ANALYSIS mean width=3 CENTER 'n';
RUN; QUIT;
ODS RTF close;

* also with non-qualified tests included;
DATA inclnonqual;
  SET pre_all(where=(conclusion NE 2));
RUN;
PROC MEANS data=inclnonqual noprint;
  VAR viability;
  CLASS laboratory name order;
  OUTPUT out=table6_5b(where=(_type_=7)) mean=meansnq std=stdsnq cv=cvsnq n=nsnq;
RUN;
DATA table6_5c;
  MERGE table6_5 table6_5b;
  BY laboratory name order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table6_5b.doc'
notoc_data;
PROC REPORT data=table6_5c NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS order laboratory,(("_Q_" stds cvs ns) ("_Q+NQ_" stdsnq cvsnq nsnq));
  DEFINE order / GROUP width = 5 'Chemical';
  DEFINE laboratory/ACROSS "_laboratory_";
  DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std';
  DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv';
  DEFINE ns/ANALYSIS mean width=3 CENTER 'n';
  DEFINE stdsnq/ANALYSIS mean format=8.1 CENTER 'std';
  DEFINE cvsnq/ANALYSIS mean format=8.1 CENTER 'cv';
  DEFINE nsnq/ANALYSIS mean width=3 CENTER 'n';
RUN; QUIT;
ODS RTF close;


/* ---------------------------------------------- */
/* Section 7 of SAP: Interlaboratory variability */
/* ---------------------------------------------- */

/* at least one qualified tests per laboratory*/
PROC SORT data=pre_all; BY laboratory name; RUN;
PROC FREQ data=pre_all noprint;
  TABLES conclusion/out=pre_BLV;
  BY laboratory name;
RUN;
DATA pre_BLV2;
  SET pre_BLV (where=(conclusion = 0 AND count >=1));
RUN;
PROC SORT data=pre_BLV2; BY name; RUN:
PROC TRANSPOSE data=pre_BLV2 out=pre_BLV2t;
  VAR count;
  ID laboratory;
  BY name;
RUN;
DATA pre_BLV2t2;
  SET pre_BLV2t;
  IF Beiersdorf IN (0 .) OR Harlan IN (0 .) OR IIVS IN (0 .) THEN DELETE;
RUN;
```

```
PROC SORT data=pre_all; BY name; RUN;
DATA pre  BLV3;
  MERGE pre_all(drop=test where=(conclusion NOT IN (1 2))) pre_BLV2t2 (in=ok);
  BY name;
  IF ok;
  IF viability > 50 THEN predINI = 'NI';
  ELSE predINI = 'I';
RUN;
PROC SORT data=pre_BLV3; BY laboratory name; RUN;
DATA BLV;
  SET pre_BLV3;
  BY laboratory name;
  RETAIN test 0;
  test = test+1;
  IF first.name THEN test=1;
  IF test > 3 THEN DELETE;
RUN;

/* 7.1 Table with means, std, cv and pred */
PROC MEANS data=BLV noprint;
  CLASS laboratory name order;
  VAR viability;
  OUTPUT out=pre7_1(where=(_type_ = 7)) mean = meanlab std = stdlab cv=cvlab n=nlab;
RUN;
PROC MEANS data=pre7_1 noprint;
  CLASS name order;
  VAR stdlab;
  OUTPUT out=table7_1(where=(_type_ = 3)) mean = means std = stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table7_1.doc'
notoc_data;
PROC REPORT data=table7_1 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS order  means stds cvs;
  DEFINE order / GROUP width = 5 'Chemical';
  DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean SD';
  DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std SD';
  DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv SD';
RUN; QUIT;
ODS RTF close;
DATA table7_1b;
  SET pre7_1;
  IF meanlab > 50 THEN finalINI = 0;
  ELSE finalINI = 1;
  FORMAT finalINI fmtINI.;
RUN;

/* 7.1 Table with means, std, cv and pred - including NQ as well*/
PROC SORT data=pre_all; BY name; RUN;
DATA pre_BLV3_NQ;
  MERGE pre_all(drop=test where=(conclusion NOT IN ( 2))) pre_BLV2t2 (in=ok);
  BY name;
  IF ok;
  IF viability > 50 THEN predINI = 'NI';
  ELSE predINI = 'I';
RUN;
PROC SORT data=pre_BLV3_NQ; BY laboratory name; RUN;
DATA BLV_NQ;
  SET pre_BLV3_NQ;
  BY laboratory name;
  RETAIN test 0;
  test = test+1;
  IF first.name THEN test=1;
  *IF test > 3 THEN DELETE;
RUN;

PROC MEANS data=BLV  NQ noprint;
  CLASS laboratory name order;
  VAR viability;
  OUTPUT out=pre7_1_NQ(where=(_type_ = 7)) mean = meanlab std = stdlab cv=cvlab n=nlab;
RUN;
PROC MEANS data=pre7_1_NQ noprint;
  CLASS name order;
  VAR stdlab;
  OUTPUT out=table7_1_NQ(where=(_type_ = 3)) mean = means std = stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table7_1_NQ.doc'
notoc_data;
PROC REPORT data=table7_1_NQ NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS order  means stds cvs;
  DEFINE order / GROUP width = 5 'Chemical';
  DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean SD';
  DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std SD';
  DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv SD';
RUN; QUIT;
ODS RTF close;

/* 7.2 concordance final classifications */
PROC SORT data=table7_1b out=pre7_2; BY name order; RUN;
PROC FREQ data=pre7_2 noprint;
  TABLES finalINI/out=pre7_2b;
  BY name order;
RUN;
DATA pre7_2c;
  SET pre7_2b;
  IF percent NE 100 THEN BLV_concordant = 'NO ';
  ELSE BLV_concordant = 'YES';
RUN;
```

```
PROC SORT data=pre7_2c out=pre7_2d nodupkey;
  BY name order;
RUN;
DATA pre7_2e;
  MERGE pre7_2d pre7_2;
  BY name order;
RUN;
PROC SORT data=BLV; BY laboratory name order; RUN;
PROC SORT data=pre7_2e; BY laboratory name order; RUN;
DATA pre7_2f;
  MERGE BLV(where=(test=1)) pre7_2e(keep = laboratory name order BLV_concordant meanlab);
  BY laboratory name order;
RUN;
DATA pre7_2g;
  SET pre7_2f(where=(BLV_concordant = 'NO '));
  KEEP laboratory order name LS coloring MTT predGHS meanlab;
RUN;
PROC SORT data=pre7_2g; BY order name order name LS coloring mTT predGHS; RUN;
PROC TRANSPOSE data=pre7_2g out=pre7_2t(drop=_name_);
  BY order name LS coloring mTT predGHS;
  VAR meanlab;
  ID laboratory;
RUN;
DATA table7_2;
  RETAIN order name LS coloring mtt predGHS Beiersdorf Harlan IIVS;
  SET pre7_2t;
RUN;
* view in excel to create table for report;

/* 7.3 descriptive statistics non-concordant results */
* see 7.2 ;

/* 7.4 statement regarding BLV */
PROC FREQ data=pre7_2d;
  TABLES BLV_concordant/out=tmp;
RUN;
DATA table7_4 ;
  SET tmp;
  WHERE BLV_concordant = 'YES';
  BLV_criteria = 'not fulfilled';
  IF percent >= 80 THEN BLV_criteria = 'fulfilled';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table7_4.doc'
notoc_data;
PROC REPORT data=table7_4 NOWINDOWS HEADLINE HEADSKIP ;
  COLUMNS percent BLV_criteria;
  DEFINE BLV_criteria / DISPLAY width=15 'Statement: criteria is ';
  DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
RUN;
ODS RTF close;

/* 7.5&7.6 Two-way ANOVA with laboratory and chemicals as factor */
DATA pre7_5;
  SET pre7_1 (keep = laboratory name order meanlab);
  IF meanlab NE 0 THEN meanlog = log(meanlab);
RUN;
ODS trace off;
ODS listing close;
PROC MIXED data=pre7_5;
  CLASS laboratory name;
  MODEL meanlog = laboratory name /outp=tmp1;
  LSMEANS laboratory/pdiff cl adjust=tukey;
  ODS OUTPUT tests3 = table7_5;
  ODS OUTPUT lsmeans = table7_5partial;
  ODS OUTPUT diffs = table7_6;
  ODS OUTPUT covparms = covparms;
RUN;
ODS listing;
PROC GPLOT data=tmp1;
  PLOT resid * pred;
RUN;QUIT;
DATA pre7_5_nooutlier (drop=tmp0) table7_5_outliers(drop=tmp0);
  MERGE tmp1 covparms;
  RETAIN tmp0;
  IF estimate NE . THEN tmp0 = estimate; ELSE estimate = tmp0;
  IF abs(resid) <= 3*sqrt(estimate) THEN OUTPUT pre7_5_nooutlier;
  ELSE OUTPUT table7_5_outliers;
RUN;
ODS listing close;
PROC MIXED data=pre7_5_nooutlier;
  CLASS laboratory name;
  MODEL meanlog = laboratory name /outp=tmp1;
  LSMEANS laboratory/pdiff cl adjust=tukey;
  ODS OUTPUT tests3 = table7_5;
  ODS OUTPUT lsmeans = table7_5partial;
  ODS OUTPUT diffs = table7_6;
  ODS OUTPUT covparms = covparms;
RUN;
ODS listing;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\EpiOcular_Table7_5residualplot.doc' notoc_data;
PROC GPLOT data=tmp1;
  PLOT resid * pred;
RUN;QUIT;
ODS RTF close;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table7_5.doc'
notoc_data;
```

```
PROC PRINT data=table7_5 NOOBS; RUN;
ODS RTF close;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table7_6.doc'
notoc_data;
PROC REPORT data=table7_6 NOWINDOWS HEADLINE HEADSKIP ;
  COLUMNS laboratory _laboratory estimate stderr DF adjP;
  DEFINE laboratory / DISPLAY;
  DEFINE _laboratory /DISPLAY 'vs';
  DEFINE estimate/DISPLAY;
  DEFINE stderr/DISPLAY;
  DEFINE DF/DISPLAY;
  DEFINE adjP/DISPLAY 'Tukey-corrected p-value' width=15;
RUN;
ODS RTF close;

/* 7.7 Pearson correlations */
PROC SORT data=pre7_1; BY name; RUN;
PROC TRANSPOSE data=pre7_1 out=pre7_7;
  BY name;
  ID laboratory;
  VAR meanlab;
RUN;
PROC CORR data=pre7_7 noprint outp=pearson outs=spearman;
  VAR Beiersdorf Harlan IIVS;
RUN;
/*PROC GPLOT data=pre7_7; */
/*   PLOT Beiersdorf * Harlan Beiersdorf * IIVS Harlan * IIVS;*/
/*RUN; QUIT;*/
DATA set1p (keep= _name_ Beiersdorf where=(_name_ NE 'Beiersdorf'))
    set2p (keep= _name_ Harlan where=(_name_ NE 'Harlan'))  ;
  SET pearson;
  WHERE _TYPE_ = 'CORR';
RUN;
DATA pre  pearson7  7(keep = laboratories pearson);
  SET set1p(in=s1 rename=(Beiersdorf = pearson)) set2p(in=s2 rename=(Harlan = pearson));
  IF s1 THEN with = 'Beiersdorf';
  IF s2 THEN with = 'Harlan';
  IF _name_ = 'Beiersdorf' THEN DELETE;
  Laboratories = TRIM(LEFT(with))||'-'||TRIM(LEFT(_name_));
RUN;
DATA set1s (keep= _name_ Beiersdorf where=(_name_ NE 'Beiersdorf'))
    set2s (keep= _name_ Harlan where=(_name_ NE 'Harlan'))  ;
  SET spearman;
  WHERE _TYPE_ = 'CORR';
RUN;
DATA pre_spearman7_7(keep = laboratories spearman);
  SET set1s(in=s1 rename=(Beiersdorf = spearman)) set2s(in=s2 rename=(Harlan = spearman));
  IF s1 THEN with = 'Beiersdorf';
  IF s2 THEN with = 'Harlan';
  IF _name_ = 'Beiersdorf' THEN DELETE;
  Laboratories = TRIM(LEFT(with))||'-'||TRIM(LEFT(_name_));
RUN;
DATA table7_7;
  RETAIN laboratories pearson spearman;
  MERGE pre_pearson7_7 pre_spearman7_7;
  BY laboratories;
  FORMAT pearson spearman 8.3;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table7_7.doc'
notoc_data;
PROC REPORT data=table7_7 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS laboratories pearson spearman;
  DEFINE laboratories / DISPLAY;
  DEFINE pearson/ DISPLAY  format=8.3 width = 15 CENTER;
  DEFINE spearman/ DISPLAY format=8.3 width = 15 CENTER;
RUN; QUIT;
ODS RTF close;

/* ------------------------------------ */
/* Section 8 of SAP: Predictive capacity */
/* ------------------------------------ */

PROC SORT data= pre_all; BY laboratory name; RUN;
DATA PCA;
  SET pre_all (drop=test);
  BY laboratory name;
  WHERE conclusion = 0;
  RETAIN test 0;
  test = test+1;
  IF first.name THEN test=1;
  IF test>3 THEN DELETE;
  IF viability > 50 THEN predINI = 'NI';
  ELSE predINI = 'I';
RUN;
/* 8.1 sens, spec, acc */
%MACRO predmodel(lab=, output=);
DATA pre8_1;
  SET PCA;
  %IF &lab NE %THEN %DO;
    WHERE laboratory = &lab;
  %END;
  IF trueINI = 'I' THEN DO;
    IF predINI = 'I' THEN result = 'TP';
      ELSE IF predINI = 'NI' THEN result = 'FN';
  END;
  ELSE IF trueINI = 'NI' THEN DO;
    IF predINI = 'NI' THEN result = 'TN';
```

```
      ELSE IF predINI = 'I' THEN result = 'FP';
  END;
RUN;
PROC SORT data=pre8_1;
  BY trueINI predINI;
RUN;
DATA pre8_1b (drop=result);
  SET pre8_1;
  BY trueINI;
  retain tp tn fp fn;
  if (first.trueINI) then do;
    tp=0; tn=0; fp=0; fn=0;
  end;
  if (result in ("TP")) then tp=tp+1;
  if (result in ("TN")) then tn=tn+1;
  if (result in ("FN")) then fn=fn+1;
  if (result in ("FP")) then fp=fp+1;
  else ;
  if (last.trueINI) then output;
run;
DATA pre8_1C;
  SET pre8_1B;
  tntp=tn+tp;
  fnfp=fn+fp;
RUN;
PROC SQL;
  CREATE TABLE pre8_1D as
  select sum(tp) as tp, sum(tn) as tn, sum(fp)as fp, sum(fn) as fn, sum(tntp) as
      tntp, sum(fnfp) as fnfp
  from pre8_1C;
QUIT;
PROC SQL;
  CREATE TABLE pre8_1E as
  select tp/(tp+fn) as sensitivity, tn/(tn+fp) as specificity,
      (tn+tp)/(tn+tp+fn+fp) as accuracy
   from pre8_1D;
QUIT;
PROC TRANSPOSE data=pre8_1D out=pre8_1F;
  VAR tp tn fn fp tntp fnfp;
RUN;
DATA pre8_1G (drop=_name_ col1);
  LENGTH group $20;
  SET pre8_1F;
  count=col1;
  if _name_="tp" then do;
    group="Sensitivity";
    response=0;
    output;
  end;
  else if _name_="fn" then do;
    group="Sensitivity";
    response=1;
    output;
  end;
  else if _name_="tn" then do;
    group="Specificity";
    response=0;
    output;
  end;
  else if _name_="fp" then do;
    group="Specificity";
    response=1;
    output;
  end;
  else if _name_="tntp" then do;
    group="Accuracy";
    response=0;
    output;
  end;
  else if _name_="fnfp" then do;
    group="Accuracy";
    response=1;
    output;
  end;
RUN;
PROC SORT data=pre8_1G; BY group; RUN;
ODS trace off;
ODS listing close;
PROC FREQ data= pre8_1G;
  WEIGHT count;
  BY group;
  TABLES response/alpha=0.05 binomial(p=0.5);
  exact binomial;
  ODS OUTPUT BinomialProp = pre8_1CI;
RUN;
ODS listing;
DATA pre8_1TOTAL;
  SET pre8_1CI;
  WHERE name1 IN ('_BIN_' 'XL_BIN' 'XU_BIN');
RUN;
PROC TRANSPOSE data=pre8_1TOTAL out=pre8_1TOTALt;
  VAR nvalue1;
  ID name1;
  BY group;
RUN;
PROC TRANSPOSE data=pre8_1G out=pre8_1H;
  VAR count;
```

```
  ID response;
  BY group;
RUN;
DATA &output;
  MERGE pre8_1TOTALt pre8_1H;
  BY group;
RUN;
%MEND;
%predmodel(lab=,output=table8_1TOTAL);
%predmodel(lab='Beiersdorf',output=table8_1BDF);
%predmodel(lab='Harlan',output=table8_1HARLAN);
%predmodel(lab='IIVS',output=table8_1IIVS);

DATA table8_1 (keep = group laboratory _BIN_ XL_BIN XU_BIN abs);
  SET table8_1BDF (in=set1) table8_1HARLAN (in=set2)
      table8_1IIVS (in=set3) table8_1TOTAL (in=set4);
  IF set1 THEN laboratory = 'Beiersdorf';
  IF set2 THEN laboratory = 'Harlan';
  IF set3 THEN laboratory = 'IIVS';
  IF set4 THEN laboratory = 'Total';
  x = PUT(_1,$3.);
  y = PUT(_0+_1,$3.);
  abs = x||'/'||y;
RUN;
* report @8.2;

/* 8.2 statement regarding predictive capacity */
DATA table8_2;
  SET table8_1;
  LENGTH PC_criteria $25;
  IF group = 'Sensitivity' THEN DO;
    PC_criteria = 'further evaluation';
    IF _BIN_ >= 0.90 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.80 THEN PC_criteria = 'definitely unacceptable';
  END;
  IF group = 'Specificity' THEN DO;
    PC_criteria = 'further evaluation';
    IF _BIN_ >= 0.60 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.50 THEN PC_criteria = 'definitely unacceptable';
  END;
  IF group = 'Accuracy' THEN DO;
    PC_criteria = 'further evaluation';
    IF _BIN_ >= 0.75 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.65 THEN PC_criteria = 'definitely unacceptable';
  END;
RUN;

ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table8_1.doc'
notoc_data;
PROC REPORT data=table8_2 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS laboratory group abs _BIN_ XL_BIN XU_BIN PC_criteria;
  DEFINE laboratory/GROUP;
  DEFINE group/DISPLAY 'Characteristic' width = 15;
  DEFINE abs/DISPLAY 'No.';
  DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
  DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
  DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
  DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
  BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

/* 8.3 sens, spec, acc per subgroup */
%MACRO predmodel2(lab=, output=, state=);
DATA pre8_1 %IF &state NE %THEN %DO; (WHERE=(LS =&state)) %END; ;
  SET PCA;
  %IF &lab NE %THEN %DO;
    WHERE laboratory = &lab;
  %END;
  IF trueINI = 'I' THEN DO;
    IF predINI = 'I' THEN result = 'TP';
      ELSE IF predINI = 'NI' THEN result = 'FN';
  END;
  ELSE IF trueINI = 'NI' THEN DO;
    IF predINI = 'NI' THEN result = 'TN';
      ELSE IF predINI = 'I' THEN result = 'FP';
  END;
RUN;
PROC SORT data=pre8_1;
  BY trueINI predINI;
RUN;
DATA pre8_1b (drop=result);
  SET pre8_1;
  BY trueINI;
  retain tp tn fp fn;
  if (first.trueINI) then do;
    tp=0; tn=0; fp=0; fn=0;
  end;
  if (result in ("TP")) then tp=tp+1;
  if (result in ("TN")) then tn=tn+1;
  if (result in ("FN")) then fn=fn+1;
  if (result in ("FP")) then fp=fp+1;
  else ;
  if (last.trueINI) then output;
run;
DATA pre8_1C;
  SET pre8_1B;
```

```
  tntp=tn+tp;
  fnfp=fn+fp;
RUN;
PROC SQL;
  CREATE TABLE pre8_1D as
  select sum(tp) as tp, sum(tn) as tn, sum(fp)as fp, sum(fn) as fn, sum(tntp) as
       tntp, sum(fnfp) as fnfp
  from pre8_1C;
QUIT;
PROC SQL;
  CREATE TABLE pre8_1E as
  select tp/(tp+fn) as sensitivity, tn/(tn+fp) as specificity,
       (tn+tp)/(tn+tp+fn+fp) as accuracy
   from pre8_1D;
QUIT;
PROC TRANSPOSE data=pre8_1D out=pre8_1F;
  VAR tp tn fn fp tntp fnfp;
RUN;
DATA pre8_1G (drop=_name_ col1);
  LENGTH group $20;
  SET pre8_1F;
  count=col1;
  if _name_="tp" then do;
    group="Sensitivity";
    response=0;
    output;
  end;
  else if _name_="fn" then do;
    group="Sensitivity";
    response=1;
    output;
  end;
  else if _name_="tn" then do;
    group="Specificity";
    response=0;
    output;
  end;
  else if _name_="fp" then do;
    group="Specificity";
    response=1;
    output;
  end;
  else if _name_="tntp" then do;
    group="Accuracy";
    response=0;
    output;
  end;
  else if _name_="fnfp" then do;
    group="Accuracy";
    response=1;
    output;
  end;
RUN;
PROC SORT data=pre8_1G; BY group; RUN;
ODS trace off;
ODS listing close;
PROC FREQ data= pre8_1G;
  WEIGHT count;
  BY group;
  TABLES response/alpha=0.05 binomial(p=0.5);
  exact binomial;
  ODS OUTPUT BinomialProp = pre8_1CI;
RUN;
ODS listing;
DATA pre8_1TOTAL;
  SET pre8_1CI;
  WHERE name1 IN ('_BIN_' 'XL_BIN' 'XU_BIN');
RUN;
PROC TRANSPOSE data=pre8_1TOTAL out=pre8_1TOTALt;
  VAR nvalue1;
  ID name1;
  BY group;
RUN;
PROC TRANSPOSE data=pre8_1G out=pre8_1H;
  VAR count;
  ID response;
  BY group;
RUN;
DATA &output;
  MERGE pre8_1TOTALt pre8_1H;
  BY group;
RUN;
%MEND;
%predmodel2(lab=,output=table8_1TOTAL_L,state='liquid');
%predmodel2(lab='Beiersdorf',output=table8_1BDF_L,state='liquid');
%predmodel2(lab='Harlan',output=table8_1HARLAN_L,state='liquid');
%predmodel2(lab='IIVS',output=table8_1IIVS_L,state='liquid');
%predmodel2(lab=,output=table8_1TOTAL_S,state='solid');
%predmodel2(lab='Beiersdorf',output=table8_1BDF_S,state='solid');
%predmodel2(lab='Harlan',output=table8_1HARLAN_S,state='solid');
%predmodel2(lab='IIVS',output=table8_1IIVS_S,state='solid');

DATA table8_3 (keep = group laboratory state abs _BIN_ XL_BIN XU_BIN);
  SET table8_1BDF_L (in=set1) table8_1HARLAN_L (in=set2)
     table8_1IIVS_L (in=set3) table8_1TOTAL_L (in=set4)
     table8_1BDF_S (in=set1b) table8_1HARLAN_S (in=set2b)
     table8_1IIVS_S (in=set3b) table8_1TOTAL_S (in=set4b);
```

```
  IF set1 OR set1b THEN laboratory = 'Beiersdorf';
  IF set2 OR set2b THEN laboratory = 'Harlan';
  IF set3 OR set3b THEN laboratory = 'IIVS';
  IF set4 OR set4b THEN laboratory = 'Total';
  IF set1 OR set2 OR set3 OR set4 THEN state='Liquid';
  IF set1b OR set2b OR set3b OR set4b THEN state='Solid';
    x = PUT(_1,$3.);
  y = PUT(_0+_1,$3.);
  abs = x||'/'||y;
RUN;

DATA table8_3b;
  SET table8_3;
  LENGTH PC_criteria $25;
  IF group = 'Sensitivity' THEN DO;
    PC_criteria = 'Further evaluation';
    IF _BIN_ >= 0.90 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.80 THEN PC_criteria = 'definitely unacceptable';
  END;
  IF group = 'Specificity' THEN DO;
    PC_criteria = 'Further evaluation';
    IF _BIN_ >= 0.60 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.50 THEN PC_criteria = 'definitely unacceptable';
  END;
  IF group = 'Accuracy' THEN DO;
    PC_criteria = 'Further evaluation';
    IF _BIN_ >= 0.75 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.65 THEN PC_criteria = 'definitely unacceptable';
  END;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table8_3.doc'
notoc_data;
PROC REPORT data=table8_3b(where=(state='Liquid')) NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS  laboratory group abs _BIN_ XL_BIN XU_BIN PC_criteria;
  DEFINE laboratory/GROUP;
  DEFINE abs / DISPLAY 'No.';
  DEFINE group/DISPLAY 'Characteristic' width = 15;
  DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
  DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
  DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
  DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
  BREAK after laboratory/SKIP;
RUN; QUIT;
PROC REPORT data=table8_3b(where=(state='Solid')) NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS  laboratory group abs _BIN_ XL_BIN XU_BIN PC_criteria;
  DEFINE laboratory/GROUP;
  DEFINE abs / DISPLAY 'No.';
  DEFINE group/DISPLAY 'Characteristic' width = 15;
  DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
  DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
  DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
  DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
  BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

/* ---------------------------------------------- */
/* Section 9 of SAP: Summary and recommendations */
/* ---------------------------------------------- */

* in report;

/* ---------------------- */
/* Additional tables */
/* ---------------------- */

* some chemicals are treated differently by the labs concerning the coloring or mtt;
PROC SORT data=pre_all out=extra0s (keep = order name laboratory mtt coloring) nodupkey;
  BY order laboratory mtt coloring;
RUN;
PROC TRANSPOSE data=extra0s out=extra0a;
  VAR mtt;
  BY order name;
  ID laboratory;
RUN;
DATA extra0_mtt(keep = order name beiersdorf harlan iivs mttcheck) ;
  SET extra0a ;
  BY order;
  mttcheck = 'not ok';
  IF beiersdorf = harlan AND beiersdorf = IIVS and harlan = IIVS THEN mttcheck = ' ';
  ELSE mttcheck = '#';
  *IF mttcheck = 'not ok' THEN OUTPUT;
RUN;
PROC TRANSPOSE data=extra0s out=extra0b;
  VAR coloring;
  BY order name;
  ID laboratory;
RUN;
DATA extra0_color( keep = order name beiersdorf harlan iivs colorcheck);
  SET  extra0b;
  BY order;
  colorcheck = 'not ok';
  IF beiersdorf = harlan AND beiersdorf = IIVS and harlan = IIVS THEN colorcheck = ' ';
  ELSE colorcheck = '#';
  *IF colorcheck = 'not ok' THEN OUTPUT;
RUN;
```

```
 * falsepos/falseneg;
PROC SORT data=PCA; BY order predGHS; RUN;
DATA PCA2;
  SET PCA;
  IF predINI = 'NI' THEN value = 0;
  ELSE value = 1;
  IF trueINI = 'NI' THEN true = 0;
  ELSE true = 1;
  mis=0;
  IF value = 1 AND true = 0 THEN mis = 1;
  IF value = 0 AND true = 1 THEN mis = 1;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'Beiersdorf')) out=extra1a prefix=B;
  VAR value;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'Harlan')) out=extra1b prefix=H;
  VAR value;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'IIVS')) out=extra1c prefix=V;
  VAR value;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'Beiersdorf')) out=extra1d prefix=misB;
  VAR mis;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'Harlan')) out=extra1e prefix=misH;
  VAR mis;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'IIVS')) out=extra1f prefix=misV;
  VAR mis;
  BY order name predGHS LS;
  ID test;
RUN;
PROC SORT data=PCA2 out=PCA2b nodupkey; BY order; RUN;
PROC TRANSPOSE data=PCA2b out=extra1g(rename=(count=true));
  VAR true;
  BY order name;
RUN;
DATA extra1/*(keep = order name predGHS LS mis med) */;
  MERGE extra1a extra1b extra1c extra1d extra1e extra1f extra1g;
  BY order name;
  med = MEDIAN(B1,B2,B3,H1,H2,H3,V1,V2,V3);
  summis = SUM(misB1,misB2,misB3,misH1,misH2,misH3,misV1,misV2,misV3);
  mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/9';
  IF order = 33 THEN DO;
       med = MEDIAN(H1,H2,H3,V1,V2,V3);
       summis = SUM(misH1,misH2,misH3,misV1,misV2,misV3);
       mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/6';
  END;
  FORMAT B1--V3 med fmtini.;
  label mis = 'Mispredicted tests/Total'
              med = 'Final classification based on median';
RUN;
PROC SORT data=extra1;
  BY LS order;
RUN;
* view in excel to create table for report;
data tmp;
  set pca;
  where order = 33;
run;

/* ---------- */
/* Appendix I */
/* ---------- */
PROC sort data=pre_all out=appendix1 (keep = order name mtt coloring  protocol
                                                where=(UPCASE(MTT) NE 'NO' OR UPCASE(coloring) NE 'NO')) nodupkey ;
  BY order name;
RUN;
/* ---------- */
/* Appendix IV */
/* ----------*/
PROC SORT data=rht.Epiocular_remarks out=remarks;
  BY chemical_code;
RUN;
PROC SORT data=chemorder2 out=chemorder3;
  BY chemical_code;
RUN;
DATA appIV;
  MERGE remarks(in=ok) chemorder3;
  BY chemical_code;
  IF ok;
RUN;
PROC SORT data=appIV; BY order; RUN;
DATA appIVfinal(keep = order filename remark);
  RETAIN order filename remark;
  SET appIV;
RUN;
```

```
/* ---------------- */
/* Appendix VI */
/* ----------------*/

DATA appVI;
  SET pre_all;
  IF viability > 50 THEN pred50 = 'NI';
  ELSE pred50 = 'I';
  IF viability > 60 THEN pred60 = 'NI';
  ELSE pred60 = 'I';
RUN;
PROC SORT data=appVI; BY laboratory order test; RUN;

/* ======================= */
/* ======================= */
/* USING THE 60% CUT-OFF */
/* ======================= */
/* ======================= */

/* ------------------------------------------------ */
/* Section 6 of SAP: Intralaboratory variability */
/* ------------------------------------------------ */

/* at least two qualified tests */
PROC SORT data=pre_all; BY laboratory name; RUN;
PROC FREQ data=pre_all noprint;
  TABLES conclusion/out=pre_WLV;
  BY laboratory name;
RUN;
DATA pre_WLV2;
  SET pre_WLV (where=(conclusion = 0 AND count >=2));
RUN;
DATA pre_WLV3;
  MERGE pre  all(drop=test where=(conclusion NOT IN (1 2))) pre_WLV2 (in=ok);
  BY laboratory name;
  IF ok;
  IF viability > 60 THEN predINI = 'NI';
  ELSE predINI = 'I';
RUN;
DATA WLV;
  SET pre_WLV3;
  BY laboratory name;
  RETAIN test 0;
  test = test+1;
  IF first.name THEN test=1;
  IF test > 3 THEN DELETE;
RUN;

/* 6.1 Table with concordance of classifications */
PROC SORT data=WLV; BY laboratory name; RUN;
PROC TRANSPOSE data=WLV out=pre6_1;
  BY laboratory name order;
  ID test;
  VAR predINI;
RUN;
PROC FREQ data=WLV noprint;
  TABLES predINI/out=pre6_1;
  BY laboratory name order;
RUN;
DATA pre6_1b;
  SET pre6_1;
  IF percent NE 100 THEN WLV_concordant = 'NO ';
  ELSE WLV_concordant = 'YES';
RUN;
PROC SORT data=pre6_1b out=pre6_1c nodupkey;
  BY laboratory name order;
RUN;
PROC FREQ data=pre6_1c noprint;
  TABLES WLV_concordant/out=table6_1LAB;
  BY laboratory;
RUN;
PROC FREQ data=pre6_1c noprint;
  TABLES WLV_concordant/out=table6_1TOTAL;
RUN;
DATA table6_1;
  SET table6  1LAB table6  1TOTAL(in=ok);
  IF ok THEN laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table6_1_p60.doc'
notoc_data;
PROC REPORT data=table6_1 NOWINDOWS HEADLINE HEADSKIP ;
  COLUMNS laboratory WLV_concordant count percent;
  DEFINE laboratory / GROUP width = 10;
  DEFINE WLV_concordant / DISPLAY width=15 'WLV concordant';
  DEFINE count / DISPLAY FLOW 'No.';
  DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
  BREAK after laboratory/SKIP;
RUN;
ODS RTF close;

/* 6.2 Additional descriptives of non-concordant results */
DATA pre6_2;
  MERGE WLV pre6_1c(keep = laboratory name order WLV_concordant);
  BY laboratory name order;
RUN;
/* 16082012 CdJ revision */
DATA pre6_2b;
```

```
  SET pre6_2(where=(WLV_concordant = 'NO '));
  KEEP laboratory order name LS coloring MTT predGHS viability test;
RUN;
PROC SORT data=pre6_2b; BY laboratory order name test;
PROC TRANSPOSE data=pre6_2b out=pre6_2t(drop=_name_);
  BY laboratory order name LS coloring mTT predGHS;
  VAR viability;
  ID test;
RUN;
DATA table6_2;
  RETAIN laboratory order name LS coloring mtt predGHS _1 _2 _3;
  SET pre6_2t;
RUN;
* view in excel to create table for report;

/* 6.3 Statement per laboratory regarding WLV */
DATA table6_3 ;
  SET table6_1LAB table6_1TOTAL(in=total);
  IF total THEN laboratory = 'Total';
  WHERE WLV_concordant = 'YES';
  WLV_criteria = 'not fulfilled';
  IF percent >= 85 THEN WLV_criteria = 'fulfilled';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table6_3_p60.doc'
notoc_data;
PROC REPORT data=table6_3 NOWINDOWS HEADLINE HEADSKIP ;
  COLUMNS laboratory percent WLV_criteria;
  DEFINE laboratory / GROUP width = 10;
  DEFINE WLV_criteria / DISPLAY width=15 'Statement: criteria is ';
  DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
RUN;
ODS RTF close;

/* 6.4 Pearson Correlations */
/* is not depending on cut-off value */

/* 6.5 mean and mean diff */
/* is not depending on cut-off value */

/* ---------------------------------------------- */
/* Section 7 of SAP: Interlaboratory variability */
/* ---------------------------------------------- */

/* at least one qualified tests per laboratory*/
PROC SORT data=pre_all; BY laboratory name; RUN;
PROC FREQ data=pre_all noprint;
  TABLES conclusion/out=pre_BLV;
  BY laboratory name;
RUN;
DATA pre_BLV2;
  SET pre_BLV (where=(conclusion = 0 AND count >=1));
RUN;
PROC SORT data=pre_BLV2; BY name; RUN:
PROC TRANSPOSE data=pre_BLV2 out=pre_BLV2t;
  VAR count;
  ID laboratory;
  BY name;
RUN;
DATA pre_BLV2t2;
  SET pre_BLV2t;
  IF Beiersdorf IN (0 .) OR Harlan IN (0 .) OR IIVS IN (0 .) THEN DELETE;
RUN;
PROC SORT data=pre_all; BY name; RUN;
DATA pre_BLV3;
  MERGE pre_all(drop=test) pre_BLV2t2 (in=ok);
  BY name;
  IF ok;
  IF conclusion IN (1 2) THEN DELETE;
  IF viability > 60 THEN predINI = 'NI';
  ELSE predINI = 'I';
RUN;
PROC SORT data=pre_BLV3; BY laboratory name; RUN;
DATA BLV;
  SET pre_BLV3;
  BY laboratory name;
  RETAIN test 0;
  test = test+1;
  IF first.name THEN test=1;
  IF test > 3 THEN DELETE;
RUN;

/* 7.1 Table with means, std, cv and pred */
/* is not depending on cut-off value */
PROC MEANS data=BLV noprint;
  CLASS laboratory name order;
  VAR viability;
  OUTPUT out=pre7_1(where=(_type_ = 7)) mean = meanlab std = stdlab cv=cvlab n=nlab;
RUN;
PROC MEANS data=pre7_1 noprint;
  CLASS name order;
  VAR stdlab;
  OUTPUT out=table7_1(where=(_type_ = 3)) mean = means std = stds cv=cvs n=ns;
RUN;
DATA table7_1b;
  SET pre7_1;
  IF meanlab > 60 THEN finalINI = 0;
  ELSE finalINI = 1;
```

```
  FORMAT finalINI fmtINI.;
RUN;

/* 7.2 concordance final classifications */
PROC SORT data=table7_1b out=pre7_2; BY name order; RUN;
PROC FREQ data=pre7_2 noprint;
  TABLES finalINI/out=pre7_2b;
  BY name order;
RUN;
DATA pre7_2c;
  SET pre7_2b;
  IF percent NE 100 THEN BLV  concordant = 'NO ';
  ELSE BLV_concordant = 'YES';
RUN;
PROC SORT data=pre7_2c out=pre7_2d nodupkey;
  BY name order;
RUN;
PROC FREQ data=pre7_2d noprint;
  TABLES BLV_concordant / out=table7_2;
RUN;
DATA pre7_2e;
  MERGE pre7_2d pre7_2;
  BY name order;
RUN;
PROC SORT data=BLV; BY laboratory name order; RUN;
PROC SORT data=pre7_2e; BY laboratory name order; RUN;
DATA pre7_2f;
  MERGE BLV(where=(test=1)) pre7_2e(keep = laboratory name order BLV_concordant meanlab);
  BY laboratory name order;
RUN;
DATA pre7_2g;
  SET pre7_2f(where=(BLV_concordant = 'NO '));
  KEEP laboratory order name LS coloring MTT predGHS meanlab;
RUN;
PROC SORT data=pre7_2g; BY order name order name LS coloring mTT predGHS; RUN;
PROC TRANSPOSE data=pre7_2g out=pre7_2t(drop=_name_);
  BY order name LS coloring mTT predGHS;
  VAR meanlab;
  ID laboratory;
RUN;
DATA table7_2b;
  RETAIN order name LS coloring mtt predGHS Beiersdorf Harlan IIVS;
  SET pre7_2t;
RUN;
* view in excel to create table for report;

/* 7.3 descriptive statistics non-concordant results */
* see 7.2 ;

/* 7.4 statement regarding BLV */
PROC FREQ data=pre7_2d;
  TABLES BLV_concordant/out=tmp;
RUN;
DATA table7_4 ;
  SET tmp;
  WHERE BLV_concordant = 'YES';
  BLV_criteria = 'not fulfilled';
  IF percent >= 80 THEN BLV_criteria = 'fulfilled';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table7_4_p60.doc'
notoc_data;
PROC REPORT data=table7_4 NOWINDOWS HEADLINE HEADSKIP ;
  COLUMNS percent BLV_criteria;
  DEFINE BLV_criteria / DISPLAY width=15 'Statement: criteria is ';
  DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
RUN;
ODS RTF close;

/* 7.5&7.6  Two-way ANOVA with laboratory and chemicals as factor */
/* is not depending on cut-off value */

/* 7.7 Pearson correlations */
/* is not depending on cut-off value */


/* ------------------------------------- */
/* Section 8 of SAP: Predictive capacity */
/* ------------------------------------- */

PROC SORT data= pre_all; BY laboratory name; RUN;
DATA PCA;
  SET pre_all (drop=test);
  BY laboratory name;
  WHERE conclusion = 0;
  RETAIN test 0;
  test = test+1;
  IF first.name THEN test=1;
  IF test>3 THEN DELETE;
  IF viability > 60 THEN predINI = 'NI';
  ELSE predINI = 'I';
RUN;
/* 8.1 sens, spec, acc */
%MACRO predmodel(lab=, output=);
DATA pre8_1;
  SET PCA;
  %IF &lab NE %THEN %DO;
    WHERE laboratory = &lab;
```

```
  %END;
  IF trueINI = 'I' THEN DO;
    IF predINI = 'I' THEN result = 'TP';
      ELSE IF predINI = 'NI' THEN result = 'FN';
  END;
  ELSE IF trueINI = 'NI' THEN DO;
    IF predINI = 'NI' THEN result = 'TN';
      ELSE IF predINI = 'I' THEN result = 'FP';
  END;
RUN;
PROC SORT data=pre8_1;
  BY trueINI predINI;
RUN;
DATA pre8_1b (drop=result);
  SET pre8_1;
  BY trueINI;
  retain tp tn fp fn;
  if (first.trueINI) then do;
    tp=0; tn=0; fp=0; fn=0;
  end;
  if (result in ("TP")) then tp=tp+1;
  if (result in ("TN")) then tn=tn+1;
  if (result in ("FN")) then fn=fn+1;
  if (result in ("FP")) then fp=fp+1;
  else ;
  if (last.trueINI) then output;
run;
DATA pre8_1C;
  SET pre8_1B;
  tntp=tn+tp;
  fnfp=fn+fp;
RUN;
PROC SQL;
  CREATE TABLE pre8  1D as
  select sum(tp) as tp, sum(tn) as tn, sum(fp)as fp, sum(fn) as fn, sum(tntp) as
       tntp, sum(fnfp) as fnfp
  from pre8_1C;
QUIT;
PROC SQL;
  CREATE TABLE pre8_1E as
  select tp/(tp+fn) as sensitivity, tn/(tn+fp) as specificity,
      (tn+tp)/(tn+tp+fn+fp) as accuracy
   from pre8_1D;
QUIT;
PROC TRANSPOSE data=pre8_1D out=pre8_1F;
  VAR tp tn fn fp tntp fnfp;
RUN;
DATA pre8_1G (drop=_name_ col1);
  LENGTH group $20;
  SET pre8_1F;
  count=col1;
  if _name_="tp" then do;
    group="Sensitivity";
    response=0;
    output;
  end;
  else if _name_="fn" then do;
    group="Sensitivity";
    response=1;
    output;
  end;
  else if _name_="tn" then do;
    group="Specificity";
    response=0;
    output;
  end;
  else if _name_="fp" then do;
    group="Specificity";
    response=1;
    output;
  end;
  else if _name_="tntp" then do;
    group="Accuracy";
    response=0;
    output;
  end;
  else if _name_="fnfp" then do;
    group="Accuracy";
    response=1;
    output;
  end;
RUN;
PROC SORT data=pre8_1G; BY group; RUN;
ODS trace off;
ODS listing close;
PROC FREQ data= pre8_1G;
  WEIGHT count;
  BY group;
  TABLES response/alpha=0.05 binomial(p=0.5);
  exact binomial;
  ODS OUTPUT BinomialProp = pre8_1CI;
RUN;
ODS listing;
DATA pre8_1TOTAL;
  SET pre8_1CI;
  WHERE name1 IN ('_BIN_' 'XL_BIN' 'XU_BIN');
RUN;
```

```
PROC TRANSPOSE data=pre8_1TOTAL out=pre8_1TOTALt;
  VAR nvalue1;
  ID name1;
  BY group;
RUN;
PROC TRANSPOSE data=pre8_1G out=pre8_1H;
  VAR count;
  ID response;
  BY group;
RUN;
DATA &output;
  MERGE pre8_1TOTALt pre8_1H;
  BY group;
RUN;
%MEND;
%predmodel(lab=,output=table8_1TOTAL);
%predmodel(lab='Beiersdorf',output=table8_1BDF);
%predmodel(lab='Harlan',output=table8_1HARLAN);
%predmodel(lab='IIVS',output=table8_1IIVS);

DATA table8_1 (keep = group laboratory _BIN_ XL_BIN XU_BIN abs);
  SET table8_1BDF (in=set1) table8_1HARLAN (in=set2)
      table8_1IIVS (in=set3) table8_1TOTAL (in=set4);
  IF set1 THEN laboratory = 'Beiersdorf';
  IF set2 THEN laboratory = 'Harlan';
  IF set3 THEN laboratory = 'IIVS';
  IF set4 THEN laboratory = 'Total';
  x = PUT(_1,$3.);
  y = PUT(_0+_1,$3.);
  abs = x||'/'||y;
RUN;
* report @8.2;

/* 8.2 statement regarding predictive capacity */
DATA table8_2;
  SET table8_1;
  LENGTH PC_criteria $25;
  IF group = 'Sensitivity' THEN DO;
    PC_criteria = 'further evaluation';
    IF _BIN_ >= 0.90 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.80 THEN PC_criteria = 'definitely unacceptable';
  END;
  IF group = 'Specificity' THEN DO;
    PC  criteria = 'further evaluation';
    IF _BIN_ >= 0.60 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.50 THEN PC_criteria = 'definitely unacceptable';
  END;
  IF group = 'Accuracy' THEN DO;
    PC_criteria = 'further evaluation';
    IF _BIN_ >= 0.75 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.65 THEN PC_criteria = 'definitely unacceptable';
  END;
RUN;

ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table8_1_P60.doc'
notoc_data;
PROC REPORT data=table8_2 NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS laboratory group abs _BIN_ XL_BIN XU_BIN PC_criteria;
  DEFINE laboratory/GROUP;
  DEFINE group/DISPLAY 'Characteristic' width = 15;
  DEFINE abs/DISPLAY 'No.';
  DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
  DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
  DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
  DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
  BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

/* 8.3 sens, spec, acc per subgroup */

/*%let lab='';*/
/*%let output=table8_1TOTAL_L;*/
/*%let state='LIQUID';*/

%MACRO predmodel2(lab=, output=, state=);
DATA pre8_1 %IF &state NE %THEN %DO; (WHERE=(UPCASE(LS) =&state)) %END; ;
  SET PCA;
  %IF &lab NE %THEN %DO;
    WHERE laboratory = &lab;
  %END;
  IF trueINI = 'I' THEN DO;
    IF predINI = 'I' THEN result = 'TP';
      ELSE IF predINI = 'NI' THEN result = 'FN';
  END;
  ELSE IF trueINI = 'NI' THEN DO;
    IF predINI = 'NI' THEN result = 'TN';
      ELSE IF predINI = 'I' THEN result = 'FP';
  END;
RUN;

PROC SORT data=pre8_1;
  BY trueINI predINI;
RUN;
DATA pre8_1b (drop=result);
  SET pre8_1;
  BY trueINI;
```

```
  retain tp tn fp fn;
  if (first.trueINI) then do;
    tp=0; tn=0; fp=0; fn=0;
  end;
  if (result in ("TP")) then tp=tp+1;
  if (result in ("TN")) then tn=tn+1;
  if (result in ("FN")) then fn=fn+1;
  if (result in ("FP")) then fp=fp+1;
  else ;
  if (last.trueINI) then output;
run;
DATA pre8_1C;
  SET pre8_1B;
  tntp=tn+tp;
  fnfp=fn+fp;
RUN;
PROC SQL;
  CREATE TABLE pre8_1D as
  select sum(tp) as tp, sum(tn) as tn, sum(fp)as fp, sum(fn) as fn, sum(tntp) as
       tntp, sum(fnfp) as fnfp
  from pre8_1C;
QUIT;
PROC SQL;
  CREATE TABLE pre8_1E as
  select tp/(tp+fn) as sensitivity, tn/(tn+fp) as specificity,
      (tn+tp)/(tn+tp+fn+fp) as accuracy
   from pre8_1D;
QUIT;
PROC TRANSPOSE data=pre8_1D out=pre8_1F;
  VAR tp tn fn fp tntp fnfp;
RUN;
DATA pre8_1G (drop=_name_ col1);
  LENGTH group $20;
  SET pre8_1F;
  count=col1;
  if _name_="tp" then do;
    group="Sensitivity";
    response=0;
    output;
  end;
  else if _name_="fn" then do;
    group="Sensitivity";
    response=1;
    output;
  end;
  else if _name_="tn" then do;
    group="Specificity";
    response=0;
    output;
  end;
  else if _name_="fp" then do;
    group="Specificity";
    response=1;
    output;
  end;
  else if _name_="tntp" then do;
    group="Accuracy";
    response=0;
    output;
  end;
  else if _name_="fnfp" then do;
    group="Accuracy";
    response=1;
    output;
  end;
RUN;
PROC SORT data=pre8_1G; BY group; RUN;
ODS trace off;
ODS listing close;
PROC FREQ data= pre8_1G;
  WEIGHT count;
  BY group;
  TABLES response/alpha=0.05 binomial(p=0.5);
  exact binomial;
  ODS OUTPUT BinomialProp = pre8_1CI;
RUN;
ODS listing;
DATA pre8_1TOTAL;
  SET pre8_1CI;
  WHERE name1 IN ('_BIN_' 'XL_BIN' 'XU_BIN');
RUN;
PROC TRANSPOSE data=pre8_1TOTAL out=pre8_1TOTALt;
  VAR nvalue1;
  ID name1;
  BY group;
RUN;
PROC TRANSPOSE data=pre8_1G out=pre8_1H;
  VAR count;
  ID response;
  BY group;
RUN;
DATA &output;
  MERGE pre8_1TOTALt pre8_1H;
  BY group;
RUN;
%MEND;
%predmodel2(lab=,output=table8_1TOTAL_L,state='LIQUID');
```

```
%predmodel2(lab='Beiersdorf',output=table8_1BDF_L,state='LIQUID');
%predmodel2(lab='Harlan',output=table8_1HARLAN_L,state='LIQUID');
%predmodel2(lab='IIVS',output=table8_1IIVS_L,state='LIQUID');
%predmodel2(lab=,output=table8_1TOTAL_S,state='SOLID');
%predmodel2(lab='Beiersdorf',output=table8_1BDF_S,state='SOLID');
%predmodel2(lab='Harlan',output=table8_1HARLAN_S,state='SOLID');
%predmodel2(lab='IIVS',output=table8_1IIVS_S,state='SOLID');

DATA table8_3 (keep = group laboratory state abs _BIN_ XL_BIN XU_BIN);
  SET table8_1BDF_L (in=set1) table8_1HARLAN_L (in=set2)
     table8_1IIVS_L (in=set3) table8_1TOTAL_L (in=set4)
     table8_1BDF_S (in=set1b) table8_1HARLAN_S (in=set2b)
     table8_1IIVS_S (in=set3b) table8_1TOTAL_S (in=set4b);
  IF set1 OR set1b THEN laboratory = 'Beiersdorf';
  IF set2 OR set2b THEN laboratory = 'Harlan';
  IF set3 OR set3b THEN laboratory = 'IIVS';
  IF set4 OR set4b THEN laboratory = 'Total';
  IF set1 OR set2 OR set3 OR set4 THEN state='Liquid';
  IF set1b OR set2b OR set3b OR set4b THEN state='Solid';
    x = PUT(_1,$3.);
  y = PUT(_0+_1,$3.);
  abs = x||'/'||y;
RUN;

DATA table8_3b;
  SET table8_3;
  LENGTH PC_criteria $25;
  IF group = 'Sensitivity' THEN DO;
    PC_criteria = 'further evaluation';
    IF _BIN_ >= 0.90 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.80 THEN PC_criteria = 'definitely unacceptable';
  END;
  IF group = 'Specificity' THEN DO;
    PC  criteria = 'further evaluation';
    IF _BIN_ >= 0.60 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.50 THEN PC_criteria = 'definitely unacceptable';
  END;
  IF group = 'Accuracy' THEN DO;
    PC_criteria = 'further evaluation';
    IF _BIN_ >= 0.75 THEN PC_criteria = 'definitely acceptable';
    IF _BIN_ <= 0.65 THEN PC_criteria = 'definitely unacceptable';
  END;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Reports\Revision\EpiOcular_Table8_3_p60.doc'
notoc_data;
PROC REPORT data=table8_3b(where=(state='Liquid')) NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS  laboratory group abs _BIN_ XL_BIN XU_BIN PC_criteria;
  DEFINE laboratory/GROUP;
  DEFINE abs / DISPLAY 'No.';
  DEFINE group/DISPLAY 'Characteristic' width = 15;
  DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
  DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
  DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
  DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
  BREAK after laboratory/SKIP;
RUN; QUIT;
PROC REPORT data=table8_3b(where=(state='Solid')) NOWINDOWS HEADLINE HEADSKIP;
  COLUMNS  laboratory group abs _BIN_ XL_BIN XU_BIN PC_criteria;
  DEFINE laboratory/GROUP;
  DEFINE abs / DISPLAY 'No.';
  DEFINE group/DISPLAY 'Characteristic' width = 15;
  DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
  DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
  DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
  DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
  BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

* additional table;
PROC SORT data=PCA; BY order predGHS; RUN;
DATA PCA2;
  SET PCA;
  IF predINI = 'NI' THEN value = 0;
  ELSE value = 1;
  IF trueINI = 'NI' THEN true = 0;
  ELSE true = 1;
  mis=0;
  IF value = 1 AND true = 0 THEN mis = 1;
  IF value = 0 AND true = 1 THEN mis = 1;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'Beiersdorf')) out=extra1a prefix=B;
  VAR value;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'Harlan')) out=extra1b prefix=H;
  VAR value;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'IIVS')) out=extra1c prefix=V;
  VAR value;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'Beiersdorf')) out=extra1d prefix=misB;
```

```
  VAR mis;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'Harlan')) out=extra1e prefix=misH;
  VAR mis;
  BY order name predGHS LS;
  ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'IIVS')) out=extra1f prefix=misV;
  VAR mis;
  BY order name predGHS LS;
  ID test;
RUN;
PROC SORT data=PCA2 out=PCA2b nodupkey; BY order; RUN;
PROC TRANSPOSE data=PCA2b out=extra1g(rename=(count=true));
  VAR true;
  BY order name;
RUN;
DATA extra1/*(keep = order name predGHS LS mis med)*/ ;
  MERGE extra1a extra1b extra1c extra1d extra1e extra1f extra1g;
  BY order name;
  med = MEDIAN(B1,B2,B3,H1,H2,H3,V1,V2,V3);
  summis = SUM(misB1,misB2,misB3,misH1,misH2,misH3,misV1,misV2,misV3);
  mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/9';
  IF order = 33 THEN DO;
      med = MEDIAN(H1,H2,H3,V1,V2,V3);
      summis = SUM(misH1,misH2,misH3,misV1,misV2,misV3);
      mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/6';
  END;
  FORMAT B1--V3 med fmtini.;
  label mis = 'Mispredicted tests/Total'
              med = 'Final classification based on median';
RUN;
PROC SORT data=extra1;
  BY LS order;
RUN;
```

Appendix III Receipt of data

Liquids

No	Remark	Used	Filename	Saved as	version	date										
1		YES	EIVS_Harlan_liquids_14225A_10_01.xls		1	11/03/2011	H9(1)	H21(1)	H22(1)	H26(1)	H27(1)	H35(1)	H56(1)	H59(1)	H65(1)	H127(1)
2	wrong run numbers	NO	EIVS_Harlan_liquids_14234D_11_02.xls		1	22/03/2011	H9(1)	H21(1)	H22(1)	H26(1)	H27(1)	H35(1)	H56(1)	H59(1)	H65(1)	H127(1)
3	replacement of 3	YES	EIVS_Harlan_liquids_14234D_11_02.xls		2	22/03/2011	H9(2)	H21(2)	H22(2)	H26(2)	H27(2)	H35(2)	H56(2)	H59(2)	H65(2)	H127(2)
4		YES	EIVS_Harlan_liquids_14241E_12_03.xls		1	28/03/2011	H9(3)	H21(3)	H22(3)	H26(3)	H27(3)	H35(3)	H56(3)	H59(3)	H65(3)	H127(3)
5		YES	EIVS_Harlan_liquids_14248E_13_04.xls		1	05/04/2011	H16(1)	H34(1)	H42(1)	H47(1)	H52(1)	H67(1)	H68(1)	H77(1)	H79(1)	H96(1)
6		YES	EIVS_Harlan_liquids_14263D_15_05.xls		1	19/04/2011	H16(2)	H34(2)	H42(2)	H47(2)	H52(2)	H67(2)	H68(2)	H77(2)	H79(2)	H96(2)
7		YES	EIVS_Harlan_liquids_14270A_16_06.xls		1	28/04/2011	H16(3)	H34(3)	H42(3)	H47(3)	H52(3)	H67(3)	H68(3)	H77(3)	H79(3)	H96(3)
8		YES	EIVS_BDF_liquids_14219F_08_01.xls		1	29/04/2011	B8(1)	B64(1)	B138(1)	B18(1)	B53(1)	B3(1)	B6(1)	B9(1)	B10(1)	B25(1)
9		YES	EIVS_BDF_liquids_14222B_09_04.xls		1	30/04/2011	B8(2)	B64(2)	B138(2)	B18(2)	B53(2)	B3(2)	B6(2)	B9(2)	B10(2)	B25(2)
10		YES	EIVS_BDF_liquids_14225D_10_07.xls		1	01/05/2011	B8(3)	B64(3)	B138(3)	B18(3)	B53(3)	B3(3)	B6(3)	B9(3)	B10(3)	B25(3)
11	replaced by 80	NO	EIVS_BDF_liquids_14225E_10_06.xls		1	02/05/2011	B39(1)	B56(1)	B58(1)	B63(1)	B78(1)	B22(1)	B7(1)	B11(1)	B45(1)	B60(1)
12	replaced by 81	NO	EIVS_BDF_liquids_14234C_11_09.xls		1	03/05/2011	B39(2)	B56(2)	B58(2)	B63(2)	B78(2)	B22(2)	B7(2)	B11(2)	B45(2)	B60(2)
13	replaced by 82	NO	EIVS_BDF_liquids_14241C_12_13.xls		1	04/05/2011	B39(3)	B56(3)	B58(3)	B63(3)	B78(3)	B22(3)	B7(3)	B11(3)	B45(3)	B60(3)
14		YES	EIVS_Harlan_liquids_14283D_18_08.xls		1	09/05/2011	H24(2)	H25(2)	H87(2)	H104(2)	H107(2)	H117(2)	H130(2)	H136(2)	H138(2)	
15		YES	EIVS_IIVS_liquids_14219_week1_number1_HI.xls		1	10/05/2011	V10(1)	V11(1)	V15(1)	V19(1)	V29(1)	V36(1)	V38(1)	V42(1)	V88(1)	V118(1)
16		YES	EIVS_IIVS_liquids_14222_week2_number2_HI.xls		1	10/05/2011	V10(2)	V11(2)	V15(2)	V19(2)	V29(2)	V36(2)	V38(2)	V42(2)	V88(2)	V118(2)
17		YES	EIVS_IIVS_liquids_14225_week3_number3_HI.xls		1	10/05/2011	V10(3)	V11(3)	V15(3)	V19(3)	V29(3)	V36(3)	V38(3)	V42(3)	V88(3)	V118(3)
18		YES	EIVS_IIVS_liquids_14234_week4_number4_HI.xls		1	10/05/2011	V2(1)	V3(1)	V20(1)	V33(1)	V47(1)	V50(1)	V75(1)	V83(1)	V84(1)	V98(1)
19		YES	EIVS_IIVS_liquids_14234_week5_number5KC_HI.xls		1	10/05/2011	V11(Kt)	V15(Kt)	V38(Kt)	V2(Kt)	V20(Kt)	V47(Kt)	V50(Kt)	V84(Kt)		
20		YES	EIVS_IIVS_liquids_14241_week5_number6_HI.xls		1	10/05/2011	V2(2)	V3(2)	V20(2)	V33(2)	V47(2)	V50(2)	V75(2)	V83(2)	V84(2)	V98(2)
21		YES	EIVS_IIVS_liquids_14248_week6_number7_HI.xls		1	11/05/2011	V2(3)	V3(3)	V20(3)	V33(3)	V47(3)	V50(3)	V75(3)	V83(3)	V84(3)	V98(3)
22		YES	EIVS_Harlan_liquids_14289A_19_09.xls		1	13/05/2011	H24(3)	H25(3)	H87(3)	H104(3)	H107(3)	H117(3)	H130(3)	H136(3)	H138(3)	
23		YES	EIVS_Harlan_liquids_14277B_17_07.xls		1	13/05/2011	H24(1)	H25(1)	H87(1)	H104(1)	H107(1)	H117(1)	H130(1)	H136(1)	H138(1)	
24	PC code missing	NO	EIVS_HARLAN_LIQUIDS_14296D_20_10.xls		1	20/05/2011	H48(1)	H71(1)	H78(1)	H98(1)						
25		YES	EIVS_HARLAN_LIQUIDS_KC.xls		1	20/05/2011	H48(Kt)	H71(Kt)	H78(Kt)	H98(Kt)						
26	replaced by 83	NO	EIVS_BDF_liquids_14248A_13_17.xls		1	27/05/2011	B73(1)	B61(1)	B28(1)	B30(1)	B54(1)	B129(1)	B118(1)	B44(1)	B27(1)	B16(1)
27		YES	EIVS_BDF_liquids_14248D_16_25.xls		1	27/05/2011	B54Kt	B129Kt	B118Kt	B44Kt	B27Kt	B16Kt				
28	replaced by 84	NO	EIVS_BDF_liquids_14256A_14_19.xls		1	27/05/2011	B73(2)	B61(2)	B28(2)	B30(2)	B54(2)	B129(2)	B118(2)	B44(2)	B27(2)	B16(2)
29	replaced by 85	NO	EIVS_BDF_liquids_14263A_15_22.xls		1	27/05/2011	B73(3)	B61(3)	B28(3)	B30(3)	B54(3)	B129(3)	B118(3)	B44(3)	B27(3)	B16(3)
30	PC code missing	NO	EIVS_HARLAN_LIQUIDS_15003C_21_11.xls		1	01/06/2011	H48(2)	H71(2)	H78(2)	H98(2)						
31	same as 25	NO	EIVS_HARLAN_LIQUIDS_KC_11.xls		1	01/06/2011	H48(Kt)	H71(Kt)	H78(Kt)	H98(Kt)						
32		YES	EIVS_IIVS_liquids_14219_week1_number1_AH.xls		1	13/07/2011	V48(1)	V49(1)	V52(1)	V81(1)	V90(1)	V92(1)	V93(1)	V95(1)	V96(1)	V104(1)
33		YES	EIVS_IIVS_liquids_14222_week2_number2_AH.xls		1	13/07/2011	V48(2)	V49(2)	V52(2)	V81(2)	V90(2)	V92(2)	V93(2)	V95(2)	V96(2)	V104(2)
34		YES	EIVS_IIVS_liquids_14225_week3_number3_AH.xls		1	13/07/2011	V48(3)	V49(3)	V52(3)	V81(3)	V90(3)	V92(3)	V93(3)	V95(3)	V96(3)	V104(3)
35		YES	EIVS_IIVS_liquids_14241_week6_number4KC_AH.xls		1	13/07/2011	V40Kt	V93Kt	V96Kt	V120Kt	V126Kt	V127Kt	V128Kt	V134Kt		
36		YES	EIVS_IIVS_liquids_14248_week6_number5_AH.xls		1	13/07/2011	V40(1)	V103(1)	V115(1)	V120(1)	V126(1)	V127(1)	V128(1)	V132(1)	V133(1)	V134(1)
37		YES	EIVS_IIVS_liquids_14256_week7_number6_AH.xls		1	13/07/2011	V40(2)	V103(2)	V115(2)	V120(2)	V126(2)	V127(2)	V128(2)	V132(2)	V133(2)	V134(2)
38		YES	EIVS_IIVS_liquids_14263_week8_number8_AH.xls		1	13/07/2011	V40(3)	V103(3)	V115(3)	V120(3)	V126(3)	V127(2)	V128(3)	V132(3)	V133(3)	V134(3)
39	PC code missing	NO	EIVS_HARLAN_LIQUIDS_15029A_27_14		1	13/07/2011	H6(1)	H15(1)	H70(1)	H72(1)	H122(1)	H124(1)	H128(1)			

No	Remark	Used	Filename	Saved as	version	date										
40		YES	EIVS_HARLAN_LIQUIDS_KC_14.xls		1	13/07/2011	H6Kt	H15Kt	H70Kt	H72Kt	H122Kt	H124Kt	H128Kt			
41	B137 is not correct reported	NO	EIVS_BDF_liquids_14256C_14_21.xls		1	14/07/2011	B121(1)	B137(1)	B38(1)	B130(1)	B133(1)	B134(1)	B14(1)	B113(1)	B84(1)	B24(1)
42		YES	EIVS_BDF_liquids_14263B_15_24.xls		1	14/07/2011	B137(2)	B137-CC(1)	B121(2)	B38(2)	B130(2)	B133(2)	B134(2)	B14(2)	B84(2)	B24(2)
43		YES	EIVS_BDF_liquids_14277E_17_27.xls		1	14/07/2011	B137(3)	B137-CC(2)	B121(3)	B38(3)	B130(3)	B133(3)	B134(3)	B14(3)	B84(3)	B24(3)
44	same as 32	NO	EIVS_IIVS_liquids_14219_week1_number1_AH.xls		1	03/08/2011	V48(1)	V49(1)	V52(1)	V81(1)	V90(1)	V92(1)	V93(1)	V95(1)	V96(1)	V104(1)
45	same as 33	NO	EIVS_IIVS_liquids_14222_week2_number2_AH.xls		1	03/08/2011	V48(2)	V49(2)	V52(2)	V81(2)	V90(2)	V92(2)	V93(2)	V95(2)	V96(2)	V104(2)
46	same as 34	NO	EIVS_IIVS_liquids_14225_week3_number3_AH.xls		1	03/08/2011	V48(3)	V49(3)	V52(3)	V81(3)	V90(3)	V92(3)	V93(3)	V95(3)	V96(3)	V104(3)
47	same as 35	NO	EIVS_IIVS_liquids_14241_week6_number4KC_AH.xls		1	03/08/2011	V40Kt	V93Kt	V96Kt	V120Kt	V126Kt	V127Kt	V128Kt	V134Kt		
48	same as 36	NO	EIVS_IIVS_liquids_14248_week6_number5_AH.xls		1	03/08/2011	V40(1)	V103(1)	V115(1)	V120(1)	V126(1)	V127(1)	V128(1)	V132(1)	V133(1)	V134(1)
49	same as 37	NO	EIVS_IIVS_liquids_14256_week7_number6_AH.xls		1	03/08/2011	V40(2)	V103(2)	V115(2)	V120(2)	V126(2)	V127(2)	V128(2)	V132(2)	V133(2)	V134(2)
50	same as 38	NO	EIVS_IIVS_liquids_14263_week8_number8_AH.xls		1	03/08/2011	V40(1)	V103(1)	V115(1)	V120(1)	V126(1)	V127(2)	V128(1)	V132(1)	V133(1)	V134(1)
51		YES	EIVS_BDF_liquids_14277F_26_47.xls		1	28/07/2011	B17_KC	B20_KC	B100_KC							
52	wrong filename (solid)	NO	EIVS_BDF_liquids_14277F_26_49.xls		1	28/07/2011	B169_KC	B177_KC								
53		YES	EIVS_BDF_liquids_14283A_18_29.xls		1	28/07/2011	B17(1)	B20(1)	B31(1)	B48(1)	B57(1)	B67(1)	B85(1)	B100(1)	B106(1)	B35(1)
54		YES	EIVS_BDF_liquids_14289D_19_32.xls		1	28/07/2011	B17(2)	B20(2)	B31(2)	B48(2)	B57(2)	B67(2)	B85(2)	B100(2)	B106(2)	B35(2)
55		YES	EIVS_BDF_liquids_14296A_20_34.xls		1	28/07/2011	B17(3)	B20(3)	B31(3)	B48(3)	B57(3)	B67(3)	B85(3)	B100(3)	B106(3)	B35(3)
56		YES	EIVS_BDF_liquids_15003B_21_38.xls		1	28/07/2011	B113(2)	B125(1)	B155(1)	B174(1)	B191(1)					
57		YES	EIVS_BDF_liquids_15007B_23_40.xls		1	28/07/2011	B113(3)	B125(2)	B155(2)	B174(2)	B137(4)	B137-CC(4)	B191(2)			
58		YES	EIVS_BDF_liquids_15013A_24_42.xls		1	28/07/2011	B113(4)	B125(3)	B155(3)	B174(3)	B191(3)					
59		YES	EIVS_BDF_liquids_15019A_26_45.xls		1	28/07/2011	B125_KC	B155_KC	B174_KC	B191_KC						
60		YES	EIVS_IIVS_liquids_14256_week12_number16KC_AH.xls		1	05/08/2011	V8_KC	V26_KC	V150_KC							
61		YES	EIVS_IIVS_liquids_14270_week9_number10_AH.xls		1	05/08/2011	V40(4)	V127(3)	V6(1)	V8(1)	V26(1)	V41(1)	V55(1)	V71(1)	V114(1)	V131(1)
62		YES	EIVS_IIVS_liquids_14277_week10_number12_AH.xls		1	05/08/2011	V6(2)	V8(2)	V26(2)	V41(2)	V55(2)	V71(2)	V114(2)	V131(2)	V150(1)	V170(1)
63		YES	EIVS_IIVS_liquids_14283_week11_number13_AH.xls		1	05/08/2011	V6(3)	V8 (ppt)	V26(3)	V41(3)	V55(3)	V71(3)	V114(3)	V131(3)	V150(2)	V170(2)
64		YES	EIVS_IIVS_liquids_14289_week12_number14_AH.xls		1	05/08/2011	V25(1)	V25-CC(1)	V61(1)	V61-CC(1)	V94(1)	V94-CC(1)				
65		YES	EIVS_IIVS_liquids_14289_week12_number15_AH.xls		1	05/08/2011	V8(4)	V191(1)								
66	PC code missing	NO	EIVS_HARLAN_LIQUIDS_15030A_28_15.xls		1	17/08/2011	H6(2)	H15(2)	H70(2)	H72(2)	H122(2)	H124(2)	H128(2)			
67	PC code missing	NO	EIVS_HARLAN_LIQUIDS_15033A_31_16.xls		1	17/08/2011	H6(3)	H15(3)	H70(3)	H72(3)	H122(3)	H124(3)	H128(3)			
68		YES	EIVS_HARLAN_LIQUIDS_15033B_31_16.xls		1	17/08/2011	H28(1)	H30(1)	H66(1)	H73(1)	H82(1)	H102(1)	H103(1)	H115(1)	H126(1)	H159(1)
69		YES	EIVS_HARLAN_LIQUIDS_15034A_32_17.xls		1	17/08/2011	H28(2)	H30(2)	H66(2)	H73(2)	H82(2)	H102(2)	H103(2)	H115(2)	H126(2)	H159(2)
70	replacement of 41	YES	EIVS_BDF_liquids_14256C_14_21.xls		2	26/08/2011	B121(1)	B137(1)	B38(1)	B130(1)	B133(1)	B134(1)	B14(1)	B113(1)	B84(1)	B24(1)
71		YES	EIVS_IIVS_liquids_14234_week15_number21KC_AH.xls		1	30/08/2011	V25_KC	V61_KC								
72		YES	EIVS_IIVS_liquids_14296_week13_number17_AH.xls		1	30/08/2011	V25(2)	V25_CC(2)	V61(2)	V61_CC(2)	V94(2)	V94_CC(2)				
73		YES	EIVS_IIVS_liquids_14296_week13_number18_AH.xls		1	30/08/2011	V170(3)	V191(2)								
74		YES	EIVS_IIVS_liquids_15003_week14_number19_AH.xls		1	30/08/2011	V25(3)	V25_CC(3)	V61(3)	V61_CC(3)	V94(3)	V94_CC(3)				
75		YES	EIVS_IIVS_liquids_15003_week14_number20_AH.xls		1	30/08/2011	V170(4)	V191(3)								
76		YES	EIVS_IIVS_liquids_15007_week16_number22_AH.xls		1	30/08/2011	V83(4)	V150(3)								

No	Remark	Used	Filename	Saved as	version	date										
77		YES	EIVS_IIVS_liquids_15007_week17_number25KC_AH.xls		1	30/08/2011	V191_KC									
78		YES	EIVS_BDF_liquids_14277F_26_48.xls		1	05/09/2011	B11_KC	B45_KC								
79		YES	EIVS_BDF_liquids_15032A_31_52.xls		1	05/09/2011	B44_KC									
80	replacement of 11	YES	EIVS_BDF_liquids_14225E_10_06_updated.xls	EIVS_BDF_liquids_14225E_10_06.xls	1	07/09/2011	B39(1)	B56(1)	B58(1)	B63(1)	B78(1)	B22(1)	B7(1)	B11(1)	B45(1)	B60(1)
81	replacement of 12	YES	EIVS_BDF_liquids_14234C_11_09_updated.xls	EIVS_BDF_liquids_14234C_11_09.xls	1	07/09/2011	B39(2)	B56(2)	B58(2)	B63(2)	B78(2)	B22(2)	B7(2)	B11(2)	B45(2)	B60(2)
82	replacement of 13	YES	EIVS_BDF_liquids_14241C_12_13_updated.xls	EIVS_BDF_liquids_14241C_12_13.xls	1	07/09/2011	B39(3)	B56(3)	B58(3)	B63(3)	B78(3)	B22(3)	B7(3)	B11(3)	B45(3)	B60(3)
83	replacement of 26	YES	EIVS_BDF_liquids_14248A_13_17_updated.xls	EIVS_BDF_liquids_14248A_13_17.xls	1	07/09/2011	B73(1)	B61(1)	B28(1)	B30(1)	B54(1)	B129(1)	B118(1)	B44(1)	B27(1)	B16(1)
84	replacement of 28	YES	EIVS_BDF_liquids_14256A_14_19_updated.xls	EIVS_BDF_liquids_14256A_14_19.xls	1	07/09/2011	B73(2)	B61(2)	B28(2)	B30(2)	B54(2)	B129(2)	B118(2)	B44(2)	B27(2)	B16(2)
85	replacement of 29	YES	EIVS_BDF_liquids_14263A_15_22_updated.xls	EIVS_BDF_liquids_14263A_15_22.xls	1	07/09/2011	B73(3)	B61(3)	B28(3)	B30(3)	B54(3)	B129(3)	B118(3)	B44(3)	B27(3)	B16(3)
86		YES	EIVS_HARLAN_LIQUIDS_15035A_33_18.xls		1	19/09/2011	H28(3)	H30(3)	H66(3)	H73(3)	H82(3)	H102(3)	H103(3)	H115(3)	H126(3)	H159(3)
87		YES	EIVS_HARLAN_LIQUIDS_15037A_34_19.xls		1	26/09/2011	H46(1)	H89(1)	H175(1)	H186(1)						
88		YES	EIVS_HARLAN_LIQUIDS_KC34.xls		1	26/09/2011	H46_KC	H89_KC	H175_KC	H186_KC						
89		YES	EIVS_HARLAN_LIQUIDS_15040B_38_20.xls		1	14/10/2011	H46(2)	H89(2)	H175(2)	H186(2)						
90	same as 21	NO	EIVS_IIVS_liquids_14248_week6_number7_HI.xls		1	20/10/2011	V2(3)	V3(3)	V20(3)	V33(3)	V47(3)	V50(3)	V75(3)	V83(3)	V84(3)	V98(3)
91		YES	EIVS_HARLAN_LIQUIDS_15046B_41_21.xls		1	27/10/2011	H46(3)	H89(3)	H175(3)	H186(3)						
92	PC code missing	NO	EIVS_HARLAN_LIQUIDS_15007C_23_12.xls		1	31/10/2011	H48(3)	H71(3)	H78(3)	H98(3)						
93	replacement of 24	YES	EIVS_HARLAN_LIQUIDS_14296D_20_10.xls		2	28/11/2011	H48(1)	H71(1)	H78(1)	H98(1)						
94	replacement of 30	YES	EIVS_HARLAN_LIQUIDS_15003C_21_11.xls		2	28/11/2011	H48(2)	H71(2)	H78(2)	H98(2)						
95	replacement of 92	YES	EIVS_HARLAN_LIQUIDS_15007C_23_12.xls		2	28/11/2011	H48(3)	H71(3)	H78(3)	H98(3)						
96	replacement of 39	YES	EIVS_HARLAN_LIQUIDS_15029A_27_14		2	28/11/2011	H6(1)	H15(1)	H70(1)	H72(1)	H122(1)	H124(1)	H128(1)			
97	replacement of 66	YES	EIVS_HARLAN_LIQUIDS_15030A_28_15.xls		2	28/11/2011	H6(2)	H15(2)	H70(2)	H72(2)	H122(2)	H124(2)	H128(2)			
98	replacement of 67	YES	EIVS_HARLAN_LIQUIDS_15033A_31_16.xls		2	28/11/2011	H6(3)	H15(3)	H70(3)	H72(3)	H122(3)	H124(3)	H128(3)			

Solids

No	Remark	Used	Filename	Saved as	version	date	content									
1		YES	EIVS_Harlan_solids_14225B_10_01.xls		1	11/03/2011	H3(1)	H4(1)	H14(1)	H41(1)	H44(1)	H61(1)	H62(1)	H86(1)	H95(1)	H111(1)
2	wrong run numbers	NO	EIVS_Harlan_solids_14234E_11_02.xls		1	22/03/2011	H3(1)	H4(1)	H14(1)	H41(1)	H44(1)	H61(1)	H62(1)	H86(1)	H95(1)	H111(1)
3	replacement of 3	YES	EIVS_Harlan_solids_14234E_11_02.xls		2	22/03/2011	H3(2)	H4(2)	H14(2)	H41(2)	H44(2)	H61(2)	H62(2)	H86(2)	H95(2)	H111(2)
4		YES	EIVS_Harlan_solids_14241D_12_03.xls		1	28/03/2011	H3(3)	H4(3)	H14(3)	H41(3)	H44(3)	H61(3)	H62(3)	H86(3)	H95(3)	H111(3)
5		YES	EIVS_Harlan_solids_14248F_13_04.xls		1	05/04/2011	H12(1)	H19(1)	H33(1)	H74(1)	H90(1)	H91(1)	H123(1)	H125(1)	H131(1)	H135(1)
6		YES	EIVS_Harlan_solids_14263E_15_05.xls		1	19/04/2011	H12(2)	H19(2)	H33(2)	H74(2)	H90(2)	H91(2)	H123(2)	H125(2)	H131(2)	H135(2)
7		YES	EIVS_Harlan_solids_14270B_16_06.xls		1	28/04/2011	H12(3)	H19(3)	H33(3)	H74(3)	H90(3)	H91(3)	H123(3)	H125(3)	H131(3)	H135(3)

No	Remark	Used	Filename	Saved as	version	date	content									
8		NO	EIVS_BDF_solids_14219D_08_02.xls		1	29/04/2011	B15(1)	B21(1)	B43(1)	B52(1)	B70(1)	B13(1)	B36(1)	B46(1)	B99(1)	B71(1)
9		YES	EIVS_BDF_solids_14219E_09_03.xls		1	30/04/2011	B13_KC	B36_KC	B46_KC	B99_KC	B71_KC					
10		NO	EIVS_BDF_solids_14222A_09_05.xls		1	01/05/2011	B15(2)	B21(2)	B43(2)	B52(2)	B70(2)	B13(2)	B36(2)	B46(2)	B99(2)	B71(2)
11	replaced by 69	NO	EIVS_BDF_solids_14225C_10_08.xls		1	02/05/2011	B15(3)	B21(3)	B43(3)	B52(3)	B70(3)	B13(3)	B36(3)	B46(3)	B99(3)	B71(3)
12		YES	EIVS_Harlan_solids_14283E_18_08.xls		1	09/05/2011	H85(2)	H92(2)	H106(2)	H108(2)	H109(2)	H112(2)	H121(2)	H133(2)	H134(2)	H139(2)
13		YES	EIVS_Harlan_solids_14277C_17_07.xls		1	13/05/2011	H85(1)	H92(1)	H106(1)	H108(1)	H109(1)	H112(1)	H121(1)	H133(1)	H134(1)	H139(1)
14		YES	EIVS_Harlan_solids_14289B_19_09.xls		1	13/05/2011	H85(3)	H92(3)	H106(3)	H108(3)	H109(3)	H112(3)	H121(3)	H133(3)	H134(3)	H139(3)
15	replacement of 8; replaced by 67	NO	EIVS_BDF_solids_14219D_08_02 revised.xls	EIVS_BDF_solids_14219D_08_02.xls	1	29/04/2011	B15(1)	B21(1)	B43(1)	B52(1)	B70(1)	B13(1)	B36(1)	B46(1)	B99(1)	B71(1)
16	replacement of 10; replaced by 68	NO	EIVS_BDF_solids_14222A_09_05 revised.xls	EIVS_BDF_solids_14222A_09_05.xls	1	01/05/2011	B15(2)	B21(2)	B43(2)	B52(2)	B70(2)	B13(2)	B36(2)	B46(2)	B99(2)	B71(2)
17	PC code missing	NO	EIVS_HARLAN_SOLIDS_14296E_20_10.xls		1	20/05/2011	H10(1)	H60(1)	H105(1)	H110(1)						
18		YES	EIVS_HARLAN_SOLIDS_KC.xls		1	20/05/2011	H10(Kt)	H60(Kt)	H105(Kt)	H110(Kt)						
19		YES	EIVS_BDF_solids_14219C_11_12.xls		1	27/05/2011	B109(Kt)	B76(Kt)	B136(Kt)	B122(Kt)	B124(Kt)					
20		YES	EIVS_BDF_solids_14234A_11_10.xls		1	27/05/2011	B115(1)	B33(1)	B2(1)	B81(1)	B104(1)	B109(1)	B76(1)	B136(1)	B122(1)	B124(1)
21		YES	EIVS_BDF_solids_14241B_12_14.xls		1	27/05/2011	B115(2)	B33(2)	B2(2)	B81(2)	B104(2)	B109(2)	B76(2)	B136(2)	B122(2)	B124(2)
22		YES	EIVS_BDF_solids_14248B_13_16.xls		1	27/05/2011	B115(3)	B33(3)	B2(3)	B81(3)	B104(3)	B109(3)	B76(3)	B136(3)	B122(3)	B124(3)
23	wrong run numbers	NO	EIVS_HARLAN_SOLIDS_15003C_21_11.xls		1	01/06/2011	H10(1)	H60(1)	H105(1)	H110(1)						
24	same as 18	NO	EIVS_HARLAN_SOLIDS_KC_11.xls		1	01/06/2011	H10(Kt)	H60(Kt)	H105(Kt)	H110(Kt)						
25	replacement of 23; pc code missing	NO	EIVS_HARLAN_SOLIDS_15003C_21_11.xls		1	01/06/2011	H10(2)	H60(2)	H105(2)	H110(2)						
26	replaced by 70	NO	EIVS_BDF_solids_14234B_11_11.xls		1	01/06/2011	B59(1)	B101(1)	B80(1)	B80CC(1)	B34(1)	B105(1)	B87(1)	B87CC(1)	B131(1)	
27	replaced by 71	NO	EIVS_BDF_solids_14241A_12_15.xls		1	01/06/2011	B80(2)	B80CC(2)	B87(2)	B87CC(2)	B59(2)	B101(2)	B34(2)	B105(2)	B131(2)	B99(4)
28	replaced by 72	NO	EIVS_BDF_solids_14248C_13_18.xls		1	01/06/2011	B80(3)	B80CC(3)	B87(3)	B87CC(3)	B59(3)	B101(3)	B34(3)	B105(3)	B131(3)	
29		YES	EIVS_BDF_solids_14256B_14_20.xls		1	01/06/2011	B132(1)	B40(1)	B88(1)	B107(1)	B117(1)	B119(1)	B135(1)	B110(1)	B108(1)	B23(1)
30		YES	EIVS_BDF_solids_14263C_15_23.xls		1	01/06/2011	B132(2)	B40(2)	B88(2)	B107(2)	B117(2)	B119(2)	B135(2)	B110(2)	B108(2)	B23(2)
31		YES	EIVS_BDF_solids_14277D_17_26.xls		1	01/06/2011	B132(3)	B40(3)	B88(3)	B107(3)	B117(3)	B119(3)	B135(3)	B110(3)	B108(3)	B23(3)
32		YES	EIVS_BDF_solids_14283C_18_28.xls		1	01/06/2011	B132(3)	B40(3)	B88(3)	B107(3)	B117(3)	B119(3)	B135(3)	B110(3)	B108(3)	B23(3)
33		YES	EIVS_HARLAN_SOLIDS_15013B_24_13.xls		1	13/07/2011	H20(1)	H39(1)	H54(1)	H76(1)						
34		YES	EIVS_HARLAN_SOLIDS_15029B_27_14.xls		1	13/07/2011	H20(2)	H39(2)	H54(2)	H76(2)						
35		YES	EIVS_HARLAN_SOLIDS_KC_13.xls		1	13/07/2011	H20Kt	H39Kt	H54Kt	H76Kt						
36		YES	EIVS_BDF_solids_14283B_18_30.xls		1	14/07/2011	B74(1)	B74CC(1)	B102(1)	B102CC(1)	B37(1)	B37CC(1)	B55(1)	B55CC(1)	B128(1)	B168(1)
37		YES	EIVS_BDF_solids_14289E_19_33.xls		1	14/07/2011	B74(2)	B74CC(2)	B102(2)	B102CC(2)	B37(2)	B37CC(2)	B55(2)	B55CC(2)	B128(2)	B168(2)
38		YES	EIVS_BDF_solids_14296C_20_35.xls		1	14/07/2011	B74(3)	B74CC(3)	B102(3)	B102CC(3)	B37(3)	B37CC(3)	B55(3)	B55CC(3)	B128(3)	B168(3)

No	Remark	Used	Filename	Saved as	version	date	content									
39		YES	EIVS_BDF_solids_15019B_26_46.xls		1	14/07/2011	B71_KC	B101_KC	B80KC	B87KC	B102_KC	B128_KC	B168_KC	B199_KC	B178_KC	B99_KC
40	empty 1st sheet	NO	EIVS_BDF_solids_14277F_26_49.xls		1	02/08/2011	B169_KC	B177_KC								
41		YES	EIVS_BDF_solids_14277F_26_49.xls		1	02/08/2011	B169_KC	B177_KC								
42		YES	EIVS_BDF_solids_14289C_19_31.xls		1	28/07/2011	B169(1)	B177(1)	B26(1)	B29(1)	B112(1)	B178(1)	B47(1)	B79(1)	B92(1)	B145(1)
43		YES	EIVS_BDF_solids_14296B_20_36.xls		1	28/07/2011	B169(2)	B177(2)	B26(2)	B29(2)	B112(2)	B178(2)	B47(2)	B79(2)	B92(2)	B145(2)
44		YES	EIVS_BDF_solids_15003A_21_37.xls		1	28/07/2011	B169(3)	B177(3)	B26(3)	B29(3)	B112(3)	B178(3)	B47(3)	B79(3)	B92(3)	B145(3)
45		YES	EIVS_IIVS_solids_14256_week7_number7_AH.xls		1	05/08/2011	V105(1)	V106(1)	V107(1)	V113(1)	V117(1)	V119(1)				
46		YES	EIVS_IIVS_solids_14263_week8_number9_AH.xls		1	05/08/2011	V105(2)	V106(2)	V107(2)	V113(2)	V117(2)	V119(2)				
47		YES	EIVS_IIVS_solids_14270_week9_number11_AH.xls		1	05/08/2011	V105(3)	V106(3)	V107(3)	V113(3)	V117(3)	V119(3)	V154(1)	V156(1)	V164(1)	V166(1)
48		YES	EIVS_HARLAN_Solids_15033C_31_16.xls		1	17/08/2011	H50(1)	H51(1)	H53(1)	H88(1)	H116(1)	H161(1)	H163(1)	H167(1)	H176(1)	H188(1)
49		YES	EIVS_HARLAN_Solids_15034B_32_17.xls		1	17/08/2011	H50(2)	H51(2)	H53(2)	H88(2)	H116(2)	H161(2)	H163(2)	H167(2)	H176(2)	H188(2)
50		YES	EIVS_IIVS_solids_15007_week16_number23_AH.xls		1	30/08/2011	V154(2)	V156(2)	V164(2)	V166(2)						
51		YES	EIVS_IIVS_solids_15013_week17_number24_AH.xls		1	30/08/2011	V154(3)	V156(3)	V164(3)	V166(3)						
52		YES	EIVS_IIVS_solids_14219_week1_number1_MK.xls		1	31/08/2011	V5(1)	V16(1)	V21(1)	V22(1)	V27(1)	V30(1)	V39(1)	V39_CC(1)	V53(1)	V69(1)
53		YES	EIVS_IIVS_solids_14222_week2_number2_MK.xls		1	31/08/2011	V5(2)	V16(2)	V21(2)	V22(2)	V27(2)	V30(2)	V39(2)	V39_CC(2)	V53(2)	V69(2)
54		YES	EIVS_IIVS_solids_14225_week3_number3_MK.xls		1	31/08/2011	V5(3)	V16(3)		V22(3)	V27(3)	V30(3)	V39(3)	V39_CC(3)	V53(3)	V69(3)
55		YES	EIVS_IIVS_solids_14234_week4_number4_MK.xls		1	31/08/2011	V18(1)	V28(1)	V37(1)	V37_CC(1)	V66(1)	V72(1)	V80(1)	V108(1)	V109(1)	V111(1)
56		YES	EIVS_IIVS_solids_14241_week5_number5_MK.xls		1	31/08/2011	V18(2)	V28(2)	V37(2)	V37_CC(2)	V66(2)	V72(2)	V80(2)	V108(2)	V109(2)	V111(2)
57		YES	EIVS_IIVS_solids_14248_week6_number6_MK.xls		1	31/08/2011	V18(3)	V28(3)	V37(3)	V37_CC(3)	V66(3)	V72(3)	V80(3)	V108(3)	V109(3)	V111(3)
58		YES	EIVS_IIVS_solids_14256_week7_number7_MK.xls		1	31/08/2011	V32(1)	V34(1)	V45(1)	V56(1)	V58(1)	V58_CC(1)	V85(1)	V86(1)	V87(1)	V101(1)
59		YES	EIVS_IIVS_solids_14263_week8_number8_MK.xls		1	31/08/2011	V32(2)	V34(2)	V45(2)	V56(2)	V37(4)	V37_CC(4)	V85(2)	V86(2)	V87(2)	V101(2)
60		YES	EIVS_IIVS_solids_14263_week9_number9KC_MK.xls		1	31/08/2011	V5_KC	V18_KC	V37_KC	V39_KC	V58_KC	V66_KC	V80_KC	V111_KC	V129_KC	
61		YES	EIVS_BDF_solids_15003B_21_39.xls		1	05/09/2011	B55(4)	B55_CC(4)	B199(1)							
62		YES	EIVS_BDF_solids_15007B_23_41.xls		1	05/09/2011	B199(2)									
63	incorrect batch no	NO	EIVS_BDF_solids_15013A_24_43.xls		1	05/09/2011	B199(3)	B47(4)	B23(5)							
64		YES	EIVS_BDF_solids_15019A_25_44.xls		1	05/09/2011	B87(4)	B87_CC(4)	B74(4)	B74_CC(4)	B128(4)	B168(4)				
65		YES	EIVS_BDF_solids_15025A_26_50.xls		1	05/09/2011	B87(5)	B87_CC(5)	B74(5)	B74_CC(5)	B55(5)	B55_CC(5)				
66		YES	EIVS_BDF_solids_15025A_27_51.xls		1	05/09/2011	B168_KC	B87_KC								
67	replacement of 15	YES	EIVS_BDF_solids_14219D_08_02 revised_updated.xls	EIVS_BDF_solids_14219D_08_02.xls	1	07/09/2011	B15(1)	B21(1)	B43(1)	B52(1)	B70(1)	B13(1)	B36(1)	B46(1)	B99(1)	B71(1)

No	Remark	Used	Filename	Saved as	version	date	content									
68	replacement of 16	YES	EIVS_BDF_solids_14222A_09_05 revised_updated.xls	EIVS_BDF_solids_14222A_09_05.xls	1	07/09/2011	B15(2)	B21(2)	B43(2)	B52(2)	B70(2)	B13(2)	B36(2)	B46(2)	B99(2)	B71(2)
69	replacement of 11	YES	EIVS_BDF_solids_14225C_10_08_updated.xls	EIVS_BDF_solids_14225C_10_08.xls	1	07/09/2011	B15(3)	B21(3)	B43(3)	B52(3)	B70(3)	B13(3)	B36(3)	B46(3)	B99(3)	B71(3)
70	replacement of 26	YES	EIVS_BDF_solids_14234B_11_11_updated.xls	EIVS_BDF_solids_14234B_11_11.xls	1	07/09/2011	B59(1)	B101(1)	B80(1)	B80CC(1)	B34(1)	B105(1)	B87(1)	B87CC(1)	B131(1)	
71	replacement of 27	YES	EIVS_BDF_solids_14241A_12_15_updated.xls	EIVS_BDF_solids_14241A_12_15.xls	1	07/09/2011	B80(2)	B80CC(2)	B87(2)	B87CC(2)	B59(2)	B101(2)	B34(2)	B105(2)	B131(2)	B99(4)
72	replacement of 28	YES	EIVS_BDF_solids_14248C_13_18_updated.xls	EIVS_BDF_solids_14248C_13_18.xls	1	07/09/2011	B80(3)	B80CC(3)	B87(3)	B87CC(3)	B59(3)	B101(3)	B34(3)	B105(3)	B131(3)	
73		YES	B74_colorant_dilution_EIVS_BDF_solids_14283B_18_30.xls		1	07/09/2011	B74(1)	B74CC(1)	B74(1)2.5%	B74CC(1)2.5%						
74		YES	B74_colorant_dilution_EIVS_BDF_solids_14289E_19_33.xls		1	07/09/2011	B74(2)	B74CC(2)	B74(2)5%	B74CC(2)5%						
75		YES	B74_colorant_dilution_EIVS_BDF_solids_14296C_20_35.xls		1	07/09/2011	B74(3)	B74CC(3)	B74(3)5%	B74CC(3)5%						
76	run?	YES	B74_colorant_dilution_EIVS_BDF_solids_15025A_26_50.xls		1	07/09/2011	B74(4) 2.5%	B74CC(4) 2.5%								
77		YES	B87_B74__colorant_dilution_EIVS_BDF_solids_15019A_25_44.xls		1	07/09/2011	B74(4)	B74CC(4)	B87(4)	B87CC(4)						
78		YES	B87_colorant_dilution_EIVS_BDF_solids_14234B_11_11.xls		1	07/09/2011	B87(1)	B87CC(1)	B87(1)5%	B87CC(1)5%						
79		YES	B87_colorant_dilution_EIVS_BDF_solids_14241A_12_15.xls		1	07/09/2011	B87(2)	B87CC(2)	B87(2)5%	B87CC(2)5%						
80		YES	B87_colorant_dilution_EIVS_BDF_solids_14248C_13_18.xls		1	07/09/2011	B87(3)	B87CC(3)	B87(3)5%	B87CC(3)5%						
81		YES	EIVS_HARLAN_Solids_15035B_33_18.xls		1	19/09/2011	H50(3)	H51(3)	H53(3)	H88(3)	H116(3)	H161(3)	H163(3)	H167(3)	H176(3)	H188(3)
82		YES	EIVS_HARLAN_SOLIDS_15037B_34_19.xls		1	26/09/2011	H23(1)	H23CC(1)	H36(1)	H36CC(1)	H83(1)	H83CC(1)	H20(4)	H20CC(4)	H155(1)	H58(1)
83		YES	EIVS_HARLAN_SOLIDS_KC34.xls		1	26/09/2011	H23_KC	H36_KC	H83_KC	H155_KC						
84		YES	EIVS_IIVS_solids_14270_week9_number10_MK.xls		1	19/10/2011	V32(3)	V34(3)	V45(3)	V56(3)	V58(2)	V58CC(2)	V85(3)	V86(3)	V87(3)	V101(3)
85		YES	EIVS_IIVS_solids_14277_week10_number11_MK.xls		1	19/10/2011	V37(5)	V37CC(5)	V130(1)	V137(1)	V140(1)	V9(1)	V9CC(1)	V13(1)	V13CC(1)	
86		YES	EIVS_IIVS_solids_14283_week11_number12_MK.xls		1	19/10/2011	V123(1)	V129(1)	V130(2)	V137(2)	V139(1)	V140(2)	V9(2)	V9CC(2)	V13(2)	V13CC(2)
87		YES	EIVS_IIVS_solids_14289_week12_number13_MK.xls		1	19/10/2011	V123(2)	V129(2)	V130(3)	V137(3)	V139(2)	V140(3)	V9(3)	V9CC(3)	V13(3)	V13CC(3)
88		YES	EIVS_IIVS_solids_14296_week13_number14_MK.xls		1	19/10/2011	V1(1)	V14(1)	V14CC(1)	V54(1)	V59(1)	V65(1)	V68(1)	V136(1)	V146(1)	V197(1)
89		YES	EIVS_IIVS_solids_15003_week14_number15_MK.xls		1	19/10/2011	V1(2)	V14(2)	V14CC(2)	V54(2)	V59(2)	V65(2)	V68(2)	V136(2)	V146(2)	V197(2)
90		YES	EIVS_IIVS_solids_15007_week15_number16_MK.xls		1	19/10/2011	V1(3)	V14(3)	V14CC(3)	V54(3)	V59(3)	V65(3)	V68(3)	V136(3)	V146(3)	V197(3)
91		YES	EIVS_IIVS_solids_15007_week17_number18KC_MK.xls		1	19/10/2011	V9_KC(1)	V13_KC(1)	V14_KC(2)	V58_KC(2)	V129_KC(1)	V146_KC(1)	V197_KC(1)			
92		YES	EIVS_IIVS_solids_15013_week16_number17_MK.xls		1	19/10/2011	V14(4)	V14CC(4)	V58(3)	V58CC(3)	V45(4)	V123(3)	V129(3)	V139(3)		
93		YES	EIVS_IIVS_solids_15030_week18_number19_MK.xls		1	19/10/2011	V14(5)	V14CC(5	V58(4)	V58CC(4						

No	Remark	Used	Filename	Saved as	version	date	content									
								)		)						
94		YES	EIVS_HARLAN_SOLIDS_15040A_38_20.xls		1	14/10/2011	H23(2)	H23CC(2)	H36(2)	H36CC(2)	H83(2)	H83CC(2)	H155(2)	H58(2)		
95	run?	NO	EIVS_Harlan_Solids_15046A_41_21.xls		1	27/10/2011	H23	H23CC	H36	H36CC	H83	H83CC	H155	H58		
96	run?	NO	EIVS_Harlan_Solids_15048A_42_22.xls		1	28/10/2011	H23	H23CC	H36	H36CC	H83	H83CC	H155	H58		
97	replacement of 95	YES	EIVS_Harlan_Solids_15046A_41_21.xls		1	31/10/2011	H23(3)	H23CC(3)	H36(3)	H36CC(3)	H83(3)	H83CC(3)	H155(3)	H58(3)		
98	replacement of 96	YES	EIVS_Harlan_Solids_15048A_42_22.xls		1	31/10/2011	H23(4)	H23CC(4)	H36(4)	H36CC(4)	H83(4)	H83CC(4)	H155(4)	H58(4)		
99	PC code missing	NO	EIVS_HARLAN_SOLIDS_15007A_23_12.xls		1	31/10/2011	H10(3)	H60(3)	H105(3)	H110(3)						
100		YES	EIVS_HARLAN_SOLIDS_15007A_23_12.xls		1	31/10/2011	H20(3)	H39(3)	H54(3)	H76(3)	H20CC(3)	H39CC(3)	H54CC(3)	H76CC(3)		
101	replacement of 63	YES	EIVS_BDF_solids_15013A_24_43-revised.xls	EIVS_BDF_solids_15013A_24_43.xls	1	09/12/2011	B199(3)	B47(4)	B23(5)							
102	replacement of 17	YES	EIVS_HARLAN_SOLIDS_14296E_20_10.xls		2	28/11/2011	H10(1)	H60(1)	H105(1)	H110(1)						
103	replacemebt of 25	YES	EIVS_HARLAN_SOLIDS_15003C_21_11.xls		2	28/11/2011	H10(2)	H60(2)	H105(2)	H110(2)						
104	replacemebt of 99	YES	EIVS_HARLAN_SOLIDS_15007A_23_12.xls		2	28/11/2011	H10(3)	H60(3)	H105(3)	H110(3)						

Appendix IV Remarks and special observations by the study personal

Chemical	filename	remark
5	EIVS_BDF_liquids_14241C_12_13.xls	After treatment precipitation of the substance in the original container was recognized. By warming at 37øC the precipitate dissolved partly.
7	EIVS_IIVS_liquids_14222_week2_number2_AH.xls	Tissue 1: Small amount of moisture observed during pulling of tissues- moisture removed by blotting insert on sterile, absorbant towels.
10	EIVS_IIVS_liquids_14248_week6_number5_AH.xls	Variability observed between tissues during the MTT incubation
11	EIVS_Harlan_liquids_14248E_13_04.xls	Both tissues stained pink after TI exposure and rinsing
11	EIVS_Harlan_liquids_14263D_15_05.xls	Both tissues stained pink after TI exposure and rinsing
11	EIVS_Harlan_liquids_14270A_16_06.xls	Both tissues stained pink after TI exposure and rinsing
11	EIVS_IIVS_liquids_14219_week1_number1_AH.xls	Tissue 2: Blister covering entire tissue noticed after 12 minute soak (blister appeared filled with media)
11	EIVS_IIVS_liquids_14225_week3_number3_AH.xls	Tissue 1 & 2: Blisters covering entire surface of tissue noticed during rinsing. Tissue 2: Blister covering entire tissue remained after soak- blister appeared to be filled with media. Tissue 2: Blister popped during blotting on paper towels prio
12	EIVS_BDF_liquids_14283A_18_29.xls	"cream-like residues after treatment and post-soak, causes turbid suspension after extraction, mean OD 1,915
12	EIVS_BDF_liquids_14283A_18_29.xls	centrifugation as described in SOP, "
12	EIVS_BDF_liquids_14289D_19_32.xls	"cream-like residues after treatment and post-soak, causes turbid suspension after extraction, mean OD 1,51
12	EIVS_BDF_liquids_14289D_19_32.xls	centrifugation as described in SOP, "
12	EIVS_BDF_liquids_14296A_20_34.xls	"cream-like residues after treatment and post-soak, causes turbid suspension after extraction, mean OD 1,458
12	EIVS_BDF_liquids_14296A_20_34.xls	centrifugation as described in SOP, "
12	EIVS_HARLAN_LIQUIDS_15033B_31_16.xls	Residual test item on tissues following rinsing
12	EIVS_HARLAN_LIQUIDS_15034A_32_17.xls	Residual test item on tissues after rinsing and post soak
12	EIVS_HARLAN_LIQUIDS_15035A_33_18.xls	Residual test item on tissues after rinsing and post soak
12	EIVS_IIVS_liquids_14289_week12_number14_AH.xls	Tissues 1&2: residual test article after rinse/soak- after soak, soak media cloudy
12	EIVS_IIVS_liquids_14296_week13_number17_AH.xls	Tissues 1&2: Residual test article after rinse/soak. Soak wells cloudy after soak. Possible small blisters noticed on tissues during rinsing.
12	EIVS_IIVS_liquids_15003_week14_number19_AH.xls	Tissue 1&2: residual test article after rinse/soak. Soak wells cloudy after soak. Possible small blisters noticed on tissues after rinse/soak.
13	EIVS_BDF_liquids_14283A_18_29.xls	"cream-like residues after treatment and post-soak, causes turbid suspension after extraction, mean OD 3,369
13	EIVS_BDF_liquids_14283A_18_29.xls	centrifugation as described in SOP, "
13	EIVS_BDF_liquids_14289D_19_32.xls	"cream-like residues after treatment and post-soak, causes turbid suspension after extraction, mean OD 2.00
13	EIVS_BDF_liquids_14289D_19_32.xls	centrifugation as described in SOP, "
13	EIVS_BDF_liquids_14296A_20_34.xls	"cream-like residues after treatment and post-soak, causes turbid suspension after extraction, mean OD 1.914
13	EIVS_BDF_liquids_14296A_20_34.xls	centrifugation as described in SOP, "
13	EIVS_HARLAN_LIQUIDS_15033B_31_16.xls	Residual test item on tissues following rinsing
13	EIVS_HARLAN_LIQUIDS_15034A_32_17.xls	Residual test item on tissues after rinsing and post soak
13	EIVS_HARLAN_LIQUIDS_15035A_33_18.xls	Residual test item on tissues after rinsing and post soak
13	EIVS_IIVS_liquids_14289_week12_number14_AH.xls	Tissues 1&2: residual test article after rinse/soak- after soak, soak media cloudy. After overnight extraction, both tissues were noticed to have a dark purple ring around the perimeter of the tissue.
13	EIVS_IIVS_liquids_14296_week13_number17_AH.xls	Tissues 1&2: Residual test article after rinse/soak. Soak wells cloudy after soak. After isopropanol extraction, purple ring noted around the perimeter of the tissues.
13	EIVS_IIVS_liquids_15003_week14_number19_AH.xls	Tissues 1&2: residual test article after rinse/soak. Soak wells cloudy after soak. Dark purple ring around perimeter of the tissues observed after isopropanol extraction.
17	EIVS_IIVS_liquids_14234_week4_number4_HI.xls	possible residual test article (clear/shiny)
17	EIVS_IIVS_liquids_14241_week5_number6_HI.xls	possible residual test article (clear/shiny)
17	EIVS_IIVS_liquids_14248_week6_number7_HI.xls	possible residual test article
20	EIVS_IIVS_liquids_14277_week10_number12_AH.xls	Tissues 1&2: residual test article after rinse/soak
20	EIVS_IIVS_liquids_14283_week11_number13_AH.xls	Tissues 1 & 2: residual test article after rinse/soak. V8 samples loaded into wells designated for TA11 after centrifugation.
20	EIVS_IIVS_liquids_14289_week12_number15_AH.xls	"Tissues 1&2: residual test article noticed after addition to MTT. After the 2 hour plate shake, precipitate noticed in the in 24-wells containing isopropanol; 1mL of the extractant was transferred to a centrifuge tube and centrifuged at ~13,000 g f
21	EIVS_IIVS_liquids_14256_week7_number6_AH.xls	Tissue 1: small amount of excess media noticed prior to adding 20 æL DPBS. Media was blotted on sterile towels before DPBS addition.
22	EIVS_BDF_liquids_14248A_13_17.xls	After postincubation there are bubbles below the tissues and crustifications on the rim of the insert.
22	EIVS_BDF_liquids_14256A_14_19.xls	After postincubation there are bubbles below the tissues and crustifications on the rim of the insert.
22	EIVS_BDF_liquids_14263A_15_22.xls	After postincubation there are bubbles below the tissues and crustifications on the rim of the insert.
22	EIVS_IIVS_liquids_14234_week4_number4_HI.xls	MTT pattern of reduction is consistent with immiscibility of test article after dosing. (the part of the tissue actually making contact with the test article was completely dead)
22	EIVS_IIVS_liquids_14241_week5_number6_HI.xls	Tissue 1: MTT pattern of reduction is consistent with immiscibility of test article after dosing. (the part of the tissue actually making contact with the test article was completely dead)
23	EIVS_BDF_liquids_14248A_13_17.xls	"After incubation the medium is light yellow (pH8,5).
23	EIVS_BDF_liquids_14248A_13_17.xls	Crustification on the rim of the insert after postincubation.
23	EIVS_BDF_liquids_14248A_13_17.xls	After MTT-staining the color of the rest of the MTT-medium has turned to blue."
23	EIVS_BDF_liquids_14256A_14_19.xls	"After incubation the medium is light yellow (pH8,5).
23	EIVS_BDF_liquids_14256A_14_19.xls	Crustification on the rim of the insert after postincubation.
23	EIVS_BDF_liquids_14256A_14_19.xls	After MTT-staining the color of the rest of the MTT-medium has turned to blue."
23	EIVS_BDF_liquids_14263A_15_22.xls	"After incubation the medium is light yellow (pH8,5).
23	EIVS_BDF_liquids_14263A_15_22.xls	Crustification on the rim of the insert after postincubation.
23	EIVS_BDF_liquids_14263A_15_22.xls	After MTT-staining the color of the rest of the MTT-medium has turned to blue."
23	EIVS_HARLAN_LIQUIDS_15029A_27_14.xls	Media turned paler pink after exposure.
23	EIVS_HARLAN_LIQUIDS_15030A_28_15.xls	Media turned paler pink after exposure.

Chemical	filename	remark
23	EIVS_HARLAN_LIQUIDS_15033A_31_16.xls	Media turned lighter pink after exposure.
23	EIVS_IIVS_liquids_14248_week6_number5_AH.xls	Tissues 1&2: Media in wells slightly orange
23	EIVS_IIVS_liquids_14256_week7_number6_AH.xls	"Immediately after dosing, the test article was attempted to be spread; the millicell was dropped onto its side- some test article may have spilled into the media (media turned slightly orange)- after the 30 minute dosing period, both wells of tis
23	EIVS_IIVS_liquids_14263_week8_number8_AH.xls	Tissues 1&2: Media in wells turned slightly orange during 30 minute dosing period
23	EIVS_IIVS_liquids_14270_week9_number10_AH.xls	Tissues 1 & 2: media in wells turned slightly orange during dosing period
26	EIVS_BDF_liquids_15003B_21_38.xls	light yellow residues (like jelly) after washing, postsoak, postinkubation, MTT and extraction.
26	EIVS_BDF_liquids_15007B_23_40.xls	light yellow residues (like jelly) after washing, postsoak, postinkubation, MTT and extraction
26	EIVS_BDF_liquids_15013A_24_42.xls	light yellow residues (like jelly) after washing, postsoak, postinkubation, MTT and extraction
26	EIVS_HARLAN_LIQUIDS_15033B_31_16.xls	Residual test item on tissues following rinsing
26	EIVS_HARLAN_LIQUIDS_15034A_32_17.xls	Residual test item on tissues after rinsing and post soak
26	EIVS_HARLAN_LIQUIDS_15035A_33_18.xls	Residual test item on tissues after rinsing and post soak
26	EIVS_IIVS_liquids_14277_week10_number12_AH.xls	"Tissue 2: large residual test article after rinse/soak. Tissues 1 & 2: After 2 hour post-incubation soak, droplets of test article noticed floating in the media of both wells. This floating test article may have been stuck to the outside of the
26	EIVS_IIVS_liquids_14283_week11_number13_AH.xls	Tissues 1 & 2; residual test article after rinse/soak. Extra care taken to wipe the outside of the millicells with sterile towels after soak
26	EIVS_IIVS_liquids_14296_week13_number18_AH.xls	Tissues 1&2: Residual test article remained on tissues after rinse/soak
26	EIVS_IIVS_liquids_15003_week14_number20_AH.xls	Tissue 1&2: residual test article after rinse/soak.
29	EIVS_BDF_solids_14283B_18_30.xls	residues after washing, post-soak, postincubation, MTT test and extraction
29	EIVS_BDF_solids_14289E_19_33.xls	no residues
29	EIVS_BDF_solids_14296C_20_35.xls	residues after washing and post-soak
29	EIVS_BDF_solids_15019A_25_44.xls	Residues after washing and post-soak.
29	EIVS_HARLAN_Solids_15033C_31_16.xls	Residual test item on tissues after rinsing and post soak.
29	EIVS_IIVS_solids_14296_week13_number14_MK.xls	Small amount of residual test article following rinsing and soaking.
29	EIVS_IIVS_solids_15003_week14_number15_MK.xls	Small amount of residual test article following rinsing and soaking. Tissue # 2 had twice as much residual test article in comparison to tissue # 1.
29	EIVS_IIVS_solids_15007_week15_number16_MK.xls	Small amount of residual test article following rinsing and soaking.
30	EIVS_BDF_solids_14234A_11_10.xls	solubilize in prewetting water -> liquid
30	EIVS_BDF_solids_14241B_12_14.xls	solubilize in prewetting water -> liquid
30	EIVS_BDF_solids_14248B_13_16.xls	solubilize in prewetting water -> liquid
30	EIVS_Harlan_solids_14277C_17_07.xls	For both tissues the test item was dissolved during the exposure period.
30	EIVS_Harlan_solids_14283E_18_08.xls	For both tissues the test item was dissolved during the exposure period.
30	EIVS_Harlan_solids_14289B_19_09.xls	For both tissues the test item was dissolved during the exposure period.
30	EIVS_IIVS_solids_14277_week10_number11_MK.xls	Media pooled within the millicells, observed following test article exposure.
30	EIVS_IIVS_solids_14283_week11_number12_MK.xls	Media pooled within the millicells following test aricle exposure time.
30	EIVS_IIVS_solids_14289_week12_number13_MK.xls	Media was observed to have pooled within the millicells following test article exposure time.
31	EIVS_Harlan_solids_14277C_17_07.xls	For both tissues the test item was dissolved during the exposure period.
32	EIVS_BDF_solids_14234B_11_11.xls	Medium yellow after exposure and washing .
32	EIVS_BDF_solids_14241A_12_15.xls	Small residues after rinsing and post-soak.
32	EIVS_BDF_solids_14248C_13_18.xls	Residues after rinsing an post soak. Medium yellow after exposure and post incubation.
32	EIVS_HARLAN_SOLIDS_15013B_24_13.xls	Media stained yellow after exposure. Tissues stained yellow/brown after rinsing and soaking.
32	EIVS_HARLAN_SOLIDS_15013B_24_13.xls	Media stained yellow after exposure. Tissues stained yellow/brown after rinsing and soaking.
32	EIVS_HARLAN_SOLIDS_15029B_27_14.xls	Media stained yellow after exposure. Tissues stained yellow/brown after rinsing and soaking.
32	EIVS_HARLAN_SOLIDS_15029B_27_14.xls	Media stained yellow after exposure. Tissues stained yellow/brown after rinsing and soaking.
32	EIVS_HARLAN_SOLIDS_15030B_28_15.xls	Media stained orange after exposure. Tissues stained brown/yellow after rinsing and soaking.
32	EIVS_HARLAN_SOLIDS_15030B_28_15.xls	Media stained orange after exposure. Tissues stained brown/yellow after rinsing and soaking.
32	EIVS_IIVS_solids_14234_week4_number4_MK.xls	"Media beneath millicells had turned a pale orange after test article exposure time. For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. Tissues appeared to be stained a br
32	EIVS_IIVS_solids_14241_week5_number5_MK.xls	"Media beneath millicells had turned a pale orange after test article exposure time. For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. Tissues appeared to be stained a br
32	EIVS_IIVS_solids_14248_week6_number6_MK.xls	"Media beneath millicells had turned a pale orange after test article exposure time. For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. Tissues appeared to be stained a br
33	EIVS_BDF_solids_14234B_11_11.xls	"Different amount of residues after washing and post-soak.
33	EIVS_BDF_solids_14234B_11_11.xls	In contrast to CC of B87 qualified! "
33	EIVS_BDF_solids_14234B_11_11.xls	"B87CC: Much more residues than B87 after washing and post-soak. The formazan-extracts were diluted 5% in isopropanol (additional spreadsheets: B87_colorant-1dilution_solids_14234B_11_11 and B87_colorant-dilution_solids_14234B_11_11
33	EIVS_BDF_solids_14234B_11_11.xls	NOT QUALIFIED!! OD >> 3,000"
33	EIVS_BDF_solids_14241A_12_15.xls	"Medium dark blue after exposure and post incubation, tissue 2 much more residues after rinsing and postsoak than tissue The formazan-extracts were diluted 5% in isopropanol (additional spreadsheets: B87_colorant-1dilution_solids_14241A_12_15 and
33	EIVS_BDF_solids_14241A_12_15.xls	NOT QUALIFIED!! OD >> 3,000"
33	EIVS_BDF_solids_14241A_12_15.xls	"B87CC: Medium dark blue after exposure and post incubation, both tissues more residues after rinsing and postsoak than B87 tissues.The formazan-extracts were diluted 5% in isopropanol (additional spreadsheets: B87_colorant-1dilution_solids_14241A_12
33	EIVS_BDF_solids_14241A_12_15.xls	NOT QUALIFIED!! OD >> 3,000"
33	EIVS_BDF_solids_14248C_13_18.xls	"Medium dark blue after exposure and post incubation, tissue 1 much more residues after rinsing and postsoak than tissue 2. The formazan-extracts were diluted 5% in isopropanol (additional spreadsheets: B87_colorant-1dilution_solids_14248C_13_18 a
33	EIVS_BDF_solids_14248C_13_18.xls	NOT QUALIFIED!! OD of tissue 1 >> 3,000"
33	EIVS_BDF_solids_14248C_13_18.xls	"B87CC: Medium dark blue after exposure and post incubation, both tissues more residues after rinsing and postsoak than B87 tissues.The formazan-extracts were diluted 5% in isopropanol (additional spreadsheets: B87_colorant-

Chemical	filename	remark
		1dilution_solids_14248C_13
33	EIVS_BDF_solids_14248C_13_18.xls	NOT QUALIFIED!! OD >> 3,000"
33	EIVS_BDF_solids_15019A_25_44.xls	"Different amount of residues after washing and post-soak. Tissue 1 = OD >> 3,000
33	EIVS_BDF_solids_15019A_25_44.xls	NOT QUALIFIED!! "
33	EIVS_BDF_solids_15019A_25_44.xls	"B87CC: Residues after washing and post-soak. The formazan-extracts were diluted 2,5% in isopropanol (additional spreadsheets: B87_colorant-dilution_solids_15019A-25_44)
33	EIVS_BDF_solids_15019A_25_44.xls	NOT QUALIFIED!! OD >> 3,000"
33	EIVS_BDF_solids_15025A_26_50.xls	Little Residues after washing and post-soak.
33	EIVS_BDF_solids_15025A_26_50.xls	B87CC:Little Residues after washing and post-soak.
33	EIVS_HARLAN_SOLIDS_15013B_24_13.xls	Media stained purple after exposure. Residual test item on tissues after rinsing and soaking. Media stained purple after 18 hour post exposure incubation.
33	EIVS_HARLAN_SOLIDS_15013B_24_13.xls	Media stained purple after exposure. Residual test item on tissues after rinsing and soaking. Media stained purple after 18 hour post exposure incubation.
33	EIVS_HARLAN_SOLIDS_15029B_27_14.xls	Media stained purple after exposure. Small amount of residual test item on tissues after rinsing and soaking.
33	EIVS_HARLAN_SOLIDS_15029B_27_14.xls	Media stained purple after exposure. Small amount of residual test item on tissues after rinsing and soaking.
33	EIVS_HARLAN_SOLIDS_15030B_28_15.xls	Media stained purple after exposure. Small amount of residual test item on tissues after rinsing and soaking.
33	EIVS_HARLAN_SOLIDS_15030B_28_15.xls	Media stained purple after exposure. Small amount of residual test item on tissues after rinsing and soaking.
33	EIVS_HARLAN_SOLIDS_15037B_34_19.xls	Media turned purple during exposure. Residual test item on tissues after rinsing and post soak. Tissues stained purple.
33	EIVS_HARLAN_SOLIDS_15037B_34_19.xls	Media turned purple during exposure. Residual test item on tissues after rinsing and post soak. Tissues stained purple.
33	EIVS_IIVS_solids_14256_week7_number7_MK.xls	Media beneath millicells had turned purple following test article exposure time. Tissues had slight staining following rinsing and soaking.
33	EIVS_IIVS_solids_14256_week7_number7_MK.xls	Media beneath millicells had turned purple following test article exposure time. Tissues had slight staining following rinsing and soaking.
33	EIVS_IIVS_solids_14270_week9_number10_MK.xls	Media beneath millicells turned purple after test article exposure time. Tissue staining observed around the outside perimeter after rinsing and soaking.
33	EIVS_IIVS_solids_14270_week9_number10_MK.xls	Media beneath millicells turned purple after test article exposure time. Tissue staining observed around the outside perimeter after rinsing and soaking. Residual test article on Tissue # 2 after rinsing and soaking. The media beneath the millicell
33	EIVS_IIVS_solids_15013_week16_number17_MK.xls	"Media beneath millicells observed to have turned purple following test article exposure time. Tissues were stained purple and large amount of residual test article following rinsing and soaking. Media beneath millicells turned purple, observed fol
33	EIVS_IIVS_solids_15013_week16_number17_MK.xls	"Media beneath millicells observed to have turned purple following test article exposure time. Tissues were stained purple and large amount of residual test article following rinsing and soaking. Media beneath millicells turned purple, observed fol
33	EIVS_IIVS_solids_15030_week18_number19_MK.xls	"Media beneath millicells observed to have turned purple following test article exposure time. Tissues stained purple in patchy areas and residual test article following rinsing and soaking. Tissue #2 had much less staining and residual test articl
33	EIVS_IIVS_solids_15030_week18_number19_MK.xls	"Media beneath millicells observed to have turned purple following test article exposure time. Tissues stained purple in patchy areas and residual test article following rinsing and soaking. Media beneath millicells turned dark purple, observed fol
34	EIVS_BDF_solids_14234B_11_11.xls	Red residues after washing , small residues after post-soak.
34	EIVS_BDF_solids_14234B_11_11.xls	B80CC: Red residues after washing , small residues after post-soak.
34	EIVS_BDF_solids_14241A_12_15.xls	Small residues after rinsing and post-soak.
34	EIVS_BDF_solids_14241A_12_15.xls	B80CC: Small residues after rinsing and post-soak.
34	EIVS_BDF_solids_14248C_13_18.xls	Small residues after rinsing an post soak.
34	EIVS_BDF_solids_14248C_13_18.xls	B80CC: Small residues after rinsing an post soak.
34	EIVS_HARLAN_SOLIDS_15013B_24_13.xls	Test item liquified in inserts during exposure. Tissues stained brown/purple after rinsing and soaking.
34	EIVS_HARLAN_SOLIDS_15013B_24_13.xls	Test item liquified in inserts during exposure. Tissues stained brown/purple after rinsing and soaking.
34	EIVS_HARLAN_SOLIDS_15029B_27_14.xls	Test item liquified in inserts during exposure. Tissues stained brown/purple after rinsing and soaking.
34	EIVS_HARLAN_SOLIDS_15029B_27_14.xls	Test item liquified in inserts during exposure. Tissues stained brown/purple after rinsing and soaking.
34	EIVS_HARLAN_SOLIDS_15030B_28_15.xls	Test item liquified during exposure. Tissues stained brown/purple after rinsing and soaking.
34	EIVS_HARLAN_SOLIDS_15030B_28_15.xls	Test item liquified during exposure. Tissues stained brown/purple after rinsing and soaking.
34	EIVS_IIVS_solids_14234_week4_number4_MK.xls	"For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. A small amount of extractant pooled into the millicell of tissue #1 during extraction period. Both tissues appeared to
34	EIVS_IIVS_solids_14234_week4_number4_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. Both tissues appeared to be stained orange after the extraction period
34	EIVS_IIVS_solids_14241_week5_number5_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. Both tissues appeared to be stained a brownish-orange after the extraction period
34	EIVS_IIVS_solids_14241_week5_number5_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. Both tissues appeared to be stained orange after the extraction period
34	EIVS_IIVS_solids_14248_week6_number6_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. Both tissues appeared to be stained a brownish-orange after the extraction period
34	EIVS_IIVS_solids_14248_week6_number6_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking. Both tissues appeared to be stained orange after the extraction period
34	EIVS_IIVS_solids_14263_week8_number8_MK.xls	Tissue staining observed following rinsing and soaking. Tissues appeared to be stained a brownish orange after extraction period.
34	EIVS_IIVS_solids_14263_week8_number8_MK.xls	Tissue staining observed following rinsing and soaking. Tissues appeared to be stained orange after extraction period.
34	EIVS_IIVS_solids_14277_week10_number11_MK.xls	Possible residual test article or tissue staining, observed following rinsing and soaking. Tissues stained a brownish orange after extraction.
34	EIVS_IIVS_solids_14277_week10_number11_MK.xls	Possible residual test article or tissue staining, observed following rinsing and soaking. Tissues stained orange after extraction.

Chemical	filename	remark
35	EIVS_BDF_solids_14219D_08_02.xls	After rinsing little residues left.
35	EIVS_BDF_solids_14222A_09_05.xls	More substance needed on both tissues (2x syringe), small residues after rinsing and postsoak on both tissues.
35	EIVS_BDF_solids_14225C_10_08.xls	Residues after rinsing and postsoak.
35	EIVS_BDF_solids_14225C_10_08.xls	No data because of cancelling B36. Two tissues were saved for using as killed contols.
35	EIVS_HARLAN_SOLIDS_14296E_20_10.xls	Residual test items on both tissues post rinsing
35	EIVS_HARLAN_SOLIDS_15003C_21_11.xls	Residual test item on both tissues post rinsing
35	EIVS_HARLAN_SOLIDS_15007A_23_12.xls	Residual test item on tissues post rinsing
36	EIVS_BDF_solids_14219D_08_02.xls	After rinsing small residues left.
36	EIVS_BDF_solids_14222A_09_05.xls	More substance needed on both tissues (2x syringe), very small residues after rinsing and postsoak on both tissues.
36	EIVS_IIVS_solids_14234_week4_number4_MK.xls	Small residual test article remained on tissues after rinsing and soaking
36	EIVS_IIVS_solids_14248_week6_number6_MK.xls	Small residual test article remained on tissues after rinsing and soaking.
37	EIVS_BDF_liquids_14256C_14_21.xls	viscous substance, not washed off, see photo " 113_after post soak", D>20 possibly because of pipetting mistake
37	EIVS_BDF_liquids_15003B_21_38.xls	foams during washing, residues (like jelly) after washing and postsoak
37	EIVS_BDF_liquids_15007B_23_40.xls	foams during washing, residues (like jelly) after washing and postsoak
37	EIVS_BDF_liquids_15013A_24_42.xls	foams during washing, residues (like jelly) after washing and postsoak
37	EIVS_Harlan_liquids_14277B_17_07.xls	Residual test item noted on both tissues following rinsing
37	EIVS_Harlan_liquids_14283D_18_08.xls	Residual test item noted on both tissues following rinsing
37	EIVS_Harlan_liquids_14289A_19_09.xls	Residual test item noted on both tissues following rinsing
37	EIVS_IIVS_liquids_14248_week6_number5_AH.xls	Tissue 1&2: Residual test article remained after dosing/rinsing
37	EIVS_IIVS_liquids_14256_week7_number6_AH.xls	Tissues 1 & 2: Residual test article remained after dosing/ rinsing
37	EIVS_IIVS_liquids_14263_week8_number8_AH.xls	Tissues 1&2: residual test article remained after rinsing/soaking
38	EIVS_BDF_solids_14289C_19_31.xls	Few residues after post soak on the inner wall of the inserts.
38	EIVS_BDF_solids_14296B_20_36.xls	Few residues after post soak on the inner wall of the inserts.
38	EIVS_IIVS_solids_14296_week13_number14_MK.xls	Small amount of residual test article following rinsing and soaking.
38	EIVS_IIVS_solids_15003_week14_number15_MK.xls	Very small amount of residual test article following rinsing and soaking.
38	EIVS_IIVS_solids_15007_week15_number16_MK.xls	Very small amount of residual test article following rinsing and soaking.
39	EIVS_BDF_solids_14289C_19_31.xls	Few residues after post soak.
39	EIVS_BDF_solids_14296B_20_36.xls	Few residues after post soak on the tissues and on the inner wall of the inserts.
39	EIVS_BDF_solids_15003A_21_37.xls	Few residues after post soak on the tissues and on the inner wall of the inserts.
39	EIVS_IIVS_solids_14296_week13_number14_MK.xls	"Immediately after dosing, it was noticed that some test article had spilled into the 6-well plate of tissue # 1. The millicell was placed into a new 6-well plate containing fresh media. Small amount of residual test article on both tissues followin
39	EIVS_IIVS_solids_15003_week14_number15_MK.xls	Small amount of residual test article on both tissues following rinsing and soaking.
39	EIVS_IIVS_solids_15007_week15_number16_MK.xls	Small amount of residual test article on both tissues following rinsing and soaking.
40	EIVS_BDF_solids_14289C_19_31.xls	Substance remains completely on the tissue after washing. After post soak substance still on the tissue. Some liquid (yellow-brown) is above the substance.
40	EIVS_BDF_solids_14296B_20_36.xls	Substance remains completely on the tissue after washing. After post soak substance still on the tissue. Some liquid (yellow-brown) is above the substance.
40	EIVS_BDF_solids_15003A_21_37.xls	Substance remains completely on the tissue after washing. After post soak substance still on the tissue. Some liquid (yellow-brown) is above the substance.
40	EIVS_HARLAN_SOLIDS_15037B_34_19.xls	Test item turned to gel in insert during exposure. Residual test item on tissues after rinsing and post soak
40	EIVS_Harlan_Solids_15046A_41_21.xls	Test item turned to gel on tissues during exposure. Residual test item on tissues after rinsing and post soak.
40	EIVS_Harlan_Solids_15048A_42_22.xls	Test item turned to gel during exposure. Residual test item on tissues after rinsing and post soak.
40	EIVS_IIVS_solids_14296_week13_number14_MK.xls	Large amount of residual test article, the test article seemed to turn into a gel following rinsing and soaking.
40	EIVS_IIVS_solids_15003_week14_number15_MK.xls	Large amount of residual test article, the test article seemed to turn into a gel following rinsing and soaking.
40	EIVS_IIVS_solids_15007_week15_number16_MK.xls	Large amount of residual test article, the test article seemed to turn into a gel following rinsing and soaking.
41	EIVS_IIVS_solids_14234_week4_number4_MK.xls	Small residual test article remained on tissues after rinsing and soaking
41	EIVS_IIVS_solids_14248_week6_number6_MK.xls	Small residual test article remained on tissues after rinsing and soaking.
42	EIVS_BDF_solids_14234A_11_10.xls	solubilize in prewetting water -> liquid
42	EIVS_BDF_solids_14241B_12_14.xls	solubilize in prewetting water -> liquid
42	EIVS_BDF_solids_14248B_13_16.xls	solubilize in prewetting water -> liquid
42	EIVS_HARLAN_SOLIDS_14296E_20_10.xls	Test item liquified in tissue inserts
42	EIVS_HARLAN_SOLIDS_15003C_21_11.xls	Test item liquified in tissue inserts
42	EIVS_HARLAN_SOLIDS_15007A_23_12.xls	Test item liquified in tissue inserts
42	EIVS_IIVS_solids_14234_week4_number4_MK.xls	Media pooled into millicell of both tissues, noticed prior to treatment termination
42	EIVS_IIVS_solids_14241_week5_number5_MK.xls	Media pooled into millicell of both tissues, noticed prior to treatment termination
42	EIVS_IIVS_solids_14248_week6_number6_MK.xls	Media pooled into millicell of both tissues, noticed prior to treatment termination
44	EIVS_IIVS_solids_14256_week7_number7_AH.xls	Tissue 2: Small amount of residual test article
44	EIVS_IIVS_solids_14263_week8_number9_AH.xls	Tissues 1&2: Small residual test article after rinsing/soaking.
44	EIVS_IIVS_solids_14270_week9_number11_AH.xls	Tissue 2: small amount of residual test article after rinse/soak
46	EIVS_BDF_solids_14256B_14_20.xls	solubilized/wax after treatment, sticks even after postsoak
46	EIVS_BDF_solids_14263C_15_23.xls	solubilized/wax after treatment, sticks even after postsoak
46	EIVS_BDF_solids_14277D_17_26.xls	solubilized/wax after treatment, sticks even after postsoak
46	EIVS_BDF_solids_14283C_18_28.xls	solubilized/wax after treatment, sticks even after postsoak
46	EIVS_Harlan_solids_14277C_17_07.xls	Test item became a gel following exposure and as such it was not possible to remove it from the tissues during the rinsing process.
46	EIVS_Harlan_solids_14283E_18_08.xls	Test item became a gel following exposure and as such it was not possible to remove it from the tissues during the rinsing process.
46	EIVS_Harlan_solids_14289B_19_09.xls	Test item became a gel following exposure and as such it was not possible to remove it from the tissues during the rinsing process.
46	EIVS_IIVS_solids_14256_week7_number7_AH.xls	"Large amount of residual test article- test article appeared to ""gel"" atop tissue after rinsing. After 18 hr post-exposure incubation, the ""gel"" (possible residual test article) atop the tissue surfaces appears to possibly contain media- the
46	EIVS_IIVS_solids_14263_week8_number9_AH.xls	"Tissues 1& 2: residual test article after rinsing/soaking- test article appeared to ""gel"" atop tissue. ""Gel"" appeared to increase in size during overnight (18 hr) incubation and ""gel"" contained pink coloration (possible media). Tissues were
46	EIVS_IIVS_solids_14270_week9_number11_AH.xls	"Tissues 1&2: Test article ""gelled"" atop tissue- residual test article after rinse/soak. After 18 hr post exposure incubation, the ""gel"" appeared to increase in size (possible media within ""gel""). After isopropanol extraction, spots of black
47	EIVS_BDF_solids_14234B_11_11.xls	"Substance dissolved or melted on the surface of the tissue after exposure.
47	EIVS_HARLAN_SOLIDS_14296E_20_10.xls	Test item liquified in tissue inserts

Chemical	filename	remark
47	EIVS_HARLAN_SOLIDS_15003C_21_11.xls	Test item liquified in tissue inserts
47	EIVS_HARLAN_SOLIDS_15007A_23_12.xls	Test item liquified in tissue inserts
47	EIVS_IIVS_solids_14270_week9_number11_AH.xls	Tissues 1&2: Small amount of residual test article remained after rinse/soak
48	EIVS_BDF_solids_14234A_11_10.xls	solubilize in prewetting water -> liquid, medium yellow after treatment pH 5,5
48	EIVS_BDF_solids_14241B_12_14.xls	solubilize in prewetting water -> liquid, medium yellow after treatment pH 5,5
48	EIVS_BDF_solids_14248B_13_16.xls	solubilize in prewetting water -> liquid, medium yellow after treatment pH 5,5
48	EIVS_Harlan_solids_14248F_13_04.xls	Test item dissolved by medium (both tissues) and assay medium turned yellow
48	EIVS_Harlan_solids_14263E_15_05.xls	Test item dissolved by medium (both tissues) and assay medium turned yellow
48	EIVS_Harlan_solids_14270B_16_06.xls	Test item dissolved by medium (both tissues) and assay medium turned yellow
48	EIVS_IIVS_solids_14283_week11_number12_MK.xls	Media beneath millicells had turned yellow, observed after exposure time. Media had also pooled within each millicell.
48	EIVS_IIVS_solids_14289_week12_number13_MK.xls	Media beneath millicells had turned yellow, observed after test article exposure time. Media had also pooled within each millicell.
48	EIVS_IIVS_solids_15013_week16_number17_MK.xls	Media beneath millicells observed to have turned yellow following test article exposure time; media was also noticed to have pooled within millicells.
49	EIVS_HARLAN_SOLIDS_15040A_38_20.xls	Tissues partially detatched from inserts after rinsing.
50	EIVS_BDF_solids_14283B_18_30.xls	small residues after washing, post-soak, postincubation, MTT test and extraction
50	EIVS_BDF_solids_14289E_19_33.xls	no residues
50	EIVS_BDF_solids_14296C_20_35.xls	residues after washing and post-soak
50	EIVS_BDF_solids_15019A_25_44.xls	Little residues after washing and post-soak.
51	EIVS_BDF_solids_14296B_20_36.xls	Few residues after washing and post soak.
51	EIVS_IIVS_solids_15007_week16_number23_AH.xls	Tissue 2: During blotting after the rinse/soak, the millicell fell outside of the hood- the tissue was rinsed in the assay media soak well, blotted, and then transferred to the 6-well plate for the post-exposure 18 hr incubation.
52	EIVS_BDF_solids_14289C_19_31.xls	Few residues after post soak on the tissues and on the inner wall of the inserts.
52	EIVS_BDF_solids_14296B_20_36.xls	Few residues after post soak on the tissues and on the inner wall of the inserts.
52	EIVS_BDF_solids_15003A_21_37.xls	Few residues after post soak on the tissues.
52	EIVS_IIVS_solids_15007_week16_number23_AH.xls	Tissues 1&2: residual test article noticed after rinse/soak- residual test article appears to adhere to the inside of the millicell only.
53	EIVS_BDF_solids_14289C_19_31.xls	Few residues after washing and post soak.
53	EIVS_BDF_solids_14296B_20_36.xls	Few residues after washing and post soak.
53	EIVS_BDF_solids_15003A_21_37.xls	Few residues after washing and post soak.
53	EIVS_IIVS_solids_14270_week9_number11_AH.xls	Tissue 2: During dosing it was noticed that the media may have some test article (3 small particles). This test article may have stuck to the outside and may have fallen into the media from the outside of the millicell. The tissue (millicell) was
53	EIVS_IIVS_solids_15007_week16_number23_AH.xls	Tissues 1&2: residual test article noticed after rinse/soak.
53	EIVS_IIVS_solids_15013_week17_number24_AH.xls	Tissues 1&2: possible residual test article remained after rinse soak.
54	EIVS_Harlan_liquids_14248E_13_04.xls	Both tissues stained pink after TI exposure and rinsing
54	EIVS_Harlan_liquids_14263D_15_05.xls	Both tissues stained pink after TI exposure and rinsing
54	EIVS_Harlan_liquids_14270A_16_06.xls	Both tissues stained pink after TI exposure and rinsing
55	EIVS_BDF_liquids_14256C_14_21.xls	Substance stinks(!) and flows out of the closed container! See photos "B121-container-a" and "B121-container-b". Medium yellow after exposure, after rinsing and postincubation medium o.k.
55	EIVS_BDF_liquids_14263B_15_24.xls	Substance stinks(!) and flows out of the closed container! Medium yellow after exposure, after rinsing and postincubation medium o.k.
55	EIVS_BDF_liquids_14277E_17_27.xls	Substance stinks(!) and spreads out of the closed container! Medium yellow after exposure, after rinsing and postincubation medium o.k.
55	EIVS_Harlan_liquids_14277B_17_07.xls	The media was stained yellow following exposure. Both tissues stained yellow following rinsing.
55	EIVS_Harlan_liquids_14283D_18_08.xls	The media was stained yellow following exposure. Both tissues stained yellow following rinsing.
55	EIVS_Harlan_liquids_14289A_19_09.xls	The media was stained yellow following exposure. Both tissues stained yellow following rinsing.
55	EIVS_IIVS_liquids_14248_week6_number5_AH.xls	Tissues 1&2: Media in wells turned orange/yellow during 30 minute test article dose
55	EIVS_IIVS_liquids_14256_week7_number6_AH.xls	Media in both wells yellow (noticed during rinsing).
55	EIVS_IIVS_liquids_14263_week8_number8_AH.xls	Tissues 1&2: Media in wells turned yellow during 30 minute dosing period.
56	EIVS_BDF_liquids_14248A_13_17.xls	The sealing is seperated into two layers.
56	EIVS_BDF_liquids_14256A_14_19.xls	The sealing is seperated into two layers.
56	EIVS_BDF_liquids_14263A_15_22.xls	The sealing is seperated into two layers.
57	EIVS_Harlan_liquids_14248E_13_04.xls	Both tissues partially detached from insert.
57	EIVS_Harlan_liquids_14270A_16_06.xls	Partially detached tissue (1 tissue only)
61	EIVS_BDF_solids_14234B_11_11.xls	Medium yellow after exposure, yellow resudues after washing and soak step.
61	EIVS_BDF_solids_14241A_12_15.xls	Small residues after rinsing and post-soak.
61	EIVS_BDF_solids_14248C_13_18.xls	Small residues after rinsing an post soak. Medium yellow after exposure and post incubation.
61	EIVS_Harlan_solids_14225B_10_01.xls	The assay medium in the wells of treatment plate and the tissue surface were stained orange (both tissues)
61	EIVS_Harlan_solids_14234E_11_02.xls	The assay medium in the wells of treatment plate and the tissue surface were stained orange (both tissues)
61	EIVS_Harlan_solids_14241D_12_03.xls	The assay medium in the wells of treatment plate and the tissue surface were stained orange (both tissues)
61	EIVS_IIVS_solids_14219_week1_number1_MK.xls	Media beneath millicells of both tissues appeared to have turned orange following the test article exposure time. Both tissues also had possible residual test article and/or tissue staining observed after rinsing and soaking.
61	EIVS_IIVS_solids_14222_week2_number2_MK.xls	Media beneath millicells of both tissues appeared to have turned orange following the test article exposure time. Both tissues also had possible residual test article and/or tissue staining observed after rinsing and soaking.
61	EIVS_IIVS_solids_14225_week3_number3_MK.xls	Media beneath millicells of both tissues appeared to have turned orange following the test article exposure time. Both tissues also had possible residual test article and/or tissue staining observed after rinsing and soaking.
65	EIVS_BDF_solids_14256B_14_20.xls	wax, no direct contact between chemical and surface possible at whole area. Spotted blue areas after MTT -> no contact = no cytotox?
65	EIVS_BDF_solids_14263C_15_23.xls	"wax, pressed to a bar (~2 mm high), used a biopsy punch (diameter 8mm) to prepare a round plate, applicated on surface of tissues with a spatula
65	EIVS_BDF_solids_14263C_15_23.xls	found during preparation pretesting that chemical evaporates"
65	EIVS_BDF_solids_14277D_17_26.xls	"wax, pressed to a bar (~2 mm high), used a biopsy punch (diameter 8mm) to prepare a round plate, applicated on surface of tissues with a spatula
65	EIVS_BDF_solids_14277D_17_26.xls	found during preparation pretesting that chemical evaporates"
65	EIVS_BDF_solids_14283C_18_28.xls	"wax, pressed to a bar (~2 mm high), used a biopsy punch (diameter 8mm) to prepare a round plate, applicated on surface of tissues with a spatula
65	EIVS_BDF_solids_14283C_18_28.xls	found during preparation pretesting that chemical evaporates"

Chemical	filename	remark
65	EIVS_Harlan_solids_14277C_17_07.xls	Due to the physical naute of the test item the test item was moulded into a disc of a size to totally cover the tissue surface during exposure and was removed as a disc following exposure.
65	EIVS_Harlan_solids_14283E_18_08.xls	Due to the physical naute of the test item the test item was moulded into a disc of a size to totally cover the tissue surface during exposure and was removed as a disc following exposure.
65	EIVS_Harlan_solids_14289B_19_09.xls	Due to the physical naute of the test item the test item was moulded into a disc of a size to totally cover the tissue surface during exposure and was removed as a disc following exposure.
66	EIVS_BDF_solids_14256B_14_20.xls	solubilized after treatment
66	EIVS_BDF_solids_14263C_15_23.xls	solubilized after treatment
66	EIVS_BDF_solids_14277D_17_26.xls	solubilized after treatment
66	EIVS_BDF_solids_14283C_18_28.xls	solubilized after treatment
66	EIVS_Harlan_solids_14277C_17_07.xls	For both tissues the test item was dissolved during the exposure period.
66	EIVS_Harlan_solids_14283E_18_08.xls	For both tissues the test item was dissolved during the exposure period.
66	EIVS_Harlan_solids_14289B_19_09.xls	For both tissues the test item was dissolved during the exposure period.
66	EIVS_IIVS_solids_14283_week11_number12_MK.xls	Media pooled within the millicells following test aricle exposure time.
66	EIVS_IIVS_solids_14289_week12_number13_MK.xls	Media was observed to have pooled within the millicells following test article exposure time.
66	EIVS_IIVS_solids_15013_week16_number17_MK.xls	Media pooled within millicells, observed following test article exposure time.
67	EIVS_Harlan_liquids_14248E_13_04.xls	Both tissues stained pink after TI exposure and rinsing
67	EIVS_Harlan_liquids_14263D_15_05.xls	Both tissues stained pink after TI exposure and rinsing
67	EIVS_Harlan_liquids_14270A_16_06.xls	Both tissues stained pink after TI exposure and rinsing
68	EIVS_BDF_liquids_14225E_10_06.xls	"Parts of the sealing stick on the lid.
68	EIVS_BDF_liquids_14225E_10_06.xls	After post-soak a part of the tissue detaches from the membrane."
68	EIVS_BDF_liquids_14234C_11_09.xls	"Parts of the sealing stick on the lid.
68	EIVS_BDF_liquids_14234C_11_09.xls	After post-soak a part of the tissue detaches from the membrane."
68	EIVS_BDF_liquids_14241C_12_13.xls	"Parts of the sealing stick on the lid.
71	EIVS_BDF_liquids_14248A_13_17.xls	Parts of the sealing stick on the rim.
71	EIVS_BDF_liquids_14256A_14_19.xls	Parts of the sealing stick on the rim.
71	EIVS_BDF_liquids_14263A_15_22.xls	Parts of the sealing stick on the rim.
71	EIVS_Harlan_liquids_14289A_19_09.xls	One tissue partially detached post rinsing
72	EIVS_BDF_liquids_14256C_14_21.xls	"TECHNICAL ISSUE according to VMG decision! Both tissues pink after exposure, see photos, after extraction both tissues remain pink, however, a small amount of color maybe dissolved in isopropanol. Conclusion: Because this chemical is originally n
72	EIVS_BDF_liquids_14256C_14_21.xls	Medium turbid after exposure and postincubation, precipitate at the bottom of the wells, can be scracht off, see photos."
72	EIVS_BDF_liquids_14263B_15_24.xls	"Both tissues pink after exposure, see photos, after extraction both tissues remain pink.
72	EIVS_BDF_liquids_14263B_15_24.xls	Medium turbid after exposure and postincubation, precipitate at the bottom of the wells, can be scracht off."
72	EIVS_BDF_liquids_14263B_15_24.xls	"B137CC:Both tissues pink after exposure, see photos, after extraction both tissues remain pink.
72	EIVS_BDF_liquids_14263B_15_24.xls	Medium turbid after exposure and postincubation, precipitate at the bottom of the wells, can be scracht off."
72	EIVS_BDF_liquids_14277E_17_27.xls	"Both tissues pink after exposure, after extraction both tissues remain pink.
72	EIVS_BDF_liquids_14277E_17_27.xls	Medium turbid after exposure and postincubation, precipitate at the bottom of the wells, can be scracht off, although the testchemical is a liquid!"
72	EIVS_BDF_liquids_14277E_17_27.xls	"137CC:Both tissues pink after exposure, after extraction both tissues remain pink.
72	EIVS_BDF_liquids_14277E_17_27.xls	Medium turbid after exposure and postincubation, precipitate at the bottom of the wells, can be scracht off,although the testchemical is a liquid! "
72	EIVS_BDF_liquids_15007B_23_40.xls	B137CC
72	EIVS_HARLAN_LIQUIDS_15029A_27_14.xls	Media turned turbid after exposure. Tissues stained pink after rinsing and post-soak.
72	EIVS_HARLAN_LIQUIDS_15030A_28_15.xls	Media turned turbid after exposure. Tissues stained pink after rinsing and post-soak.
72	EIVS_HARLAN_LIQUIDS_15033A_31_16.xls	Media turned turbid during exposure. Tissues stained pink after rinsing and post-soak.
72	EIVS_IIVS_liquids_14248_week6_number5_AH.xls	Tissues 1&2: Tissues stained pink ; 1st tissue well contained possible precipitate in media after dosing
72	EIVS_IIVS_liquids_14256_week7_number6_AH.xls	Tissues 1 & 2: Tissues stained pink after rinse/soak. Possible precipitate noticed in wells (media) under tissues.
72	EIVS_IIVS_liquids_14263_week8_number8_AH.xls	Tissues 1&2: tissues stained pink after rinse/soak; media in wells appears to have precipitate after 30 minute dosing period. Small amount of possible precipitate noticed in isopropanol 24-well plate.
73	EIVS_BDF_solids_14222A_09_05.xls	On one tissue small residues after rinsing and postsoak.
73	EIVS_BDF_solids_14225C_10_08.xls	Small residues after rinsing and postsoak.
73	EIVS_Harlan_solids_14225B_10_01.xls	Scattered residual test item adhered to tissue surface post risning and post soak (both tissues)
73	EIVS_Harlan_solids_14234E_11_02.xls	Scattered residual test item adhered to tissue surface post risning and post soak (both tissues)
73	EIVS_Harlan_solids_14241D_12_03.xls	Small amounts of test item still present on tissue surface post rinsing and post soak (both tissues)
74	EIVS_BDF_solids_14219D_08_02.xls	"After rinsing small residues left.
74	EIVS_BDF_solids_14219D_08_02.xls	After MTT-Term.: Tissue 2: small white area on the surface (residues?)."
74	EIVS_BDF_solids_14222A_09_05.xls	Residues after rinsing and postsoak on both tissues.
74	EIVS_BDF_solids_14225C_10_08.xls	Residues after rinsing and postsoak.
74	EIVS_BDF_solids_14241A_12_15.xls	Small brown residues after rinsing and post-soak.
74	EIVS_HARLAN_SOLIDS_15013B_24_13.xls	Residual test item on tissues after rinsing.
74	EIVS_HARLAN_SOLIDS_15013B_24_13.xls	Residual test item on tissues after rinsing.
74	EIVS_HARLAN_SOLIDS_15029B_27_14.xls	Residual test item on tissues after rinsing.
74	EIVS_HARLAN_SOLIDS_15029B_27_14.xls	Residual test item on tissues after rinsing.
74	EIVS_HARLAN_SOLIDS_15030B_28_15.xls	Residual test item on tissues after rinsing.
74	EIVS_HARLAN_SOLIDS_15030B_28_15.xls	Residual test item on tissues after rinsing.
74	EIVS_IIVS_solids_14219_week1_number1_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking.
74	EIVS_IIVS_solids_14219_week1_number1_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking.
74	EIVS_IIVS_solids_14222_week2_number2_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking.
74	EIVS_IIVS_solids_14222_week2_number2_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking.

Chemical	filename	remark
74	EIVS_IIVS_solids_14225_week3_number3_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking.
74	EIVS_IIVS_solids_14225_week3_number3_MK.xls	For both tissue replicates, there was possible residual test article and/or tissue staining observed after rinsing and soaking.
75	EIVS_BDF_solids_14277D_17_26.xls	"tissue1: medium in insert after treatment, chemical solubilised -> dead/damaged tissue
75	EIVS_BDF_solids_14277D_17_26.xls	tissue2: no medium in insert, chemical dry, not solubilised (like run1 and run2)"
75	EIVS_BDF_solids_14283C_18_28.xls	"tissue1: medium in insert after treatment, chemical solubilised -> dead/damaged tissue
75	EIVS_BDF_solids_14283C_18_28.xls	tissue2: no medium in insert, chemical dry, not solubilised (like run1 and run2)"
75	EIVS_BDF_solids_15013A_24_43.xls	Little residues after washing and post-soak.
75	EIVS_Harlan_solids_14283E_18_08.xls	Test item turned to liquid during exposure period
75	EIVS_Harlan_solids_14289B_19_09.xls	Test item turned to liquid during exposure period
75	EIVS_IIVS_solids_14234_week4_number4_MK.xls	Media pooled into millicell of both tissue, noticed prior to treatment termination
75	EIVS_IIVS_solids_14241_week5_number5_MK.xls	Media pooled into millicell of both tissue, noticed prior to treatment termination
75	EIVS_IIVS_solids_14248_week6_number6_MK.xls	Media pooled into millicell of both tissue, noticed prior to treatment termination
76	EIVS_BDF_solids_14234A_11_10.xls	"powder red-brown with crystal structure after treatment, removes from insert like a crust (whole piece) at rinsing
76	EIVS_BDF_solids_14234A_11_10.xls	small rests remain on surface of tissues after rinsing"
76	EIVS_BDF_solids_14241B_12_14.xls	"powder red-brown with crystal structure after treatment, removes from insert like a crust (whole piece) at rinsing
76	EIVS_BDF_solids_14241B_12_14.xls	small rests remain on surface of tissues after rinsing"
76	EIVS_BDF_solids_14248B_13_16.xls	"powder red-brown with crystal structure after treatment, removes from insert like a crust (whole piece) at rinsing
76	EIVS_BDF_solids_14248B_13_16.xls	small rests remain on surface of tissues after rinsing"
76	EIVS_IIVS_solids_14270_week9_number10_MK.xls	Small amount of residual test article on tissues after rinsing and soaking.
79	EIVS_BDF_solids_14234B_11_11.xls	Two tissues were rejected because there were only two (instead of three) feet below the inserts.
79	EIVS_BDF_solids_14248C_13_18.xls	Both tissues from Kit D, because of change of the surface, four tissues from kit C were rejected.
79	EIVS_Harlan_solids_14248F_13_04.xls	Test item dissolved by medium (both tissues)
79	EIVS_Harlan_solids_14263E_15_05.xls	Test item dissolved by medium (both tissues)
79	EIVS_Harlan_solids_14270B_16_06.xls	Test item dissolved by medium (both tissues)
80	EIVS_BDF_liquids_14225E_10_06.xls	"After treatment the medium has changed its color to yellow (pH7). The tissue is light yellow too.
80	EIVS_BDF_liquids_14225E_10_06.xls	After MTT-staining the color of the rest of the MTT-medium has turned to blue. An absorption spectrum is measured.
80	EIVS_BDF_liquids_14225E_10_06.xls	The substance stinks strongly therefore it is treated in seperate well-plates."
80	EIVS_BDF_liquids_14234C_11_09.xls	"Tissue2: Pre-incubation: PBS doesn't spread all over the tissue. After treatment the medium has changed its color to yellow (pH7). The tissue is light yellow too.
80	EIVS_BDF_liquids_14234C_11_09.xls	After MTT-staining the color of the rest of the MTT-medium has turned to blue.
80	EIVS_BDF_liquids_14234C_11_09.xls	The substance stinks strongly therefore it is incubated/treated in seperate well-plates. "
80	EIVS_BDF_liquids_14241C_12_13.xls	"The sealing is strongly corooded and sticky and greasy. The substance stinks strongly therefore it is incubated/treated in seperate well-plates.
80	EIVS_BDF_liquids_14241C_12_13.xls	After treatment the medium has changed its color to yellow (pH7). The tissue is light yellow too.
80	EIVS_BDF_liquids_14241C_12_13.xls	After MTT-staining the color of the rest of the MTT-medium has turned to blue.
80	EIVS_HARLAN_LIQUIDS_14296D_20_10.xls	Media turned yellow after exposure. After 3 hours MTT exposure the MTT in the well had turned blue.
80	EIVS_HARLAN_LIQUIDS_15003C_21_11.xls	Media turned yellow after exposure. After 3 hours MTT exposure the MTT in the well had turned blue.
80	EIVS_HARLAN_LIQUIDS_15007C_23_12.xls	Media turned yellow after exposure. After 3 hours MTT exposure the MTT in the well had turned blue.
81	EIVS_BDF_liquids_14248A_13_17.xls	After postincubation the tissues were light yellow.
81	EIVS_BDF_liquids_14256A_14_19.xls	After postincubation the tissues were light yellow.
81	EIVS_BDF_liquids_14263A_15_22.xls	After postincubation the tissues were light yellow.
82	EIVS_HARLAN_LIQUIDS_15033B_31_16.xls	Medium turned yellow following exposure
82	EIVS_HARLAN_LIQUIDS_15034A_32_17.xls	Medium stained yellow after exposure
82	EIVS_HARLAN_LIQUIDS_15035A_33_18.xls	Medium stained yellow after exposure
85	EIVS_BDF_liquids_14225E_10_06.xls	Parts of the sealing are in the sample.
85	EIVS_BDF_liquids_14234C_11_09.xls	Parts of the sealing are in the sample.
85	EIVS_BDF_liquids_14241C_12_13.xls	Parts of the sealing are in the sample.
86	EIVS_HARLAN_LIQUIDS_15033B_31_16.xls	Medium turned yellow following exposure
86	EIVS_HARLAN_LIQUIDS_15034A_32_17.xls	Medium stained yellow after exposure
86	EIVS_HARLAN_LIQUIDS_15035A_33_18.xls	Medium stained yellow after exposure
86	EIVS_IIVS_liquids_14283_week11_number13_AH.xls	Tissues 1&2: during 30 minute test article dosing period, test article appeared as cloudy yellow prior to rinsing
88	EIVS_BDF_liquids_14283A_18_29.xls	medium purple after treatment, ph ~9, tissue slightly red
88	EIVS_BDF_liquids_14289D_19_32.xls	medium purple after treatment, ph ~9, tissue slightly red
88	EIVS_BDF_liquids_14296A_20_34.xls	medium purple after treatment, ph ~9, tissue slightly red
88	EIVS_HARLAN_LIQUIDS_15037A_34_19.xls	Media stained bright pink after exposure. Tissues stained bright pink after rinsing and post soak.
88	EIVS_HARLAN_LIQUIDS_15040B_38_20.xls	Media turnned bright pink during exposure. Tissues stained pink after rinsing and post soak.
88	EIVS_HARLAN_LIQUIDS_15046B_41_21.xls	Media stained bright pink after exposure. Tissues stained pink after rinsing and post soak.
88	EIVS_IIVS_liquids_14289_week12_number14_AH.xls	Tissues 1&2: Tissues stained pink-observed after rinse/soak
88	EIVS_IIVS_liquids_14296_week13_number17_AH.xls	Tissues 1&2: Tissues observed stained pink after rinse/soak
88	EIVS_IIVS_liquids_15003_week14_number19_AH.xls	Tissues 1&2: tissues observed to be stained pink after rinse/soak
89	EIVS_BDF_liquids_14248A_13_17.xls	During the washing the substance began to foam.
89	EIVS_BDF_liquids_14256A_14_19.xls	During the washing the substance began to foam.
89	EIVS_BDF_liquids_14263A_15_22.xls	During the washing the substance began to foam.
90	EIVS_BDF_liquids_14256C_14_21.xls	foams during washing
90	EIVS_BDF_liquids_14263B_15_24.xls	foams during washing
90	EIVS_BDF_liquids_14277E_17_27.xls	foams during washing
90	EIVS_HARLAN_LIQUIDS_15029A_27_14.xls	Residual test item left on tissues after rinsing.
90	EIVS_HARLAN_LIQUIDS_15030A_28_15.xls	Residual test item left on tissues after rinsing.
90	EIVS_HARLAN_LIQUIDS_15033A_31_16.xls	Residual test item left on tissues after rinsing.
90	EIVS_IIVS_liquids_14234_week4_number4_HI.xls	possible residual test article (clear/shiny)
90	EIVS_IIVS_liquids_14241_week5_number6_HI.xls	possible residual test article (clear/shiny)

Chemical	filename	remark
90	EIVS_IIVS_liquids_14248_week6_number7_HI.xls	possible residual test article (more on tissue 1 than tissue 2)
90	EIVS_IIVS_liquids_15007_week16_number22_AH.xls	Tissues 1&2: Possible residual test article observed after rinse/soak. Tissues appeared slightly orange in color after 2 hour post incubation period.
91	EIVS_BDF_liquids_14248A_13_17.xls	"The sealing is broken and parts of it are colored orange. It looks like that the substance crystillized on the rim.
91	EIVS_BDF_liquids_14248A_13_17.xls	After post-soak the color of the medium has changed to pink (pH9). After postincubation there is one big bubble below the tissues. Liquid is on the tissues after postincubation. The tissues are pink after extraction and there is a pink rubber-like layer on
91	EIVS_BDF_liquids_14256A_14_19.xls	"The sealing is broken and parts of it are colored orange. It looks like that the substance crystillized on the rim.
91	EIVS_BDF_liquids_14256A_14_19.xls	After post-soak the color of the medium has changed to pink and there is big bubble below the tissue. After postincubation the bubbles are gone. Liquid is on the tissues after postincubation. The tissues are pink after extraction and there is a pink rubber
91	EIVS_BDF_liquids_14263A_15_22.xls	"The sealing is broken and parts of it are colored orange. It looks like that the substance crystillized on the rim.
91	EIVS_BDF_liquids_14263A_15_22.xls	After post-soak the color of the medium has changed to pink and there is big bubble below the tissue. Liquid is on the tissues after postincubation. The tissues are pink after extraction and there is a pink rubber-like layer on the tissue."
91	EIVS_IIVS_liquids_14234_week4_number4_HI.xls	possible residual test article (clear/shiny)
91	EIVS_IIVS_liquids_14241_week5_number6_HI.xls	possible residual test article (clear/shiny)
91	EIVS_IIVS_liquids_14248_week6_number7_HI.xls	possible residual test article
93	EIVS_BDF_solids_14219D_08_02.xls	More substance needed to cover the surface of the tissues (2x syringe).
93	EIVS_BDF_solids_14222A_09_05.xls	More substance needed on both tissues (2x syringe), small residues after rinsing and postsoak on both tissues.
93	EIVS_Harlan_solids_14225B_10_01.xls	Assay medium drawn into tissue insert during exposure and had completely dissolved the test item (both tissues)
93	EIVS_Harlan_solids_14234E_11_02.xls	Assay medium drawn into tissue insert during exposure and had completely dissolved the test item (both tissues)
93	EIVS_Harlan_solids_14241D_12_03.xls	Assay medium drawn into tissue insert during exposure and had dissolved the test item (both tissues)
93	EIVS_IIVS_solids_14219_week1_number1_MK.xls	Tissue # 1 appeared very wrinkly after rinse step. Tissue # 2 detached from the millicell and was found in rinse cup 2, the tissue was gently placed back into the millicell using forceps.
93	EIVS_IIVS_solids_14222_week2_number2_MK.xls	~90% of tissue detached from each millicell
94	EIVS_BDF_solids_14234A_11_10.xls	remains on surface of tissues after rinsing, medium slightly yellow after post inc.
94	EIVS_BDF_solids_14241B_12_14.xls	remains on surface of tissues after rinsing, medium slightly yellow after post inc.
94	EIVS_BDF_solids_14248B_13_16.xls	remains on surface of tissues after rinsing, medium slightly yellow after post inc.
94	EIVS_Harlan_solids_14263E_15_05.xls	residual test item on tissues
94	EIVS_Harlan_solids_14270B_16_06.xls	Residual test item on both tissues
94	EIVS_IIVS_solids_14256_week7_number7_MK.xls	Small amount of residual test article on tissues following rinsing and soaking.
94	EIVS_IIVS_solids_14263_week8_number8_MK.xls	Residual test article on tissues following rinsing and soaking.
94	EIVS_IIVS_solids_14270_week9_number10_MK.xls	Residual test article on tissues following rinsing and soaking.
95	EIVS_BDF_solids_14219D_08_02.xls	exposure: substance dissolved or melted on the surface of the tissue.
95	EIVS_HARLAN_SOLIDS_14296E_20_10.xls	Test item liquified in tissue inserts/medium turned pink
95	EIVS_HARLAN_SOLIDS_15003C_21_11.xls	Test item liquified in tissue inserts/medium turned pink
95	EIVS_HARLAN_SOLIDS_15007A_23_12.xls	Test item liquified in tissue inserts/medium turned bright pink
96	EIVS_BDF_solids_14219D_08_02.xls	More substance needed to cover the surface of the tissues (2x syringe). After rinsing small residues left.
96	EIVS_BDF_solids_14222A_09_05.xls	Small residues after rinsing and postsoak on both tissues.
96	EIVS_BDF_solids_14225C_10_08.xls	Small residues after rinsing and postsoak.
98	EIVS_BDF_solids_14283B_18_30.xls	"Orange powder, after application blue border around the substance on the tissues. After washing and post-soak, the tissues are blue and have blue residues. The PBS is blue after washing .
98	EIVS_BDF_solids_14283B_18_30.xls	"B102CC: Orange powder, after application blue border around the substance on the tissues. After washing and post-soak, the tissues are blue and have blue residues. The PBS is blue after washing .
98	EIVS_BDF_solids_14283B_18_30.xls	MTT test: The medium of the CCs is blue, although the MTT-solution of the viabilty-test is not blue. "
98	EIVS_BDF_solids_14289E_19_33.xls	"Orange powder, after application blue border around the substance on the tissues. After washing and post-soak, the tissues are blue and have blue residues. The PBS is blue after washing .
98	EIVS_BDF_solids_14289E_19_33.xls	B102CC: Orange powder, after application blue border around the substance on the tissues. After washing and post-soak, the tissues are blue and have blue residues. The PBS is blue after washing .
98	EIVS_BDF_solids_14296C_20_35.xls	Orange powder, after application blue border around the substance on the tissues. After washing and post-soak, the tissues are blue and have blue residues. The PBS is blue after washing .
98	EIVS_BDF_solids_14296C_20_35.xls	B102CC: Orange powder, after application blue border around the substance on the tissues. After washing and post-soak, the tissues are blue and have blue residues. The PBS is blue after washing .
98	EIVS_HARLAN_SOLIDS_15037B_34_19.xls	Residual test itemon tissues after rinsing and post soak. Tissues stained blue.
98	EIVS_HARLAN_SOLIDS_15037B_34_19.xls	Residual test itemon tissues after rinsing and post soak. Tissues stained blue.
98	EIVS_HARLAN_SOLIDS_15040A_38_20.xls	Residual test item on tissues after rinsing and post soak. Tissues stained blue.
98	EIVS_HARLAN_SOLIDS_15040A_38_20.xls	Residual test item on tissues after rinsing and post soak. Tissues stained blue.
98	EIVS_Harlan_Solids_15046A_41_21.xls	Residual test item on tissues after rinsing and post soak. Tissues sained blue.
98	EIVS_Harlan_Solids_15046A_41_21.xls	Residual test item on tissues after rinsing and post soak. Tissues sained blue.
98	EIVS_Harlan_Solids_15048A_42_22.xls	Tissues stained blue after rinsing and post soak.
98	EIVS_Harlan_Solids_15048A_42_22.xls	Tissues stained blue after rinsing and post soak.
98	EIVS_IIVS_solids_14277_week10_number11_MK.xls	Possible residual test article or tissue staining, observed following rinsing and soaking. Media beneath millicells turned blue following post-incubation. Tissues stained a dark blue after extraction. Isopropanol was a pale blue color.
98	EIVS_IIVS_solids_14277_week10_number11_MK.xls	Possible residual test article or tissue staining, observed following rinsing and soaking. Media beneath millicells turned blue following post-incubation. Tissues stained a dark blue after extraction. Isopropanol was a pale blue color.
98	EIVS_IIVS_solids_14283_week11_number12_MK.xls	Possible residual test article or tissue staining observed following rinsing and soaking. Media beneath millicells turned blue following post incubation. Tissues were stained dark blue after extraction. Isopropanol was a light blue color.
98	EIVS_IIVS_solids_14283_week11_number12_MK.xls	Possible residual test article or tissue staining observed following rinsing and soaking. Media beneath millicells turned blue following post incubation. Tissues were stained dark blue after extraction. Isopropanol was a light blue color.
98	EIVS_IIVS_solids_14289_week12_number13_MK.xls	Possible residual test article or tissue staining observed following rinsing and

Chemical	filename	remark
		soaking. Media beneath millicells turned blue following post incubation. Tissues were stained dark blue after extraction. Isopropanol was a light blue color.
98	EIVS_IIVS_solids_14289_week12_number13_MK.xls	Possible residual test article or tissue staining observed following rinsing and soaking. Media beneath millicells turned blue following post incubation. Tissues were stained dark blue after extraction. Isopropanol was a light blue color.
99	EIVS_Harlan_solids_14277C_17_07.xls	Scattered residual test item noted on both tissues following rinsing.
100	EIVS_BDF_solids_15003B_21_39.xls	"White powder / after exposure: powder dissolved on the surface of the tissues, tissues pink / after washing: PBS is turbid / after postincubation: below the inserts, precipitate at the bottom of the wells, can be scracht off / after extraction: t
100	EIVS_BDF_solids_15007B_23_41.xls	"White powder / after exposure: powder dissolved on the surface of the tissues, tissues pink / after washing: PBS is turbid / after postincubation: below the inserts, precipitate at the bottom of the wells, can be scracht off / after extraction: t
100	EIVS_BDF_solids_15013A_24_43.xls	"White powder / after exposure: powder dissolved on the surface of the tissues, tissues pink / after washing: PBS is turbid / after postincubation: below the inserts, precipitate at the bottom of the wells, can be scracht off / after extraction: t
100	EIVS_HARLAN_Solids_15033C_31_16.xls	Test item liquified in inserts during exposure. Tissues stained pink after rinsing and post soak.
100	EIVS_HARLAN_Solids_15034B_32_17.xls	Test item liquified in inserts during exposure. Tissues stained pink/brown after rinsing and post soak.
100	EIVS_HARLAN_Solids_15035B_33_18.xls	Test item liquified in inserts during exposure. Tissues stained pink after rinsing and post soak.
100	EIVS_IIVS_solids_14270_week9_number11_AH.xls	Tissues 1&2: Possible precipitate under tissues in well after test article incubation. Tissues stained dark pink after rinse/soak. Dark pink spots noticed in 6-well plates under tissues after 18 hr incubation. MTT media was yellow after 3 hr incub
100	EIVS_IIVS_solids_15007_week16_number23_AH.xls	Tissues 1&2: Tissues stained pink-observed after rinse/soak. 6-well plate that was used to incubate/dose test article contained pink spots- observed during rinse. Pink spots noticed on 6-well plate under tissues after 18 hr post incubation period.
100	EIVS_IIVS_solids_15013_week17_number24_AH.xls	Tissues 1&2: 6-well plate pink under tissues-observed during rinse/soak. Tissues stained pink after rinse/soak. 6-well plates pink under tissues observed after 18 hour incubation. MTT media wells were yellow/orange after 3 hr MTT incubation. Liqui
101	EIVS_BDF_solids_14283B_18_30.xls	after exposure: chemical dissolved on the surface of the tissues, tissues yellow
101	EIVS_BDF_solids_14283B_18_30.xls	B37CC: after exposure: chemical dissolved on the surface of the tissues, tissues yellow
101	EIVS_BDF_solids_14289E_19_33.xls	after exposure: chemical dissolved on the surface of the tissues, tissues yellow
101	EIVS_BDF_solids_14289E_19_33.xls	B37CC: after exposure: chemical dissolved on the surface of the tissues, tissues yellow
101	EIVS_BDF_solids_14296C_20_35.xls	after exposure: chemical dissolved on the surface of the tissues, tissues yellow
101	EIVS_BDF_solids_14296C_20_35.xls	B37CC: after exposure: chemical dissolved on the surface of the tissues, tissues yellow
101	EIVS_HARLAN_Solids_15033C_31_16.xls	Test item liquified in inserts during exposure. Media stained orange after exposure. Tissues stained orange after rinsing and post soak.
101	EIVS_HARLAN_Solids_15034B_32_17.xls	Test item liquified in inserts during exposure. Media stained orange after exposure. Tissues stained yellow after rinsing and post soak.
101	EIVS_HARLAN_Solids_15035B_33_18.xls	Test item liquified in inserts during exposure. Media stained orange after exposure. Tissues stained orange after rinsing and post soak.
101	EIVS_IIVS_solids_14296_week13_number14_MK.xls	"Media beneath millicells turned orange, observed following test article exposure time. Media was also noticed to have pooled within the millicells. Tissues stained yellow following rinsing and soaking. Media beneath millicells turned yellow, obser
101	EIVS_IIVS_solids_15003_week14_number15_MK.xls	"Media beneath millicells turned orange, observed following test article exposure time. Media was also noticed to have pooled within the millicells. Tissues stained yellow following rinsing and soaking. Media beneath millicells turned yellow, obser
101	EIVS_IIVS_solids_15007_week15_number16_MK.xls	"Media beneath millicells turned orange, observed following test article exposure time. Media was also noticed to have pooled within the millicells. Tissues stained yellow following rinsing and soaking. Media beneath millicells turned yellow, obser
102	EIVS_BDF_solids_14289C_19_31.xls	A lot of residues on the tissues after washing. Few residues after post soak. Immediately after transfering the inserts into the MTT-Medium the color of the tissues turns to apricot.
102	EIVS_BDF_solids_14296B_20_36.xls	Few residues on the tissues after washing. Few residues after post soak.
102	EIVS_BDF_solids_15003A_21_37.xls	Some residues on the tissues after washing and post soak.
102	EIVS_BDF_solids_15013A_24_43.xls	"Little residues after washing and post-soak.
102	EIVS_BDF_solids_15013A_24_43.xls	MISTAKE!: Because of missunderstanding an internal list this chemical was tested unnecessary !!"
102	EIVS_HARLAN_Solids_15033C_31_16.xls	Residual test item on tissues after rinsing and post soak.
102	EIVS_HARLAN_Solids_15034B_32_17.xls	Residual test item on tissues after rinsing and post soak.
102	EIVS_HARLAN_Solids_15035B_33_18.xls	Residual test item on tissues after rinsing and post soak.
102	EIVS_IIVS_solids_14296_week13_number14_MK.xls	Residual test article following rinsing and soaking. Tissue # 2 was noticed to have about half the viability in comparison to tissue # 1 following MTT incubation.
102	EIVS_IIVS_solids_15003_week14_number15_MK.xls	Small amount of residual test article following rinsing and soaking.
102	EIVS_IIVS_solids_15007_week15_number16_MK.xls	Small amount of residual test article following rinsing and soaking.
103	EIVS_BDF_solids_14234A_11_10.xls	solubilize in prewetting water -> liquid
103	EIVS_BDF_solids_14241B_12_14.xls	solubilize in prewetting water -> liquid
103	EIVS_BDF_solids_14248B_13_16.xls	solubilize in prewetting water -> liquid
103	EIVS_Harlan_solids_14248F_13_04.xls	Test item dissolved by medium (both tissues)
103	EIVS_Harlan_solids_14263E_15_05.xls	Test item dissolved by medium (both tissues)
103	EIVS_Harlan_solids_14270B_16_06.xls	Test item dissolved by medium (both tissues)
104	EIVS_BDF_solids_14256B_14_20.xls	sticks on surface like dots after postsoak and at MTT (photo), total dots area >1/2 of tissue area
104	EIVS_BDF_solids_14263C_15_23.xls	sticks on surface like dots after postsoak and at MTT (photo), total dots area >1/2 of tissue area
104	EIVS_BDF_solids_14277D_17_26.xls	sticks on surface like dots after postsoak and at MTT (photo), total dots area >1/2 of tissue area
104	EIVS_BDF_solids_14283C_18_28.xls	sticks on surface like dots after postsoak and at MTT (photo), total dots area >1/2 of tissue area
104	EIVS_Harlan_solids_14248F_13_04.xls	Areas of scattered residual test item post rinsing (both tissues)
104	EIVS_Harlan_solids_14263E_15_05.xls	Areas of scattered residual test item post rinsing (both tissues)
104	EIVS_Harlan_solids_14270B_16_06.xls	Residual test item ontissues post rinsing (both tissues)
104	EIVS_IIVS_solids_14256_week7_number7_MK.xls	Small amount of residual test article on tissues following rinsing and soaking.
104	EIVS_IIVS_solids_14263_week8_number8_MK.xls	Residual test article on tissues following rinsing and soaking.
104	EIVS_IIVS_solids_14270_week9_number10_MK.xls	Residual test article on tissues following rinsing and soaking. Tissue # 2 had about half as much residual test article in comparison to Tissue # 1
104	EIVS_IIVS_solids_15013_week16_number17_MK.xls	Small residual test article following rinsing and soaking.
105	EIVS_BDF_solids_14234A_11_10.xls	solubilize in prewetting water -> liquid, medium yellow after treatment pH1,5

Chemical	filename	remark
105	EIVS_BDF_solids_14241B_12_14.xls	solubilize in prewetting water -> liquid, medium yellow after treatment pH1,5
105	EIVS_BDF_solids_14248B_13_16.xls	solubilize in prewetting water -> liquid, medium yellow after treatment pH1,5
105	EIVS_Harlan_solids_14225B_10_01.xls	Assay medium in wells of treatment plate turned yellow and the medium was drawn into the tissue inserts during exposure completely dissolveing the test item (both tissues)
105	EIVS_Harlan_solids_14234E_11_02.xls	Assay medium in wells of treatment plate turned yellow and the medium was drawn into the tissue inserts during exposure completely dissolveing the test item (both tissues)
105	EIVS_Harlan_solids_14241D_12_03.xls	Assay medium in wells of treatment plate turned yellow and the medium was drawn into the tissue inserts during exposure dissolving the test item (both tissues)
105	EIVS_IIVS_solids_14256_week7_number7_MK.xls	Media beneath millicells had turned yellow following test article exposure time. Media had also pooled within each millicell during that time.
105	EIVS_IIVS_solids_14263_week8_number8_MK.xls	Media beneath millicells had turned yellow following test article exposure time, media also pooled within each millicell.
105	EIVS_IIVS_solids_14270_week9_number10_MK.xls	Media beneath millicells turned yellow after test article exposure time, media was also observed to have pooled within each millicell.
106	EIVS_BDF_solids_14283B_18_30.xls	"dark blue powder, residues after washing and post-soak
106	EIVS_BDF_solids_14283B_18_30.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_14283B_18_30.xls	"B74CC: dark blue powder, residues after washing and post-soak
106	EIVS_BDF_solids_14283B_18_30.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_14289E_19_33.xls	"dark blue powder, residues after washing and post-soak
106	EIVS_BDF_solids_14289E_19_33.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_14289E_19_33.xls	"B74CC: dark blue powder, residues after washing and post-soak
106	EIVS_BDF_solids_14289E_19_33.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_14296C_20_35.xls	"dark blue powder, residues after washing and post-soak
106	EIVS_BDF_solids_14296C_20_35.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_14296C_20_35.xls	"B74CC: dark blue powder, residues after washing and post-soak
106	EIVS_BDF_solids_14296C_20_35.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_15019A_25_44.xls	"Dark blue powder, residues after washing and post-soak
106	EIVS_BDF_solids_15019A_25_44.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_15019A_25_44.xls	"B74CC: dark blue powder, residues after washing and post-soak
106	EIVS_BDF_solids_15019A_25_44.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_15025A_26_50.xls	"A lot of residues after washing and post-soak.
106	EIVS_BDF_solids_15025A_26_50.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_BDF_solids_15025A_26_50.xls	"B74CC: A lot of residues after washing and post-soak.
106	EIVS_BDF_solids_15025A_26_50.xls	NOT QUALIFIED!! OD >> 3,000"
106	EIVS_HARLAN_SOLIDS_15037B_34_19.xls	Test item solidified on tissues during exposureResidual test item on tissues after rinsing and post soak.
106	EIVS_HARLAN_SOLIDS_15037B_34_19.xls	Test item solidified on tissues during exposureResidual test item on tissues after rinsing and post soak.
106	EIVS_HARLAN_SOLIDS_15040A_38_20.xls	Residual test item on tissues after rinsing and post soak.
106	EIVS_HARLAN_SOLIDS_15040A_38_20.xls	Residual test item on tissues after rinsing and post soak.
106	EIVS_Harlan_Solids_15046A_41_21.xls	Test item solidified on tissues during exposure. Residual test item on tissues after rinsing and post soak.
106	EIVS_Harlan_Solids_15046A_41_21.xls	Test item solidified on tissues during exposure. Residual test item on tissues after rinsing and post soak.
106	EIVS_Harlan_Solids_15048A_42_22.xls	Test item solidified on tissues during exposure. Residual test item on tissues after rinsing and post soak.
106	EIVS_Harlan_Solids_15048A_42_22.xls	Test item solidified on tissues during exposure. Residual test item on tissues after rinsing and post soak.
106	EIVS_IIVS_solids_14277_week10_number11_MK.xls	Residual test article and possible tissue staining, observed following rinsing and soaking. Media beneath millicells turned bright pink following post-incubation. Tissues stained a purplish pink after extraction. Isopropanol was bright pink.
106	EIVS_IIVS_solids_14277_week10_number11_MK.xls	Residual test article and possible tissue staining, observed following rinsing and soaking. Media beneath millicells turned bright pink following post-incubation. Tissues stained a purplish pink after extraction. Isopropanol was bright pink.
106	EIVS_IIVS_solids_14283_week11_number12_MK.xls	Possible tissue staining and residual test article following rinsing and soaking. Media beneath millicells turned bright pink following post incubation. Tissues were stained a purplish pink after extraction. Isopropanol was bright pink.
106	EIVS_IIVS_solids_14283_week11_number12_MK.xls	"Possible tissue staining and residual test article following rinsing and soaking. Media beneath millicells turned bright pink following post incubation. Tissues were stained a purplish pink after extraction. Isopropanol was bright pink. Following
106	EIVS_IIVS_solids_14289_week12_number13_MK.xls	Possible tissue staining and residual test article following rinsing and soaking. Media beneath millicells turned bright pink following post incubation. Tissues were stained a purplish pink after extraction. Isopropanol was bright pink.
106	EIVS_IIVS_solids_14289_week12_number13_MK.xls	Possible tissue staining and residual test article following rinsing and soaking. Tissue # 2 had about half as much residual test article in comparison to tissue # 1. Media beneath millicells turned bright pink following post incubation. Tissues w
107	EIVS_BDF_solids_14283B_18_30.xls	small residues after washing and post-soak, tissues pink
107	EIVS_BDF_solids_14283B_18_30.xls	B55CC: small residues after washing and post-soak, tissues pink
107	EIVS_BDF_solids_14289E_19_33.xls	small residues after washing and post-soak, tissues pink
107	EIVS_BDF_solids_14289E_19_33.xls	B55CC: small residues after washing and post-soak, tissues pink
107	EIVS_BDF_solids_14296C_20_35.xls	small residues after washing and post-soak, tissues pink
107	EIVS_BDF_solids_14296C_20_35.xls	B55CC: small residues after washing and post-soak, tissues pink
107	EIVS_BDF_solids_15003B_21_39.xls	tissues pink after exposure, little pink residues after washing and postsoak
107	EIVS_BDF_solids_15025A_26_50.xls	Residues after washig and post-soak.
107	EIVS_BDF_solids_15025A_26_50.xls	B55CC: Residues after washig and post-soak.
107	EIVS_HARLAN_SOLIDS_15037B_34_19.xls	Tissues stained pink after exposure, rinsing and post soak.
107	EIVS_HARLAN_SOLIDS_15040A_38_20.xls	Tissues stained pink after exposure, rinsing and post soak. Tissues partially detatched from inserts.
107	EIVS_HARLAN_SOLIDS_15040A_38_20.xls	Tissues stained pink after exposure, rinsing and post soak. Tissues partially detatched from inserts.
107	EIVS_Harlan_Solids_15046A_41_21.xls	Tissues stained bright pink after exposure, rinsing and post soak.
107	EIVS_Harlan_Solids_15046A_41_21.xls	Tissues stained bright pink after exposure, rinsing and post soak.
107	EIVS_Harlan_Solids_15048A_42_22.xls	Tissues stained bright pink after exposure, rinsing and post soak. Residual test item on tissues.
107	EIVS_Harlan_Solids_15048A_42_22.xls	Tissues stained bright pink after exposure, rinsing and post soak. Residual test item on tissues.
107	EIVS_IIVS_solids_14296_week13_number14_MK.xls	"Small amount of residual test article, tissues also stained bright pink following rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was a purplish-pink color. Tissue
107	EIVS_IIVS_solids_14296_week13_number14_MK.xls	Small amount of residual test article, tissues also stained bright pink following rinsing

Chemical	filename	remark
		and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was pink.
107	EIVS_IIVS_solids_15003_week14_number15_MK.xls	"Small amount of residual test article, tissues also stained bright pink following rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was a purplish-pink color. Tissue
107	EIVS_IIVS_solids_15003_week14_number15_MK.xls	Small amount of residual test article, tissues also stained bright pink following rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was pink.
107	EIVS_IIVS_solids_15007_week15_number16_MK.xls	"Small amount of residual test article, tissues also stained bright pink following rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was a purplish-pink color, with t
107	EIVS_IIVS_solids_15007_week15_number16_MK.xls	Small amount of residual test article, tissues also stained bright pink following rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was pink.
107	EIVS_IIVS_solids_15013_week16_number17_MK.xls	"Tissues were stained pink, small amount of residual test article following rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was a purplish-pink color. Tissues stain
107	EIVS_IIVS_solids_15013_week16_number17_MK.xls	Tissues were stained pink, small amount of residual test article following rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was pink.
107	EIVS_IIVS_solids_15030_week18_number19_MK.xls	"Tissues stained pink, small amount of residual test aricle following rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was a purplish-pink color. Tissues stained a p
107	EIVS_IIVS_solids_15030_week18_number19_MK.xls	Tissues stained pink, small amount of residual test aricle followind rinsing and soaking. Media beneath millicells turned bright pink, observed following post incubation period. Isopropanol extractant was a pink.
.	EIVS_BDF_liquids_14277E_17_27.xls	"The tissues were delivered one day later, on Wednesday instead of Tuesday, because the delivery were delayed at the airport. So the tests started on Thursday.
.	EIVS_BDF_liquids_14277E_17_27.xls	(According to SOP)"
.	EIVS_BDF_solids_14277D_17_26.xls	tissues delivered on wednesday (1 day later than normal), testing performed on thursday/friday
.	EIVS_BDF_solids_14296B_20_36.xls	"The tissues were delivered one day later, on Wednesday instead of Tuesday, because the delivery were delayed at the airport. So the tests started on Thursday
.	EIVS_BDF_solids_14296B_20_36.xls	(According to SOP).
.	EIVS_BDF_solids_14296B_20_36.xls	Because of this delay the maesurements were performed by Ute Demitz."
.	EIVS_BDF_solids_14296C_20_35.xls	"The tissues were delivered one day later, on Wednesday instead of Tuesday, because the delivery were delayed at the airport. So the tests started on Thursday.
.	EIVS_BDF_solids_14296C_20_35.xls	(According to SOP)"
.	EIVS_IIVS_liquids_14222_week2_number2_AH.xls	Insert appeared to be interacting with MTT. Outside of insert blue/black color. (Noticed within minutes of transferring to MTT). Prior to adding to isopropanol, outside of inserts wiped with Kim wipe.
.	EIVS_BDF_solids_14277D_17_26.xls	used an empty aliquot and did not remark that...
.	EIVS_IIVS_liquids_14289_week12_number14_AH.xls	Tissues 1&2: Tissues stained pink-observed after rinse/soak
.	EIVS_IIVS_liquids_15003_week14_number19_AH.xls	Tissues 1&2: tissues observed to be stained pink after rinse/soak
.	EIVS_IIVS_liquids_14296_week13_number17_AH.xls	Tissues 1&2: Tissues observed stained pink after rinse/soak
.	EIVS_IIVS_liquids_14289_week12_number14_AH.xls	Tissues 1&2: residual test article after rinse/soak- after soak, soak media cloudy. After overnight extraction, both tissues were noticed to have a darker red ring around the perimeter of the tissue.
.	EIVS_IIVS_liquids_15003_week14_number19_AH.xls	"Tissue1: Upon pulling of tissues for 1 hour incubation, a small black spot noticed on tissue. Tissues 1&2: residual test article after rinse/soak. Soak wells cloudy after soak. Darker pink ring around perimeter of the tissues noticed after iso
.	EIVS_IIVS_liquids_14296_week13_number17_AH.xls	Tissues 1&2: Residual test article after rinse/soak. Soak wells cloudy after soak. After isopropanol extraction, pink ring noted around the perimeter of the tissues.
.	EIVS_IIVS_liquids_14283_week11_number13_AH.xls	"V8 was initially loaded onto the 96-well plate, when precipitate was noticed in the wells; therefore, 1 mL of the isopropanol extract for each tissue was centrifuged (~13,000 rpm for 2 minutes at room temperature) and then placed into the wel
.	EIVS_IIVS_liquids_14289_week12_number14_AH.xls	Tissues 1&2: residual test article after rinse/soak- after soak, soak media cloudy
.	EIVS_IIVS_liquids_15003_week14_number19_AH.xls	Tissue 1&2: residual test article after rinse/soak. Soak wells cloudy after soak. Possible small blisters noticed on tissues after rinse/soak.
.	EIVS_IIVS_liquids_14296_week13_number17_AH.xls	Tissues 1&2: Residual test article after rinse/soak. Soak wells cloudy after soak. Possible small blisters noticed on tissues during rinsing.

Appendix V Reasoning for non-qualified and excluded test results

conclusion	laboratory	Chemical	run	NCqual	PCqual	TAqual	color_call	MTT_call
Excluded	Beiersdorf	80[1]	1	Qualified	Qualified	Qualified		meanKC>50
		80[1]	2	Qualified	Qualified	Qualified		meanKC>50
		80[1]	3	Qualified	Qualified	Qualified		
		33	1	Qualified	Qualified	Qualified	meanCC>50	
		33	2	Qualified	Qualified	Non-qualified	meanCC>50	
		33	3	Qualified	Qualified	Non-qualified	meanCC>50	
		33	4	Qualified	Qualified	Non-qualified	meanCC>50	
		33	5	Qualified	Qualified	Qualified		
	Harlan	80[1]	1	Qualified	Qualified	Qualified		meanKC>50
		80[1]	2	Qualified	Qualified	Qualified		meanKC>50
		80[1]	3	Qualified	Qualified	Qualified		meanKC>50
	IIVS	80[1]	1	Qualified	Qualified	Qualified		meanKC>50
		80[1]	2	Qualified	Qualified	Qualified		meanKC>50
		80[1]	3	Qualified	Qualified	Qualified		meanKC>50
		23[1]	1	Qualified	Qualified	Qualified		meanKC>50
		23[1]	2	Qualified	Qualified	Qualified		meanKC>50
		23[1]	3	Qualified	Qualified	Qualified		meanKC>50
Non-Qualified	Beiersdorf	75	3	Qualified	Non-qualified	Non-qualified		
		75	3	Qualified	Qualified	Non-qualified		
		78	3	Qualified	Non-qualified	Qualified		
		104	3	Qualified	Non-qualified	Qualified		
		74	1	Qualified	Qualified	Non-qualified		
		44	3	Qualified	Non-qualified	Qualified		
		46	3	Qualified	Non-qualified	Qualified		
		43	3	Qualified	Non-qualified	Qualified		
		37	1	Qualified	Qualified	Non-qualified		
		65	3	Qualified	Non-qualified	Qualified		
		66	3	Qualified	Non-qualified	Qualified		
		29	3	Qualified	Qualified	Non-qualified		
		63	3	Qualified	Non-qualified	Qualified		
		31	3	Qualified	Non-qualified	Qualified		
		50	3	Qualified	Qualified	Non-qualified		
	Harlan	40	2	Non-qualified	Qualified	Qualified		
		98	2	Non-qualified	Qualified	Qualified		
		49	2	Non-qualified	Qualified	Qualified		
	IIVS	20	2	Qualified	Qualified	Non-qualified		
		34	2	Qualified	Qualified	Non-qualified		
		34	4	Qualified	Qualified	Non-qualified		
		10	1	Qualified	Qualified	Non-qualified		
		104	1	Qualified	Qualified	Non-qualified		
		33	3	Qualified	Qualified	Non-qualified	meanCC>50	
		90	3	Qualified	Qualified	Non-qualified		
		26	1	Qualified	Qualified	Non-qualified		

[1] The core VMG overrode the rule identifying 50% NSMTT as a cut-off to consider a chemical compatible with the test method for chemicals 23 and 80 after an evaluation of the first draft of the statistics report during the VMG meeting at May 10th 2012. So, chemical 23 and 80 are included for statistical analysis.

Appendix VI Summary of all test results for EpiOcular™ EIT

NQ = Non-qualified
EX = Excluded
Diff = Difference or range
Qual = Qualification (NQ = non-qualified)

Note to chemical 23 (IIVS only) and to chemical 80 (Beiersdorf, Harlan and IIVS):

On May 10th 2012, after an evaluation of the first draft of the statistics report, the core VMG overrode the rule identifying 50% NSMTT as a cut-off to consider a chemical compatible with the test system as described in Chapter 2.5.1. of this report. In all these cases, rule 3 in Chapter 2.5.1. is fulfilled since the mean %NSC of all qualified tests is greater than (>) 50% and the classification of these qualified tests changes upon correction (from non-irritant to irritant). However, the viability values obtained in the qualified tests are definitely within the linear range of the OD measurements (within the 100% scale) and therefore, even though there is a strong MTT reduction occurring this is not interfering with the analytical capacity to measure formazan production. Moreover, the variability obtained between the different tests and controls is low. As such, these chemicals were considered compatible with the test method and their data were therefore included in all of the statistical analyses.

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	1	liquid	no cat	No	No	1	1.7	3.4		39.2	3.5		67.8	2.4								67.8		NI	NI
Beiersdorf	1	liquid	no cat	No	No	2	1.7	6.1		40.6	1.6		68.8	16.5								68.8		NI	NI
Beiersdorf	1	liquid	no cat	No	No	3	1.9	3.6		29.2	3		71.3	3.1								71.3		NI	NI
Beiersdorf	2	liquid	no cat	No	No	1	1.7	3.4		39.2	3.5		83	6.3								83		NI	NI
Beiersdorf	2	liquid	no cat	No	No	2	1.7	6.1		40.6	1.6		80.1	1.7								80.1		NI	NI
Beiersdorf	2	liquid	no cat	No	No	3	1.9	3.6		29.2	3		77.3	8								77.3		NI	NI
Beiersdorf	3	liquid	no cat	No	No	1	1.8	10.1		37.4	6.3		55.4	4.2								55.4		NI	I
Beiersdorf	3	liquid	no cat	No	No	2	1.6	5.6		43.5	4.4		63	0.3								63		NI	NI
Beiersdorf	3	liquid	no cat	No	No	3	1.6	0.3		46.4	1.2		64.2	6.8								64.2		NI	NI
Beiersdorf	4	liquid	no cat	Yes	No	1	1.6	1.2		42.4	7		108.4	2.4					1.5	0.3		106.9		NI	NI
Beiersdorf	4	liquid	no cat	Yes	No	2	2	7.9		33	4.3		105.9	1.3					1.3	0.2		104.6		NI	NI
Beiersdorf	4	liquid	no cat	Yes	No	3	1.7	7.7		41	2.1		117	1.8					1.5	0.3		115.5		NI	NI
Beiersdorf	5	liquid	no cat	Yes	No	1	1.7	3.4		39.2	3.5		83.6	0.6					0	0		83.5		NI	NI
Beiersdorf	5	liquid	no cat	Yes	No	2	1.7	6.1		40.6	1.6		72.2	5.7					0	0		72.2		NI	NI
Beiersdorf	5	liquid	no cat	Yes	No	3	1.9	3.6		29.2	3		86.4	3.2					0	0		86.4		NI	NI
Beiersdorf	6	liquid	no cat	No	No	1	1.8	10.1		37.4	6.3		81.2	1.2								81.2		NI	NI
Beiersdorf	6	liquid	no cat	No	No	2	1.6	5.6		43.5	4.4		83.7	1.4								83.7		NI	NI
Beiersdorf	6	liquid	no cat	No	No	3	1.6	0.3		46.4	1.2		90.9	6.6								90.9		NI	NI
Beiersdorf	7	liquid	no cat	No	No	1	1.8	10.1		37.4	6.3		34.6	3.1								34.6		I	I
Beiersdorf	7	liquid	no cat	No	No	2	1.6	5.6		43.5	4.4		42.3	6.8								42.3		I	I
Beiersdorf	7	liquid	no cat	No	No	3	1.6	0.3		46.4	1.2		38.7	4.6								38.7		I	I
Beiersdorf	8	liquid	no cat	No	No	1	1.8	10.1		37.4	6.3		101.4	3.1								101.4		NI	NI
Beiersdorf	8	liquid	no cat	No	No	2	1.6	5.6		43.5	4.4		97.3	1.5								97.3		NI	NI
Beiersdorf	8	liquid	no cat	No	No	3	1.6	0.3		46.4	1.2		102.8	8.3								102.8		NI	NI
Beiersdorf	9	liquid	no cat	No	No	1	1.8	10.1		37.4	6.3		95.4	11.5								95.4		NI	NI
Beiersdorf	9	liquid	no cat	No	No	2	1.6	5.6		43.5	4.4		101.9	4.1								101.9		NI	NI
Beiersdorf	9	liquid	no cat	No	No	3	1.6	0.3		46.4	1.2		98	11.2								98		NI	NI
Beiersdorf	10	liquid	no cat	No	No	1	1.9	1.3		29	7.7		33	0.8								33		I	I
Beiersdorf	10	liquid	no cat	No	No	2	2	4.3		33.3	7.8		31.1	8.2								31.1		I	I
Beiersdorf	10	liquid	no cat	No	No	3	2	6.2		34.9	3		35.4	1.2								35.3		I	I
Beiersdorf	11	liquid	no cat	No	No	1	1.7	3.4		39.2	3.5		29.8	2.9								29.8		I	I
Beiersdorf	11	liquid	no cat	No	No	2	1.7	6.1		40.6	1.6		27.5	2.3								27.5		I	I
Beiersdorf	11	liquid	no cat	No	No	3	1.9	3.6		29.2	3		29.9	1.4								29.8		I	I
Beiersdorf	12	liquid	no cat	No	No	1	1.7	6		37.5	4.2		94.1	15.6								94.1		NI	NI
Beiersdorf	12	liquid	no cat	No	No	2	1.4	0.5		18.3	4.9		91.5	9.6								91.5		NI	NI
Beiersdorf	12	liquid	no cat	No	No	3	1.4	1.8		42.2	10.3		91.6	15.1								91.6		NI	NI
Beiersdorf	13	liquid	no cat	No	No	1	1.7	6		37.5	4.2		107.9	9.8								107.9		NI	NI
Beiersdorf	13	liquid	no cat	No	No	2	1.4	0.5		18.3	4.9		87.8	4								87.8		NI	NI
Beiersdorf	13	liquid	no cat	No	No	3	1.4	1.8		42.2	10.3		105.4	9.8								105.4		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	14	liquid	no cat	No	No	1	1.6	1.2		42.4	7		98.3	1.5								98.3		NI	NI
Beiersdorf	14	liquid	no cat	No	No	2	2	7.9		33	4.3		98.7	2.9								98.7		NI	NI
Beiersdorf	14	liquid	no cat	No	No	3	1.7	7.7		41	2.1		104.9	0.4								104.9		NI	NI
Beiersdorf	15	liquid	no cat	No	No	1	1.7	6		37.5	4.2		97.2	5.4								97.2		NI	NI
Beiersdorf	15	liquid	no cat	No	No	2	1.4	0.5		18.3	4.9		101.7	8.1								101.7		NI	NI
Beiersdorf	15	liquid	no cat	No	No	3	1.4	1.8		42.2	10.3		109.5	14.4								109.5		NI	NI
Beiersdorf	16	liquid	no cat	No	No	1	1.8	10.1		37.4	6.3		100.4	1.8								100.4		NI	NI
Beiersdorf	16	liquid	no cat	No	No	2	1.6	5.6		43.5	4.4		110.9	10.1								110.9		NI	NI
Beiersdorf	16	liquid	no cat	No	No	3	1.6	0.3		46.4	1.2		103.3	12.2								103.3		NI	NI
Beiersdorf	17	liquid	no cat	No	No	1	1.9	1.3		29	7.7		102.5	0.9								102.5		NI	NI
Beiersdorf	17	liquid	no cat	No	No	2	2	4.3		33.3	7.8		98.1	5.1								98.1		NI	NI
Beiersdorf	17	liquid	no cat	No	No	3	2	6.2		34.9	3		91.9	2.4								91.9		NI	NI
Beiersdorf	18	liquid	no cat	No	No	1	1.7	6		37.5	4.2		112.3	5.3								112.3		NI	NI
Beiersdorf	18	liquid	no cat	No	No	2	1.4	0.5		18.3	4.9		69.6	8.1								69.6		NI	NI
Beiersdorf	18	liquid	no cat	No	No	3	1.4	1.8		42.2	10.3		109.5	7.1								109.5		NI	NI
Beiersdorf	19	liquid	no cat	No	No	1	1.7	6		37.5	4.2		106.4	8.8								106.4		NI	NI
Beiersdorf	19	liquid	no cat	No	No	2	1.4	0.5		18.3	4.9		106.4	12.7								106.4		NI	NI
Beiersdorf	19	liquid	no cat	No	No	3	1.4	1.8		42.2	10.3		111.8	4.3								111.8		NI	NI
Beiersdorf	20	liquid	no cat	Yes	No	1	1.7	6		37.5	4.2		58.7	0.9					27.5	11.4		31.1		I	I
Beiersdorf	20	liquid	no cat	Yes	No	2	1.4	0.5		18.3	4.9		90.4	1.9					33.2	13.7		57.2		NI	I
Beiersdorf	20	liquid	no cat	Yes	No	3	1.4	1.8		42.2	10.3		82	6.8					32.2	13.3		49.8		I	I
Beiersdorf	21	liquid	no cat	No	No	1	1.9	1.3		29	7.7		82.9	10								82.8		NI	NI
Beiersdorf	21	liquid	no cat	No	No	2	2	4.3		33.3	7.8		82.9	2.1								82.9		NI	NI
Beiersdorf	21	liquid	no cat	No	No	3	2	6.2		34.9	3		83.2	1.6								83.2		NI	NI
Beiersdorf	22	liquid	no cat	Yes	No	1	1.6	1.2		42.4	7		55.4	9.7					3.8	0.1		51.6		NI	I
Beiersdorf	22	liquid	no cat	Yes	No	2	2	7.9		33	4.3		42.5	10.1					3.1	0.1		39.3		I	I
Beiersdorf	22	liquid	no cat	Yes	No	3	1.7	7.7		41	2.1		48.8	3.1					3.7	0.1		45.1		I	I
Beiersdorf	23	liquid	no cat	Yes	No	1	1.6	1.2		42.4	7		73.5	1.6					32.6	0.8		40.8		I	I
Beiersdorf	23	liquid	no cat	Yes	No	2	2	7.9		33	4.3		72.9	1.5					26.9	0.6		46		I	I
Beiersdorf	23	liquid	no cat	Yes	No	3	1.7	7.7		41	2.1		71.9	7.1					32.4	0.8		39.5		I	I
Beiersdorf	24	liquid	no cat	No	No	1	1.9	1.3		29	7.7		48.4	9								48.4		I	I
Beiersdorf	24	liquid	no cat	No	No	2	2	4.3		33.3	7.8		45.6	4.5								45.6		I	I
Beiersdorf	24	liquid	no cat	No	No	3	2	6.2		34.9	3		43.5	2.3								43.5		I	I
Beiersdorf	25	liquid	no cat	Yes	No	1	1.9	1.3		29.7	3.1		107.7	1.5					0	1		107.6		NI	NI
Beiersdorf	25	liquid	no cat	Yes	No	2	1.8	3.6		30.7	2.4		105	4.7					0	1.1		105		NI	NI
Beiersdorf	25	liquid	no cat	Yes	No	3	2.1	4.1		30.3	2.8		101.3	0.6					0	0.9		101.3		NI	NI
Beiersdorf	26	liquid	no cat	Yes	No	1	1.9	1.3		29.7	3.1		31.7	1.1					9	3.1		22.7		I	I
Beiersdorf	26	liquid	no cat	Yes	No	2	1.8	3.6		30.7	2.4		28.7	5.2					9.3	3.2		19.4		I	I
Beiersdorf	26	liquid	no cat	Yes	No	3	2.1	4.1		30.3	2.8		30.5	0.6					8	2.7		22.4		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	28	solid	no cat	No	No	1	1.7	5.1		37.4	6.5		99.4	9.9								99.4		NI	NI
Beiersdorf	28	solid	no cat	No	No	2	1.7	2.5		34.4	2.8		99.6	2.2								99.6		NI	NI
Beiersdorf	28	solid	no cat	No	No	3	2	7.3		30.5	2.1		95.8	4.3								95.8		NI	NI
Beiersdorf	29	solid	no cat	Yes	No	1	2	0.1		33.3	4.7		83.3	15.2					0.4	0.1		82.9		NI	NI
Beiersdorf	29	solid	no cat	Yes	No	2	1.7	0.6		37.4	0.6		92.2	4.6					0.5	0.1		91.8		NI	NI
Beiersdorf	29	solid	no cat	Yes	No	3	1.7	5.1		35.9	1.9		84.5	21.3	NQ				0.5	0.1		84	NQ	NI	NI
Beiersdorf	29	solid	no cat	Yes	No	4	1.8	2.5		24.3	1.6		88.6	16					0.4	0.1		88.2		NI	NI
Beiersdorf	30	solid	no cat	Yes	No	1	1.6	0.1		29	2.6		55.6	4.5					0	0.2		55.6		NI	I
Beiersdorf	30	solid	no cat	Yes	No	2	1.6	1.6		32.9	3.3		39	5					0	0.2		39		I	I
Beiersdorf	30	solid	no cat	Yes	No	3	1.8	10.4		27.4	1.2		46.8	1.5					0	0.1		46.8		I	I
Beiersdorf	31	solid	no cat	No	No	1	1.7	2.6		32	8.3		82.1	3.8								82.1		NI	NI
Beiersdorf	31	solid	no cat	No	No	2	1.5	0.2		29.3	1.5		90.3	8.6								90.3		NI	NI
Beiersdorf	31	solid	no cat	No	No	3	1.6	2		96.1	1.9	NQ	74	5.8								74	NQ	NI	NI
Beiersdorf	31	solid	no cat	No	No	4	1.6	0.7		35.1	19.5		62.3	10.4								62.3		NI	NI
Beiersdorf	32	solid	no cat	Yes	No	1	1.7	5.3		31.6	3.9		3	0					3.2	0.1		0		I	I
Beiersdorf	32	solid	no cat	Yes	No	2	1.9	1.2		31.2	2.7		3.8	0.6					2.9	0.1		0.9		I	I
Beiersdorf	32	solid	no cat	Yes	No	3	1.7	0.8		26.4	10.8		3.5	0.3					3.3	0.1		0.2		I	I
Beiersdorf	33	solid	no cat	Yes	Yes	1	1.7	5.3		31.6	3.9		89	17		4605.5	0		5.2	4.4		0	EX	I	I
Beiersdorf	33	solid	no cat	Yes	Yes	2	1.9	1.2		31.2	2.7		2949.4	114.5	NQ	4094	0		4.6	3.9		0	EX	I	I
Beiersdorf	33	solid	no cat	Yes	Yes	3	1.7	0.8		26.4	10.8		6452.6	152.7	NQ	9506.4	0		5.4	4.5		0	EX	I	I
Beiersdorf	33	solid	no cat	Yes	Yes	4	1.8	2.5		24.3	1.6		5396.7	166.8	NQ	8732.6	0		4.9	4.2		0	EX	I	I
Beiersdorf	33	solid	no cat	Yes	Yes	5	1.7	0.4		27.5	5.7		85.4	4.5		0.5	0		5.2	4.4		79.7	EX	NI	NI
Beiersdorf	34	solid	no cat	Yes	Yes	1	1.7	5.3		31.6	3.9		118	0.8		5.1	0.7		1.8	0		111.1		NI	NI
Beiersdorf	34	solid	no cat	Yes	Yes	2	1.9	1.2		31.2	2.7		122.4	3.3		9.3	3.8		1.6	0		111.5		NI	NI
Beiersdorf	34	solid	no cat	Yes	Yes	3	1.7	0.8		26.4	10.8		125.8	7.1		7.4	0.5		1.9	0		116.5		NI	NI
Beiersdorf	35	solid	no cat	Yes	No	1	1.7	5.1		37.4	6.5		74.2	15.8					0.5	0		73.7		NI	NI
Beiersdorf	35	solid	no cat	Yes	No	2	1.7	2.5		34.4	2.8		72.4	4.1					0.5	0		72		NI	NI
Beiersdorf	35	solid	no cat	Yes	No	3	2	7.3		30.5	2.1		77.4	1.4					0.4	0		77		NI	NI
Beiersdorf	36	solid	no cat	Yes	No	1	1.7	5.1		37.4	6.5		110.9	5.4					0	0.3		110.9		NI	NI
Beiersdorf	36	solid	no cat	Yes	No	2	1.7	2.5		34.4	2.8		102.8	2.8					0	0.3		102.8		NI	NI
Beiersdorf	36	solid	no cat	Yes	No	3	2	7.3		30.5	2.1		107.5	11.8					0	0.3		107.5		NI	NI
Beiersdorf	37	liquid	no cat	No	No	1	1.9	1.3		29	7.7		62.9	46.5	NQ							62.9	NQ	NI	NI
Beiersdorf	37	liquid	no cat	No	No	2	1.9	1.3		29.7	3.1		80.4	6.1								80.4		NI	NI
Beiersdorf	37	liquid	no cat	No	No	3	1.8	3.6		30.7	2.4		75	3								75		NI	NI
Beiersdorf	37	liquid	no cat	No	No	4	2.1	4.1		30.3	2.8		79.7	10.8								79.7		NI	NI
Beiersdorf	38	solid	no cat	No	No	1	1.6	3.2		26.8	5.5		102.8	0								102.8		NI	NI
Beiersdorf	38	solid	no cat	No	No	2	1.7	2.9		35.5	4.7		100.9	5.2								100.9		NI	NI
Beiersdorf	38	solid	no cat	No	No	3	1.5	3.5		25.3	1.8		119.7	3.7								119.7		NI	NI
Beiersdorf	39	solid	no cat	No	No	1	1.6	3.2		26.8	5.5		101.9	0.8								101.9		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	39	solid	no cat	No	No	2	1.7	2.9		35.5	4.7		99.5	8.8								99.5		NI	NI
Beiersdorf	39	solid	no cat	No	No	3	1.5	3.5		25.3	1.8		117.3	4								117.3		NI	NI
Beiersdorf	40	solid	no cat	No	No	1	1.6	3.2		26.8	5.5		49.4	15.1								49.4		I	I
Beiersdorf	40	solid	no cat	No	No	2	1.7	2.9		35.5	4.7		59.5	7.7								59.5		NI	I
Beiersdorf	40	solid	no cat	No	No	3	1.5	3.5		25.3	1.8		62.1	5.4								62.1		NI	NI
Beiersdorf	41	solid	no cat	No	No	1	1.6	0.1		29	2.6		101.2	5.3								101.2		NI	NI
Beiersdorf	41	solid	no cat	No	No	2	1.6	1.6		32.9	3.3		98.8	0.4								98.8		NI	NI
Beiersdorf	41	solid	no cat	No	No	3	1.8	10.4		27.4	1.2		90.4	4.9								90.4		NI	NI
Beiersdorf	42	solid	no cat	Yes	No	1	1.6	0.1		29	2.6		64.8	6.4					0.1	0		64.7		NI	NI
Beiersdorf	42	solid	no cat	Yes	No	2	1.6	1.6		32.9	3.3		85.2	1.4					0.1	0		85		NI	NI
Beiersdorf	42	solid	no cat	Yes	No	3	1.8	10.4		27.4	1.2		58.8	4.3					0.1	0		58.7		NI	I
Beiersdorf	43	solid	no cat	No	No	1	1.7	2.6		32	8.3		93.9	5.7								93.9		NI	NI
Beiersdorf	43	solid	no cat	No	No	2	1.5	0.2		29.3	1.5		112.1	3.2								112.1		NI	NI
Beiersdorf	43	solid	no cat	No	No	3	1.6	2		96.1	1.9	NQ	100.3	9.2								100.3	NQ	NI	NI
Beiersdorf	43	solid	no cat	No	No	4	1.6	0.7		35.1	19.5		102.6	14.4								102.6		NI	NI
Beiersdorf	44	solid	no cat	No	No	1	1.7	2.6		32	8.3		104.5	3.7								104.5		NI	NI
Beiersdorf	44	solid	no cat	No	No	2	1.5	0.2		29.3	1.5		98.8	4.5								98.7		NI	NI
Beiersdorf	44	solid	no cat	No	No	3	1.6	2		96.1	1.9	NQ	104.1	3								104.1	NQ	NI	NI
Beiersdorf	44	solid	no cat	No	No	4	1.6	0.7		35.1	19.5		97.3	12.4								97.3		NI	NI
Beiersdorf	45	solid	no cat	No	No	1	1.6	3.2		26.8	5.5		110.6	0.6								110.6		NI	NI
Beiersdorf	45	solid	no cat	No	No	2	1.7	2.9		35.5	4.7		101.4	7								101.4		NI	NI
Beiersdorf	45	solid	no cat	No	No	3	1.5	3.5		25.3	1.8		118.8	1.2								118.8		NI	NI
Beiersdorf	46	solid	no cat	No	No	1	1.7	2.6		32	8.3		68.4	6.1								68.4		NI	NI
Beiersdorf	46	solid	no cat	No	No	2	1.5	0.2		29.3	1.5		68.9	15.9								68.9		NI	NI
Beiersdorf	46	solid	no cat	No	No	3	1.6	2		96.1	1.9	NQ	57.6	8.4								57.6	NQ	NI	I
Beiersdorf	46	solid	no cat	No	No	4	1.6	0.7		35.1	19.5		72.6	3.5								72.6		NI	NI
Beiersdorf	47	solid	no cat	No	No	1	1.7	5.3		31.6	3.9		4.4	0.8								4.4		I	I
Beiersdorf	47	solid	no cat	No	No	2	1.9	1.2		31.2	2.7		5	4.5								5		I	I
Beiersdorf	47	solid	no cat	No	No	3	1.7	0.8		26.4	10.8		4.6	3.1								4.6		I	I
Beiersdorf	48	solid	no cat	Yes	No	1	1.6	0.1		29	2.6		3.3	0.3					0.5	0.3		2.7		I	I
Beiersdorf	48	solid	no cat	Yes	No	2	1.6	1.6		32.9	3.3		4.2	0.5					0.5	0.3		3.6		I	I
Beiersdorf	48	solid	no cat	Yes	No	3	1.8	10.4		27.4	1.2		3.5	2					0.5	0.2		3		I	I
Beiersdorf	49	solid	no cat	Yes	No	1	1.6	3.2		26.8	5.5		8.6	5.1					12.2	17.2		0		I	I
Beiersdorf	49	solid	no cat	Yes	No	2	1.7	2.9		35.5	4.7		9.5	2.3					11.6	16.3		0		I	I
Beiersdorf	49	solid	no cat	Yes	No	3	1.5	3.5		25.3	1.8		8.8	2.9					13.1	18.4		0		I	I
Beiersdorf	50	solid	no cat	Yes	No	1	2	0.1		33.3	4.7		89.8	4					0.2	0.1		89.7		NI	NI
Beiersdorf	50	solid	no cat	Yes	No	2	1.7	0.6		37.4	0.6		89.8	2.2					0.2	0.1		89.6		NI	NI
Beiersdorf	50	solid	no cat	Yes	No	3	1.7	5.1		35.9	1.9		85.2	20.4	NQ				0.2	0.1		85	NQ	NI	NI
Beiersdorf	50	solid	no cat	Yes	No	4	1.8	2.5		24.3	1.6		83.7	8.7					0.2	0.1		83.5		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	51	solid	no cat	Yes	No	1	1.6	3.2		26.8	5.5		99.1	6.8					0	0.2		99.1		NI	NI
Beiersdorf	51	solid	no cat	Yes	No	2	1.7	2.9		35.5	4.7		91.5	16.3					0	0.2		91.5		NI	NI
Beiersdorf	51	solid	no cat	Yes	No	3	1.5	3.5		25.3	1.8		101.1	5.1					0	0.2		101.1		NI	NI
Beiersdorf	52	solid	no cat	No	No	1	1.6	3.2		26.8	5.5		104.8	0.1								104.8		NI	NI
Beiersdorf	52	solid	no cat	No	No	2	1.7	2.9		35.5	4.7		103.1	3.4								103.1		NI	NI
Beiersdorf	52	solid	no cat	No	No	3	1.5	3.5		25.3	1.8		130.8	5.5								130.8		NI	NI
Beiersdorf	53	solid	no cat	Yes	No	1	1.6	3.2		26.8	5.5		93.1	17.3					0.2	0.3		93		NI	NI
Beiersdorf	53	solid	no cat	Yes	No	2	1.7	2.9		35.5	4.7		105.9	10.8					0.2	0.3		105.7		NI	NI
Beiersdorf	53	solid	no cat	Yes	No	3	1.5	3.5		25.3	1.8		119.5	10.6					0.2	0.3		119.4		NI	NI
Beiersdorf	54	liquid	cat 2B	No	No	1	1.7	3.4		39.2	3.5		48.8	0.5								48.8		I	I
Beiersdorf	54	liquid	cat 2B	No	No	2	1.7	6.1		40.6	1.6		47.8	6.1								47.8		I	I
Beiersdorf	54	liquid	cat 2B	No	No	3	1.9	3.6		29.2	3		45.2	6.9								45.2		I	I
Beiersdorf	55	liquid	cat 2B	No	No	1	1.9	1.3		29	7.7		2.3	0.1								2.3		I	I
Beiersdorf	55	liquid	cat 2B	No	No	2	2	4.3		33.3	7.8		2.1	0.4								2.1		I	I
Beiersdorf	55	liquid	cat 2B	No	No	3	2	6.2		34.9	3		2.1	0.3								2.1		I	I
Beiersdorf	56	liquid	cat 2B	Yes	No	1	1.6	1.2		42.4	7		48.5	2.8					2.1	0.6		46.4		I	I
Beiersdorf	56	liquid	cat 2B	Yes	No	2	2	7.9		33	4.3		56.2	9.7					1.7	0.5		54.5		NI	I
Beiersdorf	56	liquid	cat 2B	Yes	No	3	1.7	7.7		41	2.1		62.4	1.5					2	0.6		60.3		NI	NI
Beiersdorf	57	liquid	cat 2B	No	No	1	1.6	1.2		42.4	7		24.4	4.7								24.4		I	I
Beiersdorf	57	liquid	cat 2B	No	No	2	2	7.9		33	4.3		19.9	5.8								19.8		I	I
Beiersdorf	57	liquid	cat 2B	No	No	3	1.7	7.7		41	2.1		19.1	3.7								19.1		I	I
Beiersdorf	58	liquid	cat 2B	No	No	1	1.9	1.3		29	7.7		22	0.3								22		I	I
Beiersdorf	58	liquid	cat 2B	No	No	2	2	4.3		33.3	7.8		22.7	6.9								22.7		I	I
Beiersdorf	58	liquid	cat 2B	No	No	3	2	6.2		34.9	3		22.2	3.4								22.2		I	I
Beiersdorf	59	liquid	cat 2B	No	No	1	1.9	1.3		29	7.7		62.6	11.1								62.6		NI	NI
Beiersdorf	59	liquid	cat 2B	No	No	2	2	4.3		33.3	7.8		67.5	3.7								67.5		NI	NI
Beiersdorf	59	liquid	cat 2B	No	No	3	2	6.2		34.9	3		78.3	7.1								78.3		NI	NI
Beiersdorf	60	liquid	cat 2B	Yes	No	1	1.9	1.3		29.7	3.1		20.5	1.5					0	0.3		20.5		I	I
Beiersdorf	60	liquid	cat 2B	Yes	No	2	1.8	3.6		30.7	2.4		13.6	2.7					0	0.3		13.6		I	I
Beiersdorf	60	liquid	cat 2B	Yes	No	3	2.1	4.1		30.3	2.8		12.6	2.4					0	0.3		12.6		I	I
Beiersdorf	61	solid	cat 2B	No	No	1	1.7	5.3		31.6	3.9		16	5.6								16		I	I
Beiersdorf	61	solid	cat 2B	No	No	2	1.9	1.2		31.2	2.7		15.9	5.8								15.9		I	I
Beiersdorf	61	solid	cat 2B	No	No	3	1.7	0.8		26.4	10.8		22.9	3.9								22.9		I	I
Beiersdorf	62	solid	cat 2B	Yes	No	1	1.6	0.1		29	2.6		115.2	9.9					0	0.5		115.2		NI	NI
Beiersdorf	62	solid	cat 2B	Yes	No	2	1.6	1.6		32.9	3.3		110.1	10.8					0	0.4		110.1		NI	NI
Beiersdorf	62	solid	cat 2B	Yes	No	3	1.8	10.4		27.4	1.2		101.7	14.9					0	0.4		101.7		NI	NI
Beiersdorf	63	solid	cat 2B	No	No	1	1.7	2.6		32	8.3		40.6	0.8								40.6		I	I
Beiersdorf	63	solid	cat 2B	No	No	2	1.5	0.2		29.3	1.5		34.3	0.2								34.3		I	I
Beiersdorf	63	solid	cat 2B	No	No	3	1.6	2		96.1	1.9	NQ	35.8	2.3								35.8	NQ	I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	63	solid	cat 2B	No	No	4	1.6	0.7		35.1	19.5		27	3.2								27		I	I
Beiersdorf	64	solid	cat 2B	No	No	1	1.7	5.3		31.6	3.9		36.9	9.4								36.9		I	I
Beiersdorf	64	solid	cat 2B	No	No	2	1.9	1.2		31.2	2.7		22.8	7.2								22.8		I	I
Beiersdorf	64	solid	cat 2B	No	No	3	1.7	0.8		26.4	10.8		30	2.1								30		I	I
Beiersdorf	65	solid	cat 2B	No	No	1	1.7	2.6		32	8.3		50.5	15.6								50.5		NI	I
Beiersdorf	65	solid	cat 2B	No	No	2	1.5	0.2		29.3	1.5		52.1	1								52.1		NI	I
Beiersdorf	65	solid	cat 2B	No	No	3	1.6	2		96.1	1.9	NQ	59.5	10.6								59.5	NQ	NI	I
Beiersdorf	65	solid	cat 2B	No	No	4	1.6	0.7		35.1	19.5		51.7	5.5								51.7		NI	I
Beiersdorf	66	solid	cat 2B	No	No	1	1.7	2.6		32	8.3		6	3.1								6		I	I
Beiersdorf	66	solid	cat 2B	No	No	2	1.5	0.2		29.3	1.5		8	1.4								8		I	I
Beiersdorf	66	solid	cat 2B	No	No	3	1.6	2		96.1	1.9	NQ	5.6	0								5.6	NQ	I	I
Beiersdorf	66	solid	cat 2B	No	No	4	1.6	0.7		35.1	19.5		6.4	1.3								6.4		I	I
Beiersdorf	67	liquid	cat 2A	No	No	1	1.7	3.4		39.2	3.5		15	2.9								15		I	I
Beiersdorf	67	liquid	cat 2A	No	No	2	1.7	6.1		40.6	1.6		10.8	0								10.8		I	I
Beiersdorf	67	liquid	cat 2A	No	No	3	1.9	3.6		29.2	3		10.7	0.9								10.7		I	I
Beiersdorf	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.7	3.4		39.2	3.5		3.5	0.2								3.5		I	I
Beiersdorf	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.7	6.1		40.6	1.6		2.4	0.2								2.4		I	I
Beiersdorf	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.9	3.6		29.2	3		4.3	0.9								4.3		I	I
Beiersdorf	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.8	10.1		37.4	6.3		13.2	1.5								13.2		I	I
Beiersdorf	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.6	5.6		43.5	4.4		15	3.6								15		I	I
Beiersdorf	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.6	0.3		46.4	1.2		13.9	2.2								13.9		I	I
Beiersdorf	70	liquid	cat 2A	No	No	1	1.8	10.1		37.4	6.3		12.5	1.3								12.5		I	I
Beiersdorf	70	liquid	cat 2A	No	No	2	1.6	5.6		43.5	4.4		17.9	1.8								17.9		I	I
Beiersdorf	70	liquid	cat 2A	No	No	3	1.6	0.3		46.4	1.2		15.4	3								15.4		I	I
Beiersdorf	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.6	1.2		42.4	7		5.2	0.7								5.2		I	I
Beiersdorf	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	2	7.9		33	4.3		6.2	1.3								6.2		I	I
Beiersdorf	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.7	7.7		41	2.1		4.7	2								4.7		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	72	liquid	cat 2A (ICCVAM: cat 2B)	No	Yes	1	2	4.3		33.3	7.8		8	2.6		3.3	1.4					4.7		I	I
Beiersdorf	72	liquid	cat 2A (ICCVAM: cat 2B)	No	Yes	2	2	6.2		34.9	3		4.6	2.8		2.4	0.8					2.2		I	I
Beiersdorf	72	liquid	cat 2A (ICCVAM: cat 2B)	No	Yes	3	1.8	3.6		30.7	2.4		7.5	0.4		2.6	0.9					4.9		I	I
Beiersdorf	73	solid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.7	5.1		37.4	6.5		73.9	5.2								73.9		NI	NI
Beiersdorf	73	solid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.7	2.5		34.4	2.8		88.1	0.3								88.1		NI	NI
Beiersdorf	73	solid	cat 2A (ICCVAM: cat 2B)	No	No	3	2	7.3		30.5	2.1		89	1.4								89		NI	NI
Beiersdorf	74	solid	cat 2A	Yes	No	1	1.7	5.1		37.4	6.5		76.4	31.7	NQ				3.3	0.9		73.1	NQ	NI	NI
Beiersdorf	74	solid	cat 2A	Yes	No	2	1.7	2.5		34.4	2.8		75.8	11					3.3	0.9		72.5		NI	NI
Beiersdorf	74	solid	cat 2A	Yes	No	3	2	7.3		30.5	2.1		68.8	2.7					2.9	0.8		65.9		NI	NI
Beiersdorf	74	solid	cat 2A	Yes	No	4	1.9	1.2		31.2	2.7		91.8	7.2					3	0.8		88.8		NI	NI
Beiersdorf	75	solid	cat 2A	No	No	1	1.7	2.6		32	8.3		74.8	10.2								74.8		NI	NI
Beiersdorf	75	solid	cat 2A	No	No	2	1.5	0.2		29.3	1.5		81.1	1.1								81.1		NI	NI
Beiersdorf	75	solid	cat 2A	No	No	3	1.6	2		96.1	1.9	NQ	41.3	76.9	NQ							41.3	NQ	I	I
Beiersdorf	75	solid	cat 2A	No	No	4	1.6	0.7		35.1	19.5		28.9	52	NQ							28.9	NQ	I	I
Beiersdorf	75	solid	cat 2A	No	No	5	1.8	2.1		24.4	4.9		83.9	6.9								83.9		NI	NI
Beiersdorf	76	solid	cat 2A	No	No	1	1.6	0.1		29	2.6		54.8	8.1								54.8		NI	I
Beiersdorf	76	solid	cat 2A	No	No	2	1.6	1.6		32.9	3.3		53.5	4.3								53.5		NI	I
Beiersdorf	76	solid	cat 2A	No	No	3	1.8	10.4		27.4	1.2		53.4	0.5								53.4		NI	I
Beiersdorf	77	solid	cat 2A	No	No	1	1.6	0.1		29	2.6		103.6	4.8								103.6		NI	NI
Beiersdorf	77	solid	cat 2A	No	No	2	1.6	1.6		32.9	3.3		94.1	17.6								94.1		NI	NI
Beiersdorf	77	solid	cat 2A	No	No	3	1.8	10.4		27.4	1.2		92.8	3.4								92.8		NI	NI
Beiersdorf	78	solid	cat 2A	No	No	1	1.7	2.6		32	8.3		79.9	3.3								79.9		NI	NI
Beiersdorf	78	solid	cat 2A	No	No	2	1.5	0.2		29.3	1.5		80.9	0.3								80.9		NI	NI
Beiersdorf	78	solid	cat 2A	No	No	3	1.6	2		96.1	1.9	NQ	84.6	11.7								84.6	NQ	NI	NI
Beiersdorf	78	solid	cat 2A	No	No	4	1.6	0.7		35.1	19.5		88.9	2.7								88.9		NI	NI
Beiersdorf	79	solid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.7	5.3		31.6	3.9		2.4	0.1								2.4		I	I
Beiersdorf	79	solid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.9	1.2		31.2	2.7		3.3	1.4								3.3		I	I
Beiersdorf	79	solid	cat 2A	No	No	3	1.7	0.8		26.4	10.8		2.2	0.1								2.2		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
			(ICCVAM: cat 2B)																						
Beiersdorf	80[1]	liquid	cat 1	Yes	No	1	1.7	3.4		39.2	3.5		70.9	1.9					52.7	1.6		18.1		I	I
Beiersdorf	80[1]	liquid	cat 1	Yes	No	2	1.7	6.1		40.6	1.6		68.6	8.6					52	1.6		16.6		I	I
Beiersdorf	80[1]	liquid	cat 1	Yes	No	3	1.9	3.6		29.2	3		66.5	0.2					48.8	1.5		17.7		I	I
Beiersdorf	81	liquid	cat 1	Yes	No	1	1.6	1.2		42.4	7		2.6	0.2					0.1	0.3		2.5		I	I
Beiersdorf	81	liquid	cat 1	Yes	No	2	2	7.9		33	4.3		1.8	0.1					0.1	0.2		1.8		I	I
Beiersdorf	81	liquid	cat 1	Yes	No	3	1.7	7.7		41	2.1		3.2	0.4					0.1	0.3		3.1		I	I
Beiersdorf	82	liquid	cat 1	No	No	1	1.7	6		37.5	4.2		4.5	3.6								4.5		I	I
Beiersdorf	82	liquid	cat 1	No	No	2	1.4	0.5		18.3	4.9		1.6	0.3								1.6		I	I
Beiersdorf	82	liquid	cat 1	No	No	3	1.4	1.8		42.2	10.3		5.4	1								5.4		I	I
Beiersdorf	83	liquid	cat 1	No	No	1	1.8	10.1		37.4	6.3		5.5	2.9								5.5		I	I
Beiersdorf	83	liquid	cat 1	No	No	2	1.6	5.6		43.5	4.4		6.1	1.8								6.1		I	I
Beiersdorf	83	liquid	cat 1	No	No	3	1.6	0.3		46.4	1.2		5.3	3.1								5.3		I	I
Beiersdorf	84	liquid	cat 1	Yes	No	1	1.7	6		37.5	4.2		12.7	4.6					0	0.3		12.6		I	I
Beiersdorf	84	liquid	cat 1	Yes	No	2	1.4	0.5		18.3	4.9		5.7	1.1					0.1	0.4		5.6		I	I
Beiersdorf	84	liquid	cat 1	Yes	No	3	1.4	1.8		42.2	10.3		22.2	13					0.1	0.4		22.1		I	I
Beiersdorf	85	liquid	cat 1	No	No	1	1.7	3.4		39.2	3.5		15.9	3.7								15.9		I	I
Beiersdorf	85	liquid	cat 1	No	No	2	1.7	6.1		40.6	1.6		18.1	0.3								18.1		I	I
Beiersdorf	85	liquid	cat 1	No	No	3	1.9	3.6		29.2	3		26.7	1.1								26.7		I	I
Beiersdorf	86	liquid	cat 1	No	No	1	1.7	6		37.5	4.2		25.3	3.3								25.3		I	I
Beiersdorf	86	liquid	cat 1	No	No	2	1.4	0.5		18.3	4.9		20.7	4.5								20.7		I	I
Beiersdorf	86	liquid	cat 1	No	No	3	1.4	1.8		42.2	10.3		27.2	3.1								27.2		I	I
Beiersdorf	87	liquid	cat 1	No	No	1	1.8	10.1		37.4	6.3		26.3	0.3								26.3		I	I
Beiersdorf	87	liquid	cat 1	No	No	2	1.6	5.6		43.5	4.4		26.3	2.9								26.3		I	I
Beiersdorf	87	liquid	cat 1	No	No	3	1.6	0.3		46.4	1.2		33.6	8.3								33.6		I	I
Beiersdorf	88	liquid	cat 1	Yes	No	1	1.7	6		37.5	4.2		4.5	0.4					0	0.4		4.5		I	I
Beiersdorf	88	liquid	cat 1	Yes	No	2	1.4	0.5		18.3	4.9		5.3	0.1					0	0.5		5.3		I	I
Beiersdorf	88	liquid	cat 1	Yes	No	3	1.4	1.8		42.2	10.3		7.5	2.5					0	0.5		7.4		I	I
Beiersdorf	89	liquid	cat 1	No	No	1	1.6	1.2		42.4	7		10.7	3.5								10.7		I	I
Beiersdorf	89	liquid	cat 1	No	No	2	2	7.9		33	4.3		7.2	0								7.2		I	I
Beiersdorf	89	liquid	cat 1	No	No	3	1.7	7.7		41	2.1		10.7	2								10.6		I	I
Beiersdorf	90	liquid	cat 1	No	No	1	1.9	1.3		29	7.7		40.4	1.2								40.4		I	I
Beiersdorf	90	liquid	cat 1	No	No	2	2	4.3		33.3	7.8		28.5	3.4								28.5		I	I
Beiersdorf	90	liquid	cat 1	No	No	3	2	6.2		34.9	3		25.6	10.2								25.6		I	I
Beiersdorf	91	liquid	cat 1	Yes	No	1	1.6	1.2		42.4	7		20.6	0					0.6	0.1		20		I	I
Beiersdorf	91	liquid	cat 1	Yes	No	2	2	7.9		33	4.3		35.4	6.3					0.5	0.1		35		I	I
Beiersdorf	91	liquid	cat 1	Yes	No	3	1.7	7.7		41	2.1		38.9	7.9					0.6	0.1		38.3		I	I
Beiersdorf	92	liquid	cat 1	Yes	No	1	1.9	1.3		29.7	3.1		47.7	9.3					0.2	0.4		47.5		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	92	liquid	cat 1	Yes	No	2	1.8	3.6		30.7	2.4		41.3	9.4					0.3	0.4		41		I	I
Beiersdorf	92	liquid	cat 1	Yes	No	3	2.1	4.1		30.3	2.8		50	2.8					0.2	0.3		49.8		I	I
Beiersdorf	93	solid	cat 1	No	No	1	1.7	5.1		37.4	6.5		11.5	0.9								11.5		I	I
Beiersdorf	93	solid	cat 1	No	No	2	1.7	2.5		34.4	2.8		9.5	4.2								9.5		I	I
Beiersdorf	93	solid	cat 1	No	No	3	2	7.3		30.5	2.1		5.7	1.2								5.7		I	I
Beiersdorf	94	solid	cat 1	No	No	1	1.6	0.1		29	2.6		2.1	0.4								2.1		I	I
Beiersdorf	94	solid	cat 1	No	No	2	1.6	1.6		32.9	3.3		2.3	0.3								2.3		I	I
Beiersdorf	94	solid	cat 1	No	No	3	1.8	10.4		27.4	1.2		2.6	0.3								2.6		I	I
Beiersdorf	95	solid	cat 1	Yes	No	1	1.7	5.1		37.4	6.5		2.4	0.1					0	0.3		2.4		I	I
Beiersdorf	95	solid	cat 1	Yes	No	2	1.7	2.5		34.4	2.8		2.5	0.1					0	0.3		2.5		I	I
Beiersdorf	95	solid	cat 1	Yes	No	3	2	7.3		30.5	2.1		2.2	0.2					0	0.3		2.2		I	I
Beiersdorf	96	solid	cat 1	No	No	1	1.7	5.1		37.4	6.5		28.9	10.3								28.9		I	I
Beiersdorf	96	solid	cat 1	No	No	2	1.7	2.5		34.4	2.8		41.1	10								41.1		I	I
Beiersdorf	96	solid	cat 1	No	No	3	2	7.3		30.5	2.1		36.1	1.7								36.1		I	I
Beiersdorf	97	solid	cat 1	No	No	1	1.7	5.1		37.4	6.5		56.2	4.5								56.2		NI	I
Beiersdorf	97	solid	cat 1	No	No	2	1.7	2.5		34.4	2.8		47.2	1.2								47.2		I	I
Beiersdorf	97	solid	cat 1	No	No	3	2	7.3		30.5	2.1		55.5	8								55.5		NI	I
Beiersdorf	98	solid	cat 1	Yes	Yes	1	2	0.1		33.3	4.7		28.4	8.4		12	10.6		27.9	1.1		0		I	I
Beiersdorf	98	solid	cat 1	Yes	Yes	2	1.7	0.6		37.4	0.6		21.1	2.4		8.9	6.5		31.7	1.3		0		I	I
Beiersdorf	98	solid	cat 1	Yes	Yes	3	1.7	5.1		35.9	1.9		23.4	1.9		5.6	0.4		32.1	1.3		0		I	I
Beiersdorf	99	solid	cat 1	No	No	1	1.6	3.2		26.8	5.5		2.6	0.1								2.6		I	I
Beiersdorf	99	solid	cat 1	No	No	2	1.7	2.9		35.5	4.7		2.8	0.1								2.8		I	I
Beiersdorf	99	solid	cat 1	No	No	3	1.5	3.5		25.3	1.8		3.1	0.5								3.1		I	I
Beiersdorf	100	solid	cat 1	Yes	No	1	1.9	13		23.6	5		9.8	1.1					0	0.1		9.8		I	I
Beiersdorf	100	solid	cat 1	Yes	No	2	1.7	3.1		21.5	3.6		3.6	0.3					0	0.1		3.6		I	I
Beiersdorf	100	solid	cat 1	Yes	No	3	1.8	2.1		24.4	4.9		2.4	0.2					0	0.1		2.4		I	I
Beiersdorf	101	solid	cat 1	No	Yes	1	2	0.1		33.3	4.7		34.6	10.6		0.4	0.1					34.1		I	I
Beiersdorf	101	solid	cat 1	No	Yes	2	1.7	0.6		37.4	0.6		33.5	5.8		0.3	0.1					33.2		I	I
Beiersdorf	101	solid	cat 1	No	Yes	3	1.7	5.1		35.9	1.9		34.6	2.8		0.3	0					34.3		I	I
Beiersdorf	102	solid	cat 1	No	No	1	1.6	3.2		26.8	5.5		10.1	3.7								10.1		I	I
Beiersdorf	102	solid	cat 1	No	No	2	1.7	2.9		35.5	4.7		110.3	9.6								110.2		NI	NI
Beiersdorf	102	solid	cat 1	No	No	3	1.5	3.5		25.3	1.8		124.3	3.5								124.3		NI	NI
Beiersdorf	103	solid	cat 1	Yes	No	1	1.6	0.1		29	2.6		2	0.1					0	0.2		2		I	I
Beiersdorf	103	solid	cat 1	Yes	No	2	1.6	1.6		32.9	3.3		3.5	0.7					0	0.2		3.5		I	I
Beiersdorf	103	solid	cat 1	Yes	No	3	1.8	10.4		27.4	1.2		2	0.4					0	0.2		2		I	I
Beiersdorf	104	solid	cat 1	No	No	1	1.7	2.6		32	8.3		37.4	5.8								37.4		I	I
Beiersdorf	104	solid	cat 1	No	No	2	1.5	0.2		29.3	1.5		38.9	2.5								38.9		I	I
Beiersdorf	104	solid	cat 1	No	No	3	1.6	2		96.1	1.9	NQ	33.1	14.2								33.1	NQ	I	I
Beiersdorf	104	solid	cat 1	No	No	4	1.6	0.7		35.1	19.5		42.9	12								42.9		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Beiersdorf	105	solid	cat 1	No	No	1	1.6	0.1		29	2.6		2.5	0.1								2.5		I	I
Beiersdorf	105	solid	cat 1	No	No	2	1.6	1.6		32.9	3.3		2.8	0.1								2.8		I	I
Beiersdorf	105	solid	cat 1	No	No	3	1.8	10.4		27.4	1.2		2.4	0.2								2.4		I	I
Harlan	1	liquid	no cat	No	No	1	1.8	3.4		25.8	6.9		66.7	3.5								66.7		NI	NI
Harlan	1	liquid	no cat	No	No	2	1.7	13.7		29	1		62.5	7.6								62.5		NI	NI
Harlan	1	liquid	no cat	No	No	3	1.7	3.5		31.5	9.5		70.5	5.4								70.4		NI	NI
Harlan	2	liquid	no cat	No	No	1	1.7	7.2		25.4	5.6		74.6	7.9								74.6		NI	NI
Harlan	2	liquid	no cat	No	No	2	1.7	1.4		28.8	3.8		79.8	0.8								79.8		NI	NI
Harlan	2	liquid	no cat	No	No	3	1.9	6.2		31.8	1.1		78.9	4.3								78.9		NI	NI
Harlan	3	liquid	no cat	No	No	1	1.7	7.2		25.4	5.6		37.2	5.2								37.2		I	I
Harlan	3	liquid	no cat	No	No	2	1.7	1.4		28.8	3.8		38.1	4.3								38.1		I	I
Harlan	3	liquid	no cat	No	No	3	1.9	6.2		31.8	1.1		38.6	2.7								38.6		I	I
Harlan	4	liquid	no cat	Yes	No	1	1.8	5.7		15.2	0.8		98.9	5.2					38	0.2		60.8		NI	NI
Harlan	4	liquid	no cat	Yes	No	2	1.9	0.8		28.1	0.3		94.7	3					36.8	0.2		57.9		NI	I
Harlan	4	liquid	no cat	Yes	No	3	1.9	4.2		17.9	6.3		102.2	12.1					37.9	0.2		64.3		NI	NI
Harlan	5	liquid	no cat	Yes	No	1	1.3	11.3		6.8	0.7		56.7	15.5					0	1.1		56.7		NI	I
Harlan	5	liquid	no cat	Yes	No	2	1.8	0.6		16.4	0.9		41.4	5.4					0	0.8		41.4		I	I
Harlan	5	liquid	no cat	Yes	No	3	2.3	3.5		12.7	0		40.3	0.4					0	0.6		40.3		I	I
Harlan	6	liquid	no cat	No	No	1	1.8	3.4		25.8	6.9		73.2	14								73.2		NI	NI
Harlan	6	liquid	no cat	No	No	2	1.7	13.7		29	1		71.1	6.9								71.1		NI	NI
Harlan	6	liquid	no cat	No	No	3	1.7	3.5		31.5	9.5		84.7	7.4								84.7		NI	NI
Harlan	7	liquid	no cat	No	No	1	1.7	7.2		25.4	5.6		31	3.6								31		I	I
Harlan	7	liquid	no cat	No	No	2	1.7	1.4		28.8	3.8		36.8	10.6								36.8		I	I
Harlan	7	liquid	no cat	No	No	3	1.9	6.2		31.8	1.1		36.6	5.8								36.6		I	I
Harlan	8	liquid	no cat	No	No	1	1.7	7.2		25.4	5.6		89.6	6.5								89.6		NI	NI
Harlan	8	liquid	no cat	No	No	2	1.7	1.4		28.8	3.8		94.8	3.4								94.7		NI	NI
Harlan	8	liquid	no cat	No	No	3	1.9	6.2		31.8	1.1		94.8	5.3								94.8		NI	NI
Harlan	9	liquid	no cat	No	No	1	1.8	3.4		25.8	6.9		91.9	7.3								91.9		NI	NI
Harlan	9	liquid	no cat	No	No	2	1.7	13.7		29	1		82.6	13.3								82.6		NI	NI
Harlan	9	liquid	no cat	No	No	3	1.7	3.5		31.5	9.5		96.5	7.3								96.5		NI	NI
Harlan	10	liquid	no cat	No	No	1	1.9	6.1		27.3	0.5		14.4	0.3								14.4		I	I
Harlan	10	liquid	no cat	No	No	2	1.8	1.1		18.1	4.1		9.8	1.3								9.8		I	I
Harlan	10	liquid	no cat	No	No	3	1.5	2.8		22.9	2.2		13.2	1.7								13.2		I	I
Harlan	11	liquid	no cat	No	No	1	1.8	3.4		25.8	6.9		21.3	3.6								21.2		I	I
Harlan	11	liquid	no cat	No	No	2	1.7	13.7		29	1		19	0.4								19		I	I
Harlan	11	liquid	no cat	No	No	3	1.7	3.5		31.5	9.5		16.4	0.9								16.4		I	I
Harlan	12	liquid	no cat	No	No	1	1.7	1.8		15.6	2.3		92.7	3.7								92.7		NI	NI
Harlan	12	liquid	no cat	No	No	2	1.6	4.3		29.8	1.6		91.9	6.1								91.9		NI	NI
Harlan	12	liquid	no cat	No	No	3	1.6	4.2		29.4	1.1		96.7	2.7								96.7		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Harlan	13	liquid	no cat	No	No	1	1.7	1.8		15.6	2.3		88.8	4.8								88.8		NI	NI
Harlan	13	liquid	no cat	No	No	2	1.6	4.3		29.8	1.6		97.5	2.1								97.5		NI	NI
Harlan	13	liquid	no cat	No	No	3	1.6	4.2		29.4	1.1		85.1	16.3								85.1		NI	NI
Harlan	14	liquid	no cat	No	No	1	1.8	3.4		25.8	6.9		90.6	10.8								90.6		NI	NI
Harlan	14	liquid	no cat	No	No	2	1.7	13.7		29	1		97.9	4.9								97.9		NI	NI
Harlan	14	liquid	no cat	No	No	3	1.7	3.5		31.5	9.5		103.1	10								103		NI	NI
Harlan	15	liquid	no cat	No	No	1	1.7	1.8		15.6	2.3		104.9	0.7								104.9		NI	NI
Harlan	15	liquid	no cat	No	No	2	1.6	4.3		29.8	1.6		93	5.3								93		NI	NI
Harlan	15	liquid	no cat	No	No	3	1.6	4.2		29.4	1.1		106.3	1.3								106.3		NI	NI
Harlan	16	liquid	no cat	No	No	1	1.7	7.2		25.4	5.6		103.8	1.8								103.8		NI	NI
Harlan	16	liquid	no cat	No	No	2	1.7	1.4		28.8	3.8		102.1	1.2								102.1		NI	NI
Harlan	16	liquid	no cat	No	No	3	1.9	6.2		31.8	1.1		94	0.2								94		NI	NI
Harlan	17	liquid	no cat	No	No	1	1.9	6.1		27.3	0.5		86.9	3.1								86.9		NI	NI
Harlan	17	liquid	no cat	No	No	2	1.8	1.1		18.1	4.1		100.6	0.8								100.6		NI	NI
Harlan	17	liquid	no cat	No	No	3	1.5	2.8		22.9	2.2		103.9	0.6								103.9		NI	NI
Harlan	18	liquid	no cat	No	No	1	1.7	1.8		15.6	2.3		101.5	4.2								101.5		NI	NI
Harlan	18	liquid	no cat	No	No	2	1.6	4.3		29.8	1.6		91	2.4								91		NI	NI
Harlan	18	liquid	no cat	No	No	3	1.6	4.2		29.4	1.1		96.8	1.8								96.8		NI	NI
Harlan	19	liquid	no cat	No	No	1	1.7	1.8		15.6	2.3		108.8	5.2								108.8		NI	NI
Harlan	19	liquid	no cat	No	No	2	1.6	4.3		29.8	1.6		105.3	5								105.3		NI	NI
Harlan	19	liquid	no cat	No	No	3	1.6	4.2		29.4	1.1		113.1	14.5								113.1		NI	NI
Harlan	20	liquid	no cat	Yes	No	1	1.7	8.5		28	3.5		26.7	10.2					17.5	4		9.1		I	I
Harlan	20	liquid	no cat	Yes	No	2	1.4	2.9		29	0.6		20.8	5.8					21.5	4.9		0		I	I
Harlan	20	liquid	no cat	Yes	No	3	1.9	1.9		27.1	14.1		34.8	3.1					15.8	3.6		19.1		I	I
Harlan	21	liquid	no cat	No	No	1	1.9	6.1		27.3	0.5		71.8	0.4								71.8		NI	NI
Harlan	21	liquid	no cat	No	No	2	1.8	1.1		18.1	4.1		67.4	4.6								67.4		NI	NI
Harlan	21	liquid	no cat	No	No	3	1.5	2.8		22.9	2.2		77.6	6.4								77.6		NI	NI
Harlan	22	liquid	no cat	Yes	No	1	1.3	11.3		6.8	0.7		28.3	7.5					4.3	1		24		I	I
Harlan	22	liquid	no cat	Yes	No	2	1.8	0.6		16.4	0.9		26.4	4.4					3.1	0.7		23.3		I	I
Harlan	22	liquid	no cat	Yes	No	3	2.3	3.5		12.7	0		15.4	0.8					2.4	0.6		13		I	I
Harlan	23	liquid	no cat	Yes	No	1	1.8	5.7		15.2	0.8		62.8	10.5					45.3	2.2		17.5		I	I
Harlan	23	liquid	no cat	Yes	No	2	1.9	0.8		28.1	0.3		66.3	1.1					43.9	2.1		22.4		I	I
Harlan	23	liquid	no cat	Yes	No	3	1.9	4.2		17.9	6.3		50	1.9					45.1	2.2		4.9		I	I
Harlan	24	liquid	no cat	No	No	1	1.9	6.1		27.3	0.5		28	0.9								28		I	I
Harlan	24	liquid	no cat	No	No	2	1.8	1.1		18.1	4.1		19.4	7.7								19.4		I	I
Harlan	24	liquid	no cat	No	No	3	1.5	2.8		22.9	2.2		21.3	6.8								21.3		I	I
Harlan	25	liquid	no cat	Yes	No	1	1.7	8.5		28	3.5		104.8	9.1					0	0.1		104.8		NI	NI
Harlan	25	liquid	no cat	Yes	No	2	1.4	2.9		29	0.6		108.9	11.9					0	0.1		108.9		NI	NI
Harlan	25	liquid	no cat	Yes	No	3	1.9	1.9		27.1	14.1		104.9	2.8					0	0.1		104.9		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Harlan	26	liquid	no cat	No	No	1	1.7	1.8		15.6	2.3		30.6	3.1								30.6		I	I
Harlan	26	liquid	no cat	No	No	2	1.6	4.3		29.8	1.6		40.7	8.1								40.7		I	I
Harlan	26	liquid	no cat	No	No	3	1.6	4.2		29.4	1.1		35.6	4.3								35.6		I	I
Harlan	28	solid	no cat	No	No	1	1.8	3.1		22.5	0.5		95	3.5								94.9		NI	NI
Harlan	28	solid	no cat	No	No	2	2	2.4		25.1	1.4		94.5	4.3								94.5		NI	NI
Harlan	28	solid	no cat	No	No	3	2	0.2		22.9	2.6		90.9	1.3								90.9		NI	NI
Harlan	29	solid	no cat	No	No	1	1.6	16.2		35.4	2.2		57.4	12.3								57.4		NI	I
Harlan	29	solid	no cat	No	No	2	1.4	2.9		32.8	0.6		112	11.3								112		NI	NI
Harlan	29	solid	no cat	No	No	3	1.6	2.7		29.2	1.2		83	7.2								83		NI	NI
Harlan	30	solid	no cat	No	No	1	1.6	2.1		19.2	1.2		35	6.7								35		I	I
Harlan	30	solid	no cat	No	No	2	1.7	0		16.3	1.8		25.2	1.9								25.2		I	I
Harlan	30	solid	no cat	No	No	3	1.6	3.7		29	15.6		14.2	6.6								14.2		I	I
Harlan	31	solid	no cat	No	No	1	1.6	2.1		19.2	1.2		96.6	1.1								96.6		NI	NI
Harlan	31	solid	no cat	No	No	2	1.7	0		16.3	1.8		77.4	8.3								77.4		NI	NI
Harlan	31	solid	no cat	No	No	3	1.6	3.7		29	15.6		96.3	7.2								96.3		NI	NI
Harlan	32	solid	no cat	Yes	Yes	1	1.7	5.1		12.3	1.5		4.3	1		0.3	0.1		2.8	0.5		1.1		I	I
Harlan	32	solid	no cat	Yes	Yes	2	1.7	2.4		19.5	3.4		4.3	0.9		0.5	0.1		2.9	0.5		0.9		I	I
Harlan	32	solid	no cat	Yes	Yes	3	1.7	0.7		17	1.4		4.1	0.3		0.4	0.2		2.8	0.5		0.9		I	I
Harlan	33	solid	no cat	Yes	Yes	1	1.7	2.4		19.5	3.4		69.2	12.9		0.5	0.3		24.6	10.2		44.1		I	I
Harlan	33	solid	no cat	Yes	Yes	2	1.7	0.7		17	1.4		77.1	15.7		4.6	5.1		24.2	10.1		48.3		I	I
Harlan	33	solid	no cat	Yes	Yes	3	1.4	11.3		43.1	6.8		84.4	14.4		13.8	3		30.3	12.6		40.3		I	I
Harlan	34	solid	no cat	Yes	Yes	1	1.7	5.1		12.3	1.5		106.6	16.7		11.4	4.2		13.8	3.8		81.4		NI	NI
Harlan	34	solid	no cat	Yes	Yes	2	1.7	2.4		19.5	3.4		80.9	13.3		12.6	2.3		14.2	3.9		54.1		NI	I
Harlan	34	solid	no cat	Yes	Yes	3	1.7	0.7		17	1.4		89.6	1.1		12.5	1.9		14	3.9		63.2		NI	NI
Harlan	35	solid	no cat	Yes	No	1	1.6	5.3		27.3	7.7		65.1	0.7					2.8	0.1		62.3		NI	NI
Harlan	35	solid	no cat	Yes	No	2	1.6	4.7		21.3	6.6		72.1	8.1					2.8	0.1		69.3		NI	NI
Harlan	35	solid	no cat	Yes	No	3	1.6	2.2		16.2	0.7		80.3	13.3					2.9	0.1		77.4		NI	NI
Harlan	36	solid	no cat	No	No	1	1.8	3.1		22.5	0.5		103.1	3.6								103.1		NI	NI
Harlan	36	solid	no cat	No	No	2	2	2.4		25.1	1.4		88.2	14								88.2		NI	NI
Harlan	36	solid	no cat	No	No	3	2	0.2		22.9	2.6		98.5	1								98.5		NI	NI
Harlan	37	liquid	no cat	No	No	1	1.9	6.1		27.3	0.5		74.2	6.1								74.2		NI	NI
Harlan	37	liquid	no cat	No	No	2	1.8	1.1		18.1	4.1		66.5	6.8								66.5		NI	NI
Harlan	37	liquid	no cat	No	No	3	1.5	2.8		22.9	2.2		78.3	8.6								78.3		NI	NI
Harlan	38	solid	no cat	No	No	1	1.6	16.2		35.4	2.2		99.7	6.2								99.7		NI	NI
Harlan	38	solid	no cat	No	No	2	1.4	2.9		32.8	0.6		113	1.7								113		NI	NI
Harlan	38	solid	no cat	No	No	3	1.6	2.7		29.2	1.2		95.8	7.9								95.8		NI	NI
Harlan	39	solid	no cat	No	No	1	1.6	16.2		35.4	2.2		100.9	5.1								100.9		NI	NI
Harlan	39	solid	no cat	No	No	2	1.4	2.9		32.8	0.6		114.7	1.1								114.7		NI	NI
Harlan	39	solid	no cat	No	No	3	1.6	2.7		29.2	1.2		88.4	2.4								88.4		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Harlan	40	solid	no cat	No	No	1	1.4	11.3		43.1	6.8		72.9	2								72.9		NI	NI
Harlan	40	solid	no cat	No	No	2	0.7	5.5	NQ	45.1	0.4		52.9	8.8								52.9	NQ	NI	I
Harlan	40	solid	no cat	No	No	3	1.8	3.3		36.8	3.1		56.2	5.1								56.2		NI	I
Harlan	40	solid	no cat	No	No	4	1.6	1		35.9	1.2		60.2	1.5								60.2		NI	NI
Harlan	41	solid	no cat	No	No	1	1.8	3.1		22.5	0.5		98.2	4								98.2		NI	NI
Harlan	41	solid	no cat	No	No	2	2	2.4		25.1	1.4		86.4	8.4								86.4		NI	NI
Harlan	41	solid	no cat	No	No	3	2	0.2		22.9	2.6		88.8	4.1								88.8		NI	NI
Harlan	42	solid	no cat	Yes	No	1	1.6	5.3		27.3	7.7		53.5	9.8					0.1	0.2		53.4		NI	I
Harlan	42	solid	no cat	Yes	No	2	1.6	4.7		21.3	6.6		66.1	3.5					0.1	0.2		66		NI	NI
Harlan	42	solid	no cat	Yes	No	3	1.6	2.2		16.2	0.7		60.2	3.1					0.1	0.3		60		NI	NI
Harlan	43	solid	no cat	No	No	1	1.6	2.1		19.2	1.2		125.3	4.7								125.3		NI	NI
Harlan	43	solid	no cat	No	No	2	1.7	0		16.3	1.8		91.6	2.1								91.6		NI	NI
Harlan	43	solid	no cat	No	No	3	1.6	3.7		29	15.6		163.7	3.6								163.7		NI	NI
Harlan	44	solid	no cat	No	No	1	1.6	2.1		19.2	1.2		101.6	6.3								101.6		NI	NI
Harlan	44	solid	no cat	No	No	2	1.7	0		16.3	1.8		95	2.8								95		NI	NI
Harlan	44	solid	no cat	No	No	3	1.6	3.7		29	15.6		103.9	4.8								103.9		NI	NI
Harlan	45	solid	no cat	No	No	1	1.6	2.1		19.2	1.2		112.5	7.7								112.5		NI	NI
Harlan	45	solid	no cat	No	No	2	1.7	0		16.3	1.8		97.9	6.9								97.9		NI	NI
Harlan	45	solid	no cat	No	No	3	1.6	3.7		29	15.6		112.6	9.4								112.6		NI	NI
Harlan	46	solid	no cat	No	No	1	1.6	2.1		19.2	1.2		73.1	0.4								73.1		NI	NI
Harlan	46	solid	no cat	No	No	2	1.7	0		16.3	1.8		58.9	4.2								58.9		NI	I
Harlan	46	solid	no cat	No	No	3	1.6	3.7		29	15.6		80	19.7								80		NI	NI
Harlan	47	solid	no cat	Yes	No	1	1.6	5.3		27.3	7.7		3.5	2.3					0.1	0.5		3.4		I	I
Harlan	47	solid	no cat	Yes	No	2	1.6	4.7		21.3	6.6		2	0.1					0.1	0.5		2		I	I
Harlan	47	solid	no cat	Yes	No	3	1.6	2.2		16.2	0.7		3.3	1.2					0.1	0.5		3.2		I	I
Harlan	48	solid	no cat	No	No	1	1.7	3.3		24.9	1.4		2.8	0.2								2.8		I	I
Harlan	48	solid	no cat	No	No	2	1.7	2.8		20.7	1.4		3.1	0.3								3.1		I	I
Harlan	48	solid	no cat	No	No	3	1.8	6.9		16.9	9.2		2.5	0.3								2.5		I	I
Harlan	49	solid	no cat	Yes	No	1	1.4	11.3		43.1	6.8		11.7	0.9					0	0.2		11.7		I	I
Harlan	49	solid	no cat	Yes	No	2	0.7	5.5	NQ	45.1	0.4		6.3	0.6					0	0.4		6.3	NQ	I	I
Harlan	49	solid	no cat	Yes	No	3	1.8	3.3		36.8	3.1		5.5	1.1					0	0.2		5.5		I	I
Harlan	49	solid	no cat	Yes	No	4	1.6	1		35.9	1.2		3.8	3					0	0.2		3.8		I	I
Harlan	50	solid	no cat	No	No	1	1.6	16.2		35.4	2.2		99.1	13.4								99.1		NI	NI
Harlan	50	solid	no cat	No	No	2	1.4	2.9		32.8	0.6		97.2	8.6								97.1		NI	NI
Harlan	50	solid	no cat	No	No	3	1.6	2.7		29.2	1.2		96.7	0.9								96.7		NI	NI
Harlan	51	solid	no cat	No	No	1	1.6	16.2		35.4	2.2		93.3	0.3								93.3		NI	NI
Harlan	51	solid	no cat	No	No	2	1.4	2.9		32.8	0.6		100.1	3								100.1		NI	NI
Harlan	51	solid	no cat	No	No	3	1.6	2.7		29.2	1.2		84.8	2.7								84.8		NI	NI
Harlan	52	solid	no cat	No	No	1	1.6	16.2		35.4	2.2		106.5	0.1								106.5		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Harlan	52	solid	no cat	No	No	2	1.4	2.9		32.8	0.6		105.7	3.4								105.7		NI	NI
Harlan	52	solid	no cat	No	No	3	1.6	2.7		29.2	1.2		93.4	3.7								93.4		NI	NI
Harlan	53	solid	no cat	No	No	1	1.6	16.2		35.4	2.2		108.2	2.1								108.2		NI	NI
Harlan	53	solid	no cat	No	No	2	1.4	2.9		32.8	0.6		123.4	4.4								123.4		NI	NI
Harlan	53	solid	no cat	No	No	3	1.6	2.7		29.2	1.2		104	11.9								104		NI	NI
Harlan	54	liquid	cat 2B	No	No	1	1.8	3.4		25.8	6.9		17.1	3.7								17.1		I	I
Harlan	54	liquid	cat 2B	No	No	2	1.7	13.7		29	1		25.2	1.1								25.2		I	I
Harlan	54	liquid	cat 2B	No	No	3	1.7	3.5		31.5	9.5		19.9	5.9								19.9		I	I
Harlan	55	liquid	cat 2B	No	No	1	1.9	6.1		27.3	0.5		2.2	0.5								2.2		I	I
Harlan	55	liquid	cat 2B	No	No	2	1.8	1.1		18.1	4.1		1.8	0.3								1.8		I	I
Harlan	55	liquid	cat 2B	No	No	3	1.5	2.8		22.9	2.2		2.6	0.5								2.6		I	I
Harlan	56	liquid	cat 2B	Yes	No	1	1.8	5.7		15.2	0.8		22.5	0.2					1.7	3.1		20.8		I	I
Harlan	56	liquid	cat 2B	Yes	No	2	1.9	0.8		28.1	0.3		28.1	3.8					1.6	3		26.5		I	I
Harlan	56	liquid	cat 2B	Yes	No	3	1.9	4.2		17.9	6.3		28.9	11.3					1.6	3.1		27.3		I	I
Harlan	57	liquid	cat 2B	No	No	1	1.8	3.4		25.8	6.9		5	0.3								5		I	I
Harlan	57	liquid	cat 2B	No	No	2	1.7	13.7		29	1		7.7	3.5								7.7		I	I
Harlan	57	liquid	cat 2B	No	No	3	1.7	3.5		31.5	9.5		6.5	5.5								6.5		I	I
Harlan	58	liquid	cat 2B	No	No	1	1.9	6.1		27.3	0.5		6.8	0.5								6.8		I	I
Harlan	58	liquid	cat 2B	No	No	2	1.8	1.1		18.1	4.1		2.1	0.6								2.1		I	I
Harlan	58	liquid	cat 2B	No	No	3	1.5	2.8		22.9	2.2		2.6	0.3								2.6		I	I
Harlan	59	liquid	cat 2B	No	No	1	1.9	6.1		27.3	0.5		46.6	2.4								46.6		I	I
Harlan	59	liquid	cat 2B	No	No	2	1.8	1.1		18.1	4.1		36.3	1.5								36.3		I	I
Harlan	59	liquid	cat 2B	No	No	3	1.5	2.8		22.9	2.2		47	0.3								47		I	I
Harlan	60	liquid	cat 2B	No	No	1	1.7	1.8		15.6	2.3		6.7	1.4								6.7		I	I
Harlan	60	liquid	cat 2B	No	No	2	1.6	4.3		29.8	1.6		16	6.3								16		I	I
Harlan	60	liquid	cat 2B	No	No	3	1.6	4.2		29.4	1.1		9.3	0.9								9.3		I	I
Harlan	61	solid	cat 2B	No	No	1	1.8	3.1		22.5	0.5		17	3.1								17		I	I
Harlan	61	solid	cat 2B	No	No	2	2	2.4		25.1	1.4		11.4	1.6								11.3		I	I
Harlan	61	solid	cat 2B	No	No	3	2	0.2		22.9	2.6		9.4	0.9								9.4		I	I
Harlan	62	solid	cat 2B	No	No	1	1.7	3.3		24.9	1.4		101.7	9.1								101.7		NI	NI
Harlan	62	solid	cat 2B	No	No	2	1.7	2.8		20.7	1.4		104.7	6.2								104.7		NI	NI
Harlan	62	solid	cat 2B	No	No	3	1.8	6.9		16.9	9.2		105.9	13.4								105.9		NI	NI
Harlan	63	solid	cat 2B	No	No	1	1.7	3.3		24.9	1.4		56.8	3.5								56.8		NI	I
Harlan	63	solid	cat 2B	No	No	2	1.7	2.8		20.7	1.4		41	1.2								41		I	I
Harlan	63	solid	cat 2B	No	No	3	1.8	6.9		16.9	9.2		50.2	12.5								50.2		NI	I
Harlan	64	solid	cat 2B	No	No	1	1.7	3.3		24.9	1.4		16	1.8								16		I	I
Harlan	64	solid	cat 2B	No	No	2	1.7	2.8		20.7	1.4		20.7	5								20.7		I	I
Harlan	64	solid	cat 2B	No	No	3	1.8	6.9		16.9	9.2		35.1	2.4								35.1		I	I
Harlan	65	solid	cat 2B	No	No	1	1.6	2.1		19.2	1.2		20.4	0.4								20.3		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Harlan	65	solid	cat 2B	No	No	2	1.7	0		16.3	1.8		16.2	1								16.2		I	I
Harlan	65	solid	cat 2B	No	No	3	1.6	3.7		29	15.6		51.8	12.1								51.8		NI	I
Harlan	66	solid	cat 2B	No	No	1	1.6	2.1		19.2	1.2		4.8	0.7								4.8		I	I
Harlan	66	solid	cat 2B	No	No	2	1.7	0		16.3	1.8		2.7	0.8								2.7		I	I
Harlan	66	solid	cat 2B	No	No	3	1.6	3.7		29	15.6		3	0.6								3		I	I
Harlan	67	liquid	cat 2A	No	No	1	1.8	3.4		25.8	6.9		4.1	0.3								4.1		I	I
Harlan	67	liquid	cat 2A	No	No	2	1.7	13.7		29	1		4.4	0.6								4.3		I	I
Harlan	67	liquid	cat 2A	No	No	3	1.7	3.5		31.5	9.5		4.9	0.4								4.9		I	I
Harlan	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.7	7.2		25.4	5.6		4	0.6								4		I	I
Harlan	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.7	1.4		28.8	3.8		2.8	2								2.8		I	I
Harlan	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.9	6.2		31.8	1.1		3.3	1.8								3.3		I	I
Harlan	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.7	7.2		25.4	5.6		10.5	0.2								10.5		I	I
Harlan	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.7	1.4		28.8	3.8		14	2								14		I	I
Harlan	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.9	6.2		31.8	1.1		16.9	2								16.9		I	I
Harlan	70	liquid	cat 2A	No	No	1	1.7	7.2		25.4	5.6		10	0.5								9.9		I	I
Harlan	70	liquid	cat 2A	No	No	2	1.7	1.4		28.8	3.8		10.3	1.4								10.3		I	I
Harlan	70	liquid	cat 2A	No	No	3	1.9	6.2		31.8	1.1		12.9	0.3								12.9		I	I
Harlan	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.9	6.1		27.3	0.5		7.9	3.6								7.9		I	I
Harlan	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.8	1.1		18.1	4.1		7.4	1.4								7.4		I	I
Harlan	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.5	2.8		22.9	2.2		4	1.6								4		I	I
Harlan	72	liquid	cat 2A (ICCVAM: cat 2B)	Yes	No	1	1.8	5.7		15.2	0.8		5.7	0.3					0.2	0.3		5.4		I	I
Harlan	72	liquid	cat 2A (ICCVAM: cat 2B)	Yes	No	2	1.9	0.8		28.1	0.3		4	1.1					0.2	0.3		3.7		I	I
Harlan	72	liquid	cat 2A (ICCVAM: cat	Yes	No	3	1.9	4.2		17.9	6.3		4	1					0.2	0.3		3.8		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
			2B)																						
Harlan	73	solid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.8	3.1		22.5	0.5		78.4	1.2								78.4		NI	NI
Harlan	73	solid	cat 2A (ICCVAM: cat 2B)	No	No	2	2	2.4		25.1	1.4		86	6.3								86		NI	NI
Harlan	73	solid	cat 2A (ICCVAM: cat 2B)	No	No	3	2	0.2		22.9	2.6		87.8	5.3								87.8		NI	NI
Harlan	74	solid	cat 2A	Yes	Yes	1	1.7	5.1		12.3	1.5		81.3	7.4		0.2	0.1		4.4	0.9		76.7		NI	NI
Harlan	74	solid	cat 2A	Yes	Yes	2	1.7	2.4		19.5	3.4		79.2	4.1		0.2	0.1		4.5	0.9		74.5		NI	NI
Harlan	74	solid	cat 2A	Yes	Yes	3	1.7	0.7		17	1.4		86.3	1.8		0.3	0		4.4	0.9		81.6		NI	NI
Harlan	75	solid	cat 2A	No	No	1	1.6	2.1		19.2	1.2		17.4	3.2								17.4		I	I
Harlan	75	solid	cat 2A	No	No	2	1.7	0		16.3	1.8		2	0.4								2		I	I
Harlan	75	solid	cat 2A	No	No	3	1.6	3.7		29	15.6		2.7	0.2								2.7		I	I
Harlan	76	solid	cat 2A	No	No	1	1.7	3.3		24.9	1.4		59.1	0.8								59		NI	I
Harlan	76	solid	cat 2A	No	No	2	1.7	2.8		20.7	1.4		32.3	4.7								32.3		I	I
Harlan	76	solid	cat 2A	No	No	3	1.8	6.9		16.9	9.2		52.8	3.2								52.8		NI	I
Harlan	77	solid	cat 2A	No	No	1	1.8	3.1		22.5	0.5		94.7	4.2								94.7		NI	NI
Harlan	77	solid	cat 2A	No	No	2	2	2.4		25.1	1.4		61.8	9.3								61.8		NI	NI
Harlan	77	solid	cat 2A	No	No	3	2	0.2		22.9	2.6		65.2	10.1								65.2		NI	NI
Harlan	78	solid	cat 2A	No	No	1	1.7	3.3		24.9	1.4		65.8	0.1								65.8		NI	NI
Harlan	78	solid	cat 2A	No	No	2	1.7	2.8		20.7	1.4		62	6.3								62		NI	NI
Harlan	78	solid	cat 2A	No	No	3	1.8	6.9		16.9	9.2		63.4	6.1								63.4		NI	NI
Harlan	79	solid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.7	3.3		24.9	1.4		2.7	0.5								2.7		I	I
Harlan	79	solid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.7	2.8		20.7	1.4		2.9	0.2								2.8		I	I
Harlan	79	solid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.8	6.9		16.9	9.2		2.2	0.3								2.2		I	I
Harlan	80[1]	liquid	cat 1	Yes	No	1	1.3	11.3		6.8	0.7		98.4	8.5					92.2	2.4		6.3		I	I
Harlan	80[1]	liquid	cat 1	Yes	No	2	1.8	0.6		16.4	0.9		63.2	8.6					66.4	1.7		0		I	I
Harlan	80[1]	liquid	cat 1	Yes	No	3	2.3	3.5		12.7	0		67.4	12					52.1	1.4		15.3		I	I
Harlan	81	liquid	cat 1	Yes	No	1	1.8	5.7		15.2	0.8		3.7	0.2					0.1	0.2		3.6		I	I
Harlan	81	liquid	cat 1	Yes	No	2	1.9	0.8		28.1	0.3		3.3	0.9					0.1	0.2		3.2		I	I
Harlan	81	liquid	cat 1	Yes	No	3	1.9	4.2		17.9	6.3		3.6	0.3					0.1	0.2		3.4		I	I
Harlan	82	liquid	cat 1	No	No	1	1.7	1.8		15.6	2.3		1.5	1.5								1.5		I	I
Harlan	82	liquid	cat 1	No	No	2	1.6	4.3		29.8	1.6		2.1	1.9								2.1		I	I
Harlan	82	liquid	cat 1	No	No	3	1.6	4.2		29.4	1.1		1.7	1								1.7		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Harlan	83	liquid	cat 1	No	No	1	1.7	7.2		25.4	5.6		4.6	1.3								4.6		I	I
Harlan	83	liquid	cat 1	No	No	2	1.7	1.4		28.8	3.8		3.6	0.9								3.6		I	I
Harlan	83	liquid	cat 1	No	No	3	1.9	6.2		31.8	1.1		7.6	1.1								7.6		I	I
Harlan	84	liquid	cat 1	No	No	1	1.7	1.8		15.6	2.3		6.7	3.1								6.7		I	I
Harlan	84	liquid	cat 1	No	No	2	1.6	4.3		29.8	1.6		7.1	4.1								7		I	I
Harlan	84	liquid	cat 1	No	No	3	1.6	4.2		29.4	1.1		4.2	2.3								4.2		I	I
Harlan	85	liquid	cat 1	No	No	1	1.8	3.4		25.8	6.9		5.6	0.5								5.6		I	I
Harlan	85	liquid	cat 1	No	No	2	1.7	13.7		29	1		9.2	1.7								9.2		I	I
Harlan	85	liquid	cat 1	No	No	3	1.7	3.5		31.5	9.5		12.5	1.3								12.5		I	I
Harlan	86	liquid	cat 1	No	No	1	1.7	1.8		15.6	2.3		41.8	4.9								41.8		I	I
Harlan	86	liquid	cat 1	No	No	2	1.6	4.3		29.8	1.6		23.4	5.4								23.4		I	I
Harlan	86	liquid	cat 1	No	No	3	1.6	4.2		29.4	1.1		24.8	5.6								24.8		I	I
Harlan	87	liquid	cat 1	No	No	1	1.7	7.2		25.4	5.6		20	2.7								20		I	I
Harlan	87	liquid	cat 1	No	No	2	1.7	1.4		28.8	3.8		14.4	3.5								14.4		I	I
Harlan	87	liquid	cat 1	No	No	3	1.9	6.2		31.8	1.1		22.2	2.9								22.2		I	I
Harlan	88	liquid	cat 1	Yes	No	1	1.7	8.5		28	3.5		5.2	1.7					0	0.3		5.2		I	I
Harlan	88	liquid	cat 1	Yes	No	2	1.4	2.9		29	0.6		7.8	3.3					0	0.4		7.8		I	I
Harlan	88	liquid	cat 1	Yes	No	3	1.9	1.9		27.1	14.1		5.4	1.7					0	0.3		5.4		I	I
Harlan	89	liquid	cat 1	No	No	1	1.8	3.4		25.8	6.9		5.8	3.9								5.8		I	I
Harlan	89	liquid	cat 1	No	No	2	1.7	13.7		29	1		7.8	2.3								7.8		I	I
Harlan	89	liquid	cat 1	No	No	3	1.7	3.5		31.5	9.5		8.1	2								8.1		I	I
Harlan	90	liquid	cat 1	Yes	No	1	1.8	5.7		15.2	0.8		29.7	4.3					4.3	0.6		25.4		I	I
Harlan	90	liquid	cat 1	Yes	No	2	1.9	0.8		28.1	0.3		36.8	1.5					4.2	0.6		32.6		I	I
Harlan	90	liquid	cat 1	Yes	No	3	1.9	4.2		17.9	6.3		18.7	1.7					4.3	0.6		14.4		I	I
Harlan	91	liquid	cat 1	Yes	No	1	1.8	5.7		15.2	0.8		18.9	2.3					1.4	0		17.6		I	I
Harlan	91	liquid	cat 1	Yes	No	2	1.9	0.8		28.1	0.3		13.8	3.6					1.3	0		12.4		I	I
Harlan	91	liquid	cat 1	Yes	No	3	1.9	4.2		17.9	6.3		21.8	1.9					1.3	0		20.4		I	I
Harlan	92	liquid	cat 1	Yes	No	1	1.7	8.5		28	3.5		18.2	0.3					0	2.8		18.2		I	I
Harlan	92	liquid	cat 1	Yes	No	2	1.4	2.9		29	0.6		14.8	5.8					0	3.4		14.8		I	I
Harlan	92	liquid	cat 1	Yes	No	3	1.9	1.9		27.1	14.1		13.1	8.9					0	2.5		13.1		I	I
Harlan	93	solid	cat 1	No	No	1	1.8	3.1		22.5	0.5		6.2	0.9								6.2		I	I
Harlan	93	solid	cat 1	No	No	2	2	2.4		25.1	1.4		9.3	0.1								9.3		I	I
Harlan	93	solid	cat 1	No	No	3	2	0.2		22.9	2.6		8.5	0.5								8.5		I	I
Harlan	94	solid	cat 1	No	No	1	1.7	3.3		24.9	1.4		5.7	0.3								5.7		I	I
Harlan	94	solid	cat 1	No	No	2	1.7	2.8		20.7	1.4		3	0.2								3		I	I
Harlan	94	solid	cat 1	No	No	3	1.8	6.9		16.9	9.2		2.6	0.7								2.6		I	I
Harlan	95	solid	cat 1	Yes	No	1	1.6	5.3		27.3	7.7		2.5	0.7					0	0.2		2.5		I	I
Harlan	95	solid	cat 1	Yes	No	2	1.6	4.7		21.3	6.6		2.7	0.7					0	0.2		2.7		I	I
Harlan	95	solid	cat 1	Yes	No	3	1.6	2.2		16.2	0.7		2.7	0.1					0	0.3		2.7		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
Harlan	96	solid	cat 1	No	No	1	1.8	3.1		22.5	0.5		35.5	6.1								35.5		I	I
Harlan	96	solid	cat 1	No	No	2	2	2.4		25.1	1.4		35.3	2.7								35.3		I	I
Harlan	96	solid	cat 1	No	No	3	2	0.2		22.9	2.6		30.9	2.8								30.9		I	I
Harlan	97	solid	cat 1	No	No	1	1.8	3.1		22.5	0.5		55.3	4.8								55.3		NI	I
Harlan	97	solid	cat 1	No	No	2	2	2.4		25.1	1.4		51.7	1.7								51.7		NI	I
Harlan	97	solid	cat 1	No	No	3	2	0.2		22.9	2.6		51	4.1								51		NI	I
Harlan	98	solid	cat 1	Yes	Yes	1	1.4	11.3		43.1	6.8		21.7	2.4		8.5	3.3		16.1	5.7		0		I	I
Harlan	98	solid	cat 1	Yes	Yes	2	0.7	5.5	NQ	45.1	0.4		28.1	0.4		17.4	2.3		29.9	10.5		0	NQ	I	I
Harlan	98	solid	cat 1	Yes	Yes	3	1.8	3.3		36.8	3.1		17.4	3.4		8.3	0.7		12.2	4.3		0		I	I
Harlan	98	solid	cat 1	Yes	Yes	4	1.6	1		35.9	1.2		17.5	10.3		4.2	1.4		14	4.9		0		I	I
Harlan	99	solid	cat 1	No	No	1	1.6	2.1		19.2	1.2		3.3	0.2								3.3		I	I
Harlan	99	solid	cat 1	No	No	2	1.7	0		16.3	1.8		2.3	1								2.3		I	I
Harlan	99	solid	cat 1	No	No	3	1.6	3.7		29	15.6		2.4	0.3								2.4		I	I
Harlan	100	solid	cat 1	No	No	1	1.6	16.2		35.4	2.2		10	3.9								10		I	I
Harlan	100	solid	cat 1	No	No	2	1.4	2.9		32.8	0.6		14.9	3.9								14.9		I	I
Harlan	100	solid	cat 1	No	No	3	1.6	2.7		29.2	1.2		8.5	2.4								8.5		I	I
Harlan	101	solid	cat 1	No	No	1	1.6	16.2		35.4	2.2		26.2	1.3								26.2		I	I
Harlan	101	solid	cat 1	No	No	2	1.4	2.9		32.8	0.6		50.6	8.2								50.6		NI	I
Harlan	101	solid	cat 1	No	No	3	1.6	2.7		29.2	1.2		42	15.9								42		I	I
Harlan	102	solid	cat 1	No	No	1	1.6	16.2		35.4	2.2		38	11.7								38		I	I
Harlan	102	solid	cat 1	No	No	2	1.4	2.9		32.8	0.6		55	15.9								55		NI	I
Harlan	102	solid	cat 1	No	No	3	1.6	2.7		29.2	1.2		52.1	7								52.1		NI	I
Harlan	103	solid	cat 1	No	No	1	1.7	3.3		24.9	1.4		1.9	0.2								1.9		I	I
Harlan	103	solid	cat 1	No	No	2	1.7	2.8		20.7	1.4		1.9	0.1								1.9		I	I
Harlan	103	solid	cat 1	No	No	3	1.8	6.9		16.9	9.2		1.6	0.2								1.6		I	I
Harlan	104	solid	cat 1	No	No	1	1.7	3.3		24.9	1.4		40.3	2.1								40.3		I	I
Harlan	104	solid	cat 1	No	No	2	1.7	2.8		20.7	1.4		36.3	0.4								36.3		I	I
Harlan	104	solid	cat 1	No	No	3	1.8	6.9		16.9	9.2		48.4	5.1								48.4		I	I
Harlan	105	solid	cat 1	No	No	1	1.8	3.1		22.5	0.5		3.9	0.3								3.9		I	I
Harlan	105	solid	cat 1	No	No	2	2	2.4		25.1	1.4		2.6	0.2								2.6		I	I
Harlan	105	solid	cat 1	No	No	3	2	0.2		22.9	2.6		1.9	0.1								1.9		I	I
IIVS	1	liquid	no cat	No	No	1	1.8	4.9		37.8	0.5		75.3	3.5								75.3		NI	NI
IIVS	1	liquid	no cat	No	No	2	1.7	1.2		31	2.6		68.2	3.1								68.2		NI	NI
IIVS	1	liquid	no cat	No	No	3	2	2.2		32.5	7.7		62.7	0.1								62.7		NI	NI
IIVS	2	liquid	no cat	No	No	1	1.8	4.9		37.8	0.5		84.2	2.9								84.2		NI	NI
IIVS	2	liquid	no cat	No	No	2	1.7	1.2		31	2.6		79.3	2.8								79.3		NI	NI
IIVS	2	liquid	no cat	No	No	3	2	2.2		32.5	7.7		80.5	0.1								80.4		NI	NI
IIVS	3	liquid	no cat	No	No	1	1.8	1.9		34.7	3.7		51.4	0.6								51.4		NI	I
IIVS	3	liquid	no cat	No	No	2	1.9	4.1		33.7	4.2		49	3.3								49		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
IIVS	3	liquid	no cat	No	No	3	1.9	2		26.2	6.2		47.5	1.4								47.5		I	I
IIVS	4	liquid	no cat	Yes	No	1	1.8	10.1		37.6	2.3		105.7	0					4.8	4.8		100.9		NI	NI
IIVS	4	liquid	no cat	Yes	No	2	1.9	0.5		39.6	5.8		97.5	1.8					4.5	4.5		93		NI	NI
IIVS	4	liquid	no cat	Yes	No	3	1.9	0.1		39.2	7.7		99.5	2.4					4.6	4.6		94.8		NI	NI
IIVS	5	liquid	no cat	Yes	No	1	1.8	4.9		37.8	0.5		72.4	2.8					0.6	0.6		71.8		NI	NI
IIVS	5	liquid	no cat	Yes	No	2	1.7	1.2		31	2.6		66.1	4.4					0.7	0.6		65.4		NI	NI
IIVS	5	liquid	no cat	Yes	No	3	2	2.2		32.5	7.7		50.9	17.8					0.6	0.6		50.3		NI	I
IIVS	6	liquid	no cat	No	No	1	1.8	4.9		37.8	0.5		88.6	1.6								88.6		NI	NI
IIVS	6	liquid	no cat	No	No	2	1.7	1.2		31	2.6		80.7	2.3								80.7		NI	NI
IIVS	6	liquid	no cat	No	No	3	2	2.2		32.5	7.7		81.4	14.5								81.3		NI	NI
IIVS	7	liquid	no cat	No	No	1	1.8	4.9		37.8	0.5		40.5	9.2								40.5		I	I
IIVS	7	liquid	no cat	No	No	2	1.7	1.2		31	2.6		43.4	7.8								43.4		I	I
IIVS	7	liquid	no cat	No	No	3	2	2.2		32.5	7.7		32.1	12.1								32.1		I	I
IIVS	8	liquid	no cat	No	No	1	1.8	4.9		37.8	0.5		101.2	8								101.2		NI	NI
IIVS	8	liquid	no cat	No	No	2	1.7	1.2		31	2.6		99.6	5.3								99.6		NI	NI
IIVS	8	liquid	no cat	No	No	3	2	2.2		32.5	7.7		95.2	1.1								95.2		NI	NI
IIVS	9	liquid	no cat	Yes	No	1	1.8	1.9		34.7	3.7		106	0.4					0	0		106		NI	NI
IIVS	9	liquid	no cat	Yes	No	2	1.9	4.1		33.7	4.2		100.5	4.9					0	0		100.5		NI	NI
IIVS	9	liquid	no cat	Yes	No	3	1.9	2		26.2	6.2		98.3	9					0	0		98.3		NI	NI
IIVS	10	liquid	no cat	Yes	No	1	1.8	1.2		34.5	6.6		49.6	38.1	NQ				0.7	0.4		48.9	NQ	I	I
IIVS	10	liquid	no cat	Yes	No	2	1.9	3.5		36.5	2		17.3	1.9					0.7	0.4		16.6		I	I
IIVS	10	liquid	no cat	Yes	No	3	1.9	3		34.7	9.7		24.5	1.2					0.7	0.4		23.8		I	I
IIVS	10	liquid	no cat	Yes	No	4	2.1	4.8		34.8	3.9		17.4	0.8					0.6	0.4		16.8		I	I
IIVS	11	liquid	no cat	No	No	1	1.8	4.9		37.8	0.5		31.6	1.2								31.6		I	I
IIVS	11	liquid	no cat	No	No	2	1.7	1.2		31	2.6		33.7	0.9								33.7		I	I
IIVS	11	liquid	no cat	No	No	3	2	2.2		32.5	7.7		28.9	0.1								28.9		I	I
IIVS	12	liquid	no cat	No	Yes	1	1.9	3.3		30.2	1.4		96.7	2.2		0.2	0.2					96.4		NI	NI
IIVS	12	liquid	no cat	No	Yes	2	1.9	3		35	6.7		92.6	5.2		0.1	0.2					92.5		NI	NI
IIVS	12	liquid	no cat	No	Yes	3	2.1	7.1		31.2	2.1		94.8	0.2		0.2	0.2					94.6		NI	NI
IIVS	13	liquid	no cat	No	Yes	1	1.9	3.3		30.2	1.4		84.4	0.8		0.4	0.2					84		NI	NI
IIVS	13	liquid	no cat	No	Yes	2	1.9	3		35	6.7		81.7	0.4		0.2	0					81.4		NI	NI
IIVS	13	liquid	no cat	No	Yes	3	2.1	7.1		31.2	2.1		86	1.3		0.2	0					85.8		NI	NI
IIVS	14	liquid	no cat	No	No	1	1.8	10.1		37.6	2.3		94.6	1.3								94.6		NI	NI
IIVS	14	liquid	no cat	No	No	2	1.9	0.5		39.6	5.8		95.7	2.2								95.7		NI	NI
IIVS	14	liquid	no cat	No	No	3	1.9	0.1		39.2	7.7		96.9	6								96.9		NI	NI
IIVS	15	liquid	no cat	No	No	1	2.1	4.8		34.8	3.9		102.4	5								102.4		NI	NI
IIVS	15	liquid	no cat	No	No	2	2	6		33.7	2.3		93.9	2.3								93.9		NI	NI
IIVS	15	liquid	no cat	No	No	3	2	2.9		29.3	0		95.3	11								95.3		NI	NI
IIVS	16	liquid	no cat	No	No	1	1.8	1.9		34.7	3.7		95.7	3.1								95.7		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
IIVS	16	liquid	no cat	No	No	2	1.9	4.1		33.7	4.2		105.5	0.8								105.5		NI	NI
IIVS	16	liquid	no cat	No	No	3	1.9	2		26.2	6.2		103	2.1								102.9		NI	NI
IIVS	17	liquid	no cat	No	No	1	1.8	10.1		37.6	2.3		96.6	2.3								96.6		NI	NI
IIVS	17	liquid	no cat	No	No	2	1.9	0.5		39.6	5.8		98.1	0.1								98.1		NI	NI
IIVS	17	liquid	no cat	No	No	3	1.9	0.1		39.2	7.7		95.3	3.5								95.3		NI	NI
IIVS	18	liquid	no cat	No	No	1	2.1	4.8		34.8	3.9		94.1	2.5								94.1		NI	NI
IIVS	18	liquid	no cat	No	No	2	2	6		33.7	2.3		95.3	0.5								95.3		NI	NI
IIVS	18	liquid	no cat	No	No	3	2	2.9		29.3	0		95	4								95		NI	NI
IIVS	19	liquid	no cat	No	No	1	2.1	4.8		34.8	3.9		95.6	2.2								95.6		NI	NI
IIVS	19	liquid	no cat	No	No	2	2	6		33.7	2.3		98.4	1								98.4		NI	NI
IIVS	19	liquid	no cat	No	No	3	2	2.9		29.3	0		98.9	0.3								98.9		NI	NI
IIVS	20	liquid	no cat	Yes	No	1	2.1	4.8		34.8	3.9		66.9	9.8					18.9	6.4		48.1		I	I
IIVS	20	liquid	no cat	Yes	No	2	2	6		33.7	2.3		46.1	32.1	NQ				19.4	6.6		26.7	NQ	I	I
IIVS	20	liquid	no cat	Yes	No	3	2	2.9		29.3	0		52.5	0.6					19.3	6.6		33.2		I	I
IIVS	20	liquid	no cat	Yes	No	4	1.9	2.2		31.3	1.6		62.4	2					20.9	7.1		41.5		I	I
IIVS	21	liquid	no cat	No	No	1	1.8	1.2		34.5	6.6		86.2	3.8								86.2		NI	NI
IIVS	21	liquid	no cat	No	No	2	1.9	3.5		36.5	2		81.5	10.8								81.5		NI	NI
IIVS	21	liquid	no cat	No	No	3	1.9	3		34.7	9.7		85.4	1.7								85.4		NI	NI
IIVS	22	liquid	no cat	Yes	No	1	1.8	10.1		37.6	2.3		39.7	9					1.9	0.2		37.7		I	I
IIVS	22	liquid	no cat	Yes	No	2	1.9	0.5		39.6	5.8		37.4	13.8					1.8	0.2		35.5		I	I
IIVS	22	liquid	no cat	Yes	No	3	1.9	0.1		39.2	7.7		40.9	17.4					1.9	0.2		39		I	I
IIVS	23[1]	liquid	no cat	Yes	No	1	1.8	1.2		34.5	6.6		75.5	5					56.5	17.8		18.9		I	I
IIVS	23[1]	liquid	no cat	Yes	No	2	1.9	3		34.7	9.7		64.2	6.1					55.6	17.5		8.6		I	I
IIVS	23[1]	liquid	no cat	Yes	No	3	2.1	4.8		34.8	3.9		60.5	9.7					50.1	15.7		10.4		I	I
IIVS	24	liquid	no cat	Yes	No	1	1.8	1.2		34.5	6.6		54.9	2					1.9	0.8		53		NI	I
IIVS	24	liquid	no cat	Yes	No	2	1.9	3.5		36.5	2		35.7	6.5					1.8	0.7		33.9		I	I
IIVS	24	liquid	no cat	Yes	No	3	1.9	3		34.7	9.7		34.4	7.5					1.9	0.7		32.6		I	I
IIVS	25	liquid	no cat	Yes	No	1	2	6		33.7	2.3		95	10.2					0	0		95		NI	NI
IIVS	25	liquid	no cat	Yes	No	2	2	2.9		29.3	0		103.2	0.6					0	0		103.2		NI	NI
IIVS	25	liquid	no cat	Yes	No	3	2	5		34.6	3.8		107.3	0.5					0	0.1		107.3		NI	NI
IIVS	26	liquid	no cat	No	No	1	2	6		33.7	2.3		37.5	32.8	NQ							37.5	NQ	I	I
IIVS	26	liquid	no cat	No	No	2	2	2.9		29.3	0		31.6	5.6								31.6		I	I
IIVS	26	liquid	no cat	No	No	3	1.9	3.7		36.1	6.1		35.6	3.5								35.6		I	I
IIVS	26	liquid	no cat	No	No	4	2	4.6		38.3	3.6		35.3	2.1								35.3		I	I
IIVS	28	solid	no cat	No	No	1	1.6	5		20.6	1.9		105.4	1.3								105.4		NI	NI
IIVS	28	solid	no cat	No	No	2	1.5	2.6		35.8	9.7		112.9	4.1								112.9		NI	NI
IIVS	28	solid	no cat	No	No	3	2.1	4.6		22	1.7		100.6	2.4								100.6		NI	NI
IIVS	29	solid	no cat	No	No	1	1.7	4.1		31.9	0.3		102.5	6.7								102.5		NI	NI
IIVS	29	solid	no cat	No	No	2	1.7	1.7		27.9	1.2		105.7	14.9								105.7		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
IIVS	29	solid	no cat	No	No	3	1.7	6		24.8	2.2		101.4	8.3								101.4		NI	NI
IIVS	30	solid	no cat	No	No	1	1.7	6.6		33.3	8.2		55.4	9								55.4		NI	I
IIVS	30	solid	no cat	No	No	2	1.7	2.5		21.8	0.2		51.8	2.1								51.8		NI	I
IIVS	30	solid	no cat	No	No	3	1.6	4.8		30.1	4		69.2	5.2								69.2		NI	NI
IIVS	31	solid	no cat	No	No	1	1.7	6.6		33.3	8.2		98.2	6.9								98.2		NI	NI
IIVS	31	solid	no cat	No	No	2	1.7	2.5		21.8	0.2		97.8	3.8								97.8		NI	NI
IIVS	31	solid	no cat	No	No	3	1.6	4.8		30.1	4		104	0.8								103.9		NI	NI
IIVS	32	solid	no cat	Yes	No	1	1.7	1.5		31.2	1.6		3.3	0					0.8	0.4		2.5		I	I
IIVS	32	solid	no cat	Yes	No	2	1.7	6.1		27.8	4.9		3.6	0.3					0.8	0.4		2.8		I	I
IIVS	32	solid	no cat	Yes	No	3	1.7	0.3		34.3	2.2		2.9	0					0.8	0.4		2.1		I	I
IIVS	33	solid	no cat	Yes	Yes	1	1.7	3.1		24.2	8.6		89.2	7.4		0.2	0.1		0.1	0		88.9		NI	NI
IIVS	33	solid	no cat	Yes	Yes	2	1.6	1.3		29.5	5		89.7	3.5		0.4	0		0.1	0		89.2		NI	NI
IIVS	33	solid	no cat	Yes	Yes	3	1.8	0.9		24.9	0.6		133.8	74.3	NQ	170.2	2.2		0.1	0		0	NQ	I	I
IIVS	33	solid	no cat	Yes	Yes	4	1.7	5.4		24	2.1		84.1	16.1		0.8	0.3		0.1	0.1		83.2		NI	NI
IIVS	34	solid	no cat	Yes	Yes	1	1.7	1.5		31.2	1.6		108.8	0.7		7.4	1.5		5.8	3.7		95.6		NI	NI
IIVS	34	solid	no cat	Yes	Yes	2	1.7	6.1		27.8	4.9		103.5	20.2	NQ	4.7	0.4		5.8	3.6		93	NQ	NI	NI
IIVS	34	solid	no cat	Yes	Yes	3	1.7	0.3		34.3	2.2		119.3	5.8		6.4	1		5.8	3.6		107.1		NI	NI
IIVS	34	solid	no cat	Yes	Yes	4	1.7	6.5		27.9	1.8		90.8	20.5	NQ	4.7	0.2		6	3.8		80.1	NQ	NI	NI
IIVS	34	solid	no cat	Yes	Yes	5	1.7	6.6		33.3	8.2		91.6	1.9		4.8	0.9		5.8	3.7		80.9		NI	NI
IIVS	35	solid	no cat	Yes	No	1	1.7	1.5		31.2	1.6		100.6	3.4					0.7	0.4		99.9		NI	NI
IIVS	35	solid	no cat	Yes	No	2	1.7	6.1		27.8	4.9		95.9	14.7					0.7	0.3		95.2		NI	NI
IIVS	35	solid	no cat	Yes	No	3	1.7	0.3		34.3	2.2		100.2	5.1					0.7	0.4		99.4		NI	NI
IIVS	36	solid	no cat	No	No	1	1.7	1.5		31.2	1.6		110.7	0.3								110.7		NI	NI
IIVS	36	solid	no cat	No	No	2	1.7	6.1		27.8	4.9		110.8	0.5								110.8		NI	NI
IIVS	36	solid	no cat	No	No	3	1.7	0.3		34.3	2.2		105.6	3.6								105.6		NI	NI
IIVS	37	liquid	no cat	No	No	1	1.8	1.2		34.5	6.6		86.3	7.2								86.3		NI	NI
IIVS	37	liquid	no cat	No	No	2	1.9	3.5		36.5	2		80.1	4.7								80.1		NI	NI
IIVS	37	liquid	no cat	No	No	3	1.9	3		34.7	9.7		78	0.6								78		NI	NI
IIVS	38	solid	no cat	No	No	1	1.7	4.1		31.9	0.3		101.1	3.1								101.1		NI	NI
IIVS	38	solid	no cat	No	No	2	1.7	1.7		27.9	1.2		101.9	1.3								101.9		NI	NI
IIVS	38	solid	no cat	No	No	3	1.7	6		24.8	2.2		108	1.5								108		NI	NI
IIVS	39	solid	no cat	No	No	1	1.7	4.1		31.9	0.3		102.5	6.4								102.5		NI	NI
IIVS	39	solid	no cat	No	No	2	1.7	1.7		27.9	1.2		101.7	1.3								101.7		NI	NI
IIVS	39	solid	no cat	No	No	3	1.7	6		24.8	2.2		104.8	2.7								104.8		NI	NI
IIVS	40	solid	no cat	No	No	1	1.7	4.1		31.9	0.3		62.3	1.8								62.3		NI	NI
IIVS	40	solid	no cat	No	No	2	1.7	1.7		27.9	1.2		63	4.4								63		NI	NI
IIVS	40	solid	no cat	No	No	3	1.7	6		24.8	2.2		60.2	4.4								60.2		NI	NI
IIVS	41	solid	no cat	No	No	1	1.7	1.5		31.2	1.6		99.3	9.1								99.3		NI	NI
IIVS	41	solid	no cat	No	No	2	1.7	6.1		27.8	4.9		102.6	5.9								102.5		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
IIVS	41	solid	no cat	No	No	3	1.7	0.3		34.3	2.2		94	6.5								94		NI	NI
IIVS	42	solid	no cat	Yes	No	1	1.7	1.5		31.2	1.6		85.7	7.2					0.4	0		85.3		NI	NI
IIVS	42	solid	no cat	Yes	No	2	1.7	6.1		27.8	4.9		82.3	19.2					0.4	0		81.8		NI	NI
IIVS	42	solid	no cat	Yes	No	3	1.7	0.3		34.3	2.2		70.9	10.1					0.4	0		70.5		NI	NI
IIVS	43	solid	no cat	No	No	1	1.8	1.1		30.3	3.2		99.8	0.1								99.8		NI	NI
IIVS	43	solid	no cat	No	No	2	1.8	9.2		31.7	3.6		102	0.7								102		NI	NI
IIVS	43	solid	no cat	No	No	3	1.7	0.2		31.3	5.1		103.4	4.2								103.4		NI	NI
IIVS	44	solid	no cat	No	No	1	1.8	1.1		30.3	3.2		98.1	0.6								98.1		NI	NI
IIVS	44	solid	no cat	No	No	2	1.8	9.2		31.7	3.6		94.2	0.1								94.2		NI	NI
IIVS	44	solid	no cat	No	No	3	1.7	0.2		31.3	5.1		102.9	5.1								102.9		NI	NI
IIVS	45	solid	no cat	No	No	1	1.7	1.5		31.2	1.6		98.6	5.2								98.6		NI	NI
IIVS	45	solid	no cat	No	No	2	1.7	6.1		27.8	4.9		98.4	5.4								98.4		NI	NI
IIVS	45	solid	no cat	No	No	3	1.7	0.3		34.3	2.2		94.8	4.6								94.8		NI	NI
IIVS	46	solid	no cat	No	No	1	1.8	1.1		30.3	3.2		65.2	7.8								65.2		NI	NI
IIVS	46	solid	no cat	No	No	2	1.8	9.2		31.7	3.6		60.8	3.1								60.8		NI	NI
IIVS	46	solid	no cat	No	No	3	1.7	0.2		31.3	5.1		57.8	3.9								57.8		NI	I
IIVS	47	solid	no cat	No	No	1	1.8	1.1		30.3	3.2		3.2	0.2								3.2		I	I
IIVS	47	solid	no cat	No	No	2	1.8	9.2		31.7	3.6		2.9	1								2.9		I	I
IIVS	47	solid	no cat	No	No	3	1.7	0.2		31.3	5.1		2.6	0.3								2.6		I	I
IIVS	48	solid	no cat	No	No	1	1.7	2.5		21.8	0.2		2.7	0.4								2.7		I	I
IIVS	48	solid	no cat	No	No	2	1.6	4.8		30.1	4		2.5	0								2.5		I	I
IIVS	48	solid	no cat	No	No	3	1.8	0.9		24.9	0.6		2.4	0								2.4		I	I
IIVS	49	solid	no cat	Yes	No	1	1.7	4.1		31.9	0.3		11.9	4.4					0	0.1		11.9		I	I
IIVS	49	solid	no cat	Yes	No	2	1.7	1.7		27.9	1.2		15.8	3					0	0.1		15.8		I	I
IIVS	49	solid	no cat	Yes	No	3	1.7	6		24.8	2.2		15.6	2.5					0	0.1		15.6		I	I
IIVS	50	solid	no cat	Yes	No	1	1.7	4.1		31.9	0.3		95.7	0.4					0.1	0.2		95.6		NI	NI
IIVS	50	solid	no cat	Yes	No	2	1.7	1.7		27.9	1.2		92.8	12.6					0.1	0.2		92.7		NI	NI
IIVS	50	solid	no cat	Yes	No	3	1.7	6		24.8	2.2		97.5	0.5					0.1	0.2		97.4		NI	NI
IIVS	51	solid	no cat	No	No	1	1.7	0.2		31.3	5.1		95.4	2.7								95.4		NI	NI
IIVS	51	solid	no cat	No	No	2	1.9	6.6		29.8	2.1		98.7	1.3								98.7		NI	NI
IIVS	51	solid	no cat	No	No	3	1.8	1.3		28.8	1.5		106	4.3								106		NI	NI
IIVS	52	solid	no cat	No	No	1	1.7	0.2		31.3	5.1		101.3	0								101.3		NI	NI
IIVS	52	solid	no cat	No	No	2	1.9	6.6		29.8	2.1		95.1	2								95.1		NI	NI
IIVS	52	solid	no cat	No	No	3	1.8	1.3		28.8	1.5		105.7	0.6								105.7		NI	NI
IIVS	53	solid	no cat	No	No	1	1.7	0.2		31.3	5.1		106.3	3								106.3		NI	NI
IIVS	53	solid	no cat	No	No	2	1.9	6.6		29.8	2.1		101.7	3.1								101.7		NI	NI
IIVS	53	solid	no cat	No	No	3	1.8	1.3		28.8	1.5		107.2	10.1								107.2		NI	NI
IIVS	54	liquid	cat 2B	No	No	1	1.8	4.9		37.8	0.5		51.8	3.5								51.8		NI	I
IIVS	54	liquid	cat 2B	No	No	2	1.7	1.2		31	2.6		43.1	2.1								43.1		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
IIVS	54	liquid	cat 2B	No	No	3	2	2.2		32.5	7.7		30.1	4.5								30.1		I	I
IIVS	55	liquid	cat 2B	No	No	1	1.8	1.2		34.5	6.6		2.5	0.2								2.5		I	I
IIVS	55	liquid	cat 2B	No	No	2	1.9	3.5		36.5	2		2.6	0.3								2.6		I	I
IIVS	55	liquid	cat 2B	No	No	3	1.9	3		34.7	9.7		2.5	0.4								2.5		I	I
IIVS	56	liquid	cat 2B	Yes	No	1	1.8	1.2		34.5	6.6		47.9	3.2					0.4	0.4		47.5		I	I
IIVS	56	liquid	cat 2B	Yes	No	2	1.9	3.5		36.5	2		35.2	1.8					0.4	0.4		34.8		I	I
IIVS	56	liquid	cat 2B	Yes	No	3	1.9	3		34.7	9.7		30	5.2					0.4	0.4		29.6		I	I
IIVS	57	liquid	cat 2B	Yes	No	1	1.8	10.1		37.6	2.3		20.4	3.7					0	0.4		20.4		I	I
IIVS	57	liquid	cat 2B	Yes	No	2	1.9	0.5		39.6	5.8		20.3	2.1					0	0.4		20.3		I	I
IIVS	57	liquid	cat 2B	Yes	No	3	1.9	0.1		39.2	7.7		12.6	5.3					0	0.4		12.6		I	I
IIVS	58	liquid	cat 2B	Yes	No	1	1.8	1.2		34.5	6.6		16.1	2.7					1.6	1		14.4		I	I
IIVS	58	liquid	cat 2B	Yes	No	2	1.9	3.5		36.5	2		15	0.7					1.6	0.9		13.4		I	I
IIVS	58	liquid	cat 2B	Yes	No	3	1.9	3		34.7	9.7		14.6	2.9					1.6	1		13		I	I
IIVS	59	liquid	cat 2B	No	No	1	1.8	1.2		34.5	6.6		56.6	5.1								56.6		NI	I
IIVS	59	liquid	cat 2B	No	No	2	1.9	3.5		36.5	2		52.8	5.5								52.8		NI	I
IIVS	59	liquid	cat 2B	No	No	3	1.9	3		34.7	9.7		43.6	0.7								43.6		I	I
IIVS	60	liquid	cat 2B	No	No	1	2.1	4.8		34.8	3.9		26.8	7.8								26.8		I	I
IIVS	60	liquid	cat 2B	No	No	2	2	6		33.7	2.3		13.8	5.4								13.8		I	I
IIVS	60	liquid	cat 2B	No	No	3	2	2.9		29.3	0		21.2	2.6								21.2		I	I
IIVS	61	solid	cat 2B	No	No	1	1.6	5		20.6	1.9		16.3	0.9								16.3		I	I
IIVS	61	solid	cat 2B	No	No	2	1.5	2.6		35.8	9.7		16.4	10.1								16.4		I	I
IIVS	61	solid	cat 2B	No	No	3	2.1	4.6		22	1.7		21.4	4								21.4		I	I
IIVS	62	solid	cat 2B	No	No	1	1.7	2.5		21.8	0.2		109.8	4.8								109.8		NI	NI
IIVS	62	solid	cat 2B	No	No	2	1.6	4.8		30.1	4		105.2	1.6								105.2		NI	NI
IIVS	62	solid	cat 2B	No	No	3	1.8	0.9		24.9	0.6		97.1	0.3								97.1		NI	NI
IIVS	63	solid	cat 2B	No	No	1	1.7	6.6		33.3	8.2		49.6	15.3								49.6		I	I
IIVS	63	solid	cat 2B	No	No	2	1.7	2.5		21.8	0.2		38.9	6.1								38.9		I	I
IIVS	63	solid	cat 2B	No	No	3	1.6	4.8		30.1	4		43.7	9.6								43.7		I	I
IIVS	64	solid	cat 2B	No	No	1	1.7	3.1		24.2	8.6		39.6	15.7								39.6		I	I
IIVS	64	solid	cat 2B	No	No	2	1.7	6.5		27.9	1.8		29.7	10								29.7		I	I
IIVS	64	solid	cat 2B	No	No	3	1.6	1.3		29.5	5		28.2	1.4								28.2		I	I
IIVS	65	solid	cat 2B	No	No	1	1.8	1.1		30.3	3.2		63.8	15.2								63.8		NI	NI
IIVS	65	solid	cat 2B	No	No	2	1.8	9.2		31.7	3.6		41.6	0.3								41.6		I	I
IIVS	65	solid	cat 2B	No	No	3	1.7	0.2		31.3	5.1		53.9	12.6								53.9		NI	I
IIVS	66	solid	cat 2B	Yes	No	1	1.7	2.5		21.8	0.2		3.4	0.9					0.7	0.1		2.7		I	I
IIVS	66	solid	cat 2B	Yes	No	2	1.6	4.8		30.1	4		7.3	0.3					0.8	0.1		6.6		I	I
IIVS	66	solid	cat 2B	Yes	No	3	1.8	0.9		24.9	0.6		2.7	0.6					0.6	0.1		2		I	I
IIVS	67	liquid	cat 2A	Yes	No	1	1.8	1.9		34.7	3.7		13.6	2.1					0	0		13.6		I	I
IIVS	67	liquid	cat 2A	Yes	No	2	1.9	4.1		33.7	4.2		15.3	0.5					0	0		15.3		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
IIVS	67	liquid	cat 2A	Yes	No	3	1.9	2		26.2	6.2		14.6	0.8					0	0		14.6		I	I
IIVS	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.8	4.9		37.8	0.5		2.7	0.4								2.7		I	I
IIVS	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.7	1.2		31	2.6		7	4.4								7		I	I
IIVS	68	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	2	2.2		32.5	7.7		3	0.3								3		I	I
IIVS	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.8	1.9		34.7	3.7		13.6	5.7								13.6		I	I
IIVS	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.9	4.1		33.7	4.2		14.5	0.7								14.4		I	I
IIVS	69	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.9	2		26.2	6.2		14.1	4.3								14.1		I	I
IIVS	70	liquid	cat 2A	No	No	1	1.8	1.9		34.7	3.7		14.3	0.6								14.3		I	I
IIVS	70	liquid	cat 2A	No	No	2	1.9	4.1		33.7	4.2		12.3	3.5								12.3		I	I
IIVS	70	liquid	cat 2A	No	No	3	1.9	2		26.2	6.2		12.2	1.8								12.2		I	I
IIVS	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.8	10.1		37.6	2.3		7.7	0.7								7.7		I	I
IIVS	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.9	0.5		39.6	5.8		9.1	3								9.1		I	I
IIVS	71	liquid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.9	0.1		39.2	7.7		7.4	0.6								7.4		I	I
IIVS	72	liquid	cat 2A (ICCVAM: cat 2B)	Yes	No	1	1.8	1.2		34.5	6.6		6.7	5.6					1.3	0.5		5.4		I	I
IIVS	72	liquid	cat 2A (ICCVAM: cat 2B)	Yes	No	2	1.9	3.5		36.5	2		4.5	1.6					1.2	0.5		3.2		I	I
IIVS	72	liquid	cat 2A (ICCVAM: cat 2B)	Yes	No	3	1.9	3		34.7	9.7		4.3	1.5					1.3	0.5		3.1		I	I
IIVS	73	solid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.6	5		20.6	1.9		102.5	1.4								102.5		NI	NI
IIVS	73	solid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.5	2.6		35.8	9.7		105.8	2.3								105.8		NI	NI
IIVS	73	solid	cat 2A (ICCVAM: cat	No	No	3	2.1	4.6		22	1.7		82.9	1.3								82.9		NI	NI

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
			2B)																						
IIVS	74	solid	cat 2A	Yes	Yes	1	1.6	5		20.6	1.9		89.2	6.5		0.3	0.1		1.7	0.1		87.2		NI	NI
IIVS	74	solid	cat 2A	Yes	Yes	2	1.5	2.6		35.8	9.7		101.4	6		0.3	0.1		1.8	0.1		99.3		NI	NI
IIVS	74	solid	cat 2A	Yes	Yes	3	2.1	4.6		22	1.7		90.4	4.9		0.2	0.1		1.3	0.1		88.8		NI	NI
IIVS	75	solid	cat 2A	No	No	1	1.7	1.5		31.2	1.6		5	2.9								5		I	I
IIVS	75	solid	cat 2A	No	No	2	1.7	6.1		27.8	4.9		5.8	1.5								5.8		I	I
IIVS	75	solid	cat 2A	No	No	3	1.7	0.3		34.3	2.2		4.5	3.3								4.4		I	I
IIVS	76	solid	cat 2A	No	No	1	1.7	3.1		24.2	8.6		26.9	7.2								26.9		I	I
IIVS	76	solid	cat 2A	No	No	2	1.7	6.5		27.9	1.8		26.3	8								26.3		I	I
IIVS	76	solid	cat 2A	No	No	3	1.6	1.3		29.5	5		28.7	1								28.7		I	I
IIVS	77	solid	cat 2A	No	No	1	1.7	3.1		24.2	8.6		98.2	3.7								98.2		NI	NI
IIVS	77	solid	cat 2A	No	No	2	1.7	6.5		27.9	1.8		107.3	4.9								107.3		NI	NI
IIVS	77	solid	cat 2A	No	No	3	1.6	1.3		29.5	5		103.6	9								103.6		NI	NI
IIVS	78	solid	cat 2A	No	No	1	1.7	3.1		24.2	8.6		87.8	1.7								87.8		NI	NI
IIVS	78	solid	cat 2A	No	No	2	1.7	6.5		27.9	1.8		86.9	1.5								86.9		NI	NI
IIVS	78	solid	cat 2A	No	No	3	1.6	1.3		29.5	5		85.9	1.8								85.9		NI	NI
IIVS	79	solid	cat 2A (ICCVAM: cat 2B)	No	No	1	1.8	1.1		30.3	3.2		2.9	0.6								2.9		I	I
IIVS	79	solid	cat 2A (ICCVAM: cat 2B)	No	No	2	1.8	9.2		31.7	3.6		2.3	0.8								2.3		I	I
IIVS	79	solid	cat 2A (ICCVAM: cat 2B)	No	No	3	1.7	0.2		31.3	5.1		3.2	0.4								3.2		I	I
IIVS	80[1]	liquid	cat 1	Yes	No	1	1.8	4.9		37.8	0.5		78.3	3.1					69	5.4		9.3		I	I
IIVS	80[1]	liquid	cat 1	Yes	No	2	1.7	1.2		31	2.6		77.7	3.2					72.6	5.7		5		I	I
IIVS	80[1]	liquid	cat 1	Yes	No	3	2	2.2		32.5	7.7		74.1	0.8					64.4	5		9.7		I	I
IIVS	81	liquid	cat 1	Yes	No	1	1.8	10.1		37.6	2.3		5.6	0.1					0	0.3		5.6		I	I
IIVS	81	liquid	cat 1	Yes	No	2	1.9	0.5		39.6	5.8		3.9	0.5					0	0.3		3.9		I	I
IIVS	81	liquid	cat 1	Yes	No	3	1.9	0.1		39.2	7.7		3.1	1.1					0	0.3		3.1		I	I
IIVS	82	liquid	cat 1	No	No	1	2.1	4.8		34.8	3.9		5.3	1.5								5.3		I	I
IIVS	82	liquid	cat 1	No	No	2	2	6		33.7	2.3		6.9	2.8								6.9		I	I
IIVS	82	liquid	cat 1	No	No	3	2	2.9		29.3	0		2.6	0.3								2.6		I	I
IIVS	83	liquid	cat 1	No	No	1	1.8	1.9		34.7	3.7		5.4	1.9								5.4		I	I
IIVS	83	liquid	cat 1	No	No	2	1.9	4.1		33.7	4.2		6.8	0.2								6.8		I	I
IIVS	83	liquid	cat 1	No	No	3	1.9	2		26.2	6.2		4	0.8								4		I	I
IIVS	84	liquid	cat 1	Yes	No	1	2.1	4.8		34.8	3.9		17.9	1.2					0.1	1		17.8		I	I
IIVS	84	liquid	cat 1	Yes	No	2	2	6		33.7	2.3		18.8	2.9					0.1	1		18.7		I	I
IIVS	84	liquid	cat 1	Yes	No	3	2	2.9		29.3	0		9.4	3.8					0.1	1		9.3		I	I
IIVS	85	liquid	cat 1	No	No	1	1.8	1.9		34.7	3.7		14	4.4								14		I	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
IIVS	85	liquid	cat 1	No	No	2	1.9	4.1		33.7	4.2		13.1	1.9								13.1		I	I
IIVS	85	liquid	cat 1	No	No	3	1.9	2		26.2	6.2		17.8	4.9								17.8		I	I
IIVS	86	liquid	cat 1	No	No	1	2.1	4.8		34.8	3.9		31.8	2.4								31.8		I	I
IIVS	86	liquid	cat 1	No	No	2	2	6		33.7	2.3		32.7	7.6								32.7		I	I
IIVS	86	liquid	cat 1	No	No	3	2	2.9		29.3	0		20.5	13.4								20.5		I	I
IIVS	87	liquid	cat 1	No	No	1	1.8	1.9		34.7	3.7		30.8	3.7								30.8		I	I
IIVS	87	liquid	cat 1	No	No	2	1.9	4.1		33.7	4.2		17.4	1.9								17.4		I	I
IIVS	87	liquid	cat 1	No	No	3	1.9	2		26.2	6.2		24.4	0.4								24.4		I	I
IIVS	88	liquid	cat 1	Yes	Yes	1	1.9	3.3		30.2	1.4		5	0.1		0.2	0.1		0.9	0.1		3.9		I	I
IIVS	88	liquid	cat 1	Yes	Yes	2	1.9	3		35	6.7		8.1	1.5		0.2	0		0.9	0.1		7		I	I
IIVS	88	liquid	cat 1	Yes	Yes	3	2.1	7.1		31.2	2.1		4.5	0.5		0.2	0		0.8	0.1		3.5		I	I
IIVS	89	liquid	cat 1	No	No	1	1.8	10.1		37.6	2.3		9	1.6								9		I	I
IIVS	89	liquid	cat 1	No	No	2	1.9	0.5		39.6	5.8		12.6	1.9								12.6		I	I
IIVS	89	liquid	cat 1	No	No	3	1.9	0.1		39.2	7.7		9.7	0.7								9.7		I	I
IIVS	90	liquid	cat 1	No	No	1	1.8	10.1		37.6	2.3		35.5	3.5								35.5		I	I
IIVS	90	liquid	cat 1	No	No	2	1.9	0.5		39.6	5.8		34.8	6.9								34.7		I	I
IIVS	90	liquid	cat 1	No	No	3	1.9	0.1		39.2	7.7		33.2	24.5	NQ							33.2	NQ	I	I
IIVS	90	liquid	cat 1	No	No	4	2	5		34.6	3.8		30.8	7.9								30.8		I	I
IIVS	91	liquid	cat 1	Yes	No	1	1.8	10.1		37.6	2.3		21.5	0.8					0.4	0.9		21.1		I	I
IIVS	91	liquid	cat 1	Yes	No	2	1.9	0.5		39.6	5.8		20	0.3					0.4	0.8		19.6		I	I
IIVS	91	liquid	cat 1	Yes	No	3	1.9	0.1		39.2	7.7		19.9	1.7					0.4	0.8		19.5		I	I
IIVS	92	liquid	cat 1	Yes	No	1	1.9	2.2		31.3	1.6		39.9	5.2					0.3	0.4		39.6		I	I
IIVS	92	liquid	cat 1	Yes	No	2	1.9	3.7		36.1	6.1		39.6	2.9					0.3	0.4		39.3		I	I
IIVS	92	liquid	cat 1	Yes	No	3	2	4.6		38.3	3.6		51.4	9.4					0.3	0.3		51.2		NI	I
IIVS	93	solid	cat 1	No	No	1	1.6	5		20.6	1.9		10.3	3.7								10.3		I	I
IIVS	93	solid	cat 1	No	No	2	1.5	2.6		35.8	9.7		21.3	1.7								21.3		I	I
IIVS	93	solid	cat 1	No	No	3	2.1	4.6		22	1.7		18	4.4								18		I	I
IIVS	94	solid	cat 1	No	No	1	1.7	3.1		24.2	8.6		5.2	4.4								5.2		I	I
IIVS	94	solid	cat 1	No	No	2	1.7	6.5		27.9	1.8		5.8	6.3								5.8		I	I
IIVS	94	solid	cat 1	No	No	3	1.6	1.3		29.5	5		4.3	2.3								4.3		I	I
IIVS	95	solid	cat 1	Yes	No	1	1.6	5		20.6	1.9		1.8	0.1					0.2	0.2		1.6		I	I
IIVS	95	solid	cat 1	Yes	No	2	1.5	2.6		35.8	9.7		2.5	0.4					0.2	0.3		2.3		I	I
IIVS	95	solid	cat 1	Yes	No	3	2.1	4.6		22	1.7		2.3	0					0.1	0.2		2.1		I	I
IIVS	96	solid	cat 1	No	No	1	1.6	5		20.6	1.9		33.2	4.6								33.2		I	I
IIVS	96	solid	cat 1	No	No	2	1.5	2.6		35.8	9.7		38.9	19.4								38.9		I	I
IIVS	96	solid	cat 1	No	No	3	2.1	4.6		22	1.7		54.1	5.1								54.1		NI	I
IIVS	97	solid	cat 1	No	No	1	1.6	5		20.6	1.9		59	4.8								59		NI	I
IIVS	97	solid	cat 1	No	No	2	1.5	2.6		35.8	9.7		55.1	2.8								55.1		NI	I
IIVS	97	solid	cat 1	No	No	3	2.1	4.6		22	1.7		51.1	11.8								51.1		NI	I

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final	Final	Classification	
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability	Call	50% cut-off	60% cut-off
IIVS	98	solid	cat 1	Yes	Yes	1	1.7	6.6		33.3	8.2		19.1	3		5.3	5.3		17.1	1.5		0		I	I
IIVS	98	solid	cat 1	Yes	Yes	2	1.7	2.5		21.8	0.2		28.8	0.2		18.8	8.1		17.1	1.5		0		I	I
IIVS	98	solid	cat 1	Yes	Yes	3	1.6	4.8		30.1	4		20.9	5.8		4.6	0.9		18.2	1.6		0		I	I
IIVS	99	solid	cat 1	Yes	No	1	1.7	1.5		31.2	1.6		2.2	0.1					0.4	0.2		1.9		I	I
IIVS	99	solid	cat 1	Yes	No	2	1.7	6.1		27.8	4.9		2.4	0.4					0.3	0.2		2		I	I
IIVS	99	solid	cat 1	Yes	No	3	1.7	0.3		34.3	2.2		2.1	0.2					0.4	0.2		1.7		I	I
IIVS	100	solid	cat 1	No	No	1	1.7	0.2		31.3	5.1		10.5	0.7								10.5		I	I
IIVS	100	solid	cat 1	No	No	2	1.9	6.6		29.8	2.1		8.2	0.2								8.2		I	I
IIVS	100	solid	cat 1	No	No	3	1.8	1.3		28.8	1.5		8.9	1.2								8.9		I	I
IIVS	101	solid	cat 1	No	No	1	1.7	4.1		31.9	0.3		19.9	4.4								19.9		I	I
IIVS	101	solid	cat 1	No	No	2	1.7	1.7		27.9	1.2		21.6	2.3								21.6		I	I
IIVS	101	solid	cat 1	No	No	3	1.7	6		24.8	2.2		13.8	8								13.8		I	I
IIVS	102	solid	cat 1	No	No	1	1.7	4.1		31.9	0.3		76.7	10.5								76.7		NI	NI
IIVS	102	solid	cat 1	No	No	2	1.7	1.7		27.9	1.2		87.8	3.7								87.8		NI	NI
IIVS	102	solid	cat 1	No	No	3	1.7	6		24.8	2.2		108.2	8.7								108.2		NI	NI
IIVS	103	solid	cat 1	No	No	1	1.7	3.1		24.2	8.6		1.7	0.2								1.7		I	I
IIVS	103	solid	cat 1	No	No	2	1.7	6.5		27.9	1.8		2.1	0.3								2.1		I	I
IIVS	103	solid	cat 1	No	No	3	1.6	1.3		29.5	5		2.1	0.2								2.1		I	I
IIVS	104	solid	cat 1	No	No	1	1.7	3.1		24.2	8.6		68.6	32.3	NQ							68.6	NQ	NI	NI
IIVS	104	solid	cat 1	No	No	2	1.7	6.5		27.9	1.8		47.1	1.1								47.1		I	I
IIVS	104	solid	cat 1	No	No	3	1.6	1.3		29.5	5		34.9	1								34.8		I	I
IIVS	104	solid	cat 1	No	No	4	1.8	0.9		24.9	0.6		24.5	4								24.4		I	I
IIVS	105	solid	cat 1	No	No	1	1.7	3.1		24.2	8.6		2.1	0.1								2.1		I	I
IIVS	105	solid	cat 1	No	No	2	1.7	6.5		27.9	1.8		2.4	0.2								2.4		I	I
IIVS	105	solid	cat 1	No	No	3	1.6	1.3		29.5	5		2.4	0								2.4		I	I

[1] See note above table

Chemical 106 and 107 are considered incompatible with the test method because of strong colour interference and so EpiOcular™ EIT shows a limitation for colours that strongly interfere with MTT using the current system of photometry. These two chemicals are excluded for the statistical analysis.

			GHS				NC			PC			Uncorrected viability			NSC			NSMTT			Final
laboratory	chemical	LS	classification	MTT	Coloring	test	OD	diff	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	Mean%	Diff%	Qual	viability
Beiersdorf	106	Solid	cat 1	No	Yes	1	1.96549	0.1119		33.285	4.73928		8056.7	0		8056.7	0					0
Beiersdorf	106	Solid	cat 1	No	Yes	2	1.72938	0.5811		37.3921	0.56668		4578.53	0		4578.53	0					0
Beiersdorf	106	Solid	cat 1	No	Yes	3	1.70828	5.1075		35.9354	1.87031		4633.97	0		4633.97	0					0
Beiersdorf	106	Solid	cat 1	No	Yes	4	1.81303	2.5234		24.2523	1.59402		8732.59	0		4366.29	0					4366.29
Beiersdorf	106	Solid	cat 1	No	Yes	5	1.7126	0.3825		27.4597	5.73397		9245.18	0		9245.18	0					0
Beiersdorf	107	Solid	cat 1	No	Yes	1	1.96549	0.1119		33.285	4.73928		78.43	68.469	NQ	86.65	28.0516	NQ				0
Beiersdorf	107	Solid	cat 1	No	Yes	2	1.72938	0.5811		37.3921	0.56668		98.27	9.833		64.16	27.1514	NQ				34.11
Beiersdorf	107	Solid	cat 1	No	Yes	3	1.70828	5.1075		35.9354	1.87031		49.04	32.4948	NQ	56.53	22.4144	NQ				0
Beiersdorf	107	Solid	cat 1	No	Yes	4	1.85775	12.9538		23.6361	4.97107		86.28	12.0737		96.69	33.4222	NQ				0
Beiersdorf	107	Solid	cat 1	No	Yes	5	1.7126	0.3825		27.4597	5.73397		134.45	6.5485		115.32	43.2062	NQ				19.13
Harlan	106	Solid	cat 1	Yes	Yes	1	1.379	11.2763		43.1291	6.81653		722.75	0		722.75	0		719.22	0		0
Harlan	106	Solid	cat 1	Yes	Yes	2	0.74275	5.4527	NQ	45.1027	0.4039		1341.57	0		1341.57	0		1335.31	0		0
Harlan	106	Solid	cat 1	Yes	Yes	3	1.81263	3.3377		36.7768	3.11703		549.78	0		549.78	0		547.16	0		0
Harlan	106	Solid	cat 1	Yes	Yes	4	1.59113	1.0056		35.8787	1.1627		626.33	0		626.33	0		623.33	0		0
Harlan	107	Solid	cat 1	Yes	Yes	1	1.379	11.2763		43.1291	6.81653		119.92	8.9195		90.05	2.248		70.56	14.0682		0
Harlan	107	Solid	cat 1	Yes	Yes	2	0.74275	5.4527	NQ	45.1027	0.4039		78.56	30.2928	NQ	171.32	74.3184	NQ	131	26.1192	NQ	0
Harlan	107	Solid	cat 1	Yes	Yes	3	1.81263	3.3377		36.7768	3.11703		84.19	3.1722		90.28	8.3856		53.68	10.7027		0
Harlan	107	Solid	cat 1	Yes	Yes	4	1.59113	1.0056		35.8787	1.1627		162.2	18.886		93.4	12.9468		61.15	12.1926		7.65
IIVS	106	Solid	cat 1	Yes	Yes	1	1.695	6.5782		33.2891	8.20059		186.76	1.3274		188.72	0.23599		176.36	0.26549		0
IIVS	106	Solid	cat 1	Yes	Yes	2	1.69363	2.4799		21.795	0.17713		182.34	2.8342		183.21	2.33228		176.5	0.2657		0
IIVS	106	Solid	cat 1	Yes	Yes	3	1.59688	4.7906		30.0665	4.00783		192.09	3.2877		194.12	1.34638		187.19	0.2818		0
IIVS	107	Solid	cat 1	Yes	Yes	1	1.68213	4.102		31.9313	0.29724		71.76	13.0192		30.18	0.535		140.4	1.2781		0
IIVS	107	Solid	cat 1	Yes	Yes	2	1.72388	1.6533		27.9095	1.16018		71.92	10.0645		74.4	28.3663	NQ	137	1.2472		0
IIVS	107	Solid	cat 1	Yes	Yes	3	1.68425	5.967		24.833	2.22651		72.67	35.6242	NQ	57.19	28.3509	NQ	140.23	1.2765		0
IIVS	107	Solid	cat 1	Yes	Yes	4	1.812	0.9382		24.862	0.55188		85.68	21.9095	NQ	64.16	25	NQ	130.34	1.1865		0
IIVS	107	Solid	cat 1	Yes	Yes	5	1.6995	5.3545		23.9776	2.05943		79.16	30.2148	NQ	52.21	14.2101		138.98	1.2945		0

Chemical 27 was sent to all participating laboratories for testing but was excluded at a very early stage of the study on request of one of the participating laboratories because it was identified as a very strong MTT reducer.

chemical	laboratory	protocol	MTT	coloring	run	ODnc	NCdiff	NCqual	meanTA	TAdiff	TAqual	CCdiff	CCqual	KCdiff	KCqual	PCqual	meanPC	PCdiff	meanCC	meanKC	corrected viability
27	Beiersdorf	Liquids	Yes	No	1	1.7173	3.4211	Qualified	100.344	0.9521	Qualified	.	.	.	.	Qualified	39.2118	3.4852	.	.	100.344
27	Beiersdorf	Liquids	Yes	No	2	1.7408	6.0721	Qualified	107.495	1.8009	Qualified	.	.	.	.	Qualified	40.6448	1.5597	.	.	107.495
27	Beiersdorf	Liquids	Yes	No	3	1.8545	3.6478	Qualified	98.055	3.1113	Qualified	.	.	.	.	Qualified	29.1791	3.0385	.	.	98.055
27	Harlan	Liquids	Yes		1	1.2896	11.282	Qualified	132.005	5.4279	Qualified	.	.	2.5589	Qualified	Qualified	6.7558	0.6591	.	16.9429	115.063
27	Harlan	Liquids	Yes		2	1.7896	0.6147	Qualified	97.793	1.7881	Qualified	.	.	1.844	Qualified	Qualified	16.3791	0.9499	.	12.2093	85.584
27	Harlan	Liquids	Yes		3	2.2828	3.5045	Qualified	104.556	3.855	Qualified	.	.	1.4456	Qualified	Qualified	12.7368	0.0438	.	9.5718	94.984

27	IIVS	Liquids	Yes	No	1	1.7879	1.9017	Qualified	103.384	3.0203	Qualified	.	.	1.9017	Qualified	Qualified	34.699	3.6915	.	3.5937	99.79
27	IIVS	Liquids	Yes	No	2	1.85	4.1081	Qualified	104.946	1.2973	Qualified	.	.	1.8378	Qualified	Qualified	33.6757	4.2162	.	3.473	101.473
27	IIVS	Liquids	Yes	No	3	1.8655	2.037	Qualified	102.854	0.8845	Qualified	.	.	1.8226	Qualified	Qualified	26.2262	6.1914	.	3.4441	99.41

Appendix VII Performance criteria

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Institute for Health and Consumer Protection
European Centre for the Validation of Alternative Methods (ECVAM)

Eye Irritation Validation Study (EIVS)
Guidance on Eye Irritation Validation Study (EIVS) Conduct for the Reconstructed Human Tissue (RhT) Assays and Performance Criteria to Assess the Scientific Validity of SkinEthic™ HCE and EpiOcular™ EIT

Version	Author	Reviewer	Approver	Date of approval
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Document history

Version	Date	Drafted by	Comments
2	08/02/2011	João Barroso	Footnotes 3, 4, 5 and 6 were updated to include WLR, BLR, sensitivity and specificity of EpiOcular™ EIT calculated from pre-validation data considering both classification cut-offs of 50% and 60%.

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Institute for Health and Consumer Protection
European Centre for the Validation of Alternative Methods (ECVAM)

GUIDANCE ON EYE IRRITATION VALIDATION STUDY (EIVS) CONDUCT FOR THE RECONSTRUCTED HUMAN TISSUE (RhT) ASSAYS AND PERFORMANCE CRITERIA TO ASSESS THE SCIENTIFIC VALIDITY OF SkinEthic™ HCE AND EpiOcular™ EIT

Disclaimer: The Validation Management Group (VMG) of the Eye Irritation Validation Study (EIVS) proposes in this document a guidance on the conduct of certain aspects of EIVS, as well as "test method performance criteria" that describe the performance deemed by the VMG as necessary for a test method to be scientifically valid and considered for regulatory acceptance. Nevertheless, the EIVS VMG recognises that regulatory authorities ultimately make the determination of what is considered adequate performance for their relevant regulatory decisions.

1. DEFINITIONS

EpiOcular™ model/construct: A reconstructed human tissue (RhT) construct produced by MatTek Corporation, consisting of a non-keratinized multilayered epithelium prepared from non-transformed, human-derived epidermal keratinocytes.

SkinEthic™ Human Corneal Epithelium (HCE) model/construct: A RhT construct produced by SkinEthic™ Laboratories, consisting of a a multilayered epithelium prepared from immortalized human corneal epithelial cells.

EpiOcular™ Eye Irritation Test (EIT): A test method to predict eye irritation, employing the EpiOcular™ RhT construct as test system and a protocol defining different exposure and post-exposure incubations for liquids and solids (i.e., liquids: 30 min exposure followed by 120 min post-treatment incubation, and solids: 90 min exposure followed by 18 hours post-treatment incubation).

SkinEthic™ HCE Short-time Exposure (SE): A test method to predict eye irritation, employing the SkinEthic™ HCE RhT construct as test system and a short-time exposure of test chemicals (i.e., 10 min exposure without post-treatment incubation).

SkinEthic™ HCE Long-time Exposure (LE): A test method to predict eye irritation, employing the SkinEthic™ HCE RhT construct as test system and a long-time exposure of test chemicals (i.e., 1 h exposure followed by 16 h post-treatment incubation).

Eye irritation Peptide Reactivity Assay (EPRA): A test method to predict chemical reactivity, defined as the electrophilic potential of the chemical to react with cysteine or lysine containing peptides.

SkinEthic™ HCE test strategy/method: A test strategy to predict eye irritation, consisting of three separate assays (i.e., EPRA, SkinEthic™ HCE SE, and SkinEthic™ HCE LE). In the SkinEthic™ HCE test strategy, chemical reactivity, as determined by the EPRA, is used to decide if a chemical is tested with SkinEthic™ HCE SE (reactive chemicals) or SkinEthic™ HCE LE (non-reactive or inclusive chemicals).

Negative control (NC): A reference test chemical that does not induce a cytotoxic effect in the treated tissues (i.e., does not reduce their viability). It is used to verify if the viability of the tissues used for testing, as quantified by the MTT assay, is within a defined acceptance range of optical density (OD) (i.e., SkinEthic™ HCE SE/LE: $0.7 \leq OD_{NC} < 1.5$; EpiOcular™ EIT: $OD_{NC} > 1.0$).

Positive control (PC): A reference test chemical known to induce a cytotoxic effect in the treated tissues (i.e., SkinEthic™ HCE SE/LE: < 50% viability; EpiOcular™ EIT: < 50% viability), as quantified by using the MTT assay. It is used to verify if the tissue batch used for testing is responding to the reference chemical within a defined acceptance range of % viability (relative to NC). It should be noted that the positive control does not need to be an *in vivo* irritant chemical (based on the Draize eye irritation test).

Test chemical: Any chemical (substance or mixture) being tested as a single entity.

Test: A single test chemical concurrently tested in a minimum of two/three tissue replicates as defined in the corresponding SOP. A "test" for a test chemical is defined when the cytotoxic effect by using MTT is quantitatively measured. A reported technical issue before the viability measurement is not considered as a "test" for the test chemical (see section 2.2.3).

Run: A run consists of multiple tests with different test chemicals (one test per test chemical) conducted concurrently with a test with NC and a test with PC, tested by one operator, as defined in the corresponding SOP.

Qualified run: A run is qualified if it meets the test acceptance criteria for the NC and PC, as defined in the corresponding SOP. Otherwise, the run will be considered as non-qualified.

Qualified test: A test is qualified if it meets the criteria for an acceptable test, as defined in the corresponding SOP, and is within a qualified run. Otherwise, the test will be considered as non-qualified.

Test sequence: The total number of tests performed for a single test chemical in a single laboratory, which includes any re-testing. A test sequence may include both qualified and non-qualified tests. The first two tests having technical issues for each test chemical, tests included in the first two runs presenting technical issues, and tests included in the first six non-qualified runs are not considered as part of a test sequence.

Complete test sequence: A test sequence is considered complete if it contains three qualified tests. Otherwise, the test sequence will be considered as incomplete.

2. TESTING PROCEDURES

2.1 Testing Chemicals for the Eye Irritation Validation Study (EIVS)

In order to establish the reliability and relevance of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT during EIVS, **all test chemicals selected for the validation study (at least 104) should be tested with SkinEthic™ HCE SE, SkinEthic™ HCE LE and EpiOcular™ EIT in three laboratories**. SkinEthic™ HCE SE and SkinEthic™ HCE LE will be run in parallel in the same three laboratories, while three other laboratories will be responsible for running the EpiOcular™ EIT. In each laboratory, **all test chemicals should be tested in three independent qualified runs per test method performed with different production tissue batches and at sufficiently spaced time points** (at least one week apart), with the final objective of obtaining **three qualified tests per test chemical**. In each run, each test chemical, as well as the negative control (NC) and the positive control (PC) should be concurrently tested in a minimum of **three tissue replicates for SkinEthic™ HCE SE/LE and two tissue replicates for EpiOcular™ EIT (see note below), respectively**. Even if more than one test chemical is tested in the same run, one replicate set for each NC and PC is sufficient.

Any tissues pre-selection (before the testing, untreated tissues), procedural change or technical issue (during the testing, tissue treated) that may impact on test method reproducibility assessment, will be documented (see data reporting templates in the annexes to the SOPs) and reported to the core VMG.

Note on the number of replicates for the EpiOcular™ EIT:
The EpiOcular™ EIT has been developed using two concurrently tested tissue replicates on the basis of practical considerations in the technical procedures for conduct of this assay. The variability between two concurrently treated tissue replicates was found to be low in the 296 pairs of replicates produced by seven laboratories for a wide set of test chemicals during the pre-validation study of the EpiOcular™ EIT. Briefly, 99%, 95%, 90% and 74% of the 296 pairs of concurrently treated tissue replicates showed a difference of viability below 20%, 15%, 10% and 5%, repectively. Two independent biostatisticians evaluated the data and their conclusions led the VMG to consider the use of two tissue replicates for EpiOcular™ EIT in EIVS as sufficiently statistically and scientifically justified.

2.2 Re-conducting Tests/Runs ("Re-testing"/"Re-running")

It is possible that one or several tests pertaining to one or more test chemicals does/do not meet the test acceptance criteria as given in the corresponding SOP or is/are not acceptable for other reasons. It is also possible that acceptance criteria for the NC and/or PC, as defined in the corresponding SOP, are not met for one or more runs. In these cases, re-testing/re-running is allowed to complete missing data as described below. Importantly, each laboratory should not produce more than three qualified tests per test chemical, per test method, and re-testing/re-running is allowed only to try to accomplish the objective of producing three qualified tests per test chemical, per test method. Excess production of data and subsequent data selection are regarded as not appropriate. All tested tissues must be reported. The extent of unacceptable tests/runs will be documented and the basis for the likely cause of each will be provided.

2.2.1 Re-testing of test chemicals: If one or more test chemicals within a qualified run does/do not meet the test acceptance criteria (**non-qualified test(s)**), a maximum number of **two additional tests** per test chemical, per test method[1], per laboratory is/are admissible ("re-testing") to complement missing data. More precisely, since in case of re-testing also PC and NC have to be concurrently tested, a maximum number of two additional qualified runs may be conducted for each test chemical. Non-qualified tests have to be documented and reported.

2.2.2 Re-running runs: If a run does not meet the acceptance criteria for the NC and/or PC, as defined in the corresponding SOP (**non-qualified run**), **the full run must be repeated** for all test chemicals included in the non-qualified run. A maximum number of **six[2] additional runs** are admissible per laboratory, per test method[1] ("re-running") to complement missing data due to failure of NC or PC acceptance criteria. Non-qualified runs have to be documented and reported. None of the tests within the first six non-qualified runs obtained by a laboratory for each test method[1] should be considered for applying section 2.2.1, or for any calculations.

[1] SkinEthic™ HCE SE and SkinEthic™ HCE LE are considered as two separate and independent test methods when considering re-testing and re-running.

[2] This limit was defined by calculating the critical (smallest) number of repetitions that will result in a probability less then 5% assuming a binomial distribution with a failing rate of 10% and 30 runs in total.

After producing six non-qualified runs with one test method[1], a laboratory should stop testing and immediately inform the core VMG through the Coordinator Jan Lammers (jan.lammers@tno.nl), with the VMG Chair Stuart Freeman (stuart.j.freeman@talktalk.net) in copy (to take action in the absence of the Coordinator). The core VMG will then analyse in detail all the non-qualified runs obtained by the laboratory with that test method[1] to that point, looking at e.g., the consistency/inconsistency of the reason(s) leading to non-qualification and the time span between the non-qualified runs, in order to decide if the tests within further non-qualified runs should be considered as non-qualified tests. In such a case, further repetition of runs will be considered as re-testing for all test chemicals included in those runs.

Moreover, after producing three consecutive non-qualified runs with one test method[1], a laboratory should stop testing and immediately inform the core VMG through the Coordinator Jan Lammers (jan.lammers@tno.nl), with the VMG Chair Stuart Freeman (stuart.j.freeman@talktalk.net) in copy (to take action in the absence of the Coordinator). The core VMG will then investigate if the laboratory is having systematic technical problems, by looking at e.g., the consistency/inconsistency of the reason(s) leading to non-qualification.

If the core VMG identifies a systematic technical problem as the cause for non-qualified runs, the lead laboratory may be informed and involved in troubleshooting.

2.2.3 Re-testing/re-running for technical reasons: If a test/run fails because of **technical reasons** (technical issue) and the test/run was not finished (no viability measurement) **re-testing is allowed twice** for each test chemical in each laboratory, for each test method[1], and **re-running is also allowed twice** in each laboratory, for each test method[1], independently of the provisions described in sections 2.2.1 and 2.2.2. The reasons will be documented and reported to the core VMG.

Examples of technical issues include e.g. tissues that are mechanically damaged during the test or tissues for which some amount of test chemical is accidentally applied to the culture medium. If a technical issue occurs, all replicates of the corresponding test chemical should be withdrawn from any further step of the test procedure. It should be avoided that OD measurements of tissues with known unacceptable technical quality will be performed (including the remaining replicates of the test chemical).

Moreover, if **systematic technical issues** occur in one laboratory, leading to loss of data for more than one test chemical, **testing should be stopped** and the core VMG informed immediately through the Coordinator Jan Lammers (jan.lammers@tno.nl), with the VMG Chair Stuart Freeman (stuart.j.freeman@talktalk.net) in copy (to take action in the absence of the Coordinator), so that appropriate measures can be taken (e.g. the lead laboratory informed and involved in trying to solve a potential technical problem).

Tissues which feature obvious, visible damage (e.g. contamination or cuts in the epithelium) should be discarded and not used at all in order to avoid a posterior technical issue.

3. TEST ACCEPTANCE CRITERIA

The test acceptance criteria for test chemicals, NC, PC, Non Specific Color controls and Non Specific MTT reduction controls are described in the corresponding SOPs and have been approved by the VMG. For example regarding variability, these acceptance criteria were defined as follows: SkinEthic™ HCE SE/LE: SD > 18%; EpiOcular™ EIT: Range > 20%. Importantly, if during or

after completion of EIVS the predefined test acceptance criteria are found not to be appropriate due to failure of a high number of tests (non-qualified tests) and/or runs (non-qualified runs), the VMG may revise these criteria on the basis of the evaluation of the acquired data. All modifications have to be scientifically/statistically justified.

4. CALCULATION OF RELIABILITY (REPRODUCIBILITY) AND PREDICTIVE CAPACITY (ACCURACY)

The independent biostatistician assigned to the validation study will be responsible for calculating the reliability and predictive capacity values in EIVS, in accordance with the rules described below. The ECVAM biostatistician will perform an **independent review and quality assurance** on the calculations performed by the independent biostatistician.

While the reproducibility and predictive capacity of EpiOcular™ EIT will be evaluated in a single assessment (as described in sections 4.1-4.3) because each chemical will be tested in a single protocol (as a solid or a liquid), for SkinEthic™ HCE three independent assessments will be performed. Since all the selected test chemicals will be tested in both SkinEthic™ HCE SE and SkinEthic™ HCE LE, these two assays can be evaluated not only as part of a testing strategy with EPRA but also as independent test methods. Thus, the SkinEthic™ HCE testing strategy, the SkinEthic™ HCE SE and the SkinEthic™ HCE LE will all be independently evaluated for their reproducibility and predictive capacity as described in sections 4.1-4.3. Finally, the EPRA will be evaluated for its reproducibility according to sections 4.1 and 4.2 (see also Project Plan).

4.1 Within Laboratory Reproducibility (WLR)

For each laboratory, concordance of classifications and overall Standard Deviation will be calculated based only on qualified tests from test chemicals for which **at least two qualified tests** are available. The final report should state how many and which test chemicals per laboratory have none or only one qualified test (omitted from WLR calculations), as well as how many and which test chemicals per laboratory have two or three qualified tests (used for WLR calculations). In addition, the overall Standard Deviation associated with each laboratory will be calculated using all available test sequences, i.e. including both qualified and non-qualified tests.

4.2 Between Laboratory Reproducibility (BLR)

For the calculation of BLR the **final classification** for each test chemical in each participating laboratory should be obtained by using the **arithmetic mean value of viability over the different qualified tests** performed. Concordance of classifications between laboratories and overall Standard Deviation of the study will be calculated based only on qualified tests from test chemicals for which **at least one qualified test per laboratory** is available. The final report should state how many and which test chemicals do not have at least one qualified test per laboratory (omitted from BLR calculation), as well as how many and which test chemicals have 3, 4, 5, 6, 7, 8 or 9 qualified tests that can be used to calculate BLR (with at least one qualified test per laboratory). In addition, the overall Standard Deviation of the study will be calculated using all available test sequences, i.e. including both qualified and non-qualified tests.

4.3 Predictive Capacity (Accuracy)

All qualified tests for each test chemical will be used to calculate the predictive capacity values. The calculations will be based on the **individual predictions of each qualified test in each laboratory** and not on the arithmetic mean values of viability over the different qualified tests performed.

By using all qualified tests to calculate the predictive capacity values, the probability of obtaining 0% underprediction of Category 1 chemicals (0 out of about 200 tests), as requested in section 6.4 (see below), is extremely low due to the accepted fact that reproducibility of SkinEthic™ HCE SE/LE and EpiOcular™ EIT both within and between laboratories is not 100% (see section 6.3). Therefore, the rate of underprediction of Category 1 chemicals as No Category (Cat 1 → No Cat), will be calculated using the **mode of the *in vitro* predictions of all qualified tests** obtained in the three participating laboratories for each test chemical classified as UN GHS/EU CLP Category 1 based on *in vivo* Draize eye irritation data. This approach more closely reflects the real testing situation (post-validation). Thus, in a post-validation testing situation, a single qualified test obtained in one laboratory is usually sufficient to classify a test chemical, but if a borderline result, such as non-concordant replicate measurements and/or mean percent viability equal to 50±5%, is obtained, a second test may be considered, as well as a third one, in case of discordant results between the first two tests, in which case the **mode of the three classifications** is taken as the final decision.

5. STUDY QUALITY CRITERION

To limit the bias introduced in the calculations of reliability and predictive capacity due to the exclusion of the most variable tests (non-qualified tests) from some of the calculations (see section 4), and also to avoid further bias introduced by a reduction of the data used in some of the calculations (at least 104 test chemicals are needed to reach the statistical power defined for the study), the VMG decided to define a target value for the number of complete test sequences that should be available after re-testing as an objective to secure the quality of the study, i.e. to limit the amount of missing data due to the predefined test acceptance criteria (see section 3).

5.1 Target Number of Complete Test Sequences After Re-testing

In each participating laboratory, **at least 85%** of the test sequences (see definition in section 1) should contain **three qualified tests** (89 out of 104 test sequences, for 104 test chemicals).

If this criterion is not met, and before deciding that the required statistical power and study quality are not reached, the VMG may (i) investigate for potential reasons of misclassification, (ii) if deemed appropriate, revise the test acceptance criteria on the basis of the evaluation of the acquired data, as described in section 3 and/or (iii) request additional testing to complement the datasets.

6. PERFORMANCE CRITERIA TO ASSESS THE SCIENTIFIC VALIDITY OF THE TEST METHODS

Prior to the initiation of the validation study, the VMG defined test method performance criteria, which it considered appropriate for judging the performance of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT with the test chemicals selected for EIVS. The test method performance criteria described below provide some guidance on the target values which the VMG would ideally like to attain in EIVS in terms of test method performance (reliability and predictive capacity) for the SkinEthic™ HCE SE, LE and/or test strategy and for the EpiOcular™ EIT. One recommendation of a previous ESAC Peer Review Panel on cell-based assays was to receive guidance from the VMG to evaluate the performance of these cell-based assays. Therefore, within the framework of EIVS, the VMG also suggests the use of these test method performance criteria as a basis for the evaluation of the performance of the SkinEthic™ HCE LE, SE and test strategy and of the EpiOcular™ EIT by the ESAC Peer Review Panel after the completion of EIVS.

The test method performance criteria developed by the VMG for EIVS and described below took into account: (a) the background and specific objectives of the validation study (see EIVS Project Plan); (b) the requirements of regulatory authorities and industry when testing and classifying chemicals for eye irritation; (c) the within test variability in the *in vivo* Draize eye irritation data and the manner in which those data are currently used for classifying eye irritants according to UN GHS / EU CLP (UN, 2007; EC, 2008); (d) the standards of performance which are expected from the *in vitro* tests evaluated; (e) the way in which the *in vitro* tests are to be used (as a test within a tiered test strategy); and (f) the power of the design of the validation study.

It should be noted that the performance criteria on predictive capacity listed in section 6.4 should only be used to evaluate the validity of the SkinEthic™ HCE SE, LE and test test strategy and of the EpiOcular™ EIT as stand-alone test methods for the identification of chemicals not classified as eye irritants, in the framework of the Bottom-up/Top-down test strategy (please see the objective and goals of EIVS set out in the Project Plan). Therefore, even if the accuracy values obtained in EIVS for any of these RhT test methods are considered "definitely unacceptable" by the VMG as described in section 6.4, the test method(s) may still be useful for other purposes, e.g. the identification of chemicals not classified as eye irritants in combination with other appropriately validated test methods (i.e., use of more than one test method to identify the majority of non-classified chemicals). The EIVS VMG will consider these situations when evaluating the results of the validation study.

6.1 Flexibility Clause

Although the EIVS VMG is of the opinion that the definition of target values for test method performance prior to initiation of the experimental phase of a validation study is beneficial, bearing in mind the post-validation acceptance process, it also acknowledges that in a prospective validation study not all circumstances and possible outcomes can be considered beforehand. Thus, the following predefined and agreed target values are to be considered in the context of the practical study outcome. In case amendments are considered necessary, these will have to be scientifically justified.

6.2 Limitations of the Test Methods

The VMG also considers that it will be important to define the limitations of the test methods, and try to rationalize any apparent reasons for misclassifications before making a final recommendation about the scientific validity of the RhT test methods under evaluation. If potential reasons for misclassification strictly related to the test methods are identified, these should be considered for defining the limitations of the test method. If the estimated reliability and/or accuracy values of a test method can be improved by excluding identified limitations, these values should also be compared to the predefined test method performance criteria (sections 6.3-6.4).

6.3 Target Values for Reproducibility

Analysis of reproducibility will not be limited to the parameters described below. Other statistical tools, e.g. the overall Standard Deviation and Coefficient of Variation of the study calculated from all qualified tests as from all available tests (qualified and non-qualified), will also be considered before making a final decision on the reproducibility of the test methods.

6.3.1 Within one laboratory (and over time): The **concordance of classifications** (not classified / classified) for the set of chemicals tested during validation obtained in different, independent runs **within a single laboratory** should **ideally be equal or higher (≥) than 85%** for all participating laboratories[3].

6.3.2 Between laboratories: The **concordance of final classifications** (not classified / classified) for the set of chemicals tested during validation obtained **by the different participating laboratories** should **ideally be equal or higher (≥) than 80%**[4].

6.4 Target Values for Predictive Capacity (Accuracy)

The SkinEthic™ HCE SE, LE and test strategy and the EpiOcular™ EIT are being validated for their usefulness as stand-alone (independent) test methods to identify chemicals not classified as eye irritant (UN GHS/EU CLP No Category; "non-irritants") and their reliable discrimination from all classes of eye irritant chemicals as e.g. the initial step in a Bottom-Up approach (in the framework of a Bottom-Up/Top-Down test strategy, Scott L. *et al.*, 2010). The SkinEthic™ HCE test strategy and the EpiOcular™ EIT were developed for maximum sensitivity (ability to detect positives, with low rate of false negatives) rather than for optimal accuracy with balanced sensitivity and specificity (ability to detect negatives, with low rate of false positives). However, it was also sought to achieve a sufficiently high specificity in order to allow the identification of the highest number of chemicals not classified as irritant to the eye. By achievement of satisfactory

[3] The within laboratory reproducibility values obtained in the pre-validation of the SkinEthic™ HCE were of 90 to 100% concordance of classifications, and for EpiOcular™ EIT of 95 to 100% concordance of classifications (considering the classification cut-off of 60% viability) or of 90 to 100% concordance of classifications (considering the classification cut-off of 50% viability).

[4] The between laboratory reproducibility values obtained in the pre-validation of the SkinEthic™ HCE were of 95 to 100% concordance of classifications, and for EpiOcular™ EIT 100% concordance of classifications (considering the classification cut-off of 60% viability) or 96% concordance of classifications (considering the classification cut-off of 50% viability).

specificity, the SkinEthic™ HCE test strategy and the EpiOcular™ EIT would present stand-alone (independent) test methods for identification of "non-irritants".

Based on these premises, the EIVS VMG defined "definitely acceptable" and "definitely unacceptable" rates of overprediction and underprediction for determining the predictive performance of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT, which are outlined in Table 1. In particular, the following points were felt to be important to recommend the test methods as being sufficiently predictive to be considered as scientifically valid:

(a) About 10% false negatives should be "definitely acceptable" (sensitivity ≥ 90%), while more than 20% would be "definitely unacceptable"[5]. In previous validation studies for eye irritation led by ECVAM (Cytotoxicity and Cell-based assays) or ICCVAM (Organotypic assays) the Peer-Review Panels responsible for evaluating the validated test methods considered 0% false negatives as a test method performance criterion for acceptance of test methods to be used as an initial step in a Bottom-Up test strategy (identification of chemicals not classified as eye irritant). However, the Draize rabbit eye test shows the potential for up to 10% over classification of chemicals as UN GHS Cat. 2 (instead of UN GHS No Cat.) due solely to its within test variability (Zuang V. *et al.*, 2010). The actual rate of overprediction of the Draize test may be even higher when considering other factors like between laboratory variability and predictivity. Thus, the EIVS VMG is of the opinion that a False Negative rate up to 10% should be "definitely acceptable" for the UN GHS and EU CLP classification and labelling systems (UN, 2007; EC, 2008) for a test method to be considered useful for the identification of chemicals not classified as eye irritants as a stand-alone test (inititial step in a Bottom-up approach). Nevertheless, the nature, severity, duration, and frequency of *in vivo* eye injuries (based on the Draize eye irritation test) for chemicals that produce false negative results from *in vitro* tests will be fully discussed and considered by the VMG in assessing the usefulness and limitations of the *in vitro* test methods for regulatory hazard classification and labelling purposes.

(b) Ideally, no ocular corrosives/severe eye irritants (Category 1) should be underpredicted as No Category, but more than 10% Cat 1 chemicals being underclassified as No Category would be "definitely unacceptable".

(c) About 40% false positives should be "definitely acceptable" (specificity ≥ 60%), while more than 50% would be "definitely unacceptable"[6]. Since the purpose of the test methods will be the identification of chemicals not classified as eye irritant (UN GHS/EU CLP No Category) as an initial step of a Bottom-Up test strategy (Scott L. *et al.* 2010), the VMG considered that it is acceptable to have a lower specificity than sensitivity (higher false positives than false negatives). Nevertheless, specificity should not be too low in order to allow for the correct identification of the majority of the chemicals not classified as irritant to the eye.

[5] During pre-validation, the EpiOcular™ EIT showed a sensitivity of 99% (considering the classification cut-off of 60% viability) or of 96% (considering the classification cut-off of 50% viability), while the SkinEthic™ HCE test strategy showed a sensitivity of 87%.

[6] During pre-validation, the EpiOcular™ EIT showed a specificity of 65% (considering the classification cut-off of 60% viability) or of 72% (considering the classification cut-off of 50% viability), while the SkinEthic™ HCE test strategy showed a specificity of 69%.

(d) About 25% of overall misclassifications would be "definitely acceptable" (overall accuracy ≥ 75%), while more than 35% would be "definitely unacceptable". Potential reasons for misclassification will be analysed in detail, including individual tissue score lesions of misclassified chemicals, which may be considered in future regulatory acceptance of the evaluated assays.

(e) Misclassification of borderline chemicals, identified from *in vivo* Draize eye irritation data and/or structure-activity relationship considerations, would be easier to justify compared to non-borderline chemicals.

If the "definitely acceptable" rates of overprediction and underprediction defined in Table 1 are not attained in the validation study, but the rates obtained are not considered "definitely unacceptable" (Table 1), the VMG will not decide on the recommendation about the scientific validity of the test method before all the validation data have been evaluated and discussed as explained (see sections 6.1 and 6.2). If the accuracy values of any of the RhT test methods (EpiOcular™ EIT, SkinEthic™ HCE SE, SkinEthic™ HCE LE and SkinEthic™ HCE test strategy) as obtained in EIVS are considered "definitely unacceptable" by the VMG for a stand-alone test method, even taking into account any possible limitations of the test methods, these may still be useful for other purposes, e.g. the identification of chemicals not classified as eye irritants in combination with other methods. The EIVS VMG will consider these situations when evaluating the results of the validation study.

Table 1. VMG accepted rates of overprediction and underprediction for the SkinEthic™ HCE SE, LE and test strategy and for the EpiOcular™ EIT, in the framework of EIVS

	False Negatives[a] (%)	Cat 1 → No Cat[b] (%)	False Positives[c] (%)	Overall misclassifications[d] (%)
"Definitely acceptable" rates	≤ 10	0	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	0 < Cat 1 FN ≤ 10	40 < FP ≤ 50	25 < OM ≤ 35
"Definitely unacceptable" rates	> 20	> 10	> 50	> 35

[a] equal to (1-Sensitivity)
[b] based on the mode of all qualified tests (see section 4.3)
[c] equal to (1-Specificity)
[d] equal to (1-Overall accuracy)

7. REFERENCES

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EUROPEAN COMMISSION
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ADDENDUM TO THE GUIDANCE ON EYE IRRITATION VALIDATION STUDY (EIVS) CONDUCT FOR THE RECONSTRUCTED HUMAN TISSUE (RhT) ASSAYS AND PERFORMANCE CRITERIA TO ASSESS THE SCIENTIFIC VALIDITY OF SkinEthic™ HCE AND EpiOcular™ EIT

Instructions for the Testing of Direct MTT-Reducers and/or Coloured Test Chemicals

1. Controls for direct MTT-reducers and coloured test chemicals

Controls for direct MTT-reducers (freeze killed tissues with MTT) and/or coloured test chemicals (living tissues without MTT) must always be performed irrespectively of the results of the viability tests. Therefore, even though Non-Specific MTT-reduction (NSMTT) and/or Non-Specific Colour (NSC) corrections will have no effect for MTT reducers and/or coloured test chemicals that are already identified as irritant in the viability tests, NSMTT and NSC controls must still be acquired for these chemicals.

2. Test chemicals showing %NSMTT or %NSC > 50% in any of the control tests performed

A test cannot be considered as non-qualified based only on the %NSMTT or %NSC values. According to the current EpiOcular™ EIT and SkinEthic™ HCE protocols, a %NSMTT or %NSC > 50% may suggest that the chemical is incompatible with the test method, but does not per se disqualify the test where it was obtained. A test can only be considered as non-qualified based on the variability of the two (EpiOcular™ EIT) or three (SkinEthic™ HCE) tissue replicates used in the %viability measurements or controls, or if it is included in a non-qualified run, where either the positive control or the negative control did not meet the test acceptance criteria. Moreover, the %NSMTT and %NSC cut-offs for deciding whether a direct-MTT reducer or coloured test chemical is compatible with the test method (currently defined as 50%) may be revised post-hoc by the Validation Management Group (VMG) once the testing phase of the ECVAM/COLIPA Eye Irritation Validation Study (EIVS) is completed and relevant statistical analysis have been performed.

Therefore, the laboratories participating in EIVS should always try to obtain three qualified viability tests and controls for direct MTT-reducers and/or coloured test chemicals even if %NSC or %NSMTT are > 50%. It will be up to the VMG to decide whether the test chemical should be considered incompatible with the test method when analysing the data acquired by all participating laboratories.

3. Re-testing due to failure to meet test acceptance criteria

Re-testing due to failure to meet test acceptance criteria should always be performed up to the maximum number of re-tests allowed and as long as three qualified tests (a complete test sequence) have not been obtained. Importantly, **re-testing should continue** up to the maximum number of re-tests allowed **even when** it becomes clear that **a complete test sequence** (three qualified tests) **can no longer be obtained** (see below: cases 5, 9, 13 and 18). **This rule applies to all test chemicals** (including coloured, non-coloured, MTT-reducer and non-MTT-reducer chemicals) and is important because according to sections 4.1, 4.2 and 4.3 of the Guidance on EIVS Conduct and Performance Criteria, the Within Laboratory Reproducibility will be calculated for "test chemicals for which at least **two** qualified tests are available", the Between Laboratory Reproducibility will be calculated for "test chemicals for which at least **one** qualified test per laboratory is available", and the Predictive Capacity will be calculated using **all** qualified tests obtained for each test chemical. Therefore, the order of qualified/non-qualified results should not dictate whether to proceed with testing since this would artificially bias the evaluation of the robustness of the protocol.

Finally, no further testing of a chemical by a laboratory should be performed once three qualified tests have been obtained for a test method (see below: cases 1, 2, 3, 6, 7, 10, 11, 15 and 16). Excess production of data and subsequent data selection are regarded as not appropriate. All tested tissues must be reported.

3.1. Extra re-testing of NSMTT control tissues due to failure to meet the test acceptance criterion

NSMTT controls are tested independently from viability tests (and NSC controls) since they use freeze killed tissues, which can only be used after all tissues from the same batch have already been used in a previous week. Moreover, NSMTT controls for one test method[1] only need to be performed once in each laboratory, for each direct MTT-reducer test chemical. If a NSMTT control within a qualified run does not meet the test acceptance criterion (SkinEthic™ HCE SE/LE: $SD_{\%NSMTT} > 18\%$; EpiOcular™ EIT: $Range_{\%NSMTT} > 20\%$) (non-qualified NSMTT control test), a maximum number of two additional NSMTT control tests per direct MTT-reducer chemical, per test method[1], per laboratory are admissible ("re-testing") to try obtaining one qualified NSMTT control for that chemical. Each additional NSMTT control test must be acquired concurrently with the negative control. All non-qualified NSMTT control tests have to be documented and reported.

It is important to note that although only one qualified NSMTT control test needs to be performed in each laboratory for each test method[1] for each direct MTT-reducer test chemical, a different %NSMTT value must be calculated from the single NSMTT control OD to correct each qualified viability test obtained. The %NSMTT value used to correct a qualified viability test must be calculated relative to the negative control that was run concurrently to that specific viability test. Depending on the negative control OD value that is used to calculate %NSMTT, it is possible that the same NSMTT control may meet the test acceptance criterion for one (or two) viability test(s), but not for the other. Thus, **a NSMTT control only qualifies if it meets the test acceptance criterion for all the qualified viability tests it needs to correct.**

If more than one qualified NSMTT control test is obtained in one laboratory for the same test chemical with the same test method[1], the mean of the different corrected OD values obtained

[1] SkinEthic™ HCE SE and SkinEthic™ HCE LE are considered as two separate and independent test methods when considering re-testing and re-running.

for those NSMTT control tests (EpiOcular™ EIT: OD_{KC}; SkinEthic™ HCE SE/LE: OD_{KT}-OD_{KU}) should be used to calculate one single %NSMTT value per qualified viability test.

3.2. Extra re-testing of coloured test chemicals due to failure to meet the test acceptance criterion in NSC control tissues

For coloured chemicals, NSC controls must be run concurrently with every viability test since the same tissue batch must be used for a viability test and its NSC control. Therefore, a viability test that meets the test acceptance criterion (SkinEthic™ HCE SE/LE: $SD_{\%Viability} \leq 18\%$; EpiOcular™ EIT: $Range_{\%Viability} \leq 20\%$) may still not qualify if the concurrent NSC control does not meet its test acceptance criterion (SkinEthic™ HCE SE/LE: $SD_{\%NSC} > 18\%$; EpiOcular™ EIT: $Range_{\%NSC} > 20\%$) (see below: for example, cases 6, 7, 8 and 9). In order to compensate for the higher probability of obtaining a non-qualified test with a coloured chemical (where two separate test acceptance criteria must be met) as compared to a non-coloured chemical (where only one test acceptance criterion must be met), a maximum number of four additional tests per coloured chemical, per test method[1], per laboratory are admissible to try obtaining a complete test sequence. Thus, a total of seven tests may be performed with coloured test chemicals in order to try obtaining three qualified tests (where both the viability test and the NSC control qualify). This corresponds to two extra re-tests in addition to the two already permitted in the Guidance on EIVS Conduct and Performance Criteria. However, the sixth and seventh tests for coloured test chemicals can only be performed if in the first five tests there are no more than two tests with $SD_{\%Viability} > 18\%$ (SkinEthic™ HCE SE/LE) or with $Range_{\%Viability} > 20\%$ (EpiOcular™ EIT), and no more than two tests with $SD_{\%NSC} > 18\%$ (SkinEthic™ HCE SE/LE) or with $Range_{\%NSC} > 20\%$ (EpiOcular™ EIT) (see below: cases 4, 5, 8, 9, 12, 13 and 14 where a 6th and 7th test cannot be performed; and cases 15, 16, 17 and 18 where up to 7 tests must be performed to generate a complete test sequence). Each additional viability test and NSC control test must be acquired concurrently with the positive control and the negative control. All non-qualified tests (including viability tests and concurrent NSC controls) have to be documented and reported.

4. Re-running due to failure to meet test acceptance criteria for the positive or the negative control

4.1. Extra re-running in each laboratory due to failure to meet test acceptance criteria for the positive or the negative control

If a run does not meet the acceptance criteria for the negative control and/or positive control, as defined in the SkinEthic™ HCE and EpiOcular™ EIT protocols (non-qualified run), the full run must be repeated for all test chemicals included in the non-qualified run. A maximum number of eight[2] additional runs are admissible per laboratory, per test method[1] ("re-running") to complement missing data due to failure to meet the negative control or positive control acceptance criteria. Thus, in addition to the six re-runs already foreseen in the Guidance on EIVS Conduct and Performance Criteria, two extra re-runs are now permitted. This amendment is proposed because the total number of runs required to generate three tests per test chemical in one laboratory is higher than the 30 initially predicted, which did not consider the need to run NSMTT and NSC controls. Assuming that 1/3 of the chemicals (about 35) will

[2] This limit was defined by calculating the critical (smallest) number of repetitions that will result in a probability less then 5% assuming a binomial distribution with a failing rate of 10% and 40 runs in total.

require controls in three runs, an extra 10 runs will be required to generate three tests per test chemical plus controls in one laboratory. These extra 10 runs justify the two extra re-runs now permitted. Non-qualified runs have to be documented and reported. None of the tests within the first eight non-qualified runs obtained by a laboratory for each test method[1] should be considered non-qualified, nor should they be used for any calculations.

5. Re-testing due to technical issues

5.1. Extra re-testing of NSMTT control tissues due to technical issues

A NSMTT control test for a direct MTT-reducer test chemical may be repeated twice (re-tested) to replace NSMTT control tests that failed due to technical reasons (technical issue) and that were not finished (OD measurement not performed). These two re-tests are allowed in each laboratory and for each test method[1], independently of the re-testing allowed due to failure to meet the test acceptance criterion (see section 3.1 above). A NSMTT control that fails due to technical reasons does not disqualify viability tests or NSC controls since, as explained above, NSMTT controls are independent from viability tests and NSC controls (see section 3.1). All technical issues must be documented and reported to the core VMG.

5.2. Extra re-testing of coloured test chemicals due to technical issues in NSC control tissues

A coloured test chemical may be re-tested twice (including viability test and NSC control) to replace tests that failed due to a technical issue in NSC controls and that were not finished (OD measurement not performed for either the viability tissues or the NSC control tissues). Thus, four re-tests (including viability test and NSC control) due to 2 technical issues in viability tissues and 2 technical issues in NSC control tissues are allowed per coloured test chemical in each laboratory, for each test method[1], independently of the re-testing allowed due to failure to meet test acceptance criteria (see section 3.2 above). Each time a coloured test chemical is re-tested due to technical reasons, both the viability test and the NSC control must be re-tested concurrently since, as explained above, the same tissue batch must be used for the viability test and its NSC control (see section 3.1). All technical issues must be documented and reported to the core VMG.

		Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7
Case 1 (Complete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off				
	SD/range %NSC	< cut-off	< cut-off	< cut-off				
	Qualified Test	**YES**	**YES**	**YES**				
A 4th and 5th test is not required since all 3 first tests qualified.								
Case 2 (Complete Test Sequence)	SD/range %Viab.	< cut-off	> cut-off	< cut-off	< cut-off			
	SD/range %NSC	< cut-off	< cut-off	< cut-off	< cut-off			
	Qualified Test	**YES**	**No**	**YES**	**YES**			
A 5th, 6th and 7th test is not required since 3 qualified tests were obtained in 4 tests.								
Case 3 (Complete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	> cut-off	< cut-off	< cut-off		
	SD/range %NSC	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**YES**	**No**	**YES**	**YES**		
A 6th and 7th test is not required since 3 qualified tests were obtained in 5 tests.								
Case 4 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	> cut-off	< cut-off	> cut-off		
	SD/range %NSC	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**YES**	**No**	**YES**	**No**		
A 6th and 7th test cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %Viability above the cut-off.								
Case 5 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	< cut-off	> cut-off	*		
	SD/range %NSC	< cut-off	< cut-off	< cut-off	< cut-off	*		
	Qualified Test	**No**	**No**	**YES**	**No**	*		
A 6th and 7th tests cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %Viability above the cut-off. * A 5th test must be performed even though a complete test sequence (one containing 3 qualified tests) can no longer be obtained in 5 tests.								

		Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7
Case 6 (Complete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off	< cut-off			
	SD/range %NSC	< cut-off	< cut-off	> cut-off	< cut-off			
	Qualified Test	**YES**	**YES**	**No**	**YES**			
A 5th, 6th and 7th test is not required since 3 qualified tests were obtained in 4 tests.								
Case 7 (Complete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	SD/range %NSC	< cut-off	> cut-off	< cut-off	> cut-off	< cut-off		
	Qualified Test	**YES**	**No**	**YES**	**No**	**YES**		
A 6th and 7th test is not required since 3 qualified tests were obtained in 5 tests.								
Case 8 (Incomplete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	SD/range %NSC	> cut-off	> cut-off	< cut-off	< cut-off	> cut-off		
	Qualified Test	**No**	**No**	**YES**	**YES**	**No**		
A 6th and 7th test cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %NSC above the cut-off.								
Case 9 (Incomplete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off	*	*		
	SD/range %NSC	> cut-off	> cut-off	> cut-off	*	*		
	Qualified Test	**No**	**No**	**No**	*	*		
A 6th and 7th test cannot be performed under the revised rules for re-testing since there are already 3 tests with SD or range of %NSC above the cut-off in the first 3 tests. * A 4th and 5th test must be performed even though a complete test sequence (one containing 3 qualified tests) can no longer be obtained in 5 tests.								

		Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7
Case 10 (Complete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	SD/range %NSC	< cut-off	> cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**No**	**YES**	**YES**	**YES**		
A 6th and 7th test is not required since 3 qualified tests were obtained in 5 tests.								
Case 11 (Complete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off		
	SD/range %NSC	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**No**	**YES**	**YES**	**YES**		
A 6th and 7th test is not required since 3 qualified tests were obtained in 5 tests.								
Case 12 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	< cut-off	< cut-off	> cut-off		
	SD/range %NSC	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**No**	**YES**	**YES**	**No**		
A 6th and 7th test cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %Viability above the cut-off.								
Case 13 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	> cut-off	*	*		
	SD/range %NSC	> cut-off	< cut-off	< cut-off	*	*		
	Qualified Test	**No**	**No**	**No**	*	*		
A 6th and 7th test cannot be performed under the revised rules for re-testing since there are already 3 tests with SD or range of %Viability above the cut-off in the first 3 tests. * A 4th and 5th test must be performed even though a complete test sequence (one containing 3 qualified tests) can no longer be obtained in 5 tests.								
Case 14 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	> cut-off	< cut-off	> cut-off		
	SD/range %NSC	> cut-off	< cut-off	< cut-off	< cut-off	> cut-off		
	Qualified Test	**No**	**YES**	**No**	**YES**	**No**		
A 6th and 7th test cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %Viability above the cut-off.								

		Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7
Case 15 (Complete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	> cut-off	< cut-off	< cut-off	< cut-off	
	SD/range %NSC	> cut-off	< cut-off	< cut-off	< cut-off	> cut-off	< cut-off	
	Qualified Test	**No**	**YES**	**No**	**YES**	**No**	**YES**	
A 6th test must be acquired under the revised rules for re-testing to try obtaining 3 qualified tests, since within the first 5 tests there are only 2 tests with SD or range of %Viability above the cut-off and only 2 tests with SD or range of %NSC above the cut-off. A 7th test is not required since 3 qualified tests were obtained in 6 tests.								
Case 16 (Complete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off
	SD/range %NSC	< cut-off	< cut-off	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off
	Qualified Test	**No**	**No**	**No**	**No**	**YES**	**YES**	**YES**
A 6th and 7th test must be acquired under the revised rules for re-testing to try obtaining 3 qualified tests, since within the first 5 tests there are only 2 tests with SD or range of %Viability above the cut-off and only 2 tests with SD or range of %NSC above the cut-off.								
Case 17 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	< cut-off	< cut-off	< cut-off	> cut-off	< cut-off
	SD/range %NSC	< cut-off	< cut-off	> cut-off	> cut-off	< cut-off	< cut-off	> cut-off
	Qualified Test	**No**	**YES**	**No**	**No**	**YES**	**No**	**No**
A 6th and 7th test must be acquired under the revised rules for re-testing to try obtaining 3 qualified tests, since within the first 5 tests there is only 1 test with SD or range of %Viability above the cut-off and only 2 tests with SD or range of %NSC above the cut-off.								
Case 18 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	< cut-off	< cut-off	> cut-off	> cut-off	*
	SD/range %NSC	< cut-off	< cut-off	> cut-off	> cut-off	< cut-off	< cut-off	*
	Qualified Test	**No**	**YES**	**No**	**No**	**No**	**No**	*
A 6th and 7th test must be acquired under the revised rules for re-testing to try obtaining 3 qualified tests, since within the first 5 tests there are only 2 tests with SD or range of %Viability above the cut-off and only 2 tests with SD or range of %NSC above the cut-off. * A 7th test must be performed even though a complete test sequence (one containing 3 qualified tests) can no longer be obtained in 7 tests.								

Appendix VIII Project Plan

EUROPEAN COMMISSION
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Institute for Health and Consumer Protection
European Centre for the Validation of Alternative Methods (ECVAM)

Eye Irritation Validation Study (EIVS)
Validation of the SkinEthic™ HCE SE, LE and Test Strategy and of the EpiOcular™ EIT for the Prediction of Acute Eye Irritation
Project Plan

Version	Author	Reviewer	Approver	Date of approval
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Document history

Version	Date	Drafted by	Comments

EYE IRRITATION VALIDATION STUDY (EIVS)

PROJECT PLAN

Validation of the SkinEthic™ HCE SE, LE and Test Strategy and of the EpiOcular™ EIT for the Prediction of Acute Eye Irritation

1. Definitions

EpiOcular™ model/construct: A reconstructed human tissue (RhT) construct produced by MatTek Corporation, consisting of a non-keratinized multilayered epithelium prepared from non-transformed, human-derived epidermal keratinocytes.

SkinEthic™ Human Corneal Epithelium (HCE) model/construct: A RhT construct produced by SkinEthic™ Laboratories, consisting of a a multilayered epithelium prepared from immortalized human corneal epithelial cells.

EpiOcular™ Eye Irritation Test (EIT): A test method to predict eye irritation, employing the EpiOcular™ RhT construct as test system and a protocol defining different exposure and post-exposure incubations for liquids and solids (i.e., liquids: 30 min exposure followed by 120 min post-treatment incubation, and solids: 90 min exposure followed by 18 hours post-treatment incubation).

SkinEthic™ HCE Short-time Exposure (SE): A test method to predict eye irritation, employing the SkinEthic™ HCE RhT construct as test system and a short-time exposure of test chemicals (i.e., 10 min exposure without post-treatment incubation).

SkinEthic™ HCE Long-time Exposure (LE): A test method to predict eye irritation, employing the SkinEthic™ HCE RhT construct as test system and a long-time exposure of test chemicals (i.e., 1 h exposure followed by 16 h post-treatment incubation).

Eye irritation Peptide Reactivity Assay (EPRA): A test method to predict chemical reactivity, defined as the electrophilic potential of the chemical to react with cysteine or lysine containing peptides.

SkinEthic™ HCE test strategy/method: A test strategy to predict eye irritation, consisting of three separate assays (i.e., EPRA, SkinEthic™ HCE SE, and SkinEthic™ HCE LE). In the SkinEthic™ HCE test strategy, chemical reactivity, as determined by the EPRA, is used to decide if a chemical is tested with SkinEthic™ HCE SE (reactive chemicals) or SkinEthic™ HCE LE (non-reactive or inconclusive chemicals).

2. Study Objective

The objective of this study is to formally validate the SkinEthic™ HCE SE, LE and test strategy and the EpiOcular™ EIT by inter-laboratory ring trial study, to facilitate international acceptance in regulatory schemes for hazard assessment of chemicals. In particular, these test methods/strategy shall be incorporated into a tiered test strategy (so-called Bottom-Up/Top-Down test strategy, as defined in an ECVAM workshop held in 2005, Scott L. *et al.*, 2010) as e.g. the initial step in a Bottom-Up approach or the second step in a Top-Down Approach. The ultimate purpose of a tiered test strategy will be to replace the traditional *in vivo* Draize eye irritation test [Method B.5 of EC Regulation 440/2008 (EC, 2008a) or OECD TG 405 (OECD, 2002)].

3. Study Goals

The goal of the Eye Irritation Validation Study (EIVS) is to assess the relevance (predictive capacity) and reliability (reproducibility within and between laboratories) of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT, by testing a statistically significant number of coded test chemicals (substances and mixtures), supported by complete and quality assured *in vivo* Draize eye irritation data for comparative evaluation of results.

Specifically, EIVS will assess the validity of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT as stand-alone (independent) test methods to reliably discriminate chemicals not classified as eye irritant ("non-irritants") from all classes of eye irritant chemicals (in the framework of a Bottom-Up/Top-Down test strategy, Scott L. *et al.*, 2010), defined according to the United Nations Globally Harmonized System (GHS) of Classification and Labelling of Chemicals (UN GHS: No Category versus Category 1/Category 2A/Category 2B; UN, 2007) and as implemented in the European Commission Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (EU CLP: No Category versus Category 1/Category 2).

The SkinEthic™ HCE test strategy and the EpiOcular™ EIT were developed for maximum sensitivity (ability to detect positives, with low rate of false negatives) rather than for optimal overall accuracy with balanced sensitivity and specificity (ability to detect negatives, with low rate of false positives). Sensitivity had therefore a bigger weight than specificity and overall accuracy in their development. However, it was also sought to achieve a sufficiently high specificity and overall accuracy, in order to allow identification of the highest number of chemicals not classified as irritant to the eye. By achieving satisfactory specificity, the SkinEthic™ HCE test strategy and the EpiOcular™ EIT would represent stand-alone (independent) test methods for the identification of "non-irritants". Importantly, the test methods are not intended to differentiate between UN GHS/EU CLP Category 1 (irreversible effects) and UN GHS/EU CLP Category 2 (reversible effects). As proposed by the ECVAM workshop of February 2005, this differentiation would be left to another tier of the Bottom-Up/Top-Down test strategy (Scott L. *et al.*, 2010).

The EIVS will be undertaken in accordance with the principles and criteria documented in the OECD *Guidance Document on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment* (No. 34, OECD, 2005) and according to the Modular Approach to validation (Hartung T. *et al.*, 2004).

4. Test Methods

The SkinEthic™ HCE SE, LE and test strategy and the EpiOcular™ EIT have progressed through protocol optimisation and multi-laboratory assessment and will be evaluated in EIVS. The

SkinEthic™ HCE SE/LE and the EpiOcular™ EIT use as test systems reconstructed human tissue (RhT) constructs, and consist of a topical exposure of the neat test chemical to the epithelial surface of the tissue construct.

The EpiOcular™ tissue construct is a non-keratinized multilayered epithelium prepared from non-transformed, human-derived epidermal keratinocytes. It is intended to model the cornea epithelium with progressively stratified but not cornified cells. These cells are not transformed or transfected with genes to induce an extended life span in culture. The "tissue" is prepared in inserts with a porous membrane (MTI-003) through which the nutrients pass to the cells. A cell suspension is seeded into the MTI-003 membrane in specialized medium. After a period of initial cell proliferation, the medium is removed from the top of the tissue so that the epithelial surface is in direct contact with the air. This allows the test chemical to be directly applied to the epithelial surface in a fashion similar to how the corneal epithelium would be exposed *in vivo*. The ability to expose the tissue topically is essential to model the same kind of progressive injury expected *in vivo*. It also allows both solid and liquid test chemicals to be applied directly to the tissue. In the EpiOcular™ EIT, liquids and solids are treated with different exposure and post-exposure incubations (i.e., liquids: 30 min exposure followed by 120 min post-treatment incubation, and solids: 90 min exposure followed by 18 hours post-treatment incubation).

To construct SkinEthic™ HCE tissues, immortalized human corneal epithelial cells are cultured in a chemically defined medium and seeded on a polycarbonate membrane at the air–liquid interface. The tissue construct obtained is a multilayered epithelium resembling the *in vivo* corneal epithelium. As *in vivo*, columnar basal cells are present, including Wing cells. The model is characterized by the presence of specific ultra structural figures like intermediate filaments, mature hemi-desmosomes and desmosomes. Specific cytokeratins 64kD (K.3) have also been described (Nguyen D.H. *et al.*, 2003).

The SkinEthic™ HCE test strategy uses three separate assays, i.e. EPRA, SkinEthic™ HCE SE, and SkinEthic™ HCE LE. In this strategy, test chemicals are tested in a short-time exposure (SkinEthic™ HCE SE: 10 min exposure without post-treatment incubation) or a long-time exposure (SkinEthic™ HCE LE: 1 h exposure followed by 16 h post-treatment incubation) depending on their chemical reactivity (defined as the electrophilic potential to react with cysteine or lysine containing peptides), as measured by the Eye irritation Peptide Reactivity Assay (EPRA).

Following treatment with a test chemical as described above (using EpiOcular™ EIT, SkinEthic™ HCE SE or SkinEthic™ HCE LE), the relative tissue viability is determined against the negative control-treated constructs by the reduction of the vital dye MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide). Tissues treated with eye irritants (UN GHS/EU CLP Category 2 and Category 1) are expected to show a decrease in viability below a certain threshold in respect to the negative control.

5. Validation Management Group

The management structure of EIVS and the responsibilities of the different members are shown in Figure 1. The Validation Management Group (VMG), with supervisory role, comprises:

Core VMG

- Chair (Stuart Freeman)
- Co-chair (Valérie Zuang)
- COLIPA sponsor representative (Pauline McNamee; *alternate*: Penny Jones)
- ECVAM sponsor representative (João Barroso)
- TNO coordinator representative (Jan Lammers; *alternate*: Ruud Woutersen)
- TNO biostatistician (Carina de Jong-Rubingh)
- ECVAM biostatistician (André Kleensang until 30.09.2010)[1]
- Independent scientist (Chantra Eskes)
- Chemicals Selection Group (CSG) coordinator (Thomas Cole)

Representatives of the lead laboratories

- SkinEthic™ HCE test strategy lead laboratory: L'Oréal (Nathalie Alépée)
- EpiOcular™ EIT lead laboratory: Beiersdorf (Uwe Pfannenbecker)

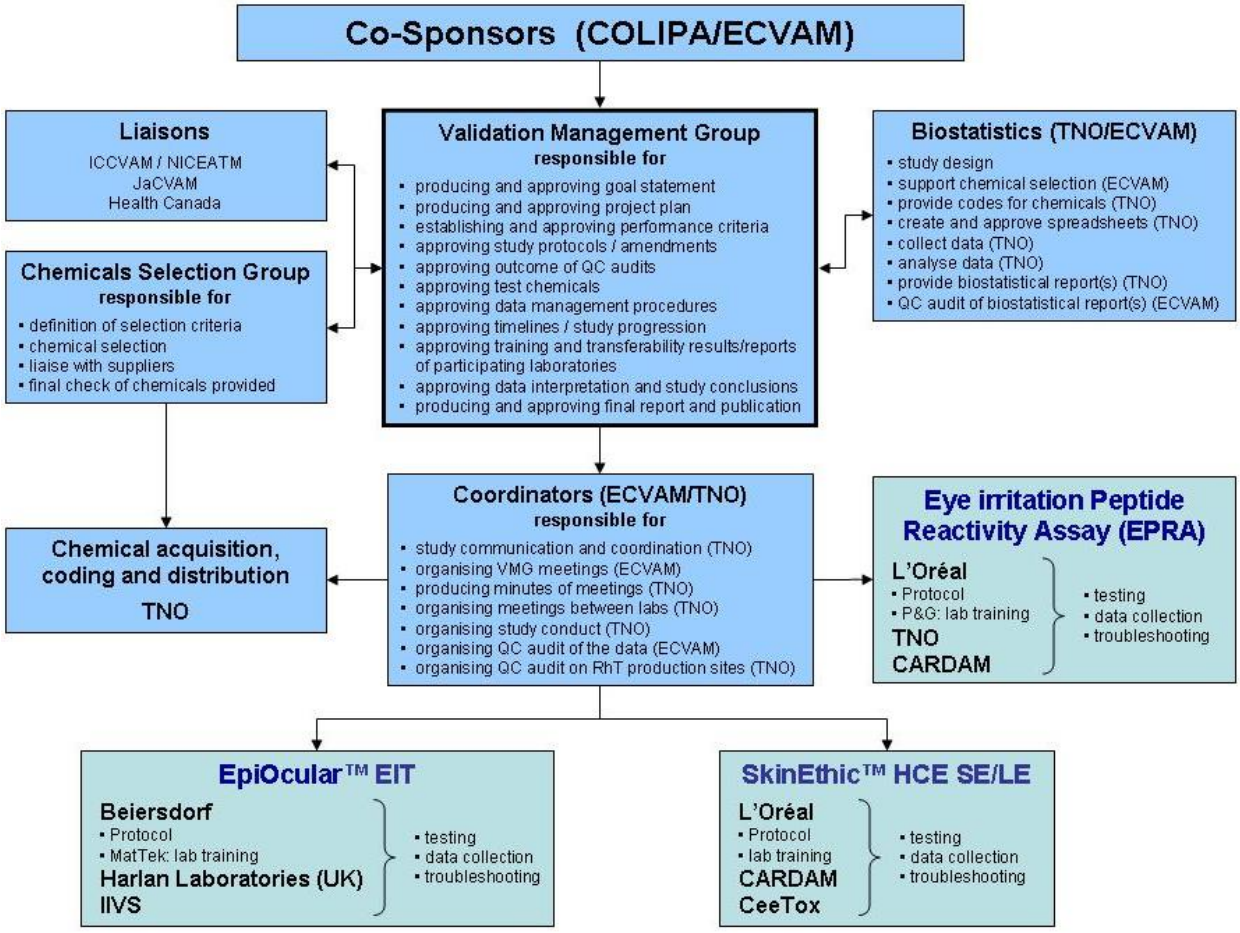
In addition, in the framework of the International Cooperation on Alternative Test Methods (ICATM), Liaisons from the USA, Japan and Canada are represented on the VMG namely:

- NICEATM (William Stokes; *alternates:* Warren Casey, David Allen, Elizabeth Lipscomb)
- ICCVAM (Jill Merrill)
- JaCVAM (Hajime Kojima)
- Health Canada (Alison McLaughlin)

Operational decisions will be taken by the core VMG only. Representation of the lead laboratories allows consultation on technical issues relating to the test systems and monitoring progress of experimental work, but will not be involved in discussions regarding the chemicals selection. The ICATM liaisons are invited to advise the VMG.

[1] From 30 September 2010, there will be no official representation from an ECVAM biostatistician in the VMG. Nevertheless, ECVAM will continue providing the planned biostatistical support to EIVS after this date.

Figure 1: Management Structure of the ECVAM Eye Irritation Validation Study



6. Study Coordination and Sponsorship

6.1. Overall study coordination

The overall study coordination will be conducted by ECVAM. This will include the organisation of all necessary VMG meetings and teleconferences, and the maintenance of a website where all EIVS documents not related to chemical selection are made available to VMG members and ICATM liaisons. ECVAM will also be responsible for organising the Quality Control audits on data collection, handling and analysis, as well as on the biostatistical reports produced by the TNO biostatistician.

6.2. Logistical coordination and communication

The TNO (Quality of Life) representative will coordinate the communication flow between all parties, draft minutes of VMG meetings and telephone conferences, organize meetings between laboratories, and organise the study conduct. TNO has also responsibility for logistics of test chemical acquisition, coding and distribution. Finally, the TNO representative will arrange quality control audits on the RhT production sites.

6.3. Study sponsorship

ECVAM and COLIPA will co-sponsor EIVS, with the main financial support being provided by COLIPA.

COLIPA will finance:

- conduct of the chemical reactivity assays
- lead and participating laboratories for the two test methods
- statistical support provided by TNO
- financial support of the independent chair of the VMG
- independent CRO responsible for the test chemicals purchase, coding and distribution to the laboratories
- overall logistical coordination of the study
- part of the independent QC audit on the RhT models production sites
- purchase cost of existing chemicals
- purchase of a proportion of the RhT tissues

ECVAM will finance:

- management and coordination of the study, including the organisation of all VMG meetings
- statistical support provided by ECVAM
- part of the independent QC audit on the RhT models production sites
- independent QC audit on data collection, handling and analysis
- independent QC audit of the biostatistical report(s)
- purchase of a proportion of the RhT tissues
- publication of the study

7. Chemicals Selection

7.1. Chemicals Selection Group (CSG)

The CSG is composed of the following members:

Tom Cole (ECVAM; coordinator)
João Barroso (ECVAM)
Chantra Eskes (independent scientist)
William Stokes (NICEATM)
Amanda Cockshott (HSE; UK Competent Authority)
Betty Hakkert (RIVM; NL Competent Authority)

The roles and responsibilities of the CSG are shown in Figure 1.

The members of Competent Authorities (Amanda Cockshott and Betty Hakkert) will give support in reviewing *in vivo* Draize eye irritation reports on CosIng ingredients provided by DG SANCO.

In the framework of the International Cooperation on Alternative Test Methods (ICATM), liaisons from NICEATM, ICCVAM, JaCVAM and Health Canada are invited to propose eligible test chemicals for selection, supported by quality assured *in vivo* Draize eye irritation data.

7.2. Chemicals selection

A principal criterion for selection of test chemicals is availability of supporting complete and quality assured *in vivo* Draize eye irritation data, for comparative evaluation of *in vitro* method predictive capacity. Complete *in vivo* Draize eye irritation data sets comprise severity and duration of ocular toxicity effects, registered over a 21 day observation period as irritation scores for corneal opacity, iritis and conjunctival chemosis/redness. Eligibility of test chemicals will be confirmed by compilation of *in vivo* Draize eye irritation data into a customised Excel template where algorithms generate systematic assignment of eye irritation EU DSD, UN GHS / EU CLP and US EPA classifications.

Intending to challenge performance of the *in vitro* tissue models, diverse chemicals will be sought that have not been previously tested during protocol R&D, optimisation and pre-validation. Therefore, in shortlisting chemicals from recognised sources (e.g., ECETOC, TSCA, ZEBET, NIHS Japan, EPA, etc.) those chemicals reported in the original test submissions will be avoided.

One potential source for screening eligible chemicals which will be considered by the CSG is the official European Commission inventory of cosmetic ingredients (CosIng). CosIng is supported by consolidated documentation (opinions) issued by the Scientific Committee on Consumer Safety (SCCS) with references to confidential *in vivo* Draize eye irritation studies archived by DG-SANCO. In collaboration with SCCS and DG-SANCO, *in vivo* Draize eye irritation data on CosIng chemicals will be reviewed, and sample material availability determined. For eligible chemicals, *in vivo* Draize eye irritation study sponsors will be requested to authorise use and eventual publication of eye irritation data and, in cases of proprietary production, to supply sample material for *in vitro* assay.

Proprietary new substances notified under Directive 67/548/EEC present another unique potential source, qualified by *in vivo* Draize eye irritation studies compliant with official guidelines and reviewed by Competent Authorities. Notification files (with summary *in vivo* Draize eye irritation data) archived in a confidential new chemicals database (NCD) accessible to authorised European Commission and Competent Authority personnel in the CSG, allow shortlisting of eligible candidates according to the notifier/producer. Under the auspices of the European Partnership for Alterative Approaches to Animal Testing (EPAA) affiliated companies will be invited to collaborate in determining availability of sample material, with release of supporting *in vivo* Draize eye irritation study reports. Initiative within cooperative companies to propose additional and/or alternative chemicals would also be welcomed.

A sample size calculation by the ECVAM biostatistician and the TNO biostatistician has shown that 104 test chemicals will be required for this validation study.

Ideally, chemical selection should achieve a balanced set of (i) irritancy (UN GHS/EU CLP categories 1 and 2 versus no category); (ii) physical state (liquids versus solids); and (iii) EPRA reactivity (reactive versus non-reactive). Acknowledging practicality of achieving a perfectly balanced set covering all three conditions, the VMG agreed the following limits: (i) an overall 50±5% split of UN GHS/EU CLP categories 1 and 2 versus no category, with a 50/50 split between category 1 and category 2, including adequate representation of UN GHS sub-categories 2A and 2B; (ii) an overall 50±10% split of solids versus liquids; and (iii) an overall 50±15% split

of reactive versus non-reactive chemicals (based on EPRA analyses). Similarly, the selection would aim for an even distribution of physical state (50±10% split of liquids versus solids) and EPRA reactivity (50±15% split of reactive versus non-reactive) among each irritancy sub-group (no category, category 2B, category 2A and category 1).

Significantly, since EPRA reactivity is not known in advance, the parameter cannot be applied as an eligibility criterion *a priori*. Thus, the VMG agreed to a wider limit of acceptance (50±15%) for the proportion of reactive versus non-reactive chemicals. In event of EPRA results demonstrating significant bias in reactivity distribution, this limit would have to be reconsidered.

The chemical selection would also aim for representation of a range of ocular toxicity effects, evident from distributions and persistence of irritation scores.

Final approval of the test chemicals proposed by the CSG is the responsibility of the core VMG. Respecting non-disclosure of chemical identities to the test facilities, the VMG lead laboratory representatives will not participate in the selection process.

The VMG recognises that commercial availability of selected test chemicals would facilitate future identification of performance standard reference chemicals, relevant to similar method catch-up studies (Performance Standards-based validation). Therefore, the CSG will limit the selection of proprietary chemicals and will aim at having at least ⅔ of commercially available chemicals (~70 chemicals) in their final chemical selection (at least 104 test chemicals), which present a balanced distribution of irritancy, physical state and reactivity similar to the overall set of selected test chemicals (see above). As such, ample scope for establishing a robust set of reference chemicals upon completion of EIVS shall be ensured.

8. Chemical Acquisition, Coding and Distribution

Independent coding and distribution of test chemicals will be contracted out by the sponsor COLIPA to TNO. TNO is certified according to ISO 9001 and GLP, and has proven experience of reliable services. TNO will purchase, code and supply existing chemicals, including cosmetic ingredients from the CosIng inventory. The CSG coordinator will ask companies producing new chemicals to send samples directly to TNO for coding and distribution. All test chemicals will be randomly coded. Each test chemical will have a code that is unique for each laboratory. The same code will be used for the SkinEthic™ HCE SE and for the SkinEthic™ HCE LE assays but otherwise distinct codes will also be used for each test method/assay (i.e., EpiOcular™ EIT, SkinEthic™ HCE SE/LE and EPRA) that is run in the same laboratory. The codes will be generated and provided by the TNO biostatistician. Expiry dates will be provided for all test chemicals. Furthermore, when available, a single Molecular Weight and a single purity for each coded test chemical will be provided to the laboratories performing the EPRA to allow preparation of Molar solutions, as required by the EPRA Protocol. This includes pure substances and mixtures. For mixtures, the single purity will be determined by the sum of the proportion of its components (excluding water), while the single Molecular Weight will be determined by considering the individual Molecular Weights of each component in the mixture (excluding water) and their individual proportions. In exceptional cases (e.g., complex mixtures or polymers) Molecular Weights and exact proportions of components may not be available.

Personnel responsible for chemical acquisition, coding and distribution shall be independent from those conducting the EPRA for EIVS.

9. Receipt and Handling of Chemicals

Coded test chemicals as well as a health and safety information package will be dispatched to the Safety Officer of each participating laboratory (see sections 10.1-10.3 and 11.4) in appropriate packaging, compliant with relevant regulatory requirements. The participating laboratories shall be notified by TNO when the test chemicals are shipped, shall make proper provision for their receipt, and promptly acknowledge that they have been received. Upon receipt at the laboratory, the test chemicals shall be stored in appropriate storage conditions as indicated in the unsealed accompanying documentation and must be stored for at least six months following submission of the final biostatistical report to the VMG.

The health and safety information package will include a sealed envelope for each test chemical identified by chemical code. Each envelope will contain a MSDS and a certificate of analysis for the respective test chemical. A sealed envelope shall be opened at the laboratory only in an emergency/need-to-know situation. At the end of EIVS, the Safety Officer shall return the health and safety information package with all unopened envelopes to the VMG (Logistics Coordinator). If a sealed envelope from the health and safety information package is opened by the laboratory, the Safety Officer shall immediately notify the VMG designated contact, i.e. the Logistics Coordinator (Jan Lammers, TNO).

The Study Director of each laboratory (see sections 10.1-10.3 and 11.1) shall receive essential information about the test chemicals (e.g. storage instructions). Upon receipt, each laboratory must complete and return the Test Chemical Receipt Report (Annex I).

Appropriate routine safety procedures shall be followed in handling the test chemicals unless otherwise specified in the unsealed documentation supplied at the time of chemical distribution. Laboratory personnel shall be instructed to treat all coded test chemicals as very hazardous and to dispose of laboratory waste as toxic waste.

10. Participating Laboratories

The laboratories participating in the study are defined as shown in Figure 1. The specific obligations and responsibilities of the participating laboratories will be specified in contracts between the sponsor COLIPA and the laboratories. These include, but are not limited to, the adherence to this project plan throughout the study, the adherence to the test method protocol, the adherence to the work program, assuring compliance with GLP-like principles, specifying and applying proper Quality Assurance procedures, and meeting the data submission deadlines. The participating laboratories shall have competence in performing the test method(s) and shall provide competent personnel, adequate facilities, equipment, supplies, and proper health and safety guidelines. The lead laboratories are further responsible for preparing detailed protocols for the EpiOcular™ EIT, SkinEthic™ HCE SE/LE and EPRA, and for providing training to the technical staff of the other testing facilities. The contracts between COLIPA and the laboratories should also clarify the ownership of results and the publication procedures.

The participating laboratories are allowed to freely communicate and meet during the training and transfer phases of EIVS. Such meetings will be organized by the lead laboratories and can occur without a formal approval by the VMG. However, during the testing phase, the participating laboratories and the personnel responsible for providing training on the test methods, will no longer contact each other regarding this validation study without the previous knowledge and approval by the VMG. All VMG approved meetings or other forms of communication between the participating laboratories during the testing phase will be organized by the Logistics Coordinator in collaboration with the lead laboratories.

10.1. Cys/Lys EPRA

Three laboratories will participate in EIVS for testing with the EPRA. These are:

- Lead laboratory – L'Oréal
  - Study Director: Nathalie Alépée
  - Safety Officer: Joan Eilstein
- Laboratory 1 – TNO
  - Study Director: Brigitte Buscher
  - Safety Officer: Hans Ram
- Laboratory 2 – CARDAM
  - Study Director: Griet Jacobs
  - Safety Officer: Frank Vander Plaetse / Katrien Smits

10.2. EpiOcular™ EIT

Three laboratories will participate in EIVS for testing with the EpiOcular™ EIT. These are:

- Lead laboratory – Beiersdorf
  - Study Director: Uwe Pfannenbecker
  - Safety Officer: Peter Klaws
- Laboratory 2 – Harlan Laboratories Ltd. (UK)
  - Study Director: Andrew Whittingham
  - Safety Officer: Christine Cauldwell
- Laboratory 3 – IIVS
  - Study Director: Hans Raabe
  - Safety Officer: Nathan Wilt

A reserve laboratory is also identified as Pierre-Fabre (Contact Person: Sandrine Bessou-Touya)

10.3. SkinEthic™ HCE SE/LE

Three laboratories will participate in EIVS for for testing with the SkinEthic™ HCE SE/LE. These are:

- Lead laboratory – L'Oréal
  - Study Director: Nathalie Alépée
  - Safety Officer: Samuel Blond
- Laboratory 2 – CARDAM
  - Study Director: An van Rompay
  - Safety Officer: Frank Vander Plaetse / An Jacobs
- Laboratory 3 – CeeTox Inc.
  - Study Director: Colleen Toole
  - Safety Officer: Karen Rutherford

A reserve laboratory is to be identified.

11. Laboratory Personnel

11.1. Study Directors

Each participating laboratory shall appoint a Study Director (see sections 10.1-10.3), a scientist of appropriate education, training, and experience in the field. The Study Director represents the single point of study control with ultimate responsibility for the overall technical conduct of the study, the documentation and reporting of the results, as well as GLP adherence or adherence to the minimum quality requirements (see section 14).

The Study Director is responsible for collecting the data of his/her laboratory and to send them to the Logistics Coordinator of the study (to be forwarded to the TNO biostatistician) according to the timelines established in the Project Plan (see section 17).

The Study Directors are also responsible for sending timely Study Reports to the contact person of the VMG, i.e. the Logistics Coordinator, who will monitor the progress of the study. Such reports should include all relevant experimental data as well as all deviations from the Project Plan and Test Method protocols.

The study directors will be the primary contact point for the communications between the VMG and the testing facilities unless otherwise requested.

11.2. Quality Assurance (QA) Officers

For participating laboratories that are GLP compliant the Quality Assurance Officer shall assure conformity with GLP requirements for all aspects of the study (facilities, equipment, personnel, methods, practices, records, controls, SOPs, Test Method protocol, final reports (for data integrity), and archives). The Quality Assurance Officer is entirely separate from and independent of the personnel engaged in the direction and conduct of the study.

Participating laboratories that are not GLP compliant, shall appoint an individual to assure that all records, documents, raw data and reports are available to the VMG if an inspection is requested, and ensure that the quality assurance provisions detailed in the section 14 (see below) have been implemented.

11.3. Experimental team

The conduct of the EpiOcular™ EIT, SkinEthic™ HCE SE/LE and EPRA requires personnel trained and competent in the specific techniques and general laboratory procedures. Each individual engaged in the conduct of, or responsible for, the supervision of a validation study shall have education, training, and experience, or combination thereof, to enable that individual to perform the assigned duties.

11.4. Safety Officers

A designated Safety Officer (not otherwise involved in the actual conduct of the validation study) at each participating laboratory (see sections 10.1-10.3) will receive the blinded (coded) test chemicals and shall transfer the test chemicals to the responsible person of the laboratory. Sealed Material Safety Data Sheets (MSDSs) will accompany the test chemicals and the Safety Officer shall retain the package until the completion of EIVS. Additional sealed MSDSs can be sent to the testing facilities upon request of the Safety Officer if this information needs to be kept in more than one location. At the end of the validation study, the Safety Officer shall return the unopened

packages to the Logistics Coordinator of the study. If any laboratory personnel should open the packages at any time during the validation study, the Safety Officer shall promptly notify the VMG through the Logistics Coordinator (Jan Lammers, TNO).

12. Study Design

12.1. Eye irritation Peptide Reactivity Assay ("chemical reactivity")

Chemical reactivity is defined in this validation study as the electrophilic potential to react with cysteine or lysine containing peptides.

The lead laboratory for the Cysteine/Lysine Eye Irritation Peptide Reactivity Assay (EPRA) is L'Oréal. Training of the other participating laboratories (TNO and CARDAM) in conducting the EPRA shall be provided by the test method developer (Procter & Gamble). The lead laboratory in collaboration with the test method developer will be responsible for issuing a final test method protocol. Upon completion of the training phase, participating laboratories shall test 5-10 test chemicals to demonstrate transferability of the assay and to confirm test method protocol adequacy. Importantly, training of TNO and CARDAM in conducting the EPRA and their respective transferability studies will not occur at the same time during EIVS because TNO will be involved in testing for chemical selection and for reliability assessment while CARDAM will only do testing for reliability assessment (see below). The trained participating laboratories will be responsible for issuing training and transfer reports upon completion of the transferability study. The results of the training phase and of the transferability study of a laboratory will be reviewed and approved by the VMG before that laboratory progresses with testing for EIVS (testing phase). If the transferability data do not meet test acceptance criteria, the VMG will work with the participating laboratory and the lead laboratory to identify the problems and make corrections where needed.

In a first stage of the EIVS testing phase, all eligible chemicals identified by the CSG will have their chemical reactivity determined based on the EPRA, in a blind study in a single laboratory (TNO), with a single test consisting of three replicate measurements. Since chemicals found eligible by the CSG will not all become available for EPRA testing at TNO at the same time (due to differences in the time required to gain access to *in vivo* Draize eye irritation study reports for different chemicals, and to differences in the time required to obtain commercially available and proprietary chemical samples), the selection of a final test chemical set will be phased, with subsets of 30-50 test chemicals being selected by the CSG in different stages, as the data from the EPRA analysis becomes available, and until the final amount of at least 104 test chemicals is reached. These chemical subsets shall be as balanced as possible considering the criteria described in section 7.2 (with some flexibility allowed) and, upon approval by the core VMG, they will be distributed to the participating laboratories for viability assessment. Importantly, the total chemical set of at least 104 test chemicals (considering all selected subsets) shall be well balanced and meet all the criteria defined in section 7.2.

Upon completion of the viability assessment study, a preliminary evaluation of the usefulness of the SkinEthic™ HCE test strategy composed of the EPRA, the SkinEthic™ HCE SE and the SkinEthic™ HCE LE assays will be performed using the reactivity data obtained by TNO for all the selected test chemicals (at least 104) and the viability data obtained with SkinEthic™ HCE SE and SkinEthic™ HCE LE for the same test chemicals. If by combining the three assays in a test strategy a better predictive capacity is obtained as compared to the SkinEthic™ HCE SE or the SkinEthic™ HCE LE assays alone, chemical reactivity data will be obtained for a subset of the full validation set, in three laboratories (L'Oréal, TNO and CARDAM), in a second step to assess the reliability of the EPRA. Each of these three laboratories will test each test chemical in this subset

in three independent tests (performed in separate runs) consisting of three replicate measurements each, in order to strictly determine reproducibility (WLR and BLR) of the EPRA. TNO, as one of the three laboratories, will be testing these chemicals in three new independent tests (performed in separate runs).

The definitive number and characteristics of the chemicals to be tested for reliability assessment of the EPRA will be decided on later by the VMG with the help of statistical power analysis performed by the biostatisticians, but at least 20 chemicals and up to the maximum number of chemicals that can be tested in two separate runs for one peptide will be tested. When selecting the subset of test chemicals to assess the reliability of the EPRA, preference will be given to test chemicals that classify differently in SkinEthic™ HCE SE and SkinEthic™ HCE LE, since this would allow the use of these data for calculating the predictive capacity of the SkinEthic™ HCE test strategy. However, if all of these cannot be included in the selection, the data of a single test acquired by TNO for the selected test chemicals (at least 104) will be used to determine the predictive capacity of the proposed SkinEthic™ HCE test strategy, and other chemicals may be chosen for reliability assessment.

12.2. Biological assays

The lead laboratories for the EpiOcular™ EIT and the SkinEthic™ HCE SE/LE are Beiersdorf and L'Oréal, respectively. Training of the participating laboratories in conducting the EpiOcular™ EIT or the SkinEthic™ HCE SE/LE assays shall be provided by the respective test method developer (MatTek Corporation for EpiOcular™ EIT and L'Oréal for SkinEthic™ HCE SE/LE). The lead laboratories in collaboration with the test method developers will be responsible for issuing final test method protocols. Upon completion of the training phase, participating laboratories shall test 5-10 chemicals to demonstrate transferability of the assay and to confirm test method protocol adequacy. The test method developers in collaboration with the participating laboratories will be responsible for issuing training and transfer reports upon completion of the transferability studies. The results of the training phase and of the transferability studies for a particular test method will be reviewed and approved by the VMG before progression of the study for that test method. If the transferability data do not meet test acceptance criteria, the VMG will work with the participating laboratory and the lead laboratory to identify the problems and make corrections where needed.

In the testing phase of EIVS, each of the test chemicals in the final chemical selection set (at least 104 test chemicals) will be tested in the three assays (EpiOcular™ EIT, SkinEthic™ HCE SE and SkinEthic™ HCE LE) in at least three independent tests (using different tissue batches and performed in separate runs) by each of three independent laboratories (see Document "Guidance on Study Conduct and Test Method Performance Criteria for EIVS"). Thus, each chemical will be tested with the two different exposure/post-treatment periods of the SkinEthic™ HCE SE/LE protocol (10 min and 1 h + 16 h post-treatment), and with one of the two EpiOcular™ EIT exposure procedures depending on the test chemical being solid or liquid (30 min + 120 min post-treatment, or 90 min + 18 h post-treatment). Importantly, the three laboratories participating in the validation of EpiOcular™ EIT will **not** be instructed on the physical state of the test chemicals. Therefore, each laboratory participating in the validation of the EpiOcular™ EIT shall decide on the physical state of each test chemical and the appropriate exposure procedure to use. Finally, each control and test chemical included in one run will be tested in two (EpiOcular™ EIT) or three (SkinEthic™ HCE SE/LE) replicate tissues.

The EIVS RhT testing phase will be conducted in two or more consecutive phases to allow for periodic opportunities to evaluate the frequency of technical errors and any other problems that might occur during testing. At least at the end of each RhT testing phase the Study Directors will forward the data acquired by their laboratories to the Logistics Coordinator after internal quality check (see Table 2 in section 17) who will provide it to the TNO biostatistician for immediate

preliminary analyses of Within Laboratory Reproducibility (WLR) and compliance with Study Quality criteria (number of complete/incomplete test sequences as described in the Performance Criteria). Once completed, these phased statistical analyses and their conclusions will be provided to the core VMG who will review them and determine if modifications to the protocol and/or study plan are warranted/appropriate in order to avoid future occurrences of identified issues. All participating laboratories should adhere to these testing phases and ideally complete testing of all chemicals in one phase (by obtaining three qualified tests per chemical) before testing chemicals of following phases. However, for practical reasons and in order to minimise the cost of the study, the participating laboratories may delay the testing of MTT reducers and/or colorants in order to test them all together in a later testing phase, provided delayed chemicals will not expire. Moreover, chemicals with short expiry dates included in later testing phases of the study may be moved to an earlier phase to avoid testing after the expiration date.

13. Data Collection, Handling, and Analysis

The Logistics Coordinator will collect the data from each participating laboratory via the Study Directors (see section 11.1) at least at the end of each RhT testing phase (see section 12.2 and Table 2 in section 17) and will forward it to the TNO biostatistician. The TNO biostatistician will organise the data in specific data collection software (MS EXCEL spreadsheets). The collected data shall be circulated to every participating laboratory for a quality check. At the end of each RhT testing phase a preliminary analysis of WLR and compliance with Study Quality criteria (see above) will be performed without decoding the test chemicals (to avoid breaking the code before completion of the study). Upon completion of the RhT testing phases by all participating laboratories and preliminary "blind" determination of WLR and Study Quality criteria for each laboratory, test chemicals will be decoded and the TNO biostatistician will do a complete statistical analysis of the data and provide a final biostatistical report to the VMG. The ECVAM biostatistician will do a quality control of the processes of data collection, handling and analysis, as well as of the final biostatistical report. The data management procedures and statistical tools that will be used for data analysis and included in the final biostatistical report will be described in a Statistical Analyses and Reporting Plan. This Plan shall be developed by the ECVAM and TNO biostatisticians before the end of the experimental phase of the study and shall be approved by the VMG before the biostatistical analyses begin.

Based on final data analysis, the VMG reserves the possibility to identify the most suitable test strategies for the identification of non classified chemicals from classified ones.

The VMG has the responsibility of producing the final report and publication of the study. These will include the results of the EIVS and the VMG conclusions/recommendations on the outcome of the study. VMG conclusions/recommendations will be supported by the Performance Criteria defined by the VMG prior to initiation of the testing phase of EIVS. The draft statistical report and the draft validation study report shall be circulated to every participating laboratory for review and comments prior to finalisation. The VMG should review all comments received and make revisions if deemed appropriate.

14. Quality Assurance, Good Laboratory Practice

14.1. Laboratories

Participating laboratories that are compliant with Good Laboratory Practices (GLP) will perform the studies in accordance with GLP standards (OECD, 1999). Non GLP-compliant laboratories shall use the OECD principles of GLP as guidelines for conducting the validation study. Any

deviations from these principles should be documented along with a discussion of their impact on the study results.

It is considered that the following requirements (Balls M. *et al.*, 1995) are essential for the mutual acceptance of information produced in the validation process:

- Qualified personnel, and appropriate facilities, equipment and materials shall be available for the timely and proper conduct of the study
- Records of the qualifications, training and experience, and a job description for each professional and technical individual involved in the study, shall be maintained.
- For each study, an individual with appropriate qualifications, training and experience shall be appointed to be responsible for its overall conduct and for any report issued (Study Director, see section 11.1).
- Instruments used for the generation of experimental data shall be inspected regularly, cleaned, maintained and calibrated according to established SOPs, if available, or to manufacturers' instructions. Records of these processes shall be kept, and made available for inspection on request.
- Reagents shall be labelled, as appropriate, to indicate their source, identity, concentration and stability. The labelling shall include the preparation and expiry dates, and specific storage conditions.
- All data generated during a study shall be recorded directly, promptly and legibly by the individual(s) responsible. These entries shall be attributable and dated.
- All changes to data shall be identified with the date and the identity of the individual responsible, and a reason for the change shall be documented at the time.

14.2. Tissue model suppliers

According to OECD GLP Consensus Document No.5 "*Compliance of Laboratory Suppliers with GLP Principles*" the responsibility for the quality and fitness for use of equipment and materials rests entirely with the management of the test facility (OECD, 1999).

The acceptability of equipment and materials in laboratories complying to GLP principles should therefore be guaranteed to any regulatory authority to whom studies are submitted. In some countries where GLP has been implemented, suppliers belong to national regulatory or voluntary accreditation schemes (for example, for laboratory animals) which can provide users with additional documentary evidence that they are using a test system of a defined quality.

The audits on the RhT tissue production sites (MatTek Corporation and EpiSkin Laboratories) will be carried out by TNO and ECVAM, and will focus on the procedures established to guarantee a defined quality of the tissue models, as defined in the audit protocol previously approved by the VMG.

15. Health and Safety

Each laboratory shall conform to all applicable statutes in effect at the time of this validation study. The designated Safety Officer (see sections 10.1-10.3 and 11.4) shall be the point of contact for health and safety issues.

16. Records and Archives

At the end of EIVS, the original raw (if applicable; not possible for GLP compliant laboratories) and processed data or copies thereof shall be submitted to ECVAM and COLIPA for storing and

archiving. In addition, other records relevant to EIVS (instrument logs, calibration records, facility logs, etc.) should be made available for inspection upon request by the VMG.

Raw and processed data or copies thereof (depending if the laboratory is or not GLP compliant) shall be stored and archived at the participating laboratory for at least five years after completion of EIVS. The data which are stored electronically shall be periodically copied, and backup files shall be produced and maintained.

17. Timelines

The following tables summarise the critical activities of the study and the estimated completion timelines. Timelines might need to be reviewed during the study.

Table 1. Study timelines

Critical activities	Timing (*finalisation)
Chemical eligibility / availability from suppliers	
o NCD	o 29 October 2010
o Existing	o VMG III 3-4 June 2009*
o CosIng	o 29 October 2010
o EPA	o 29 October 2010
Project Plan	
o Finalisation	o VMG VII 28-29 September 2010
o Approval by VMG	o 1 December 2010
Guidance on Study Conduct and Test Method Performance Criteria for EIVS	
o Finalisation	o VMG VII 28-29 September 2010
o Approval by VMG	o 1 December 2010
Study design approval by VMG	o 30 July 2009*
EPRA	
o Cut-off for EPRA	o VMG III 3-4 June 2009*
o EPRA updated/final Protocol approval	o 18 December 2009* (slightly revised and approved on VMG VII 28-29 September 2010)
o EPRA study plan	o VMG V 24-25 November 2009*
o # and identity of chemicals tested for reproducibility assessment of EPRA	o T.b.d. by July 2011
EPRA testing at TNO for chemicals selection	
o Training	o 3-4 June 2009*
o Transferability study	o 13 July-16 October 2009*
o Beginning of testing	o March 2010
EPRA reliability assessment	
o Training	o T.b.d. by March 2011
o Transferability study	o T.b.d. by March 2011
o Beginning of testing	o T.b.d. by July 2011

SkinEthic™ HCE SE/LE o Performance under UN GHS classification (TST data) o QA audit on RhT production site o Training o Transferability study o SkinEthic™ HCE SE/LE final Protocol approval o Beginning of testing (see Table 2)	 o VMG III 3-4 June 2009* o 19 March 2010* o 19-29 January 2010* o 8 February-9 April 2010* o 17 June 2010* o 21 June 2010*
EpiOcular™ EIT o QA audit on RhT production site o Insert to be used o Cut-off to be used o Training o Transferability study o Final Protocol approval o Beginning of testing (see Table 2)	 o 26 May 2010* o 9 September 2010* o 9 September 2010* o October-November 2010 o November 2010 o December 2010 o January 2011
CSG final chemical selection and Core VMG approval o 1st set (34 test chemicals) o 2nd set (46 test chemicals) o 3rd and final set (24-27 test chemicals)	 o 10 June 2010* o 8 September 2010* o 10 December 2010
Chemical coding and distribution	June 2010-January 2011
Participating laboratory contracts	December 2009-January 2011
Contract with SkinEthic Laboratories for the supply of SkinEthic™ HCE tissues	February 2010
Contract with MatTek corporation for the supply of EpiOcular™ tissues	April 2010
Delivery of final statistical report (biostatistician)	Within 2 months after completion of testing phase
Delivery of final study report (VMG)	Within 2 months after finalisation of the statistical report

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621 **Table 2. Testing and data collection timelines**

RhT testing phase	SkinEthic™ HCE SE/LE	EpiOcular™ EIT
1st Phase	**34 test chemicals (selected on 10/06/2010)** Starting date: 21 June 2010 Finishing date: February 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by February 2011	**~40 test chemicals (½ liquids, ½ solids)** Starting date: December 2010 Finishing date: March 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by March 2011
2nd Phase	**46 test chemicals (selected on 08/09/2010)** Starting date: October 2010 Finishing date: May 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by May 2011	**~40 test chemicals** Starting date: March 2011 Finishing date: May 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by May 2011
3rd Phase	**24-27 test chemicals** Starting date: March 2011 Finishing date: July 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by July 2011	**24-27 test chemicals** Starting date: May 2011 Finishing date: July 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by July 2011

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623 # 18. Documents and Data

624 1. ECVAM and/or the Logistics Coordinator, after consultation with the VMG, supplies EIVS
625 documentation 'in confidence' to participating laboratories. Unless and until ECVAM places these
626 documents in the public domain, they may not be published or communicated/distributed to other
627 third parties without the knowledge and consent of ECVAM after consultation with the VMG.

628 2. All study data generated by the contracted laboratories are the property of the European
629 Commission/ECVAM and COLIPA. These data may not be published, communicated or
630 circulated/distributed to third parties without the knowledge and consent of the European
631 Commission/ECVAM and COLIPA, and the knowledge of the VMG.

632 4. ECVAM and COLIPA reserve the right to be the first to promptly publish and communicate the
633 outcomes of the validation process.

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19. References

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Annex I - Test Chemicals Receipt Report Template

Testing Facility:

Test Chemicals Received by:

Test Chemicals Receipt Date:

General Comments:

Test Chemical Code	Storage Conditions	Expiry date	Physical Appearance (colour physico-chemical state)	Container Appearance (vial and lid)	Deviations from description of the chemical	Was the envelope included in the health and safety information package received intact and unopened?	Other remarks
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	

Test Chemical Code	Storage Conditions	Expiry date	Physical Appearance (colour physico-chemical state)	Container Appearance (vial and lid)	Deviations from description of the chemical	Was the envelope included in the health and safety information package received intact and unopened?	Other remarks
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	

Test Chemical Code	Storage Conditions	Expiry date	Physical Appearance (colour physico-chemical state)	Container Appearance (vial and lid)	Deviations from description of the chemical	Was the envelope included in the health and safety information package received intact and unopened?	Other remarks
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	

Test Chemical Code	Storage Conditions	Expiry date	Physical Appearance (colour physico-chemical state)	Container Appearance (vial and lid)	Deviations from description of the chemical	Was the envelope included in the health and safety information package received intact and unopened?	Other remarks
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	

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Annex 2

Statistical analysis on the EpiOcular™ EIT post-optimisation validation study

Eye Irritation Validation Study (EIVS)

statistical analysis of the data generated under SOP ver 8.0 of EpiOcular™ EIT -solid test substances, laboratory Beiersdorf-

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March 3, 2014

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1 Introduction

The main objective of this report is to provide statistical analysis of the data generated in the second phase of the EpiOcular^{TM} EIT validation trial, i.e. the evaluation of reproducibility and predictive capacity of an optimised solids protocol. This second phase was performed in the laboratory Beiersdorf with a set of 60 coded solid chemicals (see Table 1). The optimized EpiOcular^{TM} EIT Solids protocol is based on an amended Standard Operating Procedure (SOP) Version 8.0, which includes an extended exposure time for solid test substances. Results can be found in Sections 3 to 4.

EIVS#	Code1	GHS	CAS	Name
28	B249	NC	118-82-1	4,4'-Methylene bis-(2,6-di-tert-butylphenol)
29	B267	NC	3234-85-3	Tetradecyl tetradecanoate
30	B204	NC	598-65-2	1,1-Dimethylguanidine sulphate
31	B298	NC	14075-53-7	Potassium tetrafluoroborate
32	B285	NC	84540-47-6	2,6-Dihydroxy-3,4-dimethylpyridine
33	B232	NC	23920-15-2	2,2'-[[4-[(2-Methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol
34	B218	NC	3179-89-3	2,2'-[[3-Methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol
35	B275	NC	1603-02-7	2,5,6-Triamino-4-pyrimidinol sulphate
36	B290	NC	101-20-2	1-(4-Chlorophenyl)-3-(3,4-dichlorophenyl) urea
37	B242	NC	61788-85-0	Polyethylene glycol (PEG-40) hydrogenated castor oil
38	B237	NC	103597-45-1	2,2'-Methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol)
39	B274	NC	187393-00-6	2,2'-[6-(4-Methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol]
40	B287	NC	75150-29-7	Acrylamidopropyltrimonium chloride/acrylamide copolymer
41	B224	NC	88122-99-0	Tris(2-ethylhexyl)-4,4',4"-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate
42	B246	NC	66170-10-3	Trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate
43	B245	NC	302776-68-7	Hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate
44	B262	NC	231278-20-9	[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine
45	B284	NC	72956-09-3	1-(9H-Carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol
46	B283	NC	68610-92-4	Cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%)
47	B260	NC	120-14-9	3,4-Dimethoxy benzaldehyde
48	B243	NC	7631-90-5	Sodium hydrogensulphite
49	B266	NC	94-13-3	Propyl-4-hydroxybenzoate
50	B278	NC	144550-36-7	Iodosulfuron-methyl-sodium
51	B222	NC	33089-61-1	1,5-Di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene
52	B205	NC	53112-28-0	2-Anilino-4,6-dimethylpyrimidine
53	B299	NC	153719-23-4	3-(2-Chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine
108	B634	NC	145701-23-1	Florasulam
109	B332	NC	82-66-6	Diphacinone
61	B221	2B	83-72-7	2-Hydroxy-1,4-naphthoquinone
62	B225	2B	104-36-9	1,4-Dibutoxy benzene
63	B231	2B	62-23-7	4-Nitrobenzoic acid
64	B228	2B	96568-04-6	Ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate
65	B253	2B	79-92-5	2,2-Dimethyl-3-methylenebicyclo [2.2.1] heptane
66	B226	2B	3926-62-3	Sodium chloroacetate
110	B451	2B	82657-04-3	Bifenthrin
73	B268	2A	1119-62-6	3,3'-Dithiopropionic acid
74	B282	2A	16867-03-1	2-Amino-3-hydroxy pyridine
75	B254	2A	532-32-1	Sodium benzoate
76	B201	2A	362525-73-3	6,7-Dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one
77	B296	2A	189813-45-4	Methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate
78	B271	2A	76855-69-1	(2R,3R)-3-((R)-1-(Tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate
79	B235	2A	6484-52-2	Ammonium nitrate
111	B447	2A	619-66-9	4-Carboxybenzaldehyde
112	B608	2A	83-56-7	1,5-Naphthalenediol
113	B202	2A	74918-21-1	1,3-Bis-(2,4-diamnophenoxy)-propane tetrachloride
93	B250	1	110-03-2	2,5-Dimethyl-2,5-hexanediol
94	B213	1	143-07-7	Dodecanoic acid
95	B294	1	41253-21-8	1,2,4-Triazole sodium salt
96	B255	1	86-87-3	1-Naphthalene acetic acid
97	B291	1	62-76-0	Sodium oxalate
98*	B252*	1	4430-25-5	4,4'-(4,5,6,7-Tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide
99	B214	1	2634-33-5	1,2-Benzisothiazol-3(2H)-one
100	B233	1	60372-77-2	Ethyl lauroyl arginate HCl
101	B281	1	97404-02-9	2-[(4-Aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride
102	B279	1	27344-41-8	Disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate)
103	B244	1	2820-37-3	3,4-Dimethyl-1H-pyrazole
104	B207	1	171887-03-9	N-(2-Amino-4,6-dichloropyrimidin-5-yl) formamide
105	B261	1	54424-29-2	1,2-Dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate
114	B293	1	105812-81-5	3-piperidinemethanol, 4-(4-fluorophenyl)-1-methyl-, (3S,4R)
115	B276	1	65-85-0	Benzoic acid

EIVS#: chemicals selection number, Code1: code Beiersdorf under optimized protocol.

Table 1: Chemical Selection for Post-Optimisation Validation Activity for EpiOcular^{TM} EIT solids prtocol.

To provide a more complete information about performance of the assay, the data obtained

with the optimized EpiOcular^{TM} EIT Solids protocol at Beiersdorf are integrated with data obtained with the EpiOcular^{TM} EIT Liquids protocol at three test facilities. Two classification cut-off values 50% and 60% are considered for both solids and liquids protocols. Results can be found in Section 5.

2 Note about chemicals

Out of 60 test chemicals, one chemical was excluded from final evaluation, i.e. chemical 98(denoted by asterix in Table 1), due to a too strong colour interference on the MTT assay.(strong colorant)

Chemical 37 was originally selected by the EIVS VMG as being a solid. However, all three laboratories participating in the core validation of theEpiOcular^{TM} EIT independently considered the chemical as being liquid due to its low melting point and testing during the spring/summer period. This chemical was therefore tested during the core EIVS using the liquid protocol of EpiOcular^{TM} EIT. However, due to an oversight of the VMG, chemical 37 was again shipped to Beiersdorf as a solid to be tested during the validation of the EpiOcular^{TM} EIT optimised solids protocol and because this time the testing occurred during the autumn/winter, Beiersdorf confirmed the physical state of the chemical as being solid upon receipt and tested it as such. Thus, chemical 37 ended up being tested in both the liquids and solids protocols of EpiOcular^{TM} EIT, somehow in agreement with its borderline physical state. The VMG considered both sets of data as being valid and therefore the statistics analyses in this report include both sets of data for this chemical (produced with the original liquids and the optimised solids protocols). Nevertheless, the EpiOcular^{TM} EIT predictive capacity was also calculated considering only the optimised solids protocol data (excluding the liquids protocol data) in accordance with the fact that this chemical had been tested in vivo as a solid and had been originally considered by th VMG as a solid during chemicals selection for the study. The corresponding accuracy values are described in chapter 4.

3 Reproducibility

The objective of this section is to compare final viabilities generated at Beiersdorf and MatTek under optimized EpiOcular^{TM} EIT Solids protocol. To guarantee comparability of the results, the comparison is made on the common set of chemicals tested. Two sets of chemicals are used for the comparison:

- **Dataset 1.** Set of 11 compounds provided by Cosmetics Europe to MatTek for optimization of the EpiOcular^{TM} EIT Solids protocol,
- **Dataset 2.** largest common set of compounds (20) used at Beiersdorf and MatTek under optimized EpiOcular^{TM} EIT Solids protocol.

The Dataset 2 contains Dataset 1 and additional chemicals that belong both to a) the set of 60 chemicals tested at Beiersdorf and b) the set of 39 chemicals from an article by Kaluzhny et al. (2011) tested at MatTek under optimized EpiOcular^{TM} EIT Solids protocol.

3.1 Within laboratory reproducibility

The acceptance criterion for within laboratory reproducibility (WLR) is a minimum concordance of classifications of 85%. The Table 2 reports the WLR statistics based on the data generated under optimized EpiOcular^{TM} EIT Solids protocol at Beiersdorf as well as the WLR obtained in the validation of the original solids protocol by the three participating laboratories. It can be seen that the optimised protocol provides similar (or even slightly better) WLR than the original protocol.

		50% cut-off		**60% cut-off**	
optimized solids protocol	BDF	93.2%	(55/59)	96.6%	(57/59)
original solids protocol	BDF	92.0%	(46/50)	94.0%	(47/50)
	Harlan	90.2%	(46/51)	90.2%	(46/51)
	IIVS	96.1%	(49/51)	94.1%	(48/51)
	Total	92.8%	(141/152)	92.8%	(141/152)

Table 2: Within Laboratory Reproducibility (WLR) statistics for cut-off 50% and 60%.

3.2 Between Laboratory Reproducibility(BLR): Beiersdorf and MatTek laboratories

To calculate BLR, the final classification for each test chemical in each participating laboratory is obtained by using the arithmetic mean value of viability over different qualified tests performed. Using a 60% cut-off, the BLR (optimised solids protocol) for Dataset1 is 73% (8/11) whereas 85% (17/20) for Dataset2. Identical BLR was obtained with the same set of chemicals with the original protocol, although in this case the reproducibility is calculated for 3 labs while only 2 for the optimised protocol. Nevertheless the acceptance criterion of BLR $> 80\%$ is met in this dataset. See Tables 3-6 for detailed calculations.

				optimized protocol								original protocol								
EIVS #	Code1	Code2	GHS	MatTek				Beiersdorf				Beiersdorf			Harlan			IIVS		
				single			mean	single			mean									
35	B275	C011	NC	NI	NI	NI	NI	I	I	NI	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
37	B242	C002	NC	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
40	B287	C008	NC	NI	NI	NI	NI	NI	I	NI	NI	I	NI	NI	NI	NI	NI	NI	NI	NI
42	B246	C004	NC	I	I	I	I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
46	B283	C007	NC	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
62	B225	C001	2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
73	B268	C005	2A	I	NI	I	I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
74	B282	C006	2A	I	I	I	I	NI	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
77	B296	C003	2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
78	B271	C010	2A	NI	I		NI	NI	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
102	B279	C009	1	I	I	I	I	I	I	I	I	I	NI	NI	I	NI	NI	NI	NI	NI
			WLR	82% (9/11)				64% (7/11)				82% (9/11)			91% (10/11)			100% (11/11)		
			BLR	82% (9/11)								91% (10/11)								

EIVS #: chemicals selection number, Code1: code Beiersdorf under optimized protocol, Code2: Cosmetics Europe codes of 11 chemicals provided to MatTek for optimization

Table 3: Dataset1. Classification with a 50% cut-off.

				optimized protocol								original protocol								
EIVS #	Code1	Code2	GHS	MatTek				Beiersdorf				Beiersdorf			Harlan			IIVS		
				single			mean	single			mean									
35	B275	C011	NC	NI	I	NI	NI	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
37	B242	C002	NC	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
40	B287	C008	NC	NI	NI	NI	NI	NI	I	I	I	I	I	NI	NI	I	NI	NI	NI	NI
42	B246	C004	NC	I	I	I	I	I	I	I	I	NI	NI	I	I	NI	NI	NI	NI	NI
46	B283	C007	NC	NI	NI	NI	NI	NI	I	NI	NI	NI	NI	NI	NI	I	NI	NI	NI	I
62	B225	C001	2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
73	B268	C005	2A	I	I	I	I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
74	B282	C006	2A	I	I	I	I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
77	B296	C003	2A	NI	NI	NI	NI	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
78	B271	C010	2A	I	I		I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
102	B279	C009	1	I	I	I	I	I	I	I	I	I	NI	NI	I	I	I	NI	NI	NI
			WLR	91% (10/11)				82% (9/11)				73% (8/11)			73% (8/11)			91% (10/11)		
			BLR	73% (8/11)								73% (8/11)								

EIVS #: chemicals selection number, Code1: code Beiersdorf under optimized protocol, Code2: Cosmetics Europe codes of 11 chemicals provided to MatTek for optimization

Table 4: Dataset1. Classification with a 60% cut-off.

Looking at Table 4, there are 3 out of 8 chemicals(77, 40 and 35) in no cat GHS group classified at Beiersdorf as I wheras at MatTek as NI. The underlying averaged viabilities are quite different, 77: 57.1 vs 88.0, 40: 55.7 vs 72.7 and 35: 43.0 vs 80.8. (see Table 7)

				optimized protocol								original protocol								
EIVS #	Code1	Code2	GHS	MatTek					Beiersdorf				Beiersdorf			Harlan			IIVS		
				single				mean	single			mean									
30	B204		NC	I	I	I		I	I	I	I	I	NI	I	I	I	I	I	NI	NI	NI
31	B298		NC	NI	NI	NI		NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
35	B275	C011	NC	NI	NI	NI		NI	I	I	NI	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
37	B242	C002	NC	NI	NI	NI		NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
40	B287	C008	NC	NI	NI	NI		NI	NI	I	NI	NI	I	NI	NI	NI	NI	NI	NI	NI	NI
42	B246	C004	NC	I	I	I		I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
46	B283	C007	NC	NI	NI	NI		NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
49	B266		NC	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
62	B225	C001	2B	NI	NI	NI		NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
63	B231		2B	I	I			I	I	I	I	I	I	I	I	NI	I	NI	I	I	I
64	B228		2B	I	I			I	I	I	I	I	I	I	I	I	I	I	I	I	I
65	B253		2B	I	I	I		I	I	I	I	I	NI	NI	NI	I	I	NI	NI	I	NI
66	B226		2B	I	I			I	I	I	I	I	I	I	I	I	I	I	I	I	I
73	B268	C005	2A	I	NI	I		I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
74	B282	C006	2A	I	I	I		I	NI	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
77	B296	C003	2A	NI	NI	NI		NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
78	B271	C010	2A	NI	I			NI	NI	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
79	B235		2A	I	I	I		I	I	I	I	I	I	I	I	I	I	I	I	I	I
97	B291		1	I	I	I	I	I	I	I	I	I	NI	I	NI	NI	NI	NI	NI	NI	NI
102	B279	C009	1	I	I	I		I	I	I	I	I	I	NI	NI	I	NI	NI	NI	NI	NI
			WLR	90% (18/20)					80% (16/20)				80% (16/20)			85% (17/20)			95% (19/20)		
			BLR	90% (18/20)									85% (17/20)								

EIVS #: chemicals selection number, Code1: code Beiersdorf under optimized protocol, Code2: Cosmetics Europe codes of 11 chemicals provided to MatTek for optimization

Table 5: Dataset2. Classification with a 50% cut-off.

				optimized protocol								original protocol								
EIVS #	Code1	Code2	GHS	MatTek					Beiersdorf				Beiersdorf			Harlan			IIVS		
				single				mean	single			mean									
30	B204		NC	I	I	I		I	I	I	I	I	I	I	I	I	I	I	I	I	NI
31	B298		NC	NI	NI	NI		NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
35	B275	C011	NC	NI	I	NI		NI	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
37	B242	C002	NC	NI	NI	NI		NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
40	B287	C008	NC	NI	NI	NI		NI	NI	I	I	I	I	I	NI	NI	I	NI	NI	NI	NI
42	B246	C004	NC	I	I	I		I	I	I	I	I	NI	NI	I	I	NI	NI	NI	NI	NI
46	B283	C007	NC	NI	NI	NI		NI	NI	I	NI	NI	NI	NI	NI	NI	I	NI	NI	NI	I
49	B266		NC	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
62	B225	C001	2B	NI	NI	NI		NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
63	B231		2B	I	I			I	I	I	I	I	I	I	I	I	I	I	I	I	I
64	B228		2B	I	I			I	I	I	I	I	I	I	I	I	I	I	I	I	I
65	B253		2B	I	I	I		I	I	I	I	I	I	I	I	I	I	I	NI	I	I
66	B226		2B	I	I			I	I	I	I	I	I	I	I	I	I	I	I	I	I
73	B268	C005	2A	I	I	I		I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
74	B282	C006	2A	I	I	I		I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
77	B296	C003	2A	NI	NI	NI		NI	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
78	B271	C010	2A	I	I			I	I	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
79	B235		2A	I	I	I		I	I	I	I	I	I	I	I	I	I	I	I	I	I
97	B291		1	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
102	B279	C009	1	I	I	I		I	I	I	I	I	I	NI	NI	I	I	I	NI	NI	NI
			WLR	95% (19/20)					90% (18/20)				85% (17/20)			85% (17/20)			85% (17/20)		
			BLR	85% (17/20)									85% (17/20)								

EIVS #: chemicals selection number, Code1: code Beiersdorf under optimized protocol, Code2: Cosmetics Europe codes of 11 chemicals provided to MatTek for optimization

Table 6: Dataset2. Classification with a 60% cut-off.

				optimized protocol						original protocol								
EIVS #	Code1	Code2	GHS	MatTek				Beiersdorf			Beiersdorf			Harlan			IIVS		
30	B204		NC	7.6	3.5	5.5		3.1	3.1	2.3	55.6	39	46.8	35	25.2	14.2	55.4	51.8	69.2
31	B298		NC	124.6	101.0	117.2		91.8	88.6	85.3	82.1	90.3	62.3	96.6	77.4	96.3	98.2	97.8	103.9
35	B275	C011	NC	99.1	58.2	85.1		32.5	40.6	55.9	73.7	72	77	62.3	69.3	77.4	99.9	95.2	99.4
37	B242	C002	NC	118.9	80.1	88.2		89.2	65.2	68.1	80.4	75	79.7	74.2	66.5	78.3	86.3	80.1	78
40	B287	C008	NC	82.0	65.5	70.6		64	44.9	58.3	49.4	59.5	62.1	72.9	56.2	60.2	62.3	63	60.2
42	B246	C004	NC	18.2	11.1	21.2		3.2	4.2	2.7	64.7	85	58.7	53.4	66	60.1	85.3	81.8	70.5
46	B283	C007	NC	83.4	67.3	79.5		66	59.8	62	68.4	68.9	72.6	73.1	58.9	80	65.2	60.8	57.8
49	B266		NC	4.5	28.1	15.9	10.7	5.6	3.2	3.1	0	0	0	11.7	5.5	3.8	11.9	15.8	15.6
62	B225	C001	2B	103.8	110.8	98.4		106.5	116.5	98	115.2	110.1	101.7	101.7	104.7	105.9	109.8	105.2	97.1
63	B231		2B	15.9	3.4			6	4.7	5.8	40.6	34.3	27	56.8	41	50.2	49.6	38.9	43.7
64	B228		2B	2.8	7.8			1.9	2.1	1.9	36.9	22.8	30	16	20.7	35.1	39.6	29.7	28.2
65	B253		2B	2.2	4.5	31.4		6.2	4.8	3.2	50.5	52.1	51.7	20.3	16.2	51.8	63.8	41.6	53.9
66	B226		2B	3.4	4.8			2.3	2.7	2.1	6	8	6.4	4.8	2.7	3	2.7	6.6	2
73	B268	C005	2A	29.4	51.4	6.2		4.1	2.9	20.4	73.9	88.1	89	78.4	86	87.8	102.5	105.8	82.9
74	B282	C006	2A	17.0	16.9	11.4		51.5	23	18.3	72.5	65.9	88.8	76.7	74.5	81.6	87.2	99.3	88.8
77	B296	C003	2A	96.1	70.2	97.7		55	59.8	56.5	103.6	94.1	92.8	94.7	61.8	65.2	98.2	107.3	103.6
78	B271	C010	2A	56.6	43.9			52.8	46.4	48.4	79.9	80.9	88.9	65.8	62	63.4	87.8	86.9	85.9
79	B235		2A	3.0	2.8	5.1		2.2	2.1	2.1	2.4	3.3	2.2	2.7	2.8	2.2	2.9	2.3	3.2
97	B291		1	32.2	27.2	46.3	47.1	27.6	29.8	29.6	56.2	47.2	55.5	55.3	51.7	51	59	55.1	51.1
102	B279	C009	1	21.2	21.4	3.0		14.3	14.6	19.8	10.1	110.2	124.3	38	55	52.1	76.7	87.8	108.2

EIVS #: chemicals selection number, Code1: code Beiersdorf under optimized protocol, Code2: Cosmetics Europe codes of 11 chemicals provided to MatTek for optimization

Table 7: Average viability over qualified tests for Dataset 2.

4 Predictive Capacity (Accuracy)

Predictive Capacity was calculated on the basis of all individual predictions obtained for each chemical in each individual qualified test. Moreover, the predictive capacity was calculated considering the solids data obtained by Beiersdorf with the optimised solids protocol alone or in combination with the data obtained by Beiersdorf, Harlan and IIVS with the liquid chemicals in the main study (validation of the original liquids and solids protocols). In the latter case, the data obtained by Beiersdorf on the 59 chemicals (excluding chemical 98) listed in Table 1 (3 qualified tests for each chemical) were combined with the data obtained by Beiersdorf, Harlan and IIVS for the 52 liquid chemicals that were tested in the main study (9 qualified tests for each chemical) (see Appendices B-D). Thus, different chemicals ended up with a different number of independent classifications used for calculating predictive capacity i.e., 9 classifications (liquids) or 3 classifications (solids). To avoid that different chemicals weight differently in the calculation of predictive capacity from the combined data, a weighted calculation was used in this case (Tables 8 - 11). In summary, the result of each individual qualified test obtained for each chemical (from one or three laboratories) was captured as an independent classification in the calculations and correction factors were applied so that all chemicals ended up with an equal weight in the calculations. The positive and negative predictions for each chemical were divided by the total number of predictions for that chemical so that each chemical contributes with a final weight of 1 in the calculations. In this way, the accuracy values obtained better reflect the real predictive capacity of the test method.

4.1 Analysis of the data generated at Beiersdorf with the optimised solids protocol

The predictive capacity statistics are based on the individual predictions obtained with each qualified test. The estimates are given in Tables 8 and 9. A significant increase in sensitivity

and accuracy is observed for the optimised solids protocol as compared to the original one, but, as expected, a decrease in specificity was also observed.

All the definitely acceptable acceptance criteria defined by the VMG are met with the optimised solids protocol using the 60% cut-off (when chemical 37 is included in the calculations), while for the 50% cut-off the sensitivity is slightly lower than the definitely acceptance threshold of 90%. The accuracy of the optimised solids protocol is also higher with a 60% cut-off than with a 50% cut-off.

	optimized Solids protocol		**original Solids protocol**	
Solids Specificity (37 incl)	64.3%	(18/28)		
Solids False Positives (37 incl)	35.7%			
Solids Specificity (37 excl)	63.0%	(17/27)	79.2%	(57/72)
Solids False Positives (37 excl)	37.0%		20.8%	
Solids Sensitivity	88.2%	(27.3/31)	64.1%	(50/78)
Solids False Negatives	11.8%		35.9%	
Solids Accuracy (37 incl)	76.8%	(45.3/59)		
Solids Accuracy (37 excl)	76.4%	(44.3/58)	71.3%	(107/150)

Table 8: Beiersdorf. Predictive capacity statistics for cut-off 50%. Calculations are made with/without chemical 37 due to borderline melting temperature. Statistics reported for original Solids protocol are taken from TNO report.

	optimized Solids protocol		**original Solids protocol**	
Solids Specificity (37 incl)	60.7%	(17/28)		
Solids False Positives (37 incl)	39.3%			
Solids Specificity (37 excl)	59.3%	(16/27)	75.0%	(54/72)
Solids False Positives (37 excl)	40.7%		25.0%	
Solids Sensitivity	93.5%	(29/31)	74.4%	(58/78)
Solids False Negatives	6.5%		25.6%	
Solids Accuracy (37 incl)	78.0%	(46/59)		
Solids Accuracy (37 excl)	77.6%	(45/58)	74.7%	(112/150)

Table 9: Beiersdorf. Predictive capacity statistics for cut-off 60%. Calculations are made with/without chemical 37 due to borderline melting temperature. Statistics reported for original Solids protocol are taken from TNO report.

See Tables 14 to 17 for details.

4.2 Are final viabilities lower under optimized EpiOcular™ EIT Solids protocol?

As the main difference between optimized and original EpiOcular™ EIT Solids protocol is an extended exposure time, a natural question to ask is: "Are final viabilities lower under optimized EpiOcular™ EIT Solids protocol?"

To answer this question, the data from Beiersdorf were first split into two groups i.e. a) group of the data for chemicals with in-vivo GHS classification as category 1, 2A or 2B (denote by Group 1) and b) group of the data for chemicals not requiring classification based on vivo data (GHS no category) (denote by Group 2), see Appendix A.

A Wilcoxson matched paired test was used on both groups of data. The null hypothesis about equal viabilities generated under the two protocols is rejected for Group 1 whereas in the case of Group 2 it cannot be rejected at level $\alpha = 5\%$. In fact, on average, the underlying viability under the optimized protocol is statistically lower than under the original protocol in Group 2.

This statistical finding should be interpreted as follows. No statistical significant differences were observed between viabilities of original and optimised solids protocols for Group 1, but significant differences were observed in Group 2, with viabilities obtained with the optimised protocol being significantly lower than those obtained with the original protocol. This can also be confirmed by observing the graphs included in Appendix A.

4.3 Analysis of data generated at all test facilities. Liquids and Solids Protocols.

Sensitivity, specificity and accuracy detailed statistics for data generated under **optimized Solids & original Liquids** and **original Solids & original Liquids** EpiOcular™ EIT protocols are shown in Table 10 (50% cut-off) and Table 11 (60% cut-off). The values of statistics below the acceptance threshold are highlighted.(in orange if "further evaluation necessary" or in red if "definitely unacceptable" rates are obtained)

All the definitely acceptable acceptance criteria decided by VMG are met with 60% cut-off. For the 50% cut-off the sensitivity of the optimised solids protocol is below the definitely acceptance criterion of 90% but the combined sensitivity of the optimised solids and original liquids protocol is still higher than 90% (definitely acceptable). The total accuracy is slightly higher with 60% cut-off than with 50% cut-off. None of the cat 1 chemicals were underclassified with either cut-off.

	Optimised Solids protocol & Original Liquids protocol		**Original Solids protocol & Original Liquids protocol**	
Liquids Specificity (37 incl)	68.7%	(18.6/27)	68.7%	(167/243)
Liquids False Positives (37 incl)	31.3%		31.3%	
Solids Specificity (37 incl)	64.3%	(18/28)		
Solids False Positives (37 incl)	35.7%			
Total Specificity (37 incl twice)	66.5%	(36.6/55)		
Total False Positives(37 incl twice)	33.5%			
Liquids Specificity (37 excl)	67.5%	(17.6/26)		
Liquids False Positives (37 excl)	32.5%			
Solids Specificity (37 excl)	63.0%	(17/27)	79.7%	(177/222)
Solids False Positives (37 excl)	37.0%		20.3%	
Total Specificity (37 incl once)	65.8%	(35.6/54)	74.0%	(344/465)
Total False Positives (37 incl once)	**34.2%**		26.0%	
Liquids Sensitivity	96.2%	(25/26)	96.2%	(225/234)
Liquids False Negatives	3.8%		3.8%	
Solids Sensitivity	88.2%	(27.3/31)	66.7%	(156/234)
Solids False Negatives	11.8%		33.3%	
Total Sensitivity	91.8%	(52.3/57)	81.4%	(381/468)
Total False Negatives	**8.2%**		18.6%	
Liquids Accuracy (37 incl)	82.2%	(43.6/53)	82.2%	(392/477)
Solids Accuracy (37 incl)	76.8%	(45.3/59)		
Total Accuracy (37 incl twice)	79.4%	(88.9/112)		
Liquids Accuracy (37 excl)	81.8%	(42.6/52)		
Solids Accuracy (37 excl)	76.4%	(44.3/58)	73.0%	(333/456)
Total Accuracy (37 incl once)	**79.2%**	(87.9/111)	77.7%	(725/933)

Table 10: Predictive capacity statistics for Cut-off 50%.

	Optimised Solids protocol & Original Liquids protocol		**Original Solids protocol & Original Liquids protocol**	
Liquids Specificity (37 incl)	65.4%	(17.7/27)	65.4%	(159/243)
Liquids False Positives (37 incl)	34.6%		34.6%	
Solids Specificity (37 incl)	60.7%	(17/28)		
Solids False Positives (37 incl)	39.3%			
Total Specificity (37 incl twice)	63.0%	(34.7/55)		
Total False Positives(37 incl twice)	37.0%			
Liquids Specificity (37 excl)	64.1%	(16.7/26)		
Liquids False Positives (37 excl)	35.9%			
Solids Specificity (37 excl)	59.3%	(16/27)	74.8%	(166/222)
Solids False Positives (37 excl)	40.7%		25.2%	
Total Specificity (37 incl once)	62.4%	(33.7/54)	69.9%	(325/465)
Total False Positives (37 incl once)	**37.6%**		30.1%	
Liquids Sensitivity	98.3%	(25.6/26)	98.3%	(230/234)
Liquids False Negatives	1.7%		1.7%	
Solids Sensitivity	93.5%	(29/31)	76.9%	(180/234)
Solids False Negatives	6.5%		23.1%	
Total Sensitivity	95.7%	(54.6/57)	87.6%	(410/468)
Total False Negatives	**4.3%**		12.4%	
Liquids Accuracy (37 incl)	81.6%	(43.2/53)	81.6%	(389/477)
Solids Accuracy (37 incl)	78.0%	(46/59)		
Total Accuracy (37 incl twice)	79.7%	(89.2/112)		
Liquids Accuracy (37 excl)	81.2%	(42.2/52)		
Solids Accuracy (37 excl)	77.6%	(45/58)	75.9%	(346/456)
Total Accuracy (37 incl once)	**79.5%**	(88.2/111)	78.8%	(735/933)

Table 11: Predictive capacity statistics for Cut-off 60%.

Appendices

A Beiersdorf - optimized SOP. Graphical output.

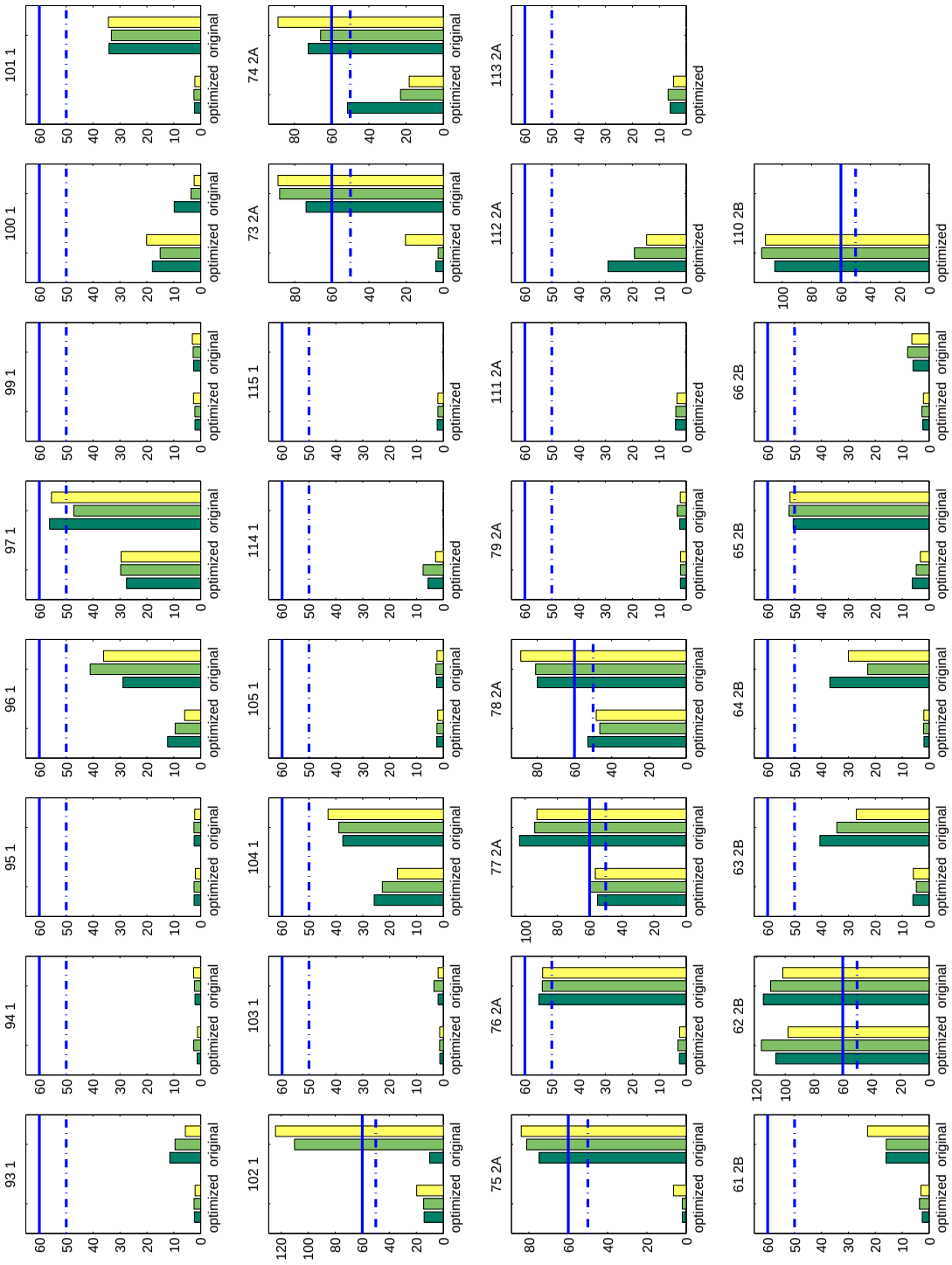

Figure 1: Viability. lab Beiersdorf. GHS classification 1, 2A and 2B

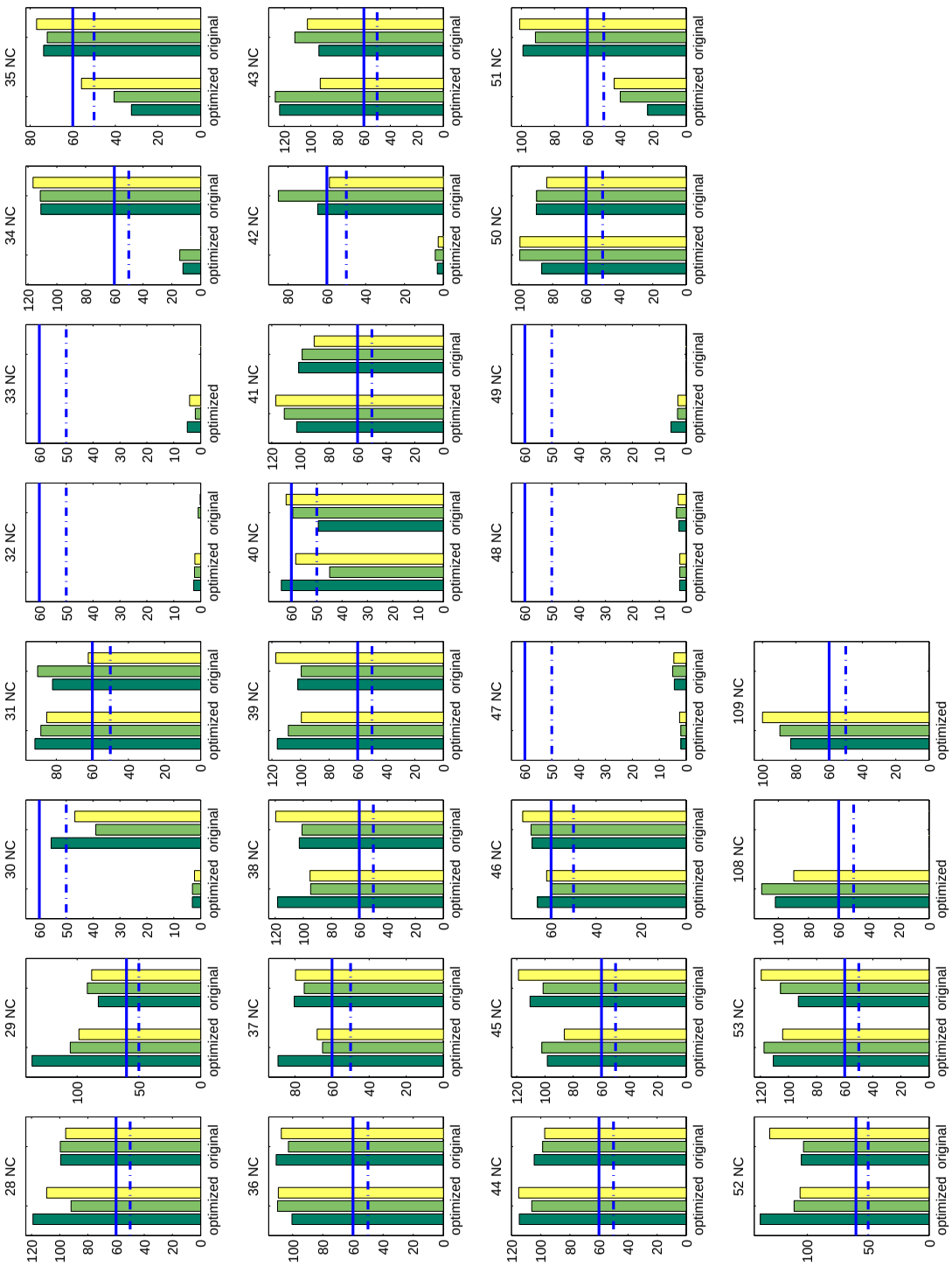

Figure 2: Viability. Beiersdorf. GHS classification non-irritants

B Final viabilities

				optimized			original protocol								
	EIVS #	Code1	GHS	Beiersdorf			Beiersdorf			Harlan			IIVS		
Liquids	1		no cat				67.8	68.8	71.3	66.7	62.5	70.4	75.3	68.2	62.7
	2		no cat				83	80.1	77.3	74.6	79.8	78.9	84.2	79.3	80.4
	3		no cat				55.4	63	64.2	37.2	38.1	38.6	51.4	49	47.5
	4		no cat				106.9	104.6	115.5	60.8	57.9	64.3	100.9	93	94.8
	5		no cat				83.5	72.2	86.4	56.7	41.4	40.3	71.8	65.4	50.3
	6		no cat				81.2	83.7	90.9	73.2	71.1	84.7	88.6	80.7	81.3
	7		no cat				34.6	42.3	38.7	31	36.8	36.6	40.5	43.4	32.1
	8		no cat				101.4	97.3	102.8	89.6	94.7	94.8	101.2	99.6	95.2
	9		no cat				95.4	101.9	98	91.9	82.6	96.5	106	100.5	98.3
	10		no cat				33	31.1	35.3	14.4	9.8	13.2	16.6	23.8	16.8
	11		no cat				29.8	27.5	29.8	21.2	19	16.4	31.6	33.7	28.9
	12		no cat				94.1	91.5	91.6	92.7	91.9	96.7	96.4	92.5	94.6
	13		no cat				107.9	87.8	105.4	88.8	97.5	85.1	84	81.4	85.8
	14		no cat				98.3	98.7	104.9	90.6	97.9	103	94.6	95.7	96.9
	15		no cat				97.2	101.7	109.5	104.9	93	106.3	102.4	93.9	95.3
	16		no cat				100.4	110.9	103.3	103.8	102.1	94	95.7	105.5	102.9
	17		no cat				102.5	98.1	91.9	86.9	100.6	103.9	96.6	98.1	95.3
	18		no cat				112.3	69.6	109.5	101.5	91	96.8	94.1	95.3	95
	19		no cat				106.4	106.4	111.8	108.8	105.3	113.1	95.6	98.4	98.9
	20		no cat				31.1	57.2	49.8	9.1	0	19.1	48.1	33.2	41.5
	21		no cat				82.8	82.9	83.2	71.8	67.4	77.6	86.2	81.5	85.4
	22		no cat				51.6	39.3	45.1	24	23.3	13	37.7	35.5	39
	23		no cat				40.8	46	39.5	17.5	22.4	4.9	18.9	8.6	10.4
	24		no cat				48.4	45.6	43.5	28	19.4	21.3	53	33.9	32.6
	25		no cat				107.6	105	101.3	104.8	108.9	104.9	95	103.2	107.3
	26		no cat				22.7	19.4	22.4	30.6	40.7	35.6	31.6	35.6	35.3
	37		no cat				80.4	75	79.7	74.2	66.5	78.3	86.3	80.1	78
Solids	28	B249	no cat	119	91.9	109.3	99.4	99.6	95.8	94.9	94.5	90.9	105.4	112.9	100.6
	29	B267	no cat	136.5	105.6	98.6	82.9	91.8	88.2	57.4	112	83	102.5	105.7	101.4
	30	B204	no cat	3.1	3.1	2.3	55.6	39	46.8	35	25.2	14.2	55.4	51.8	69.2
	31	B298	no cat	91.8	88.6	85.3	82.1	90.3	62.3	96.6	77.4	96.3	98.2	97.8	103.9
	32	B285	no cat	2.6	2.3	2.2	0	0.9	0.2	1.1	0.9	0.9	2.5	2.8	2.1
	33	B232	no cat	4.9	2	4.1				44.1	48.3	40.3	88.9	89.2	83.2
	34	B218	no cat	12.3	14.5	-1.9	111.1	111.5	116.5	81.4	54.1	63.2	95.6	107.1	80.9
	35	B275	no cat	32.5	40.6	55.9	73.7	72	77	62.3	69.3	77.4	99.9	95.2	99.4
	36	B290	no cat	100.5	110	109.5	110.9	102.8	107.5	103.1	88.2	98.5	110.7	110.8	105.6
	37	B242	no cat	89.2	65.2	68.1									
	38	B237	no cat	118.2	94.7	95.2	102.8	100.9	119.7	99.7	113	95.8	101.1	101.9	108
	39	B274	no cat	116.3	108.6	99.4	101.9	99.5	117.3	100.9	114.7	88.4	102.5	101.7	104.8
	40	B287	no cat	64	44.9	58.3	49.4	59.5	62.1	72.9	56.2	60.2	62.3	63	60.2
	41	B224	no cat	102.6	111.3	117.2	101.2	98.8	90.4	98.2	86.4	88.8	99.3	102.5	94
	42	B246	no cat	3.2	4.2	2.7	64.7	85	58.7	53.4	66	60.1	85.3	81.8	70.5
	43	B245	no cat	123.6	126.8	92.9	93.9	112.1	102.6	125.3	91.6	163.7	99.8	102	103.4
	44	B262	no cat	114.8	106.2	115.2	104.5	98.7	97.3	101.6	95	103.9	98.1	94.2	102.9
	45	B284	no cat	98.4	102.2	86.4	110.6	101.4	118.8	112.5	97.9	112.6	98.6	98.4	94.8
	46	B283	no cat	66	59.8	62	68.4	68.9	72.6	73.1	58.9	80	65.2	60.8	57.8
	47	B260	no cat	1.9	2	2.5	4.4	5	4.6	3.4	2	3.2	3.2	2.9	2.6
	48	B243	no cat	2.4	2.4	2.4	2.7	3.6	3	2.8	3.1	2.5	2.7	2.5	2.4
	49	B266	no cat	5.6	3.2	3.1	0	0	0	11.7	5.5	3.8	11.9	15.8	15.6
	50	B278	no cat	86.5	99.6	99.5	89.7	89.6	83.5	99.1	97.1	96.7	95.6	92.7	97.4
	51	B222	no cat	23.4	40	43.7	99.1	91.5	101.1	93.3	100.1	84.8	95.4	98.7	106
	52	B205	no cat	138.5	110.8	105.9	104.8	103.1	130.8	106.5	105.7	93.4	101.3	95.1	105.7
	53	B299	no cat	110.8	117.4	104.2	93	105.7	119.4	108.2	123.4	104	106.3	101.7	107.2
	108	B332	no cat	83.1	89.5	100									
	109	B634	no cat	102	111	89.8									

Table 12: No Category. Final viability for qualified tests.

				optimized			original protocol								
	EIVS #	Code1	GHS	Beiersdorf			Beiersdorf			Harlan			IIVS		
Liquids	54		cat 2B				48.8	47.8	45.2	17.1	25.2	19.9	51.8	43.1	30.1
	55		cat 2B				2.3	2.1	2.1	2.2	1.8	2.6	2.5	2.6	2.5
	56		cat 2B				46.4	54.5	60.3	20.8	26.5	27.3	47.5	34.8	29.6
	57		cat 2B				24.4	19.8	19.1	5	7.7	6.5	20.4	20.3	12.6
	58		cat 2B				22	22.7	22.2	6.8	2.1	2.6	14.4	13.4	13
	59		cat 2B				62.6	67.5	78.3	46.6	36.3	47	56.6	52.8	43.6
	60		cat 2B				20.5	13.6	12.6	6.7	16	9.3	26.8	13.8	21.2
	67		cat 2A				15	10.8	10.7	4.1	4.3	4.9	13.6	15.3	14.6
	68		cat 2A				3.5	2.4	4.3	4	2.8	3.3	2.7	7	3
	69		cat 2A				13.2	15	13.9	10.5	14	16.9	13.6	14.4	14.1
	70		cat 2A				12.5	17.9	15.4	9.9	10.3	12.9	14.3	12.3	12.2
	71		cat 2A				5.2	6.2	4.7	7.9	7.4	4	7.7	9.1	7.4
	72		cat 2A				4.7	2.2	4.9	5.4	3.7	3.8	5.4	3.2	3.1
	80		cat 1				18.1	16.6	17.7	6.3	0	15.3	9.3	5	9.7
	81		cat 1				2.5	1.8	3.1	3.6	3.2	3.4	5.6	3.9	3.1
	82		cat 1				4.5	1.6	5.4	1.5	2.1	1.7	5.3	6.9	2.6
	83		cat 1				5.5	6.1	5.3	4.6	3.6	7.6	5.4	6.8	4
	84		cat 1				12.6	5.6	22.1	6.7	7	4.2	17.8	18.7	9.3
	85		cat 1				15.9	18.1	26.7	5.6	9.2	12.5	14	13.1	17.8
	86		cat 1				25.3	20.7	27.2	41.8	23.4	24.8	31.8	32.7	20.5
	87		cat 1				26.3	26.3	33.6	20	14.4	22.2	30.8	17.4	24.4
	88		cat 1				4.5	5.3	7.4	5.2	7.8	5.4	3.9	7	3.5
	89		cat 1				10.7	7.2	10.6	5.8	7.8	8.1	9	12.6	9.7
	90		cat 1				40.4	28.5	25.6	25.4	32.6	14.4	35.5	34.7	30.8
	91		cat 1				20	35	38.3	17.6	12.4	20.4	21.1	19.6	19.5
	92		cat 1				47.5	41	49.8	18.2	14.8	13.1	39.6	39.3	51.2
Solids	61	B221	cat 2B	2.5	3.5	3	16	15.9	22.9	17	11.3	9.4	16.3	16.4	21.4
	62	B225	cat 2B	106.5	116.5	98	115.2	110.1	101.7	101.7	104.7	105.9	109.8	105.2	97.1
	63	B231	cat 2B	6	4.7	5.8	40.6	34.3	27	56.8	41	50.2	49.6	38.9	43.7
	64	B228	cat 2B	1.9	2.1	1.9	36.9	22.8	30	16	20.7	35.1	39.6	29.7	28.2
	65	B253	cat 2B	6.2	4.8	3.2	50.5	52.1	51.7	20.3	16.2	51.8	63.8	41.6	53.9
	66	B226	cat 2B	2.3	2.7	2.1	6	8	6.4	4.8	2.7	3	2.7	6.6	2
	110	B451	cat 2B	105.1	114.1	111.4									
	73	B268	cat 2A	4.1	2.9	20.4	73.9	88.1	89	78.4	86	87.8	102.5	105.8	82.9
	74	B282	cat 2A	51.5	23	18.3	72.5	65.9	88.8	76.7	74.5	81.6	87.2	99.3	88.8
	75	B254	cat 2A	1.9	2	6.5	74.8	81.1	83.9	17.4	2	2.7	5	5.8	4.4
	76	B201	cat 2A	2.5	3.1	2.4	54.8	53.5	53.4	59	32.3	52.8	26.9	26.3	28.7
	77	B296	cat 2A	55	59.8	56.5	103.6	94.1	92.8	94.7	61.8	65.2	98.2	107.3	103.6
	78	B271	cat 2A	52.8	46.4	48.4	79.9	80.9	88.9	65.8	62	63.4	87.8	86.9	85.9
	79	B235	cat 2A	2.2	2.1	2.1	2.4	3.3	2.2	2.7	2.8	2.2	2.9	2.3	3.2
	111	B447	cat 2A	3.9	3.9	3.4									
	112	B608	cat 2A	29.1	19.3	14.7									
	113	B202	cat 2A	5.9	6.7	4.7									
	93	B250	cat 1	2.3	2.5	2.1	11.5	9.5	5.7	6.2	9.3	8.5	10.3	21.3	18
	94	B213	cat 1	1.3	2.6	1.2	2.1	2.3	2.6	5.7	3	2.6	5.2	5.8	4.3
	95	B294	cat 1	2.4	2.4	2	2.4	2.5	2.2	2.5	2.7	2.7	1.6	2.3	2.1
	96	B255	cat 1	12.3	9.5	6	28.9	41.1	36.1	35.5	35.3	30.9	33.2	38.9	54.1
	97	B291	cat 1	27.6	29.8	29.6	56.2	47.2	55.5	55.3	51.7	51	59	55.1	51.1
	98	B252	cat 1				0	0	0	0	0	0	0	0	0
	99	B214	cat 1	2.1	2.2	2.7	2.6	2.8	3.1	3.3	2.3	2.4	1.9	2	1.7
	100	B233	cat 1	18	15	20.1	9.8	3.6	2.4	10	14.9	8.5	10.5	8.2	8.9
	101	B281	cat 1	2.3	2.5	2.2	34.1	33.2	34.3	26.2	50.6	42	19.9	21.6	13.8
	102	B279	cat 1	14.3	14.6	19.8	10.1	110.2	124.3	38	55	52.1	76.7	87.8	108.2
	103	B244	cat 1	1.3	1.4	1.4	2	3.5	2	1.9	1.9	1.6	1.7	2.1	2.1
	104	B207	cat 1	25.7	22.7	17.1	37.4	38.9	42.9	40.3	36.3	48.4	47.1	34.8	24.4
	105	B261	cat 1	2.4	2.4	2.1	2.5	2.8	2.4	3.9	2.6	1.9	2.1	2.4	2.4
	114	B293	cat 1	5.7	7.6	2.9									
	115	B276	cat 1	2.3	2.1	2.1									

Table 13: GHS cat 1,2A, 2B. Final viability for qualified tests.

C Final classifications cut-off 50%

				optimized			original protocol								
	EIVS #	Code1	GHS	Beiersdorf			Beiersdorf			Harlan			IIVS		
Liquids	1		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	2		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	3		no cat				NI	NI	NI	I	I	I	NI	I	I
	4		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	5		no cat				NI	NI	NI	NI	I	I	NI	NI	NI
	6		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	7		no cat				I	I	I	I	I	I	I	I	I
	8		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	9		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	10		no cat				I	I	I	I	I	I	I	I	I
	11		no cat				I	I	I	I	I	I	I	I	I
	12		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	13		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	14		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	15		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	16		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	17		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	18		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	19		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	20		no cat				I	NI	I	I	I	I	I	I	I
	21		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	22		no cat				NI	I	I	I	I	I	I	I	I
	23		no cat				I	I	I	I	I	I	I	I	I
	24		no cat				I	I	I	I	I	I	NI	I	I
	25		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	26		no cat				I	I	I	I	I	I	I	I	I
	37		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
Solids	28	B249	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	29	B267	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	30	B204	no cat	I	I	I	NI	I	I	I	I	I	NI	NI	NI
	31	B298	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	32	B285	no cat	I	I	I	I	I	I	I	I	I	I	I	I
	33	B232	no cat	I	I	I				I	I	I	NI	NI	NI
	34	B218	no cat	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	35	B275	no cat	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	36	B290	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	37	B242	no cat	NI	NI	NI									
	38	B237	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	39	B274	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	40	B287	no cat	NI	I	NI	I	NI	NI	NI	NI	NI	NI	NI	NI
	41	B224	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	42	B246	no cat	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	43	B245	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	44	B262	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	45	B284	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	46	B283	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	47	B260	no cat	I	I	I	I	I	I	I	I	I	I	I	I
	48	B243	no cat	I	I	I	I	I	I	I	I	I	I	I	I
	49	B266	no cat	I	I	I	I	I	I	I	I	I	I	I	I
	50	B278	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	51	B222	no cat	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	52	B205	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	53	B299	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	108	B634	no cat	NI	NI	NI									
	109	B332	no cat	NI	NI	NI									

Table 14: No Category. Final classification cut-off 50%.

				optimized			original protocol								
	EIVS #	Code1	GHS	Beiersdorf			Beiersdorf			Harlan			IIVS		
Liquids	54		cat 2B				I	I	I	I	I	I	NI	I	I
	55		cat 2B				I	I	I	I	I	I	I	I	I
	56		cat 2B				I	NI	NI	I	I	I	I	I	I
	57		cat 2B				I	I	I	I	I	I	I	I	I
	58		cat 2B				I	I	I	I	I	I	I	I	I
	59		cat 2B				NI	NI	NI	I	I	I	NI	NI	I
	60		cat 2B				I	I	I	I	I	I	I	I	I
	67		cat 2A				I	I	I	I	I	I	I	I	I
	68		cat 2A				I	I	I	I	I	I	I	I	I
	69		cat 2A				I	I	I	I	I	I	I	I	I
	70		cat 2A				I	I	I	I	I	I	I	I	I
	71		cat 2A				I	I	I	I	I	I	I	I	I
	72		cat 2A				I	I	I	I	I	I	I	I	I
	80		cat 1				I	I	I	I	I	I	I	I	I
	81		cat 1				I	I	I	I	I	I	I	I	I
	82		cat 1				I	I	I	I	I	I	I	I	I
	83		cat 1				I	I	I	I	I	I	I	I	I
	84		cat 1				I	I	I	I	I	I	I	I	I
	85		cat 1				I	I	I	I	I	I	I	I	I
	86		cat 1				I	I	I	I	I	I	I	I	I
	87		cat 1				I	I	I	I	I	I	I	I	I
	88		cat 1				I	I	I	I	I	I	I	I	I
	89		cat 1				I	I	I	I	I	I	I	I	I
	90		cat 1				I	I	I	I	I	I	I	I	I
	91		cat 1				I	I	I	I	I	I	I	I	I
	92		cat 1				I	I	I	I	I	I	I	I	NI
Solids	61	B221	cat 2B	I	I	I	I	I	I	I	I	I	I	I	I
	62	B225	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	63	B231	cat 2B	I	I	I	I	I	I	NI	I	NI	I	I	I
	64	B228	cat 2B	I	I	I	I	I	I	I	I	I	I	I	I
	65	B253	cat 2B	I	I	I	NI	NI	NI	I	I	NI	NI	I	NI
	66	B226	cat 2B	I	I	I	I	I	I	I	I	I	I	I	I
	110	B451	cat 2B	NI	NI	NI									
	73	B268	cat 2A	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	74	B282	cat 2A	NI	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	75	B254	cat 2A	I	I	I	NI	NI	NI	I	I	I	I	I	I
	76	B201	cat 2A	I	I	I	NI	NI	NI	NI	I	NI	I	I	I
	77	B296	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	78	B271	cat 2A	NI	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	79	B235	cat 2A	I	I	I	I	I	I	I	I	I	I	I	I
	111	B447	cat 2A	I	I	I									
	112	B608	cat 2A	I	I	I									
	113	B202	cat 2A	I	I	I									
	93	B250	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	94	B213	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	95	B294	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	96	B255	cat 1	I	I	I	I	I	I	I	I	I	I	I	NI
	97	B291	cat 1	I	I	I	NI	I	NI	NI	NI	NI	NI	NI	NI
	98	B252	cat 1				I	I	I	I	I	I	I	I	I
	99	B214	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	100	B233	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	101	B281	cat 1	I	I	I	I	I	I	I	NI	I	I	I	I
	102	B279	cat 1	I	I	I	I	NI	NI	I	NI	NI	NI	NI	NI
	103	B244	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	104	B207	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	105	B261	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	114	B293	cat 1	I	I	I									
	115	B276	cat 1	I	I	I									

Table 15: GHS cat 1, 2A, 2B. cut-off 50%

D Final classifications cut-off 60%

				optimized			original protocol								
	EIVS #	Code1	GHS	Beiersdorf			Beiersdorf			Harlan			IIVS		
Liquids	1		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	2		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	3		no cat				I	NI	NI	I	I	I	I	I	I
	4		no cat				NI	NI	NI	NI	I	NI	NI	NI	NI
	5		no cat				NI	NI	NI	I	I	I	NI	NI	I
	6		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	7		no cat				I	I	I	I	I	I	I	I	I
	8		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	9		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	10		no cat				I	I	I	I	I	I	I	I	I
	11		no cat				I	I	I	I	I	I	I	I	I
	12		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	13		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	14		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	15		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	16		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	17		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	18		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	19		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	20		no cat				I	I	I	I	I	I	I	I	I
	21		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	22		no cat				I	I	I	I	I	I	I	I	I
	23		no cat				I	I	I	I	I	I	I	I	I
	24		no cat				I	I	I	I	I	I	I	I	I
	25		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
	26		no cat				I	I	I	I	I	I	I	I	I
	37		no cat				NI	NI	NI	NI	NI	NI	NI	NI	NI
Solids	28	B249	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	29	B267	no cat	NI	NI	NI	NI	NI	NI	I	NI	NI	NI	NI	NI
	30	B204	no cat	I	I	I	I	I	I	I	I	I	I	I	NI
	31	B298	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	32	B285	no cat	I	I	I	I	I	I	I	I	I	I	I	I
	33	B232	no cat	I	I	I				I	I	I	NI	NI	NI
	34	B218	no cat	I	I	I	NI	NI	NI	NI	I	NI	NI	NI	NI
	35	B275	no cat	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	36	B290	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	37	B242	no cat	NI	NI	NI									
	38	B237	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	39	B274	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	40	B287	no cat	NI	I	I	I	I	NI	NI	I	NI	NI	NI	NI
	41	B224	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	42	B246	no cat	I	I	I	NI	NI	I	I	NI	NI	NI	NI	NI
	43	B245	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	44	B262	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	45	B284	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	46	B283	no cat	NI	I	NI	NI	NI	NI	NI	I	NI	NI	NI	I
	47	B260	no cat	I	I	I	I	I	I	I	I	I	I	I	I
	48	B243	no cat	I	I	I	I	I	I	I	I	I	I	I	I
	49	B266	no cat	I	I	I	I	I	I	I	I	I	I	I	I
	50	B278	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	51	B222	no cat	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	52	B205	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	53	B299	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	108	B634	no cat	NI	NI	NI									
	109	B332	no cat	NI	NI	NI									

Table 16: No Category. Final classification cut-off 60%.

				optimized			original protocol								
	EIVS #	Code1	GHS	Beiersdorf			Beiersdorf			Harlan			IIVS		
Liquids	54		cat 2B				I	I	I	I	I	I	I	I	I
	55		cat 2B				I	I	I	I	I	I	I	I	I
	56		cat 2B				I	I	NI	I	I	I	I	I	I
	57		cat 2B				I	I	I	I	I	I	I	I	I
	58		cat 2B				I	I	I	I	I	I	I	I	I
	59		cat 2B				NI	NI	NI	I	I	I	I	I	I
	60		cat 2B				I	I	I	I	I	I	I	I	I
	67		cat 2A				I	I	I	I	I	I	I	I	I
	68		cat 2A				I	I	I	I	I	I	I	I	I
	69		cat 2A				I	I	I	I	I	I	I	I	I
	70		cat 2A				I	I	I	I	I	I	I	I	I
	71		cat 2A				I	I	I	I	I	I	I	I	I
	72		cat 2A				I	I	I	I	I	I	I	I	I
	80		cat 1				I	I	I	I	I	I	I	I	I
	81		cat 1				I	I	I	I	I	I	I	I	I
	82		cat 1				I	I	I	I	I	I	I	I	I
	83		cat 1				I	I	I	I	I	I	I	I	I
	84		cat 1				I	I	I	I	I	I	I	I	I
	85		cat 1				I	I	I	I	I	I	I	I	I
	86		cat 1				I	I	I	I	I	I	I	I	I
	87		cat 1				I	I	I	I	I	I	I	I	I
	88		cat 1				I	I	I	I	I	I	I	I	I
	89		cat 1				I	I	I	I	I	I	I	I	I
	90		cat 1				I	I	I	I	I	I	I	I	I
	91		cat 1				I	I	I	I	I	I	I	I	I
	92		cat 1				I	I	I	I	I	I	I	I	I
Solids	61	B221	cat 2B	I	I	I	I	I	I	I	I	I	I	I	I
	62	B225	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
	63	B231	cat 2B	I	I	I	I	I	I	I	I	I	I	I	I
	64	B228	cat 2B	I	I	I	I	I	I	I	I	I	I	I	I
	65	B253	cat 2B	I	I	I	I	I	I	I	I	I	NI	I	I
	66	B226	cat 2B	I	I	I	I	I	I	I	I	I	I	I	I
	110	B451	cat 2B	NI	NI	NI									
	73	B268	cat 2A	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	74	B282	cat 2A	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	75	B254	cat 2A	I	I	I	NI	NI	NI	I	I	I	I	I	I
	76	B201	cat 2A	I	I	I	I	I	I	I	I	I	I	I	I
	77	B296	cat 2A	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	78	B271	cat 2A	I	I	I	NI	NI	NI	NI	NI	NI	NI	NI	NI
	79	B235	cat 2A	I	I	I	I	I	I	I	I	I	I	I	I
	111	B447	cat 2A	I	I	I									
	112	B608	cat 2A	I	I	I									
	113	B202	cat 2A	I	I	I									
	93	B250	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	94	B213	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	95	B294	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	96	B255	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	97	B291	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	98	B252	cat 1				I	I	I	I	I	I	I	I	I
	99	B214	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	100	B233	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	101	B281	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	102	B279	cat 1	I	I	I	I	NI	NI	I	I	I	NI	NI	NI
	103	B244	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	104	B207	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	105	B261	cat 1	I	I	I	I	I	I	I	I	I	I	I	I
	114	B293	cat 1	I	I	I									
	115	B276	cat 1	I	I	I									

Table 17: GHS cat 1, 2A, 2B. cut-off 60%

Annex 3

Statistical analysis on the SkinEthic™ HCE main validation study

TNO report

TNO 2013 R11617 | Final report

Eye Irritation Validation Study on Human Tissue Models: Statistical Analysis and Reporting on the SkinEthic™ HCE

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Project number	051.01208

Summary

The goal of the Eye Irritation Validation Study (EIVS) was to assess the relevance (predictive capacity) and reliability (reproducibility within and between laboratories) of the SkinEthic™ HCE and of the EpiOcular™ EIT, by testing a statistically significant number of coded test chemicals (substances and mixtures), supported by complete and quality assured in vivo Draize eye irritation data for comparative evaluation of results. In this report a complete, objective and transparent analysis of within-laboratory and between-laboratory reproducibility as well as predictive capacity based on the submitted test data for SkinEthic™ HCE is presented. The results for the EpiOcular™ EIT are reported elsewhere (TNO2013 R10396).

The statistical analyses are performed for the data generated using the short exposure protocol (SE), the long exposure protocol (LE) as well as based on the test strategy (selection of SE or LE based on reactivity analysis). Based on the results for the fraction of complete test sequences (100% in total for SE and 99.7% for LE), the within-laboratory variability (93.9% concordance in total for SE and 95.5% concordance in total for LE) and the between-laboratory variability (92.3% concordance in total using the SE protocol and 92.3% concordance in total using the LE protocol), the validation of the SkinEthic™ HCE was based on high-quality data. The acceptance criteria for these three characteristics were easily fulfilled.

The SkinEthic™ HCE test method is highly reproducible. The within-laboratory reproducibility (WLR) and between-laboratory reproducibility (BLR) was well above the acceptance criteria set by the VMG (i.e. WLR ≥ 85% and BLR ≥ 80%).

A cut-off value of 50% was applied, meaning that a chemical for which the mean viabililty was below 50% is classified as irritant and non-irrant otherwise. The specificity of the prediction model was ‘definitely acceptable’ according to the acceptance criteria as defined by the VMG, regardless the protocol that was used (SE: 0.885; LE: 0.655; test strategy: 0.777). Further evaluation is needed regarding the accuracy (SE: 0.656; LE: 0.686; test strategy: 0.661). The results for the sensitivity are ‘definitely unacceptable’ according to the acceptance criteria as defined by the VMG (SE: 0.427; LE: 0.716; test strategy: 0.545).

Contents

1 Introduction

The goal of the Eye Irritation Validation Study (EIVS) was to assess the relevance (predictive capacity) and reliability (reproducibility within and between laboratories) of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT, by testing a statistically significant number of coded test chemicals (substances and mixtures), supported by complete and quality assured in vivo Draize eye irritation data for comparative evaluation of results.

Specifically, EIVS assessed the validity of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT as stand-alone (independent) test methods to reliably discriminate chemicals not classified as eye irritant ("non-irritants") from all classes of eye irritant chemicals (in the framework of a Bottom-Up/Top-Down test strategy, Scott L. et al., 2010), defined according to the United Nations Globally Harmonized System (GHS) of Classification and Labelling of Chemicals (UN GHS: No Category versus Category 1/Category 2A/Category 2B; UN, 2007) and as implemented in the European Commission Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (EU CLP: No Category versus Category 1/Category 2).

The EpiOcular™ EIT was developed for maximum sensitivity (ability to detect positives, with low rate of false negatives) rather than for optimal overall accuracy with balanced sensitivity and specificity (ability to detect negatives, with low rate of false positives). Sensitivity had therefore a bigger weight than specificity and overall accuracy in their development. However, it was also sought to achieve a sufficiently high specificity and overall accuracy, in order to allow identification of the highest number of chemicals not classified as irritant to the eye. The SkinEthic™ HCE test strategy was developed to optimize the overall accuracy with balanced sensitivity and specificity. It was developed to oriented to the short or long exposure treatment based on the reactivity of the chemical, given balanced accuracy.
By achieving satisfactory specificity, the SkinEthic™ HCE test strategy and the EpiOcular™ EIT would represent stand-alone (independent) test methods for the identification of "non-irritants". Importantly, the test methods were not intended to differentiate between UN GHS/EU CLP Category 1 (irreversible effects) and UN GHS/EU CLP Category 2 (reversible effects). As proposed by the ECVAM workshop of February 2005, this differentiation would be left to another tier of the Bottom-Up/Top-Down test strategy (Scott L. et al., 2010).

The EIVS was undertaken in accordance with the principles and criteria documented in the OECD Guidance Document on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment (No. 34, OECD, 2005) and according to the Modular Approach to validation (Hartung T. et al., 2004).

The objective of this report is to summarise and present a complete, objective and transparent analysis of within-laboratory and between-laboratory reproducibility as well as predictive capacity based on the submitted test data for SkinEthic™ HCE. The analysis is performed for the data generated using the short exposure protocol (SE), the long exposure protocol (LE) as well as based on the test strategy

(selection of SE or LE based on EPRA analysis). The results for the EpiOcular™ EIT protocol have been reported in a separate report.

2 Material and Methods

2.1 Study Design

The SkinEthic™ HCE was tested in three laboratories.

Lead Laboratory	L'OREAL (FR)
Additional Laboratory 1	CARDAM (BE)
Additional Laboratory 2	CEETOX (USA)

Each laboratory tested the same 106 chemicals in three runs each, in three tissues (post-validation statistical analyses to investigate whether it would be sufficient to use two tissues instead of three tissues were conducted elsewhere; for completeness, the results of these separate analyses are given in appendix IX). These chemicals were coded and distributed by TNO (The Netherlands). The chemicals were tested blinded. Contact between the laboratories during the testing was not allowed in order to safeguard the blinding. More details regarding the study design can be found in the project plan (appendix VIII).

The chemicals that were used in the validation study are listed in Table 2.1.1.

Table 2.1.1 List of tested chemicals in EIVS validation study

Chemical	Substance name	State	CAS #	GHS Class
1	1-bromohexane	Liquid	111-25-1	no cat
2	1-methylpropyl benzene	Liquid	135-98-8	no cat
3	2-ethoxyethyl methacrylate	Liquid	2370-63-0	no cat
4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	Liquid	25103-09-7	no cat
5	4-(methylthio)-benzaldehyde	Liquid	3446-89-7	no cat
6	dipropyl disulphide	Liquid	629-19-6	no cat
7	1-bromo-4-chlorobutane	Liquid	6940-78-9	no cat
8	1-bromo-octane	Liquid	111-83-1	no cat
9	1,9-decadiene	Liquid	1647-16-1	no cat
10	2,2-dimethyl-3-pentanol	Liquid	3970-62-5	no cat
11	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	Liquid	111-90-0	no cat
12	bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated (53-57% aqueousemulsion)	Liquid	68123-18-2	no cat
13	bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated (56% aqueous emulsion)	Liquid	455946-46-0	no cat
14	dioctyl ether INCI name: DICAPRYLYL ETHER	Liquid	629-82-3	no cat
15	dioctyl carbonate INCI name: DICAPRYLYL CARBONATE	Liquid	1680-31-5	no cat
16	2-propylheptyl octanoate INCI name: PROPYLHEPTYL CAPRYLATE	Liquid	868839-23-0	no cat
17	polyglyceryl-3 diisooctadecanoate INCI name: POLYGLYCERYL-3 DIISOSTEARATE	Liquid	63705-03-3	no cat
18	steareth-10 allyl ether/acrylates copolymer (30% aqueous) INCI name: STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	Liquid	109292-17-3	no cat
19	dimethyl siloxane, mono dimethylvinylsiloxy- and mono trimethoxysiloxy-terminated (95%)	Liquid	471277-16-4	no cat
20	ricinoleic acid tin salt	Liquid	71828-07-4	no cat
21	1-ethyl-3-methylimidazolium ethylsulphate	Liquid	342573-75-5	no cat
22	3-phenoxybenzyl alcohol	Liquid	13826-35-2	no cat
23	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE	Liquid	623-51-8	no cat
24	glycidyl methacrylate	Liquid	106-91-2	no cat
25	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE	Liquid	51-03-6	no cat
26	propiconazole	Liquid	60207-90-1	no cat

Chemical	Substance name	State	CAS #	GHS Class
27[1]	2-ethylhexylthioglycolate	Liquid	7659-86-1	no cat
28	4,4'-methylene bis-(2,6-di-tert-butylphenol)	Solid	118-82-1	no cat
29	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE	Solid	3234-85-3	no cat
30	1,1-dimethylguanidine sulphate	Solid	598-65-2	no cat
31	potassium tetrafluoroborate	Solid	14075-53-7	no cat
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	Solid	84540-47-6	no cat
33	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11	Solid	23920-15-2	no cat
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	Solid	3179-89-3	no cat
35	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	Solid	1603-02-7	no cat
36	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN	Solid	101-20-2	no cat
37[3]	polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL	Solid	61788-85-0	no cat
38	2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYLBUTYLPHENOL	Solid	103597-45-1	no cat
39	2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol] INCI name: BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE	Solid	187393-00-6	no cat
40	acrylamidopropyltrimonium chloride/acrylamide copolymer	Solid	75150-29-7	no cat
41	tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate INCI name: ETHYLHEXYL TRIAZONE	Solid	88122-99-0	no cat
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	Solid	66170-10-3	no cat
43	hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE	Solid	302776-68-7	no cat
44	[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine	Solid	231278-20-9	no cat
45	1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol	Solid	72956-09-3	no cat
46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	Solid	68610-92-4	no cat
47	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE	Solid	120-14-9	no cat
48	sodium hydrogensulphite INCI name: SODIUM BISULFITE	Solid	7631-90-5	no cat
49	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN	Solid	94-13-3	no cat
50	iodosulfuron-methyl-sodium	Solid	144550-36-7	no cat
51	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz	Solid	33089-61-1	no cat
52	2-anilino-4,6-dimethylpyrimidine common name: Pyrimethanil	Solid	53112-28-0	no cat
53	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam	Solid	153719-23-4	no cat
54	3-chloropropionitrile	Liquid	542-76-7	cat 2B
55	2-methylpropanal INCI name: 2-METHYLPROPANAL	Liquid	78-84-2	cat 2B
56	isopropyl acetoacetate	Liquid	542-08-5	cat 2B
57	2-methyl-1-pentanol	Liquid	105-30-6	cat 2B
58	1-(1-methyl-2-propoxyethoxy)propan-2-ol INCI name: PPG-2 PROPYL ETHER	Liquid	29911-27-1	cat 2B
59	ethyl-2-methyl acetoacetate	Liquid	609-14-3	cat 2B
60	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET	Liquid	134-62-3	cat 2B
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	Solid	83-72-7	cat 2B
62	1,4-dibutoxy benzene	Solid	104-36-9	cat 2B
63	4-nitrobenzoic acid	Solid	62-23-7	cat 2B
64	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate	Solid	96568-04-6	cat 2B
65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	Solid	79-92-5	cat 2B
66	sodium chloroacetate	Solid	3926-62-3	cat 2B
67	gamma-butyrolactone INCI name: BUTYROLACTONE	Liquid	96-48-0	cat 2A

Chemical	Substance name	State	CAS #	GHS Class
68	cyclopentanol	Liquid	96-41-3	cat 2A (ICCVAM: cat 2B)
69	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	Liquid	383178-66-3	cat 2A (ICCVAM: cat 2B)
70	methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-oxobicyclo[2.2.1]hept-2-ylidene)methyl]anilinium sulphate (30% aqueous) INCI name: CAMPHOR BENZALKONIUM METHOSULFATE	Liquid	52793-97-2	cat 2A
71	1-propoxy-2-propanol INCI name: PROPYLENE GLYCOL PROPYL ETHER	Liquid	1569-01-3	cat 2A (ICCVAM: cat 2B)
72	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE	Liquid	18472-51-0	cat 2A (ICCVAM: cat 2B)
73	3,3'-dithiopropionic acid	Solid	1119-62-6	cat 2A (ICCVAM: cat 2B)
74	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	Solid	16867-03-1	cat 2A
75	sodium benzoate INCI name: SODIUM BENZOATE	Solid	532-32-1	cat 2A
76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	Solid	362525-73-3	cat 2A
77	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate	Solid	189813-45-4	cat 2A
78	(2R,3R)-3-((R)-1-(tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate	Solid	76855-69-1	cat 2A
79	ammonium nitrate INCI name: AMMONIUM NITRATE	Solid	6484-52-2	cat 2A (ICCVAM: cat 2B)
80	methylthioglycolate INCI name: METHYL THIOGLYCOLATE	Liquid	2365-48-2	cat 1
81	3-diethylaminopropionitrile	Liquid	02/04/5351	cat 1
82	coco alkyl dimethyl betaine (~ 30% aqueous) INCI name: COCO-BETAINE	Liquid	68424-94-2	cat 1
83	coco amidopropyl betaine (~ 30% aqueous) INCI name: COCAMIDOPROPYL BETAINE	Liquid	61789-40-0	cat 1
84	sodium coco amphoacetate (~ 30% aqueous)	Liquid	61791-32-0	cat 1
85	triethanol ammonium alkyl sulphate (~ 40% aqueous) INCI name: TEA-C12-14 ALKYL SULFATE	Liquid	90583-18-9	cat 1
86	di-sodium alkyl ether sulfosuccinate (~ 30% aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE	Liquid	68815-56-5	cat 1
87	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE	Liquid	68891-38-3	cat 1
88	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)	Liquid	118569-52-1	cat 1
89	ethoxylated (5 EO) alkyl (C10-14) alcohol	Liquid	66455-15-0	cat 1
90	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	Liquid	110615-47-9	cat 1
91	(ethylenediaminepropyl)trimethoxysilane	Liquid	1760-24-3	cat 1
92	tetraethylene glycol diacrylate	Liquid	17831-71-9	cat 1
93	2,5-dimethyl-2,5-hexanediol	Solid	110-03-2	cat 1
94	dodecanoic acid INCI name: LAURIC ACID	Solid	143-07-7	cat 1
95	1,2,4-triazole sodium salt	Solid	41253-21-8	cat 1
96	1-naphthalene acetic acid	Solid	86-87-3	cat 1
97	sodium oxalate INCI name: SODIUM OXALATE	Solid	62-76-0	cat 1
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	Solid	4430-25-5	cat 1
99	1,2-benzisothiazol-3(2H)-one INCI name: BENZISOTHIAZOLINONE	Solid	2634-33-5	cat 1
100	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	Solid	60372-77-2	cat 1
101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31	Solid	97404-02-9	cat 1
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	Solid	27344-41-8	cat 1
103	3,4-dimethyl-1H-pyrazole	Solid	2820-37-3	cat 1
104	N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide	Solid	171887-03-9	cat 1
105	1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate	Solid	54424-29-2	cat 1
106[2]	4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methylbenzenamine hydrochloride INCI name: BASIC VIOLET 2	Solid	3248-91-7	cat 1
107[2]	xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxycarbonyl)phenyl]-	Solid	134429-57-5	cat 1

Chemical	Substance name	State	CAS #	GHS Class
	tetrafluoroborate			

[1] sent to all participating laboratories for testing but excluded at a very early stage of the study on request of one of the participating laboratories because it was identified as a very strong MTT reducer

[2] extra chemicals not for statistics but for a later purpose of evaluation using an HPLC based detection system.

[3] Chemical 37 (polyethylene glycol (PEG-40) hydrogenated castor oil, INCI name: PEG-40 HYDROGENATED CASTOR OIL) was originally selected by the EIVS VMG as being a solid. However, all three laboratories participating in the validation of the EpiOcular™ EIT independently considered the chemical as being liquid due to its low melting point and tested it using the liquid protocol of EpiOcular™ EIT (see statistical report on EpiOcular™ EIT). Hence, chemical 37 was reclassified as liquid by the VMG.

Chemical 106 (*4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methylbenzenamine hydrochloride INCI name: BASIC VIOLET 2*) and chemical 107 (*xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxycarbonyl)phenyl]-tetrafluoroborate*) were sent to all participating laboratories for testing but excluded at a very early stage of the study on request of one of the participating laboratories because it was identified as a very strong MTT reducer. These two chemicals are excluded from any statistical analysis. Hence, the statistical analysis is based on 104 chemicals.

In Table 2.1.2, the decoding of the chemicals is given.

Table 2.1.2 Decoding of chemicals

Chemical	Substance name	L'OREAL	Cardam	Ceetox
1	1-bromohexane	L94	C51	X5
2	1-methylpropyl benzene	L43	C99	X22
3	2-ethoxyethyl methacrylate	L51	C76	X93
4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	L7	C53	X62
5	4-(methylthio)-benzaldehyde	L12	C104	X68
6	dipropyl disulphide	L55	C78	X7
7	1-bromo-4-chlorobutane	L66	C82	X89
8	1-bromo-octane	L98	C60	X63
9	1,9-decadiene	L20	C54	X2
10	2,2-dimethyl-3-pentanol	L87	C12	X30
11	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	L17	C65	X38
12	bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated (53-57% aqueousemulsion)	L76	C4	X61
13	bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated (56% aqueous emulsion)	L36	C20	X77
14	dioctyl ether INCI name: DICAPRYLYL ETHER	L75	C79	X59
15	dioctyl carbonate INCI name: DICAPRYLYL CARBONATE	L53	C67	X94
16	2-propylheptyl octanoate INCI name: PROPYLHEPTYL CAPRYLATE	L27	C37	X103
17	polyglyceryl-3 diisooctadecanoate INCI name: POLYGLYCERYL-3 DIISOSTEARATE	L64	C83	X53
18	steareth-10 allyl ether/acrylates copolymer (30% aqueous) INCI name: STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	L50	C71	X19
19	dimethyl siloxane, mono dimethylvinylsiloxy- and mono trimethoxysiloxy-terminated (95%)	L111	C114	X113
20	ricinoleic acid tin salt	L58	C58	X37

Chemical	Substance name	L'OREAL	Cardam	Ceetox
21	1-ethyl-3-methylimidazolium ethylsulphate	L72	C46	X82
22	3-phenoxybenzyl alcohol	L101	C47	X3
23	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE	L140	C128	X139
24	glycidyl methacrylate	L119	C139	X128
25	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE	L161	C141	X143
26	propiconazole	L185	C163	X190
27	2-ethylhexylthioglycolate	L74	C87	X17
28	4,4'-methylene bis-(2,6-di-tert-butylphenol)	L60	C85	X1
29	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE	L127	C140	X120
30	1,1-dimethylguanidine sulphate	L134	C131	X131
31	potassium tetrafluoroborate	L122	C129	X116
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	L57	C38	X91
33	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11	L90	C101	X8
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	L99	C45	X27
35	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	L85	C30	X13
36	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN	L18	C2	X72
37	polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL	L109	C109	X110
38	2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYLBUTYLPHENOL	L62	C39	X11
39	2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol] INCI name: BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE	L65	C14	X55
40	acrylamidopropyltrimonium chloride/acrylamide copolymer	L15	C55	X40
41	tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate INCI name: ETHYLHEXYL TRIAZONE	L106	C105	X115
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	L107	C113	X108
43	hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE	L115	C108	X107
44	[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine	L112	C107	X112
45	1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol	L108	C110	X114
46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	L114	C106	X109
47	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE	L113	C112	X111
48	sodium hydrogensulphite INCI name: SODIUM BISULFITE	L129	C135	X119
49	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN	L169	C195	X173
50	iodosulfuron-methyl-sodium	L148	C185	X158
51	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz	L156	C164	X169
52	2-anilino-4,6-dimethylpyrimidine common name:	L144	C166	X160

Chemical	Substance name	L'OREAL	Cardam	Ceetox
	Pyrimethanil			
53	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam	L200	C196	X157
54	3-chloropropionitrile	L81	C19	X6
55	2-methylpropanal INCI name: 2-METHYLPROPANAL	L132	C134	X117
56	isopropyl acetoacetate	L131	C127	X138
57	2-methyl-1-pentanol	L92	C50	X33
58	1-(1-methyl-2-propoxyethoxy)propan-2-ol INCI name: PPG-2 PROPYL ETHER	L120	C119	X133
59	ethyl-2-methyl acetoacetate	L133	C132	X118
60	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET	L125	C137	X127
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	L5	C96	X86
62	1,4-dibutoxy benzene	L118	C116	X125
63	4-nitrobenzoic acid	L126	C120	X123
64	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate	L79	C70	X50
65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	L137	C124	X134
66	sodium chloroacetate	L123	C125	X129
67	gamma-butyrolactone INCI name: BUTYROLACTONE	L45	C91	X45
68	cyclopentanol	L48	C26	X52
69	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	L24	C1	X98
70	methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-oxobicyclo[2.2.1]hept-2-ylidene)methyl]anilinium sulphate (30% aqueous) INCI name: CAMPHOR BENZALKONIUM METHOSULFATE	L130	C123	X121
71	1-propoxy-2-propanol INCI name: PROPYLENE GLYCOL PROPYL ETHER	L70	C11	X65
72	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE	L139	C138	X136
73	3,3'-dithiopropionic acid	L73	C49	X47
74	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	L102	C34	X39
75	sodium benzoate INCI name: SODIUM BENZOATE	L11	C35	X36
76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	L4	C84	X70
77	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate	L67	C16	X84
78	(2R,3R)-3-((R)-1-(tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate	L61	C15	X102
79	ammonium nitrate INCI name: AMMONIUM NITRATE	L136	C136	X126
80	methylthioglycolate INCI name: METHYL THIOGLYCOLATE	L9	C6	X31
81	3-diethylaminopropionitrile	L78	C90	X51
82	coco alkyl dimethyl betaine (~ 30% aqueous) INCI name: COCO-BETAINE	L80	C64	X56
83	coco amidopropyl betaine (~ 30% aqueous) INCI name: COCAMIDOPROPYL BETAINE	L82	C33	X83
84	sodium coco amphoacetate (~ 30% aqueous)	L37	C97	X29
85	triethanol ammonium alkyl sulphate (~ 40% aqueous) INCI name: TEA-C12-14 ALKYL SULFATE	L23	C66	X28
86	di-sodium alkyl ether sulfosuccinate (~ 30% aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE	L16	C29	X66
87	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE	L59	C77	X41

Chemical	Substance name	L'OREAL	Cardam	Ceetox
88	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)	L33	C48	X42
89	ethoxylated (5 EO) alkyl (C10-14) alcohol	L42	C25	X25
90	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	L104	C13	X64
91	(ethylenediaminepropyl)trimethoxysilane	L29	C3	X81
92	tetraethylene glycol diacrylate	L174	C170	X165
93	2,5-dimethyl-2,5-hexanediol	L91	C63	X16
94	dodecanoic acid INCI name: LAURIC ACID	L97	C94	X43
95	1,2,4-triazole sodium salt	L68	C75	X73
96	1-naphthalene acetic acid	L28	C88	X99
97	sodium oxalate INCI name: SODIUM OXALATE	L39	C36	X49
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	L1	C28	X24
99	1,2-benzisothiazol-3(2H)-one INCI name: BENZISOTHIAZOLINONE	L83	C21	X21
100	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	L164	C193	X196
101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31	L13	C9	X80
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	L32	C103	X75
103	3,4-dimethyl-1H-pyrazole	L56	C62	X87
104	N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide	L96	C27	X46
105	1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate	L8	C98	X14
106	4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methylbenzenamine hydrochloride INCI name: BASIC VIOLET 2	L6	C52	X95
107	xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxycarbonyl)phenyl]-tetrafluoroborate	L100	C56	X32

2.2 Archiving

One data file in a flat file format will be provided which includes all quality checked test-results from all three laboratories for possible later use. A readme-file will be provided which explains each variable in the data set.

The SAS code which was used for statistical analysis is provided in Appendix II.

2.3 Receipt of data

The study results were received by the statistician from the Trial coordinator. The receipt of data was reported in an excel file. The report on the receipt of data can be found in Appendix III.

2.4 Test acceptance criteria

2.4.1 Test acceptance criteria

The test acceptance criteria are described in detail in the SkinEthic^{TM} HCE SOP..

In short, the following test acceptance criteria are applied.

Subject	Criteria	Remark
NC response	0.7 < OD < 1.5	
PC mean viability	≤ 50%	
Tissue variability	Standard deviation ≤ 18%	Over replicates, for chemicals, PC and NC

2.4.2 Study acceptance criteria

The study acceptance criteria are described in detail in the Guidance on eye irritation validation study (EIVS) conduct for the reconstructed human tissue (RhT) assays and performance criteria to assess the scientific validity of SkinEthic™ HCE and EpiOcular™ EIT and its addendum (see appendix VII and VIII).

In short, the following study acceptance criteria are applied.

Subject	Criteria	Remark
Complete test sequences	≥ 85%	In each laboratory
Within laboratory variability (concordance of classification)	≥ 85%	Using test chemicals for which at least two qualified tests are available
Between laboratory variability (concordance of classification)	≥ 80%	Using test chemicals for which at least one qualified test per laboratory is available
Sensitivity	≥90%	Based on all qualified tests
Specificity	≥60%	Based on all qualified tests
Accuracy	≥75%	Based on all qualified tests

A test sequence is considered complete if it contains three qualified tests. Otherwise, the test sequence is considered as incomplete.

If the test method fulfils the above stated acceptance criteria, the performance of the method is considered to be 'definitely acceptable'. For sensitivity, specificity and accuracy, some additional criteria are defined to be able to distinguish between a definitely unacceptable performance and a performance which might need some further evaluation. These criteria are defined as follows:

	False Negatives[a] (%)	False Positives[b] (%)	Overall misclassifications[c] (%)
"Definitely acceptable" rates	≤ 10	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	40 < FP ≤ 50	25 < OM ≤ 35
"Definitely unacceptable" rates	> 20	> 50	> 35

[a] equal to (1-Sensitivity), [b] equal to (1-Specificity), [c] equal to (1-Overall accuracy)

2.5 Statistical methods

The statistical analyses are performed according to the Statistical Analysis and Reporting Plan for the ECVAM/COLIPA Eye Irritation Validation Study on Reconstructed Human Tissue Models (final version May 5, 2011). The statistical analysis is based on the performance criteria document Guidance on eye irritation validation study (EIVS) conduct for the reconstructed human tissue (RhT) assays and performance criteria to assess the scientific validity of SkinEthic™ HCE and EpiOcular™ EIT and its addendum (see appendix VII and VIII).

2.5.1 Quality checks

Before starting the statistical analyses, the following quality checks were done:

- Is the information complete?
- Are the test acceptance criteria always met?
- Are there any deviations from the study plan?
- Are there any remarks and special observations as given in the reporting sheet by the study personal?

Some chemicals might be incompatible with the test method. Evaluation of compatibility was evaluated for colouring or MTT-reducing chemicals by the following criteria:

RULE 1 – IF the mean of %NSC or %NSMTT of all qualified tests obtained for a chemical in one laboratory is less than or equal to (≤) 50%, THEN this chemical is considered to be compatible with the test method. The chemical should be included in the overview tables, and included in all statistical calculations of reproducibility and predictive capacity.

RULE 2 – IF the mean of %NSC or %NSMTT of all qualified tests obtained for a chemical in one laboratory is greater than (>) 50% AND their classification (I or NI) remains the same upon correction, THEN this chemical is considered to be compatible with the test method. The chemical should be included in the overview tables, and included in all statistical calculations of reproducibility and predictive capacity.

RULE 3 – IF the mean of %NSC or %NSMTT of all qualified tests obtained for a chemical in one laboratory is greater than (>) 50% AND the classification of at least one of the qualified tests changes upon correction, THEN this chemical is considered to be incompatible with the test method. The chemical should be included in the overview tables, but excluded from all statistical calculations of reproducibility and predictive capacity.

2.5.2 Descriptive statistics

The descriptive statistics contain summary tables on the chemical selection set (e.g. cross tables with long exposure (LE) and short exposure (SE)), the number of qualified tests, the number of complete test sequences, *etcetera*.

2.5.3 Within Laboratory Reproducibility (WLR)

For each laboratory, concordance of classifications and overall Standard Deviation were calculated based on qualified tests from test chemicals for which at least two qualified tests are available. For each laboratory, concordance of classifications and overall Standard Deviation were also calculated based on all tests performed,

including both qualified and non-qualified tests. The WLR is calculated using the SE protocol, the LE protocol as well as using the test strategy.

2.5.4 Between Laboratory Reproducibility (BLR)

For the calculation of BLR the final classification for each test chemical in each participating laboratory should be obtained by using the arithmetic mean value of viability over the different qualified tests performed. Concordance of classifications between laboratories and overall Standard Deviation of the study were calculated based only on qualified tests from test chemicals for which at least one qualified test per laboratory is available. The overall Standard Deviation of the study is also calculated based on all tests performed, including both qualified and non-qualified tests. The BLR is calculated using the SE protocol, the LE protocol as well as using the test strategy.

2.5.5 Predictive capacity (accuracy)

All qualified tests for each test chemical were used to calculate the predictive capacity values. The calculations were based on the individual predictions of each qualified test in each laboratory and not on the arithmetic mean values of viability over the different qualified tests performed. The predictive capacity is calculated using the SE protocol, the LE protocol as well as using the test strategy.

3 Results

3.1 Quality checks

Data were imported from the original spread sheets into a SAS data base. All test results in the data base are checked by the laboratories and their approval was given for completeness and correctness before the statistical analysis was started.

The remarks and special observations as given by the study personal in the reporting sheets are listed in Appendix IV.

In Table 3.1.1, the number of non-qualified and qualified runs are given, based on the acceptance criteria for NC and PC.

Table 3.1.1 Number of non-qualified and qualified runs, based on the acceptance criteria for NC and PC, subdivided into laboratories

Protocol	laboratory		No. Qualified	%	No .Non-Qualified	%
SE	CARDAM	NC	35	100.0	0	0.0
		PC	35	100.0	0	0.0
	CEETOX	NC	40	100.0	0	0.0
		PC	40	100.0	0	0.0
	L'OREAL	NC	34	100.0	0	0.0
		PC	34	100.0	0	0.0
LE	CARDAM	NC	33	100.0	0	0.0
		PC	33	100.0	0	0.0
	CEETOX	NC	44	100.0	0	0.0
		PC	36	81.8	8	18.2
	L'OREAL	NC	34	100.0	0	0.0
		PC	33	97.1	1	2.9

There were no major deviations from the study plan (see appendix IV for detailed remarks).

3.2 Descriptive statistics

3.2.1 Distribution of test chemicals

In Table 3.2.1 the distribution of test chemicals is given. The 104 chemicals were equally distributed among irritants (50%) and non-irritants (50%) and among liquids (50%) and solids (50%). The distribution regarding the reactivity is given as well.

Table 3.2.1 Distribution of test chemicals (upper: frequencies, lower: percentages; NR = non-reactive, R = reactive)

Classification	Liquid[1]	Solid	Total
I	26 25.0	26 25.0	52 50.0
NI	26 25.0	26 25.0	52 50.0
Total	52 50.0	52 50.0	104 100.00

Classification	NR	R	Total
I	24 23.1	28 26.9	52 50.0
NI	30 28.9	22 21.2	52 50.0
Total	52 50.0	52 50.0	104 100.00

[1] Chemical 37 (*polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL*) was listed as solid, but is statistically analysed as a liquid.

Corrections on total viability were made for MTT-reducing and/or colouring chemicals. Whether this correction had to be made was decided by the laboratory. For some chemicals, the judgement whether it regards an MTT-reducer or a colorant differed between laboratories as is shown in Table 3.2.2. In appendix I, a list is given of all MTT-reducing and/or colouring chemicals. If a chemical is treated as an MTT-reducer or a colorant in at least one of the laboratories, it is listed in appendix I.

Table 3.2.2 Colouring or MTT-reducing chemicals which are treated differently between laboratories are indicated by #.

		MTT				Colouring			
Chemical	**Name**	**Cardam**	**Ceetox**	**L'OREAL**		**Cardam**	**Ceetox**	**L'OREAL**	
1	1-bromohexane	No	No	Yes	#	No	No	No	
2	1-methylpropyl benzene	No	No	Yes	#	No	No	No	
3	2-ethoxyethyl methacrylate	No	No	No		No	No	No	
4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	Yes	Yes	Yes		No	No	No	
5	4-(methylthio)-benzaldehyde	Yes	Yes	Yes		No	No	No	
6	dipropyl disulphide	No	No	No		No	No	No	
7	1-bromo-4-chlorobutane	No	No	Yes	#	No	No	No	
8	1-bromo-octane	No	No	No		No	No	No	
9	1,9-decadiene	Yes	No	Yes	#	No	No	No	
10	2,2-dimethyl-3-pentanol	No	No	No		No	No	No	
11	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	No	No	Yes	#	No	No	No	
12	bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated (53-57% aqueousemulsion)	No	No	No		No	No	No	
13	bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated (56% aqueous emulsion)	No	No	No		No	No	No	
14	dioctyl ether INCI name: DICAPRYLYL ETHER	No	Yes	No	#	No	No	No	
15	dioctyl carbonate INCI name: DICAPRYLYL CARBONATE	No	No	No		No	No	No	
16	2-propylheptyl octanoate INCI name: PROPYLHEPTYL CAPRYLATE	No	No	Yes	#	No	No	No	
17	polyglyceryl-3 diisooctadecanoate INCI name: POLYGLYCERYL-3 DIISOSTEARATE	No	No	No		No	No	No	
18	steareth-10 allyl ether/acrylates copolymer (30% aqueous) INCI name: STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	No	No	No		No	No	No	
19	dimethyl siloxane, mono dimethylvinylsiloxy- and mono trimethoxysiloxy-terminated (95%)	No	No	No		No	No	No	
20	ricinoleic acid tin salt	Yes	No	Yes	#	No	No	No	
21	1-ethyl-3-methylimidazolium ethylsulphate	No	No	Yes	#	No	No	No	
22	3-phenoxybenzyl alcohol	No	No	No		No	No	No	
23	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE	Yes	Yes	Yes		No	No	No	
24	glycidyl methacrylate	No	No	Yes	#	No	No	No	
25	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE	Yes	Yes	Yes		No	No	No	

		MTT				Colouring			
Chemical	**Name**	**Cardam**	**Ceetox**	**L'OREAL**		**Cardam**	**Ceetox**	**L'OREAL**	
26	propiconazole	No	No	No		No	No	No	
28	4,4'-methylene bis-(2,6-di-tert-butylphenol)	No	No	No		No	No	No	
29	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE	No	No	No		No	No	No	
30	1,1-dimethylguanidine sulphate	No	No	No		No	No	No	
31	potassium tetrafluoroborate	No	No	No		No	No	No	
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	No	No	Yes	#	Yes	No	Yes	#
33	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11	Yes	Yes	Yes		Yes	Yes	Yes	
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	Yes	Yes	Yes		Yes	Yes	Yes	
35	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	Yes	Yes	Yes		No	No	No	
36	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN	No	No	No		No	No	No	
37	polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL	No	Yes	No	#	No	No	No	
38	2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYLBUTYLPHENOL	No	No	No		No	No	No	
39	2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol] INCI name: BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE	No	No	No		No	No	No	
40	acrylamidopropyltrimonium chloride/acrylamide copolymer	No	No	No		No	No	No	
41	tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate INCI name: ETHYLHEXYL TRIAZONE	No	No	No		No	No	No	
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	Yes	Yes	Yes		No	No	No	
43	hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE	No	No	No		No	No	No	
44	[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine	No	No	No		No	No	No	
45	1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol	No	No	No		No	No	No	
46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	No	Yes	No	#	No	No	No	
47	3,4-dimethoxy benzaldehyde INCI name:	No	No	No		No	No	No	

		MTT				Colouring			
Chemical	**Name**	**Cardam**	**Ceetox**	**L'OREAL**		**Cardam**	**Ceetox**	**L'OREAL**	
	VERATRALDEHYDE								
48	sodium hydrogensulphite INCI name: SODIUM BISULFITE	Yes	Yes	No	#	No	No	No	
49	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN	Yes	Yes	Yes		No	No	No	
50	iodosulfuron-methyl-sodium	No	No	No		No	No	No	
51	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz	No	No	No		No	No	No	
52	2-anilino-4,6-dimethylpyrimidine common name: Pyrimethanil	No	No	No		No	No	No	
53	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam	No	No	No		No	No	No	
54	3-chloropropionitrile	No	No	No		No	No	No	
55	2-methylpropanal INCI name: 2-METHYLPROPANAL	No	Yes	Yes	#	No	No	No	
56	isopropyl acetoacetate	No	Yes	No	#	No	No	No	
57	2-methyl-1-pentanol	No	No	No		No	No	No	
58	1-(1-methyl-2-propoxyethoxy)propan-2-ol INCI name: PPG-2 PROPYL ETHER	No	Yes	Yes	#	No	No	No	
59	ethyl-2-methyl acetoacetate	No	Yes	Yes	#	No	No	No	
60	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET	No	No	No		No	No	No	
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	No	No	No		Yes	No	Yes	#
62	1,4-dibutoxy benzene	No	No	No		No	No	No	
63	4-nitrobenzoic acid	No	No	No		No	No	No	
64	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate	No	No	No		No	No	No	
65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	No	No	No		No	No	No	
66	sodium chloroacetate	No	No	No		No	No	No	
67	gamma-butyrolactone INCI name: BUTYROLACTONE	No	No	Yes	#	No	No	No	
68	cyclopentanol	No	No	No		No	No	No	
69	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	No	No	No		No	No	No	
70	methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-oxobicyclo[2.2.1]hept-2-ylidene)methyl]anilinium sulphate (30% aqueous) INCI name: CAMPHOR BENZALKONIUM METHOSULFATE	No	No	No		No	No	No	
71	1-propoxy-2-propanol INCI name: PROPYLENE GLYCOL PROPYL ETHER	No	Yes	Yes	#	No	No	No	
72	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE	No	Yes	Yes	#	No	No	No	
73	3,3'-dithiopropionic acid	No	No	No		No	No	No	

		MTT				Colouring			
Chemical	**Name**	**Cardam**	**Ceetox**	**L'OREAL**		**Cardam**	**Ceetox**	**L'OREAL**	
74	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	Yes	Yes	Yes		Yes	No	Yes	#
75	sodium benzoate INCI name: SODIUM BENZOATE	No	No	No		No	No	No	
76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	No	No	No		No	No	No	
77	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate	No	No	No		No	No	No	
78	(2R,3R)-3-((R)-1-(tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate	No	No	No		No	No	No	
79	ammonium nitrate INCI name: AMMONIUM NITRATE	No	No	No		No	No	No	
80	methylthioglycolate INCI name: METHYL THIOGLYCOLATE	Yes	Yes	Yes		No	No	No	
81	3-diethylaminopropionitrile	Yes	Yes	No	#	No	No	No	
82	coco alkyl dimethyl betaine (~ 30% aqueous) INCI name: COCO-BETAINE	No	No	No		No	No	No	
83	coco amidopropyl betaine (~ 30% aqueous) INCI name: COCAMIDOPROPYL BETAINE	No	No	Yes	#	No	No	No	
84	sodium coco amphoacetate (~ 30% aqueous)	No	No	No		No	No	No	
85	triethanol ammonium alkyl sulphate (~ 40% aqueous) INCI name: TEA-C12-14 ALKYL SULFATE	No	No	No		No	No	No	
86	di-sodium alkyl ether sulfosuccinate (~ 30% aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE	No	No	No		No	No	No	
87	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE	No	No	Yes	#	No	No	No	
88	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)	Yes	Yes	Yes		No	No	No	
89	ethoxylated (5 EO) alkyl (C10-14) alcohol	No	No	No		No	No	No	
90	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	No	No	Yes	#	No	No	No	
91	(ethylenediaminepropyl)trimethoxysilane	Yes	Yes	Yes		No	No	No	
92	tetraethylene glycol diacrylate	Yes	Yes	Yes		No	No	No	
93	2,5-dimethyl-2,5-hexanediol	No	No	No		No	No	No	
94	dodecanoic acid INCI name: LAURIC ACID	No	No	No		No	No	No	
95	1,2,4-triazole sodium salt	Yes	No	No	#	No	No	No	
96	1-naphthalene acetic acid	No	No	No		No	No	No	
97	sodium oxalate INCI name: SODIUM OXALATE	No	No	No		No	No	No	
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	No	Yes	No	#	Yes	Yes	Yes	
99	1,2-benzisothiazol-3(2H)-one INCI name: BENZISOTHIAZOLINONE	No	No	No		No	No	No	
100	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	No	No	No		No	No	No	
101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31	No	No	No		Yes	No	Yes	#

		MTT				Colouring			
Chemical	**Name**	**Cardam**	**Ceetox**	**L'OREAL**		**Cardam**	**Ceetox**	**L'OREAL**	
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	No	No	No		No	No	No	
103	3,4-dimethyl-1H-pyrazole	No	Yes	No	#	No	No	No	
104	N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide	No	Yes	No	#	No	No	No	
105	1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate	No	No	No		No	Yes	No	#

3.2.2 Number and fraction of qualified and non-qualified tests

If the standard deviation of the viability between the three tested tissues was above 18%, the test was considered to be non-qualified. This could concern the tests for the NC, the PC and the chemicals. The number and fraction of qualified and non-qualified tests are presented in Table 3.2.3, subdivided into laboratories and total. The reasons for the non-qualification of a test is presented in Appendix V.

Table 3.2.3 Number and fraction of qualified and non-qualified tests

Procotol	**Laboratory**	**Call**	**No.**	**Fraction (%)**
SE	CARDAM	Qualified and included	312	98.7
		Non-Qualified	4	1.3
	CEETOX	Qualified and included	312	99.7
		Non-Qualified	1	0.3
	L'OREAL	Qualified and included	312	98.7
		Non-Qualified	4	1.3
	Total	Qualified and included	936	99.0
		Non-Qualified	9	1
LE	CARDAM	Qualified and included	314	99.4
		Non-Qualified	2	0.6
	CEETOX	Qualified and included	311	81.8
		Non-Qualified	69	18.2
	L'OREAL	Qualified and included	312	96.3
		Non-Qualified	12	3.7
	Total	Qualified and included	937	91.9
		Non-Qualified	83	8.1

3.2.3 Chemicals within a run

Table 3.2.4 shows the chemicals within each run subdivided into laboratories. The chemicals are tested in each run with a test with NC and a test with PC.

Table 3.2.4 Chemicals within each run subdivided into laboratories (chemicals with test numbers between brackets)

Protocol	**Laboratory**	**Run**													
SE	Cardam	EIVS_CARDAM_SE_10HCE029_35.xls	C1(1)	C2(1)	C17(1)	C19(1)	C26(1)	C30(1)	C33(1)	C34(1)	C35(1)				
		EIVS_CARDAM_SE_10HCE031_37.xls	C1(2)	C2(2)	C17(2)	C19(2)	C26(2)	C30(2)	C33(2)	C34(2)	C35(2)				
		EIVS_CARDAM_SE_10HCE032_38.xls	C1(3)	C2(3)	C17(3)	C19(3)	C26(3)	C30(3)	C77(1)	C34(3)	C35(3)				
		EIVS_CARDAM_SE_10HCE033_39(C77).xls	C77(2)												
		EIVS_CARDAM_SE_10HCE033_39.xls	C33(3)	C35(4)	C36(1)	C37(1)	C49(1)	C51(1)	C54(1)	C60(1)	C63(1)	C65(1)	C66(1)	C75(1)	C76(1)
		EIVS_CARDAM_SE_10HCE034_40(C79).xls	C79(1)												
		EIVS_CARDAM_SE_10HCE034_40.xls	C36(2)	C37(2)	C49(2)	C51(2)	C54(2)	C60(2)	C63(2)	C65(2)	C66(2)	C75(2)	C76(2)	C77(3)	C78(1)
		EIVS_CARDAM_SE1_10HCE035_41.xls	C36(3)	C37(3)	C49(3)	C51(3)	C54(3)	C60(3)	C63(3)	C65(3)	C66(3)	C75(3)	C76(3)	C78(2)	C79(2)
		EIVS_CARDAM_SE2_10HCE035_41.xls	C82(1)	C85(1)	C87(1)	C88(1)	C90(1)	C91(1)	C94(1)	C96(1)					
		EIVS_CARDAM_SE1_10HCE036_42.xls	C78(3)	C79(3)	C82(2)	C85(2)	C87(2)	C88(2)	C90(2)	C91(2)	C94(2)	C96(2)	C99(1)	C104(1)	C3(1)
		EIVS_CARDAM_SE1_10HCE037_43.xls	C82(3)	C85(3)	C87(3)	C88(3)	C90(3)	C91(3)	C94(3)	C96(3)	C99(2)	C104(2)	C3(2)	C11(2)	C12(2)
		EIVS_CARDAM_SE1_10HCE040_46.xls	C99(3)	C104(3)	C3(3)	C11(3)	C12(3)	C13(3)	C15(3)	C16(3)	C21(3)	C25(3)	C27(3)	C38(2)	C45(1)
		EIVS_CARDAM_SE1_10HCE041_47.xls	C38(3)	C45(2)	C46(2)	C47(2)	C50(2)	C53(2)	C62(2)	C70(2)	C83(2)	C84(2)	C98(1)	C101(1)	C119(1)
		EIVS_CARDAM_SE1_10HCE042_48.xls	C45(3)	C46(3)	C47(3)	C50(3)	C53(3)	C62(3)	C70(3)	C83(3)	C84(3)	C98(2)	C101(2)	C119(2)	C123(2)

Protocol	Laboratory	Run													
		EIVS_CARDAM_SE2_10HCE036_42.xls	C11(1)	C12(1)	C13(1)	C15(1)	C16(1)	C21(1)	C25(1)	C27(1)					
		EIVS_CARDAM_SE2_10HCE037_43.xls	C13(2)	C15(2)	C16(2)	C21(2)	C25(2)	C27(2)	C38(1)						
		EIVS_CARDAM_SE2_10HCE040_46.xls	C46(1)	C47(1)	C50(1)	C53(1)	C62(1)	C70(1)	C83(1)	C84(1)					
		EIVS_CARDAM_SE2_10HCE041_47.xls	C123(1)	C127(1)	C132(1)	C134(1)	C6(1)								
		EIVS_CARDAM_SE2_10HCE042_48.xls	C127(2)	C132(2)	C134(2)	C135(1)	C136(1)	C138(1)	C6(2)						
		EIVS_CARDAM_SE_10HCE044_50.xls	C45(4)	C53(4)	C98(3)	C101(3)	C119(3)	C123(3)	C127(3)	C132(3)	C83(4)	C6(3)			
		EIVS_CARDAM_SE_11HCE001_Kt_2.xls	C45(Kt)	C53(Kt)	C101(Kt)	C113(Kt)	C135(Kt)	C128(Kt)							
		EIVS_CARDAM_SE_11HCE003_3.xls	C105(1)	C106(1)	C107(1)	C108(1)	C139(1)	C110(1)	C112(1)	C134(3)	C135(2)	C136(2)	C138(2)	C128(1)	
		EIVS_CARDAM_SE_11HCE005_5.xls	C105(2)	C106(2)	C107(2)	C108(2)	C139(2)	C110(2)	C112(2)	C113(1)	C135(3)	C136(3)	C138(3)	C128(2)	
		EIVS_CARDAM_SE_11HCE006_6.xls	C105(3)	C106(3)	C107(3)	C108(3)	C139(3)	C110(3)	C112(3)	C113(2)	C116(1)	C120(1)	C124(1)	C128(3)	
		EIVS_CARDAM_SE_11HCE007_7.xls	C113(3)	C109(1)	C116(2)	C120(2)	C125(1)	C129(1)	C131(1)						
		EIVS_CARDAM_SE_11HCE008_8.xls	C124(2)	C109(2)	C125(2)	C129(2)	C131(2)								
		EIVS_CARDAM_SE_11HCE009_9.xls	C124(3)	C109(3)	C125(3)	C129(3)	C131(3)	C116(3)	C120(3)						
		EIVS_CARDAM_SE_11HCE020_18.xls	C4(1)	C9(1)	C20(1)	C39(1)	C28(1)	C48(1)	C52(1)	C55(1)	C58(1)				
		EIVS_CARDAM_SE_11HCE022_19.xls	C4(2)	C9(2)	C14(1)	C20(2)	C28(2)	C29(1)	C39(2)	C48(2)	C52(2)				
		EIVS_CARDAM_SE_11HCE024_20.xls	C4(3)	C9(3)	C14(2)	C28(3)	C29(2)	C52(3)	C56(1)	C58(2)					
		EIVS_CARDAM_SE_11HCE026_21.xls	C14(3)	C20(3)	C29(3)	C52(4)	C56(2)	C64(1)	C67(1)	C71(1)	C97(1)	C114(1)			
		EIVS_CARDAM_SE_11HCE029_23.xls	C39(3)	C48(3)	C55(2)	C52(5)	C56(3)	C58(3)	C103(1)	C137(1)	C140(1)	C141(1)			
		EIVS_CARDAM_SE_11HCE032_25.xls	C55(3)	C64(2)	C67(2)	C163(1)	C164(1)	C166(1)	C170(1)	C185(1)	C193(1)	C195(1)	C196(1)	C71(2)	
		EIVS_CARDAM_SE_11HCE034_26.xls	C97(2)	C103(2)	C114(2)	C137(2)	C140(2)	C141(2)	C163(2)	C164(2)	C166(2)	C170(2)	C185(2)	C193(2)	
		EIVS_CARDAM_SE_11HCE036_27.xls	C64(3)	C67(3)	C71(3)	C97(3)	C103(3)	C114(3)	C137(3)	C140(3)	C141(3)	C163(3)	C195(2)	C196(2)	
		EIVS_CARDAM_SE_11HCE038_28.xls	C164(3)	C166(3)	C170(3)	C185(3)	C193(3)	C195(3)	C196(3)						
	Ceetox	EIVS_CEETOX_SE_11HCE010 FK_16_v1.0 Set 2.xls	x138(1)	x139(1)											
		EIVS_CEETOX_SE_10HCE023_25_v1.0.xls	x1(1)	x2(1)	x5(1)	x6(1)	x7(1)	x16(1)	x22(1)	x28(1)	x36(1)	x38(1)			
		EIVS_CEETOX_SE_10HCE024_26_v1.0.xls	x1(2)	x2(2)	x5(2)	x6(2)	x7(2)	x16(2)	x22(2)	x28(2)	x36(2)	x38(2)			
		EIVS_CEETOX_SE_10HCE025_27_v1.0.XLS	x1(3)	x2(3)	x5(3)	x6(3)	x7(3)	x16(3)	x22(3)	x28(3)	x36(3)	x38(3)			
		EIVS_CEETOX_SE_10HCE027_29_v1.0.xls	x63(1)	x72(1)	x73(1)	x83(1)	x86(1)	x89(1)	x93(1)	x98(1)	x99(1)	x103(1)			
		EIVS_CEETOX_SE_10HCE028_30_v1.0.xls	x63(2)	x72(2)	x73(2)	x83(2)	x86(2)	x89(2)	x93(2)	x98(2)	x99(2)	x103(2)			
		EIVS_CEETOX_SE_10HCE042_48_v1.0.xls	x63(3)	x72(3)	x73(3)	x83(3)	x86(3)	x89(3)	x93(3)	x98(3)	x99(3)	x103(3)			
		EIVS_CEETOX_SE_10HCE043_49_v1.0.xls	x45(1)	x47(1)	x49(1)	x51(1)	x52(1)	x59(1)	x68(1)						
		EIVS_CEETOX_SE_10HCE044_50_v1.0.xls	x45(2)	x47(2)	x49(2)	x51(2)	x52(2)	x59(2)	x68(2)						
		EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.XLS	x45(3)	x47(3)	x49(3)	x51(3)	x52(3)	x59(3)	x68(3)						
		EIVS_CEETOX_SE_11HCE004_4_v1.0.xls	x41(1)	x17(1)	x31(1)	x91(1)	x121(1)	x3(1)	x25(1)	x30(1)	x33(1)				
		EIVS_CEETOX_SE_11HCE006_6_v1.0.xls	x41(2)	x17(2)	x31(2)	x91(2)	x121(2)	x3(2)	x25(2)	x30(2)	x33(2)				
		EIVS_CEETOX_SE_11HCE007_7_v1.0.xls	x41(3)	x17(3)	x31(3)	x91(3)	x121(3)	x3(3)	x25(3)	x30(3)	x33(3)				
		EIVS_CEETOX_SE_11HCE008_8_v1.0 JOEY.xls	x13(1)	x39(1)	x8(1)	x128(1)									
		EIVS_CEETOX_SE_11HCE008_8_v1.0 LISA.xls	x62(1)	x64(1)	x65(1)	x81(1)	x82(1)	x117(1)	x43(1)	x44(1)					
		EIVS_CEETOX_SE_11HCE013_13_v1.0 Set 1.xls	x13(3)	x39(3)	x8(3)	x128(3)	x43(3)	x62(3)	x64(3)						
		EIVS_CEETOX_SE_11HCE013_13_v1.0 Set 2.xls	x65(3)	x81(3)	x82(3)	x117(3)	x112(1)	x126(1)	x21(1)						
		EIVS_CEETOX_SE_11HCE022_19_v1.0.xls	X21(3)	X112(3)	X126(3)	X14(1)	X46(1)	X27(1)							
		EIVS_CEETOX_SE_11HCE009_9_v1.0 LISA.xls	x62(2)	x65(2)	x81(2)	x82(2)	x117(2)								
		EIVS_CEETOX_SE_11HCE009_9_v1.0.xls	x13(1)	x39(2)	x8(2)	x128(2)	x64(2)	x43(2)	x44(2)						
		EIVS_CEETOX_SE_11HCE020_18_v1.0.xls	X13(4)	X21(2)	X112(2)	X126(2)	X81 FK(2)	X108 FK(1)	X118 FK(1)						
		EIVS_CEETOX_SE_11HCE047_37_v1.0 UPDATED.xls	X14(2)	X27(2)	X46(2)	X50(1)	X53(1)	X70(1)	X84(1)	X87(1)	X102(1)	X107(1)	X108(1)	X109(1)	
		EIVS_CEETOX_SE_11HCE049_38_v1.0.xls	X14(3)	X27(3)	X46(3)	X50(2)	X53(2)	X70(2)	X84(2)	X87(2)	X102(2)	X107(2)	X108(2)	X109(2)	
		EIVS_CEETOX_SE_11HCE051_39_v1.0 SET 1.xls	X50(3)	X53(3)	X70(3)	X84(3)	X87(3)	X102(3)	X107(3)						
		EIVS_CEETOX_SE_11HCE051_39_v1.0 SET 2.xls	X108(3)	X109(3)	X110(1)	X111(1)	X114(1)	X115(1)	X116(1)						
		EIVS_CEETOX_SE_11HCE053_40_v1.0 SET 1.xls	X110(2)	X111(2)	X114(2)	X115(2)	X116(2)	X118(1)	X119(1)						
		EIVS_CEETOX_SE_11HCE053_40_v1.0 SET 2.xls	X123(1)	X125(1)	X129(1)	X131(1)	X133(1)	X134(1)	X136(1)						
		EIVS_CEETOX_SE_11HCE055_41_v1.0 SET 1.xls	X37(1)	X143(1)	X190(1)	X131(2)	X119(2)	X173(1)	X169(1)						
		EIVS_CEETOX_SE_11HCE055_41_v1.0 SET 2.xls	X133(2)	X127(1)	X139(1)	X40(1)	X111(3)	X138(1)							
		EIVS_CEETOX_SE_11HCE057_42_v1.0 SET 1.xls	X37(2)	X143(2)	X190(2)	X131(3)	X119(3)	X173(2)	X169(2)						
		EIVS_CEETOX_SE_11HCE057_42_v1.0 SET 2.xls	X133(3)	X127(2)	X139(2)	X40(2)	X138(2)								
		EIVS_CEETOX_SE_11HCE059_43_v1.0 SET 1.xls	X37(3)	X143(3)	X190(3)	X173(3)	X169(3)	X127(3)	X139(3)						
		EIVS_CEETOX_SE_11HCE059_43_v1.0 SET 2.xls	X40(3)	X138(3)	X118(2)	X125(2)	X123(2)	X134(2)	X129(2)						
		EIVS_CEETOX_SE_11HCE061_44_v1.0 SET 1.xls	X118(3)	X125(3)	X123(3)	X134(3)	X129(3)	X196(1)	X110(3)						
		EIVS_CEETOX_SE_11HCE061_44_v1.0 SET 2.xls	X114(3)	X115(3)	X116(3)	X136(2)	X11(1)	X19(1)	X29(1)						
		EIVS_CEETOX_SE_11HCE063_45_v1.0.xls	X11(2)	X19(2)	X29(2)	X196(2)	X136(3)	X24(1)	X32(1)	X42(1)	X55(1)	X56(1)			
		EIVS_CEETOX_SE_11HCE065_46_v1.0.xls	X19(3)	X196(3)	X24(2)	X32(2)	X42(2)	X55(2)	X56(2)	X61(1)	X66(1)	X75(1)	X77(1)	X80(1)	
		EIVS_CEETOX_SE_11HCE068_48_v1.0.xls	X61(2)	X66(2)	X75(2)	X77(2)	X80(2)	X94(1)	X95(1)	X113(1)	X120(1)	X157(1)	X158(1)	X160(1)	X165(1)
		EIVS_CEETOX_SE_11HCE070_49_v1.0.xls	X11(3)	X19(4)	X24(3)	X29(3)	X94(2)	X95(2)	X113(2)	X120(2)	X157(2)	X158(2)	X160(2)	X165(2)	
		EIVS_CEETOX_SE_12HCE002_2_v1.0.xls	X32(3)	X42(3)	X55(3)	X56(3)									
		EIVS_CEETOX_SE_12HCE004_3_v1.0.xls	X61(3)	X66(3)	X75(3)	X77(3)	X80(3)	X94(3)	X95(3)	X113(3)	X120(3)	X157(3)	X158(3)	X160(3)	X165(3)
	L'OREAL	EIVS_LOREAL_SE_10HCE023_25.xls	L5(1)	L9(1)	L11(1)	L12(1)	L17(1)	L18(1)	L20(1)	L23(1)	L24(1)	L27(1)	L28(1)		
		EIVS_LOREAL_SE_10HCE024_26.xls	L5(2)	L9(2)	L11(2)	L12(2)	L17(2)	L18(2)	L20(2)	L23(2)	L24(2)	L27(2)	L28(2)		
		EIVS_LOREAL_SE_10HCE025_27.xls	L30(1)	L39(1)	L43(1)	L45(1)	L48(1)	L51(1)	L55(1)	L59(1)	L60(1)	L66(1)	L68(1)	L11(3)	
		EIVS_LOREAL_SE_10HCE026_28.xls	L9(3)	L12(3)	L17(3)	L20(3)	L27(3)	L43(2)							
		EIVS_LOREAL_SE_10HCE027_29.xls	L30(2)	L39(2)	L43(3)	L45(2)	L48(2)	L51(2)	L55(2)	L59(2)	L60(2)	L66(2)	L68(2)	L73(1)	
		EIVS_LOREAL_SE_10HCE028_30.xls	L5(3)	L11(4)	L23(3)		L24(3)	L30(3)	L39(3)	L48(3)	L51(3)	L55(3)	L60(3)	L68(3)	
		EIVS_LOREAL_SE_10HCE029_35.xls	L74(1)	L75(1)	L78(1)	L81(1)	L82(1)	L85(1)	L91(1)	L94(1)	L97(1)	L98(1)	L102(1)		
		EIVS_LOREAL_SE_10HCE031_37.xls	L45(3)	L59(3)	L66(3)	L74(2)	L82(2)	L94(2)							
		EIVS_LOREAL_SE_10HCE032_38.xls	L74(3)	L75(2)	L78(2)	L81(2)	L82(3)	L85(2)	L91(2)	L94(3)	L97(2)	L98(2)	L102(2)		
		EIVS_LOREAL_SE_10HCE033_39.xls	L11(5)	L18(3)	L28(3)	L73(2)	L75(3)	L78(3)	L81(3)	L85(3)	L91(3)	L97(3)			
		EIVS_LOREAL_SE_10HCE034_40.xls	L73(3)	L98(3)	L4(1)	L7(1)	L8(1)								
		EIVS_LOREAL_SE_10HCE035_41.xls	L4(2)	L7(2)	L8(2)	L29(1)	L42(1)	L56(1)	L57(1)	L61(1)	L63(1)	L64(1)			
		EIVS_LOREAL_SE_10HCE036_42.xls	L102(3)	L7(3)	L29(2)	L57(2)									
		EIVS_LOREAL_SE_10HCE037_43.xls	L4(3)	L8(3)	L29(3)	L42(2)	L56(2)	L61(2)	L57(3)	L63(2)	L64(2)	L67(1)	L70(1)		
		EIVS_LOREAL_SE_10HCE040_46.xls	L30(4)	L42(3)	L56(3)	L61(3)	L63(3)	L64(3)	L67(2)	L70(2)	L72(1)	L79(1)	L83(1)	L87(1)	
		EIVS_LOREAL_SE_10HCE041_47.xls	L67(3)	L72(2)	L79(2)	L83(2)	L87(2)	L90(1)	L92(1)	L96(1)	L101(1)	L99(1)			
		EIVS_LOREAL_SE_10HCE042_48.xls	L87(3)	L90(2)	L92(2)	L99(2)	L104(1)	L119(1)	L120(1)	L130(1)	L131(1)	L132(1)			
		EIVS_LOREAL_SE_10HCE043_49.xls	L83(3)	L96(2)	L101(2)	L104(1)	L106(1)	L107(1)	L108(1)	L109(1)	L112(1)	L113(1)			
		EIVS_LOREAL_SE_10HCE044_50.xls	L79(3)	L96(3)	L101(3)	L106(2)	L107(2)	L108(2)	L109(2)	L112(2)	L113(2)	L114(1)	L115(1)	L118(1)	
		EIVS_LOREAL_SE_11HCE020_18.xls	L1(1)	L6(1)	L13(1)	L15(1)	L16(1)	L32(1)	L33(1)	L36(1)	L37(1)				
		EIVS_LOREAL_SE_11HCE024_20.xls	L144(1)	L148(1)	L156(1)	L161(1)	L164(1)	L169(1)	L174(1)	L185(1)	L200(1)	L15(2)	L6(2)		
		EIVS_LOREAL_SE_11HCE026_21.xls	L1(2)	L13(2)	L16(2)	L32(2)	L33(2)	L36(2)	L37(2)	L50(2)	L53(2)				
		EIVS_LOREAL_SE_11HCE032_25(2).xls	L100(3)												
		EIVS_LOREAL_SE_11HCE034_26(2).xls	L111(3)	L125(3)	L127(3)	L144(3)	L148(3)	L156(3)	L161(3)						
		EIVS_LOREAL_SE_11HCE002_2.xls	L122(1)	L123(1)	L126(1)	L129(1)	L133(1)	L134(1)	L136(1)	L137(1)	L139(1)	L140(1)	L114(2)	L115(2)	
		EIVS_LOREAL_SE_11HCE006_6.xls	L70(3)	L72(3)	L90(3)	L99(3)	L104(2)	L106(3)	L107(3)	L108(3)					
		EIVS_LOREAL_SE_11HCE007_7.xls	L109(3)	L112(3)	L113(3)	L114(3)	L115(3)	L118(2)	L119(2)	L120(2)	L122(2)	L123(2)			
		EIVS_LOREAL_SE_11HCE008_8.xls	L118(3)	L119(3)	L120(3)	L122(3)	L123(3)	L126(2)	L129(2)	L130(2)	L131(2)	L132(2)	L133(2)	L134(2)	

Protocol	Laboratory	Run													
		EIVS_LOREAL_SE_11HCE009_9.xls	L126(3)	L129(3)	L130(3)	L131(3)	L132(3)	L133(3)	L134(3)	L136(2)	L137(2)	L139(2)	L140(2)	L92(3)	L104(3)
		EIVS_LOREAL_SE_11HCE014_14.xls	L136(3)	L137(3)	L139(3)	L140(3)									
		EIVS_LOREAL_SE_11HCE022_19	L50(1)	L53(1)	L58(1)	L62(1)	L65(1)	L76(1)	L80(1)	L100(1)	L111(1)	L125(1)	L127(1)		
		EIVS_LOREAL_SE_11HCE029_23	L33(3)	L58(2)	L62(2)	L65(2)	L76(2)	L80(2)	L100(2)	L111(2)	L161(2)	L169(2)	L174(2)	L6	
		EIVS_LOREAL_SE_11HCE032_25(1)	L125(2)	L127(2)	L144(2)	L148(2)	L156(2)	L164(2)	L185(2)	L200(2)	L1(3)	L6(3)	L13(3)	L16(3)	L58(3)
		EIVS_LOREAL_SE_11HCE034_26(1)	L6(4)	L15(3)	L32(3)	L36(3)	L37(3)	L50(3)	L53(3)	L58(4)	L62(3)	L65(3)	L76(3)	L80(3)	L100(4)
		EIVS_LOREAL_SE_11HCE036_27	L6(5)	L58(5)	L164(3)	L100(5)	L169(3)	L174(3)	L185(3)	L200(3)					
LE	Cardam	EIVS_CARDAM_LE_10HCE029_35.xls	C1(1)	C2(1)	C17(1)	C19(1)	C26(1)	C30(1)	C33(1)	C34(1)	C35(1)				
		EIVS_CARDAM_LE_10HCE031_37.xls	C1(2)	C2(2)	C17(2)	C19(2)	C26(2)	C30(2)	C33(2)	C34(2)	C35(2)				
		EIVS_CARDAM_LE_10HCE032_38.xls	C1(3)	C2(3)	C17(3)	C19(3)	C26(3)	C30(3)	C77(1)	C34(3)	C35(3)				
		EIVS_CARDAM_LE_10HCE033_W39.xls	C33(3)	C35(4)	C36(1)	C37(1)	C49(1)	C51(1)	C54(1)	C60(1)	C63(1)	C65(1)	C66(1)	C75(1)	C76(1)
		EIVS_CARDAM_LE_10HCE033_W39_(C77).xls	C77(2)												
		EIVS_CARDAM_LE_10HCE034_40(C79).xls	C79(1)												
		EIVS_CARDAM_LE_10HCE034_40.xls	C36(1)	C37(1)	C49(1)	C51(1)	C54(1)	C60(1)	C63(1)	C65(1)	C66(1)	C75(1)	C76(1)	C77(1)	C78(1)
		EIVS_CARDAM_LE_10HCE044_50.xls	C45(4)	C84(2)	C98(2)	C101(2)	C119(3)	C123(2)	C127(2)	C132(2)	C135(2)	C6(3)			
		EIVS_CARDAM_LE_11HCE003_3.xls	C84(3)	C98(3)	C101(3)	C123(3)	C127(3)	C132(3)	C134(2)	C135(3)	C106(1)	C107(1)	C128(1)		
		EIVS_CARDAM_LE_11HCE005_5.xls	C105(1)	C106(2)	C107(2)	C108(1)	C110(1)	C112(1)	C134(3)	C135(4)	C136(1)	C138(1)	C139(1)	C128(2)	
		EIVS_CARDAM_LE_11HCE006_6.xls	C105(2)	C106(3)	C107(3)	C108(2)	C110(2)	C112(2)	C113(1)	C116(1)	C136(2)	C138(2)	C139(2)	C128(3)	
		EIVS_CARDAM_LE_11HCE007_7.xls	C105(3)	C109(1)	C120(1)	C108(3)	C125(1)	C129(1)	C113(2)	C116(2)	C131(1)				
		EIVS_CARDAM_LE_11HCE008_8.xls	C110(3)	C109(2)	C120(2)	C124(1)	C125(2)	C129(2)	C131(2)						
		EIVS_CARDAM_LE_11HCE009_9.xls	C136(3)	C109(3)	C120(3)	C124(2)	C138(3)	C112(3)	C113(3)	C116(3)	C139(3)				
		EIVS_CARDAM_LE_11HCE020_18.xls	C124(3)	C125(3)	C129(3)	C131(3)	C4(1)	C9(1)	C20(1)	C28(1)	C48(1)	C58(1)			
		EIVS_CARDAM_LE_11HCE022_19.xls	C4(2)	C9(2)	C14(1)	C20(2)	C28(2)	C29(1)	C39(1)	C48(2)	C52(1)				
		EIVS_CARDAM_LE_11HCE024_20.xls	C4(3)	C9(3)	C14(2)	C28(3)	C29(2)	C52(2)	C56(1)	C58(2)					
		EIVS_CARDAM_LE_11HCE026_21.xls	C14(3)	C20(3)	C29(3)	C52(3)	C56(2)	C64(1)	C67(1)	C71(1)	C97(1)	C114(1)			
		EIVS_CARDAM_LE_11HCE029_23.xls	C39(2)	C48(3)	C55(1)	C52(4)	C56(3)	C58(3)	C103(1)	C137(1)	C140(1)	C141(1)			
		EIVS_CARDAM_LE_11HCE032_25.xls	C39(3)	C55(2)	C64(2)	C67(2)	C163(1)	C164(1)	C166(1)	C185(1)	C170(1)	C193(1)	C195(1)	C196(1)	
		EIVS_CARDAM_LE_11HCE034_26.xls	C55(3)	C71(2)	C97(2)	C103(2)	C114(2)	C137(2)	C140(2)	C141(2)	C163(2)	C164(2)	C166(2)	C170(2)	
		EIVS_CARDAM_LE_11HCE036_27.xls	C64(3)	C67(3)	C71(3)	C97(3)	C103(3)	C114(3)	C137(3)	C166(3)	C185(2)	C193(2)	C195(2)	C196(2)	
		EIVS_CARDAM_LE_11HCE038_28.xls	C140(3)	C141(3)	C163(3)	C164(3)	C166(4)	C170(3)	C185(3)	C193(3)	C195(3)	C196(3)			
		EIVS_CARDAM_LE1_10HCE035_41.xls	C36(2)	C37(2)	C49(2)	C51(2)	C54(2)	C60(2)	C63(2)	C65(2)	C66(2)	C75(2)	C76(2)	C77(3)	C78(1)
		EIVS_CARDAM_LE1_10HCE036_42.xls	C36(3)	C37(3)	C49(3)	C51(3)	C54(3)	C60(3)	C63(3)	C65(3)	C66(3)	C75(3)	C76(3)	C78(2)	C79(2)
		EIVS_CARDAM_LE1_10HCE037_43.xlsx	C78(3)	C79(3)	C82(3)	C85(3)	C87(3)	C88(3)	C90(3)	C91(3)	C94(2)	C96(3)	C99(1)	C104(1)	C3(1)
		EIVS_CARDAM_LE1_10HCE040_46.xls	C94(3)	C99(2)	C104(2)	C3(2)	C11(2)	C12(2)	C13(2)	C15(2)	C16(2)	C21(2)	C25(2)	C27(2)	C38(1)
		EIVS_CARDAM_LE1_10HCE041_47.xls	C99(3)	C104(3)	C3(3)	C11(3)	C12(3)	C13(3)	C15(3)	C16(3)	C21(3)	C25(3)	C27(3)	C38(2)	C45(2)
		EIVS_CARDAM_LE1_10HCE042_48.xls	C38(3)	C45(3)	C46(3)	C47(3)	C50(3)	C53(3)	C62(3)	C70(3)	C83(3)	C84(1)	C98(1)	C101(1)	C119(2)
		EIVS_CARDAM_LE2_10HCE035_41.xls	C79(1)	C82(1)	C85(1)	C87(1)	C88(1)	C90(1)	C91(1)	C96(1)					
		EIVS_CARDAM_LE2_10HCE036_42.xls	C82(2)	C85(2)	C87(2)	C88(2)	C90(2)	C91(2)	C94(1)	C96(2)					
		EIVS_CARDAM_LE2_10HCE037_43.xlsx	C11(1)	C12(1)	C13(1)	C15(1)	C16(1)	C21(1)	C25(1)	C27(1)					
		EIVS_CARDAM_LE2_10HCE040_46.xls	C45(1)	C46(1)	C47(1)	C50(1)	C53(1)	C62(1)	C70(1)	C83(1)					
		EIVS_CARDAM_LE2_10HCE041_47.xls	C46(2)	C47(2)	C50(2)	C53(2)	C62(2)	C70(2)	C83(2)	C119(1)	C6(1)				
		EIVS_CARDAM_LE2_10HCE042_48.xls	C123(1)	C127(1)	C132(1)	C134(1)	C135(1)	C6(2)							
	Ceetox	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls	x1(1)	x2(1)	x5(1)	x6(1)	x7(1)	x16(1)	x22(1)	x28(1)	x36(1)	x38(1)			
		EIVS_CEETOX_LE_10HCE024_26_v1.0.xls	x1(2)	x2(2)	x5(2)	x6(2)	x7(2)	x16(2)	x22(2)	x28(2)	x36(2)	x38(2)			
		EIVS_CEETOX_LE_10HCE042_48_v1.0 UPDATED.xls	x1(3)	x2(3)	x5(3)	x6(3)	x7(3)	x16(3)	x22(3)	x28(3)	x36(3)	x38(3)			
		EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls	x1(4)	x2(4)	x5(4)	x6(4)	x7(4)	x16(4)	x22(4)	x28(4)	x36(4)	x38(4)			
		EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls	x1(5)	x2(5)	x5(5)	x6(5)	x7(5)	x16(5)	x22(5)	x28(5)	x36(5)	x38(5)			
		EIVS_CEETOX_LE_11HCE003_3_v1.0 .xls	x63(1)	x72(1)	x73(1)	x83(1)	x86(1)	x89(1)	x93(1)	x98(1)	x99(1)	x103(1)			
		EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY Updated.xls	x45(1)	x47(1)	x49(1)	x51(1)	x52(1)	x59(1)	x68(1)						
		EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.XLS	x72(2)	x73(2)	x83(2)	x86(2)	x89(2)	x93(2)	x98(2)	x99(2)					
		EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.XLS	x45(2)	x47(2)	x49(2)	x51(2)	x52(2)	x59(2)	x68(2)						
		EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 1.xls	x63(2)	x72(3)	x73(3)	x83(3)	x86(3)	x89(3)	x93(3)	x98(3)	x99(3)				
		EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 Joey.xls	x45(3)	x47(3)	x49(3)	x51(3)	x52(3)								
		EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls	x13(1)	x39(1)	x8(1)	x128(1)	x103(2)	x49(4)							
		EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.XLS	x62(1)	x64(1)	x65(1)	x81(1)	x82(1)	x117(1)	x43(1)	x44(1)					
		EIVS_CEETOX_LE_11HCE009_9_v1.0 Joey FAILED RUN UPDATED.XLS	x13(2)	x39(2)	x8(2)	x128(2)	x64(2)	x43(2)	x44(2)	x103(3)	x63(3)				
		EIVS_CEETOX_LE_11HCE009_9_v1.0 LISA FAILED RUN UPDATED.XLS	x62(2)	x65(2)	x81(2)	x82(2)	x117(2)								
		EIVS_CEETOX_LE_11HCE013_13_v1.0 Set 1.xls	x13(2)	x39(1)	x8(2)	x128(2)	x43(2)	x62(2)	x64(2)						
		EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 1.xls	X21(2)	X112(2)	X126(2)	X14(1)	X46(1)	X27(1)	X50(1)	X53(1)	X70(1)	X84(1)	X87(1)	X102(1)	
		EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 2.xls	X108(1)	X109(1)	X110(1)	X118(1)	X136(1)	X138(1)	X139(1)	X13(3)	X43(3)	X47(5)	X59(3)	X68(3)	
		EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 3.xls	X62(3)	X64(3)	X65(3)	X81(3)	X82(3)	X117(3)	X128(3)	X39(3)	PC2(1)	PC3(1)	X107(1)		
		EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 1.xls	X14(2)	X46(2)	X27(2)	X50(2)	X53(2)	X70(2)	X84(2)	X87(2)	X102(2)	X107(2)	X8(3)		
		EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 2.xls	X108(2)	X109(2)	X110(2)	X118(2)	X136(2)	X138(2)	X139(2)	X39(4)	X21(3)	X112(3)	X126(3)		
		EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 3.xls	X111(1)	X114(1)	X115(1)	X116(1)	X119(1)	X123(1)	X125(1)	X129(1)	X131(1)	X133(1)	X134(1)		
		EIVS_CEETOX_LE_11HCE040_29_v1.0 SET 1.xls	X14(3)	X46(3)	X27(3)	X50(3)	X53(3)	X70(3)	X84(3)	X87(3)	X102(3)	X107(3)			
		EIVS_CEETOX_LE_11HCE040_29_v1.0 SET 2.xls	X108(3)	X109(3)	X110(3)	X118(3)	X136(3)	X138(3)	X139(3)	X111(2)	X114(2)	X115(2)	X116(2)		
	L'OREAL	EIVS_LOREAL_LE_10HCE023_25.xls	L5(1)	L9(1)	L11(1)	L12(1)	L17(1)	L18(1)	L20(1)	L23(1)	L24(1)	L27(1)	L28(1)		
		EIVS_LOREAL_LE_10HCE024_26.xls	L5(2)	L9(2)	L11(2)	L12(2)	L17(2)	L18(2)	L20(2)	L23(2)	L24(2)	L27(2)	L28(2)		
		EIVS_LOREAL_LE_10HCE025_27.xls	L30(1)	L39(1)	L43(1)	L45(1)	L48(1)	L51(1)	L55(1)	L59(1)	L60(1)	L66(1)	L68(1)	L11(3)	
		EIVS_LOREAL_LE_10HCE026_28.xls	L9(3)	L12(3)	L17(3)	L20(3)	L27(3)	L43(2)							
		EIVS_LOREAL_LE_10HCE027_29.xls	L30(2)	L39(1)	L43(3)	L45(2)	L48(2)	L51(2)	L55(2)	L59(2)	L60(2)	L66(2)	L68(2)	L73(1)	
		EIVS_LOREAL_LE_10HCE028_30.xls	L5(3)	L11(4)	L23(3)		L24(3)	L30(3)	L39(2)	L48(3)	L51(3)	L55(3)	L60(3)	L68(3)	
		EIVS_LOREAL_LE_10HCE031_37.xls	L45(3)	L59(3)	L66(3)	L74(1)	L82(1)	L94(1)							
		EIVS_LOREAL_LE_10HCE032_38.xls	L74(2)	L75(1)	L78(1)	L81(1)	L82(2)	L85(1)	L91(1)	L94(2)	L97(1)	L98(1)	L102(1)		
		EIVS_LOREAL_LE_10HCE033_39.xls	L18(3)	L28(3)	L39(3)	L73(2)	L75(2)	L78(2)	L81(2)	L85(2)	L91(2)	L97(2)			
		EIVS_LOREAL_LE_10HCE034_40(1).xls	L73(3)	L74(3)	L75(3)	L78(3)	L81(3)	L82(3)	L91(3)	L94(3)	L97(3)	L98(2)	L102(2)		
		EIVS_LOREAL_LE_10HCE034_40(2).xls	L4(1)	L7(1)	L8(1)										
		EIVS_LOREAL_LE_10HCE035_41.xls	L85(3)	L98(3)	L4(2)	L7(2)	L8(2)	L29(1)	L42(1)	L56(1)	L57(1)	L61(1)	L63(1)	L64(1)	
		EIVS_LOREAL_LE_10HCE036_42.xls	L102(3)	L7(3)	L29(2)	L57(2)									
		EIVS_LOREAL_LE_10HCE037_43.xls	L4(3)	L8(3)	L29(3)	L42(2)	L56(2)	L61(2)	L57(3)	L63(2)	L64(2)	L67(1)	L70(1)		
		EIVS_LOREAL_LE_10HCE040_46.xls	L42(3)	L56(3)	L61(3)	L63(3)	L64(3)	L67(2)	L70(2)	L72(1)	L79(1)	L83(1)	L87(1)	L92(1)	
		EIVS_LOREAL_LE_10HCE041_47.xls	L67(3)	L72(2)	L79(2)	L83(2)	L87(2)	L90(1)	L92(2)	L96(1)	L99(1)	L101(1)			
		EIVS_LOREAL_LE_10HCE042_48.xls	L87(3)	L90(2)	L92(3)	L99(2)	L104(1)	L119(1)	L120(1)	L130(1)	L131(1)	L132(1)			
		EIVS_LOREAL_LE_10HCE043_49.xls	L83(3)	L96(2)	L101(2)	L104(2)	L106(1)	L107(1)	L108(1)	L109(1)	L112(1)	L113(1)			
		EIVS_LOREAL_LE_10HCE044_50.xls	L79(3)	L96(3)	L101(3)	L106(2)	L107(2)	L108(2)	L109(2)	L112(2)	L113(2)	L114(1)	L115(1)	L118(1)	
		EIVS_LOREAL_LE_11HCE002_2.xls	L122(1)	L123(1)	L126(1)	L129(1)	L133(1)	L134(1)	L136(1)	L137(1)	L139(1)	L140(1)	L114(2)	L115(2)	
		EIVS_LOREAL_LE_11HCE006_6.xls	L70(3)	L72(3)	L90(3)	L99(3)	L104(3)	L106(3)	L107(3)	L108(3)					
		EIVS_LOREAL_LE_11HCE007_7.xls	L109(3)	L112(3)	L113(3)	L114(3)	L115(3)	L118(2)	L119(2)	L120(2)	L122(2)	L123(2)			
		EIVS_LOREAL_LE_11HCE008_8.xls	L118(3)	L119(3)	L120(3)	L122(3)	L123(3)	L126(2)	L129(2)	L130(2)	L131(2)	L132(2)	L133(2)	L134(2)	
		EIVS_LOREAL_LE_11HCE009_9.xls	L126(3)	L129(3)	L130(3)	L131(3)	L132(3)	L133(3)	L134(3)	L136(2)	L137(2)	L139(2)	L140(2)		
		EIVS_LOREAL_LE_11HCE014_14.xls	L136(3)	L137(3)	L139(3)	L140(3)									

Protocol	Laboratory	Run													
		EIVS_LOREAL_LE_11HCE020_18.xls	L1(1)	L6(1)	L13(1)	L15(1)	L16(1)	L32(1)	L33(1)	L36(1)	L37(1)				
		EIVS_LOREAL_LE_11HCE022_19.xls	L50(1)	L53(1)	L58(1)	L62(1)	L65(1)	L76(1)	L80(1)	L100(1)	L111(1)	L125(1)	L127(1)		
		EIVS_LOREAL_LE_11HCE024_20.xls	L144(1)	L148(1)	L156(1)	L161(1)	L164(1)	L169(1)	L174(1)	L185(1)	L200(1)	L137(4)	L6(2)		
		EIVS_LOREAL_LE_11HCE026_21.xls	L1(2)	L13(2)	L15(2)	L16(2)	L32(2)	L33(2)	L36(2)	L37(2)	L50(2)	L53(2)	L148(1)		
		EIVS_LOREAL_LE_11HCE029_23.xls	L33(3)	L58(2)	L62(2)	L65(2)	L76(2)	L80(2)	L100(2)	L161(2)	L169(2)	L174(2)	L111(2)	L6	
		EIVS_LOREAL_LE_11HCE032_25(1).xls	L125(2)	L127(2)	L144(2)	L148(2)	L156(2)	L164(2)	L185(2)	L200(2)	L1(3)	L6(3)	L13(3)	L16(3)	L58(3)
		EIVS_LOREAL_LE_11HCE032_25(2).xls	L100(3)												
		EIVS_LOREAL_LE_11HCE034_26.xls	L6(4)	L15(3)	L32(3)	L36(3)	L37(3)	L50(3)	L53(3)	L62(3)	L65(3)	L76(3)	L80(3)	L111(3)	L125(3)
		EIVS_LOREAL_LE_11HCE036_27.xls	L6(5)	L127(3)	L144(3)	L148(3)	L156(3)	L161(3)	L164(3)	L169(3)	L174(3)	L185(3)	L200(3)		

3.2.4 Number of tests within each test sequence

In Table 3.2.5, the number of tests within each test sequence is given, subdivided into laboratories and chemicals.

Table 3.2.5a Number of tests within each test sequence (SE protocol)

	laboratory				laboratory		
Chemical	**Cardam**	**Ceetox**	**L'OREAL**	**Chemical**	**Cardam**	**Ceetox**	**L'OREAL**
1	3	3	3	55	3	3	3
2	3	3	3	56	3	3	3
3	3	3	3	57	3	3	3
4	4	3	3	58	3	3	3
5	3	3	3	59	3	3	3
6	3	3	3	60	3	3	3
7	3	3	3	61	3	3	3
8	3	3	3	62	3	3	3
9	3	3	3	63	3	3	3
10	3	3	3	64	3	3	3
11	3	3	3	65	3	3	3
12	3	3	3	66	3	3	3
13	3	3	3	67	3	3	3
14	3	3	3	68	3	3	3
15	3	3	3	69	3	3	3
16	3	3	3	70	3	3	3
17	4	3	3	71	3	3	3
18	3	4	3	72	3	3	3
19	3	3	3	73	3	3	3
20	3	3	5	74	3	3	3
21	3	3	3	75	4	3	5
22	3	3	3	76	3	3	3
23	3	3	3	77	3	3	3
24	3	3	3	78	3	3	3
25	3	3	3	79	3	3	3
26	3	3	3	80	3	3	3
28	3	3	3	81	3	3	3
29	3	3	3	82	3	3	3
30	3	3	3	83	3	3	3
31	3	3	3	84	3	3	3
32	3	3	3	85	3	3	3
33	3	3	3	86	3	3	3
34	4	3	3	87	3	3	3
35	3	3	3	88	3	3	3
36	3	3	3	89	3	3	3
37	3	3	3	90	3	3	3
38	3	3	3	91	3	3	3
39	3	3	3	92	3	3	3
40	3	3	3	93	3	3	3
41	3	3	3	94	3	3	3
42	3	3	3	95	3	3	3
43	3	3	3	96	3	3	3
44	3	3	3	97	3	3	3
45	3	3	3	98	3	3	3
46	3	3	3	99	3	3	3

	laboratory				laboratory		
Chemical	**Cardam**	**Ceetox**	**L'OREAL**	**Chemical**	**Cardam**	**Ceetox**	**L'OREAL**
47	3	3	3	100	3	3	3
48	3	3	3	101	3	3	3
49	3	3	3	102	3	3	3
50	3	3	3	103	3	3	3
51	3	3	3	104	3	3	3
52	3	3	3	105	3	3	3
53	3	3	3	106[1]	5	3	5
54	3	3	3	107[1]	3	3	5

[1] extra chemicals not for statistics but for a later purpose of evaluation using an HPLC based detection system.

Table 3.2.5b Number of tests within each test sequence (LE protocol)

	laboratory				laboratory		
Chemical	**Cardam**	**Ceetox**	**L'OREAL**	**Chemical**	**Cardam**	**Ceetox**	**L'OREAL**
1	3	5	4	55	3	5	3
2	3	5	3	56	3	3	3
3	3	3	3	57	3	3	3
4	3	5	3	58	3	4	3
5	3	4	3	59	3	3	3
6	3	5	3	60	3	3	3
7	3	3	3	61	3	3	3
8	3	4	4	62	3	3	3
9	3	5	3	63	3	3	3
10	3	3	3	64	3	4	3
11	3	5	3	65	3	4	4
12	3	3	3	66	3	3	3
13	3	3	3	67	3	3	3
14	3	4	4	68	3	3	3
15	3	3	3	69	3	3	3
16	3	4	3	70	3	3	3
17	3	3	3	71	3	5	3
18	3	4	3	72	3	3	3
19	3	4	3	73	3	6	3
20	3	3	3	74	3	5	4
21	3	5	3	75	4	4	4
22	3	3	3	76	3	3	3
23	3	3	3	77	3	3	3
24	3	5	3	78	3	3	3
25	3	3	3	79	3	4	3
26	3	3	3	80	3	3	3
28	3	5	3	81	3	3	4
29	3	4	3	82	3	3	3
30	3	3	3	83	3	3	4
31	3	3	3	84	3	4	3
32	3	3	3	85	3	5	3
33	3	5	3	86	3	3	3
34	4	3	3	87	3	3	3
35	3	5	4	88	3	4	3
36	3	3	3	89	3	3	3
37	3	3	3	90	3	5	3
38	3	4	3	91	3	5	3
39	3	4	3	92	3	4	3
40	3	3	3	93	3	5	4
41	3	3	3	94	3	5	4
42	3	3	3	95	3	3	3
43	3	3	3	96	3	3	3
44	3	4	3	97	3	3	3
45	3	3	3	98	3	5	3
46	3	3	3	99	3	4	3
47	3	3	3	100	3	3	3
48	4	3	3	101	3	3	3
49	3	4	3	102	3	3	3

	laboratory				laboratory		
Chemical	**Cardam**	**Ceetox**	**L'OREAL**	**Chemical**	**Cardam**	**Ceetox**	**L'OREAL**
50	3	4	3	103	3	3	3
51	3	3	3	104	3	3	3
52	4	4	3	105	3	3	3
53	3	4	3	106[1]	4	3	5
54	3	5	4	107[1]	3	3	3

[1] extra chemicals not for statistics but for a later purpose of evaluation using an HPLC based detection system.

3.2.5 Non-qualified and excluded chemicals

A listing of the number and fraction of non-qualified chemicals is given in Table 3.2.6.

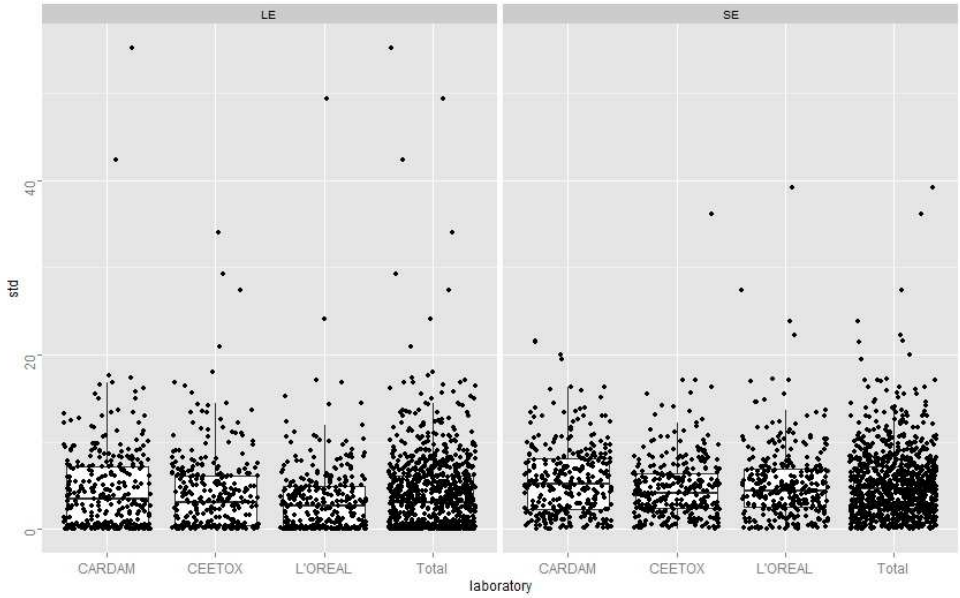
Table 3.2.6 List, number and fraction of non-qualified chemicals, subdivided into laboratories and chemicals

Protocol	Laboratory	Chemical	Reason	No.	Fraction (%)
SE	CARDAM	4	Non-Qualified	1	25
		17	Non-Qualified	1	25
		34	Non-Qualified	1	25
		75	Non-Qualified	1	25
	CEETOX	18	Non-Qualified	1	25
	L'OREAL	75	Non-Qualified	2	40
		20	Non-Qualified	2	40
LE	CARDAM	34	Non-Qualified	1	25
		52	Non-Qualified	1	25
	CEETOX	1	Non-Qualified	2	40
		2	Non-Qualified	2	40
		4	Non-Qualified	2	40
		5	Non-Qualified	1	25
		6	Non-Qualified	2	40
		8	Non-Qualified	1	25
		9	Non-Qualified	2	40
		11	Non-Qualified	2	40
		14	Non-Qualified	1	25
		16	Non-Qualified	1	25
		18	Non-Qualified	1	25
		19	Non-Qualified	1	25
		20	Non-Qualified	1	33.3
		21	Non-Qualified	2	40
		24	Non-Qualified	2	40
		28	Non-Qualified	2	40
		29	Non-Qualified	1	25
		33	Non-Qualified	2	40
		35	Non-Qualified	2	40
		38	Non-Qualified	1	25
		39	Non-Qualified	1	25
		44	Non-Qualified	1	25
		49	Non-Qualified	1	25
		50	Non-Qualified	1	25
		52	Non-Qualified	1	25
		53	Non-Qualified	1	25
		54	Non-Qualified	2	40
		55	Non-Qualified	2	40
		58	Non-Qualified	1	25
		64	Non-Qualified	1	25
		65	Non-Qualified	1	25
		71	Non-Qualified	2	40
		73	Non-Qualified	3	50

Protocol	Laboratory	Chemical	Reason	No.	Fraction (%)
		74	Non-Qualified	2	40
		75	Non-Qualified	1	25
		79	Non-Qualified	1	25
		84	Non-Qualified	1	25
		85	Non-Qualified	2	40
		88	Non-Qualified	1	25
		90	Non-Qualified	2	40
		91	Non-Qualified	2	40
		92	Non-Qualified	1	25
		93	Non-Qualified	2	40
		94	Non-Qualified	2	40
		98	Non-Qualified	2	40
		99	Non-Qualified	1	25
	L'OREAL	1	Non-Qualified	1	25
		8	Non-Qualified	1	25
		14	Non-Qualified	1	25
		35	Non-Qualified	1	25
		54	Non-Qualified	1	25
		65	Non-Qualified	1	25
		74	Non-Qualified	1	25
		75	Non-Qualified	1	25
		81	Non-Qualified	1	25
		83	Non-Qualified	1	25
		93	Non-Qualified	1	25
		94	Non-Qualified	1	25

In Figure 3.2.1, a boxplot is given of the standard deviations between uncorrected viabilities for every set of 3 tissue replicates used for each chemical, including both qualified and unqualified tests, for each independent laboratory and for all laboratories together, as well as for both protocols.

Figure 3.2.1 Standard deviations of uncorrected viabilities for every set of 3 tissue replicates, per laboratory and total, including both qualified and unqualified tests.



3.2.6 Chemicals with complete test sequences

A total of three qualified tests is considered as a complete test sequence. A list of chemicals with a complete test sequence is given in Table 3.2.7. Each of the

laboratory had a fraction of more than 98% complete test sequences, as is shown in Table 3.2.8.

Table 3.2.7a A list of chemicals with a complete test sequence (SE protocol)

Chemical	Cardam	Ceetox	L'OREAL	Chemical	Cardam	Ceetox	L'OREAL
1	3	3	3	55	3	3	3
2	3	3	3	56	3	3	3
3	3	3	3	57	3	3	3
4	3[1]	3[1]	3[1]	58	3	3	3
5	3	3	3	59	3	3	3
6	3	3	3	60	3	3	3
7	3	3	3	61	3	3	3
8	3	3	3	62	3	3	3
9	3	3	3	63	3	3	3
10	3	3	3	64	3	3	3
11	3	3	3	65	3	3	3
12	3	3	3	66	3	3	3
13	3	3	3	67	3	3	3
14	3	3	3	68	3	3	3
15	3	3	3	69	3	3	3
16	3	3	3	70	3	3	3
17	3	3	3	71	3	3	3
18	3	3	3	72	3	3	3
19	3	3	3	73	3	3	3
20	3[1]	3	3	74	3	3	3
21	3	3	3	75	3	3	3
22	3	3	3	76	3	3	3
23	3	3[1]	3	77	3	3	3
24	3	3	3	78	3	3	3
25	3	3	3	79	3	3	3
26	3	3	3	80	3	3	3
28	3	3	3	81	3	3	3
29	3	3	3	82	3	3	3
30	3	3	3	83	3	3	3
31	3	3	3	84	3	3	3
32	3	3	3	85	3	3	3
33	3	3	3	86	3	3	3
34	3	3	3	87	3	3	3
35	3	3	3	88	3	3	3
36	3	3	3	89	3	3	3
37	3	3	3	90	3	3	3
38	3	3	3	91	3	3[1]	3
39	3	3	3	92	3	3	3
40	3	3	3	93	3	3	3
41	3	3	3	94	3	3	3
42	3	3	3	95	3	3	3
43	3	3	3	96	3	3	3
44	3	3	3	97	3	3	3
45	3	3	3	98	3	3	3
46	3	3	3	99	3	3	3
47	3	3	3	100	3	3	3
48	3	3	3	101	3	3	3
49	3	3	3	102	3	3	3
50	3	3	3	103	3	3	3
51	3	3	3	104	3	3	3
52	3	3	3	105	3	3	3
53	3	3	3				
54	3	3	3				

[1]On May 10th 2012, after an evaluation of the first draft of the statistics report, the core VMG overrode the rule identifying 50% NSMTT as a cut-off to consider a chemical compatible with the test system as described in Chapter 2.5.1. of this report. In all these cases, rule 3 in Chapter 2.5.1. is fulfilled since the mean %NSC of all qualified tests is greater than (>) 50% and the classification

of these qualified tests changes upon correction (from non-irritant to irritant). However, the viability values obtained in the qualified tests are definitely within the linear range of the OD measurements (within the 100% scale) and therefore, even though there is a strong MTT reduction occurring this is not interfering with the analytical capacity to measure formazan production. Moreover, the variability obtained between the different tests and controls is low. As such, these chemicals were considered compatible with the test method and their data were therefore included in all of the statistical analyses.

Table 3.2.7b A list of chemicals with a complete test sequence (LE protocol)

Chemical	Cardam	Ceetox	L'OREAL	Chemical	Cardam	Ceetox	L'OREAL
1	3	3	3	55	3	3	3
2	3	3	3	56	3	3	3
3	3	3	3	57	3	3	3
4	3[1]	3[1]	3	58	3	3	3
5	3	3	3	59	3	3	3
6	3	3	3	60	3	3	3
7	3	3	3	61	3	3	3
8	3	3	3	62	3	3	3
9	3	3	3	63	3	3	3
10	3	3	3	64	3	3	3
11	3	3	3	65	3	3	3
12	3	3	3	66	3	3	3
13	3	3	3	67	3	3	3
14	3	3	3	68	3	3	3
15	3	3	3	69	3	3	3
16	3	3	3	70	3	3	3
17	3	3	3	71	3	3	3
18	3	3	3	72	3	3	3
19	3	3	3	73	3	3	3
20	3	2	3	74	3	3	3
21	3	3	3	75	4	3	3
22	3	3	3	76	3	3	3
23	3	3	3	77	3	3	3
24	3	3	3	78	3	3	3
25	3	3	3	79	3	3	3
26	3	3	3	80	3	3[1]	3
28	3	3	3	81	3	3	3
29	3	3	3	82	3	3	3
30	3	3	3	83	3	3	3
31	3	3	3	84	3	3	3
32	3	3	3	85	3	3	3
33	3	3	3	86	3	3	3
34	3	3	3	87	3	3	3
35	3	3	3	88	3	3	3
36	3	3	3	89	3	3	3
37	3	3	3	90	3	3	3
38	3	3	3	91	3	3	3
39	3	3	3	92	3	3	3
40	3	3	3	93	3	3	3
41	3	3	3	94	3	3	3
42	3	3	3	95	3	3	3
43	3	3	3	96	3	3	3
44	3	3	3	97	3	3	3
45	3	3	3	98	3	3	3
46	3	3	3	99	3	3	3
47	3	3	3	100	3	3	3
48	4	3	3	101	3	3	3
49	3	3	3	102	3	3	3
50	3	3	3	103	3	3	3
51	3	3	3	104	3	3	3
52	3	3	3	105	3	3	3
53	3	3	3				

54	3	3	3				

[1]On May 10th 2012, after an evaluation of the first draft of the statistics report, the core VMG overrode the rule identifying 50% NSMTT as a cut-off to consider a chemical compatible with the test system as described in Chapter 2.5.1. of this report. In all these cases, rule 3 in Chapter 2.5.1. is fulfilled since the mean %NSC of all qualified tests is greater than (>) 50% and the classification of these qualified tests changes upon correction (from non-irritant to irritant). However, the viability values obtained in the qualified tests are definitely within the linear range of the OD measurements (within the 100% scale) and therefore, even though there is a strong MTT reduction occurring this is not interfering with the analytical capacity to measure formazan production. Moreover, the variability obtained between the different tests and controls is low. As such, these chemicals were considered compatible with the test method and their data were therefore included in all of the statistical analyses.

Table 3.2.8 Fraction of chemicals with a complete test sequence, subdivided into laboratories and total

	Fraction (%)	
laboratory	**SE**	**LE**
CARDAM	100.0	100.0
CEETOX	100.0	99.0
L'OREAL	100.0	100.0
Total	100.0	99.7

Given Table 3.2.8, the criteria of at least 85% complete test sequences in each laboratory was met, as is also summarized in Table 3.2.9.

Table 3.2.9 Statement whether the test method has fulfilled the performance criteria (at least 85% complete test sequences) concerning the fraction of complete test sequences.

	SE		**LE**	
laboratory	**Fraction**	**Statement: criteria is**	**Fraction**	**Statement: criteria is**
CARDAM	100.0	fulfilled	100.0	fulfilled
CEETOX	100.0	fulfilled	99.0	fulfilled
L'OREAL	100.0	fulfilled	100.0	fulfilled
Total	100.0	fulfilled	99.7	fulfilled

3.2.7 Negative and Positive controls

The results for the negative and positive controls are presented in summarizing figures (see Figure 3.2.2, Figure 3.2.3 Figure 3.2.4, and Figure 3.2.5) as well as in Table 3.2.12.

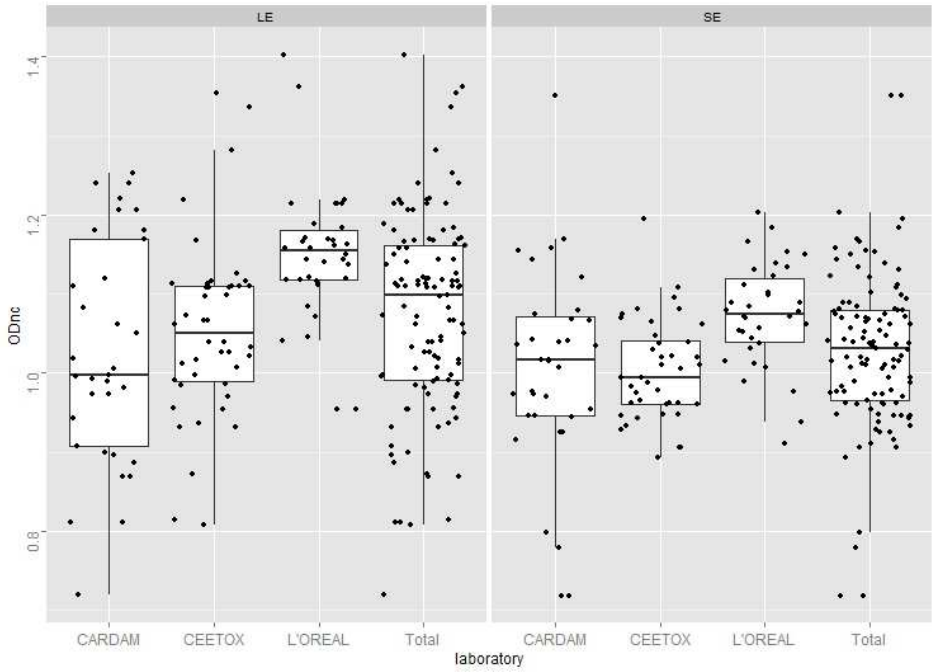


Figure 3.2.2 Mean OD-values for the Negative controls (Performance criteria: 0.7 < mean ODnc < 1.5), per laboratory and total

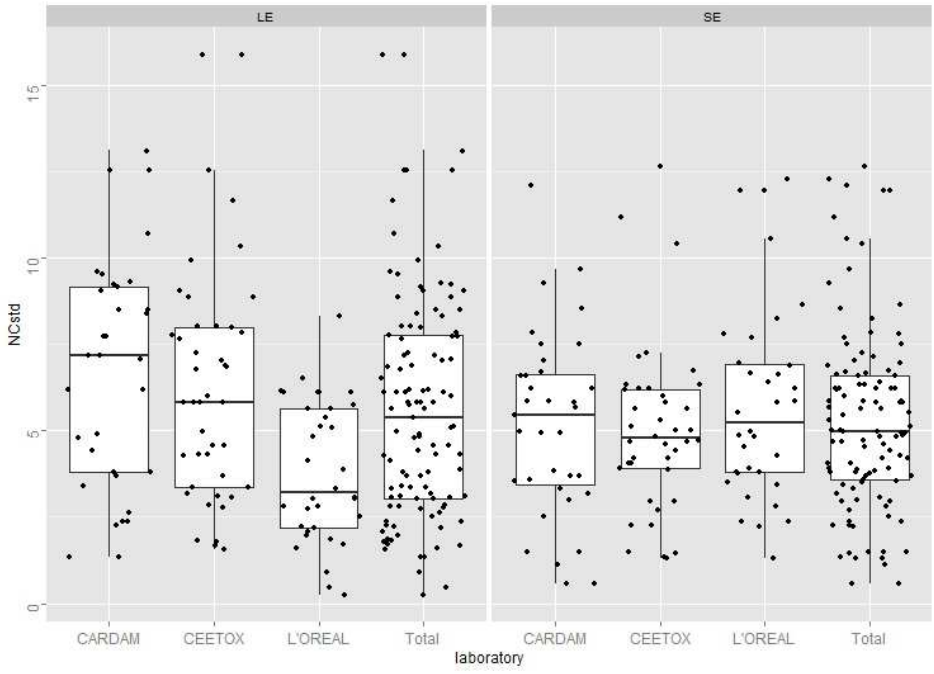


Figure 3.2.3 Standard deviations in viabilities for the Negative controls (Performance criteria: standard deviation ≤ 18%), per laboratory and total

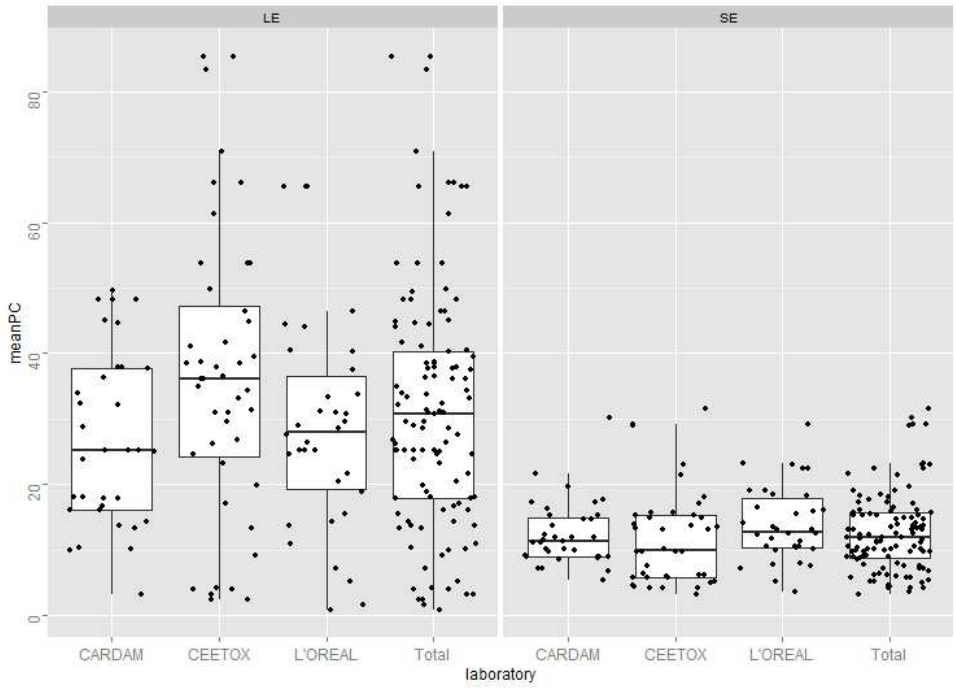


Figure 3.2.4 Mean viabilities for the Positive controls (Performance criteria: mean viability ≤ 50%)

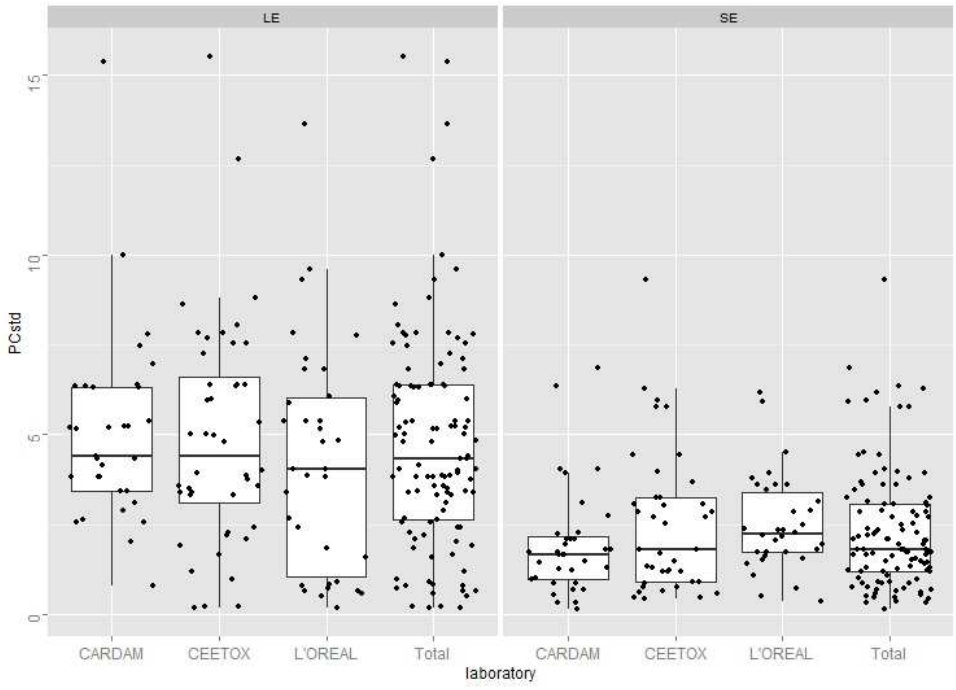


Figure 3.2.5 Standard deviations in viabilities for the Positive controls (Performance criteria: Standard deviations ≤ 18%), per laboratory and total

Table 3.2.12 Numerical statistical values for the Negative and Positive Control (lower: 25th percentile – 1.5*IQR, p25: 25th percentile, median: 50th percentile, p75: 75th percentile, upper: 75th percentile + 1.5*IQR, with IQR = 75th percentile – 25th percentile).

		SE					LE				
Variable[1]	**laboratory**	**lower**	**p25**	**median**	**p75**	**upper**	**lower**	**p25**	**median**	**p75**	**upper**
ODnc	CARDAM	0.78	0.95	1.02	1.07	1.17	0.72	0.91	1.00	1.17	1.25
	CEETOX	0.89	0.96	0.99	1.04	1.11	0.81	0.99	1.05	1.11	1.28
	L'OREAL	0.94	1.04	1.07	1.12	1.2	1.04	1.12	1.15	1.18	1.22
	Total	0.8	0.97	1.03	1.08	1.2	0.81	0.99	1.1	1.16	1.4
NCstd	CARDAM	0.57	3.44	5.47	6.64	9.67	1.34	3.81	7.2	9.19	13.12
	CEETOX	1.29	3.9	4.78	6.2	7.28	1.56	3.35	5.84	8.00	12.55
	L'OREAL	1.31	3.78	5.25	6.95	10.58	0.24	2.18	3.21	5.64	8.31
	Total	0.57	3.59	5.00	6.6	10.58	0.24	3.05	5.4	7.76	13.12
meanPC	CARDAM	5.45	8.97	11.31	14.97	21.68	3.25	16.15	25.13	37.68	49.52
	CEETOX	3.29	5.79	9.96	15.34	29.1	2.39	23.94	36.13	48.11	83.28
	L'OREAL	3.58	10.26	12.8	18.23	29.16	0.84	18.85	28.07	37.47	46.43
	Total	3.29	8.67	11.85	15.76	23.31	0.84	17.83	30.79	40.39	70.82
PCstd	CARDAM	0.15	0.99	1.67	2.17	3.95	0.79	3.43	4.4	6.31	10.00
	CEETOX	0.43	0.91	1.82	3.25	6.27	0.18	2.87	4.41	6.82	12.67
	L'OREAL	0.35	1.73	2.24	3.48	5.9	0.17	0.89	4.04	6.08	13.63
	Total	0.15	1.21	1.82	3.08	5.78	0.17	2.64	4.31	6.37	10.00

[1] ODnc = optical density for negative control, NCstd = standard deviation between replicates of the negative control, meanPC = viability for positive control, PCstd = standard devation between replicates of the positive control

3.2.8 Summary of all tests results

Finally, a summary of all tests results (including the non-qualified and excluded test results) are presented in Appendix VI.

3.3 Reproducibility and accuracy using the SE protocol

In this section, a 50% cut-off was applied to determine the irritancy of the chemical based on the SE protocol. If the viability is above 50%, the chemical is considered to be non-irritant. If the viability is 50% or below, the chemical is considered to be irritant.

3.3.1 Within-laboratory variability

For each laboratory, concordance of classification was calculated based on qualified test from test chemicals for which at least two qualified tests were available. In Table 3.3.1 the concordance within each laboratory as well as in total is given.

Table 3.3.1 Concordance within laboratories and total

		SE	
laboratory	**WLV concordant**	**No.**	**Fraction(%)**
CARDAM	NO	7	6.7
	YES	97	93.3
CEETOX	NO	8	7.7
	YES	96	92.3
L'OREAL	NO	4	3.8
	YES	100	96.2

		SE	
laboratory	**WLV concordant**	**No.**	**Fraction(%)**
Total	NO	19	6.1
	YES	293	93.9

Additional descriptive statistics can identify possible reasons for non-concordant results. These are presented in Table 3.3.2. For each non-concordant result the reactivity, GHS classification, whether it is colouring or MTTreducer and the test results are given.

Table 3.3.2 Additional descriptive statistics on non-concordant results within laboratories

	Chemical					Test		
laboratory	**& reactivity[1]**	**name**	**colouring**	**MTT**	**GHS class**	**1**	**2**	**3**
CARDAM	20 NR	Ricinoleic acid tin salt	No	Yes	no cat	46.2985	44.938	65.542
	35 R	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	No	Yes	no cat	21.820	68.206	13.977
	48 NR	sodium hydrogensulphite INCI name: SODIUM BISULFITE	No	Yes	no cat	39.332	43.625	53.660
	69 R	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	No	No	cat 2A (ICCVAM:cat2B)	81.825	34.715	68.611
	75 NR	sodium benzoate INCI name: SODIUM BENZOATE	No	No	cat 2A	61.585	19.942	10.124
	91 NR	(ethylenediaminepropyl)trimethoxysilane	No	Yes	cat 1	58.078	41.530	55.730
	100 NR	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	No	No	cat 1	28.052	55.149	27.078
CEETOX	22 NR	3-phenoxybenzyl alcohol	No	No	no cat	82.712	48.284	40.507
	35 R	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	No	Yes	no cat	9.883	66.492	4.429
	73 R	3,3'-dithiopropionic acid	No	No	cat 2A (ICCVAM:cat2B)	65.464	47.596	35.656
	74 R	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	No	Yes	cat 2A	88.001	86.080	21.660
	76 NR	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	No	No	cat 2A	44.397	58.806	75.627
	77 R	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate	No	No	cat 2A	49.749	102.332	101.634
	87 R	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE	No	No	cat 1	81.973	87.036	31.902
	89 NR	ethoxylated (5 EO) alkyl (C10-14) alcohol	No	No	cat 1	66.308	56.433	16.697
L'OREAL	20 NR	ricinoleic acid tin salt	No	Yes	no cat	56.208	45.605	41.291
	54 R	3-chloropropionitrile	No	No	cat 2B	76.698	71.114	43.178
	90 NR	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	No	Yes	cat 1	51.517	23.173	32.711
	100 NR	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	No	No	cat 1	27.798	69.408	56.670

[1] Reactivity: R = reactive, NR = non-reactive

The concordance of classifications (irritant/non-irritant) for the set of chemicals tested during validation obtained in different, independent runs within a single laboratory should ideally be equal or higher than 85% for all participating laboratories. As summarized in Table 3.3.3, this criteria was met for each laboratory as well as in total.

Table 3.3.3 Statement whether the test method has fulfilled the performance criteria concerning the concordance of classifications within one laboratory.

	SE	
laboratory	**Fraction(%)**	**Statement: criteria is**
CARDAM	93.3	fulfilled
CEETOX	92.3	fulfilled
L'OREAL	96.2	fulfilled
Total	93.9	fulfilled

The intra-laboratory variability is described by the concordance of classifications. Correlation coefficients between viability measurements give also information on this variability. Since the Pearson correlation coefficient is sensitive to outlying test results and high leverages, both the Pearson and the Spearman correlation coefficients (using ranks instead of the original test results) were calculated. These coefficients are presented in Table 3.3.4.

Table 3.3.4 Pearson and Spearman correlation coefficients between tests results within each laboratory as well as in total.

Correlation	laboratory	Qual1 - Qual2	Qual1 - Qual3	Qual2 - Qual3
Pearson	L'OREAL	0.958	0.962	0.968
	CARDAM	0.889	0.941	0.916
	CEETOX	0.940	0.922	0.933
	Mean	0.929	0.942	0.939
Spearman	L'OREAL	0.856	0.850	0.868
	CARDAM	0.727	0.818	0.770
	CEETOX	0.838	0.853	0.881
	Mean	0.807	0.841	0.840

Finally, the arithmetic mean, standard deviation and coefficient of variation from the three valid tests are given per laboratory as well as in total (see Table 3.3.5). Note that the coefficient of variation is not a useful measure if the mean is close to zero.

Table 3.3.5 Arithmetic mean, standard deviation (std) and coefficient of variation (cv) from the three valid tests are given per laboratory as well as in total (n = number of qualified tests that was used for the calculation of the mean, std and cv)

	laboratory											
	CARDAM				CEETOX				L'OREAL			
Chemical	mean	std	cv	n	mean	std	cv	n	mean	std	cv	n
1	86.7	4.9	5.6	3	85.4	3.1	3.7	3	81.8	2.7	3.3	3
2	85.6	15.7	18.4	3	92.0	10.7	11.6	3	93.3	3.6	3.9	3
3	93.4	37.2	39.8	3	79.8	8.5	10.7	3	82.9	3.7	4.4	3
4	31.0	8.0	25.7	3	0.0	0.0	.	3	8.8	4.2	48.1	3
5	87.8	12.8	14.6	3	101.8	6.0	5.9	3	88.2	1.5	1.7	3
6	110.6	6.4	5.8	3	110.6	11.0	9.9	3	112.8	5.8	5.1	3
7	78.7	12.0	15.2	3	86.8	2.5	2.9	3	91.7	4.1	4.4	3
8	109.2	13.1	12.0	3	106.2	8.5	8.0	3	104.1	1.5	1.4	3
9	102.6	8.4	8.2	3	94.8	4.6	4.9	3	94.2	5.6	6.0	3
10	37.3	9.9	26.7	3	40.8	4.4	10.9	3	30.7	3.7	11.9	3
11	73.3	7.0	9.6	3	81.7	2.5	3.1	3	80.0	5.8	7.3	3
12	104.8	2.4	2.3	3	96.1	5.1	5.3	3	89.8	5.1	5.7	3
13	99.8	3.7	3.7	3	98.4	2.2	2.2	3	95.3	2.3	2.4	3
14	101.7	7.6	7.5	3	99.3	5.5	5.6	3	87.6	2.6	2.9	3
15	96.1	4.8	5.0	3	98.9	5.2	5.3	3	93.6	8.5	9.1	3
16	98.3	5.7	5.8	3	93.9	4.9	5.2	3	105.4	5.6	5.3	3
17	97.2	14.4	14.8	3	100.1	4.8	4.8	3	97.7	5.2	5.3	3
18	92.5	7.4	8.0	3	92.3	12.7	13.8	3	100.3	4.8	4.8	3
19	100.6	5.0	4.9	3	100.5	7.4	7.4	3	99.4	3.9	3.9	3
20	52.3	11.5	22.0	3	111.2	10.3	9.2	3	47.7	7.7	16.1	3
21	80.4	17.6	21.9	3	86.3	0.4	0.4	3	85.8	1.9	2.2	3
22	82.8	19.3	23.3	3	57.2	22.5	39.3	3	68.7	16.7	24.3	3
23	0.0	0.0	.	3	0.0	0.0	.	3	1.2	0.5	42.5	3
24	70.4	8.2	11.7	3	68.1	6.3	9.2	3	68.3	3.1	4.5	3
25	106.2	15.7	14.8	3	96.0	2.5	2.6	3	93.6	6.4	6.8	3
26	103.1	3.8	3.7	3	97.9	1.7	1.7	3	94.3	7.0	7.5	3
28	90.8	15.3	16.9	3	91.7	4.2	4.6	3	98.1	2.7	2.8	3
29	104.9	4.4	4.2	3	99.2	4.1	4.1	3	90.8	0.3	0.3	3
30	93.3	10.8	11.6	3	80.2	3.2	4.0	3	89.1	6.2	7.0	3
31	100.9	10.0	9.9	3	98.9	0.4	0.4	3	93.7	4.4	4.7	3
32	61.2	8.0	13.1	3	44.7	5.1	11.5	3	23.8	6.9	28.9	3
33	88.8	10.5	11.8	3	91.5	5.7	6.2	3	91.3	7.1	7.8	3

	laboratory											
	CARDAM				CEETOX				L'OREAL			
Chemical	mean	std	cv	n	mean	std	cv	n	mean	std	cv	n
34	106.9	13.4	12.5	3	108.1	18.7	17.3	3	108.7	10.0	9.2	3
35	34.7	29.3	84.5	3	26.9	34.4	127.6	3	25.9	8.7	33.5	3
36	105.2	7.0	6.6	3	96.5	5.4	5.6	3	93.9	2.3	2.5	3
37	93.4	13.8	14.7	3	86.6	4.1	4.7	3	85.8	0.7	0.8	3
38	99.9	10.8	10.8	3	94.3	9.3	9.8	3	94.3	5.3	5.6	3
39	99.7	4.9	4.9	3	98.1	4.7	4.8	3	97.4	6.2	6.3	3
40	96.6	3.3	3.4	3	84.9	1.2	1.4	3	85.4	12.7	14.9	3
41	100.3	6.2	6.2	3	99.1	5.7	5.7	3	96.1	5.0	5.2	3
42	90.2	2.1	2.3	3	84.2	8.8	10.4	3	91.7	11.5	12.6	3
43	95.7	3.4	3.6	3	101.1	3.1	3.1	3	98.4	4.2	4.3	3
44	98.2	5.7	5.8	3	100.4	1.9	1.9	3	97.0	3.4	3.5	3
45	98.2	6.4	6.5	3	95.1	4.4	4.6	3	90.9	7.0	7.7	3
46	89.5	3.4	3.8	3	92.2	9.9	10.8	3	86.5	5.9	6.8	3
47	95.6	6.1	6.3	3	96.7	6.9	7.1	3	91.4	5.4	5.9	3
48	45.5	7.4	16.1	3	28.4	10.7	37.8	3	39.4	5.5	13.9	3
49	105.3	4.1	3.9	3	105.7	7.5	7.1	3	100.1	4.7	4.7	3
50	92.7	8.4	9.0	3	90.1	4.6	5.1	3	91.1	5.4	6.0	3
51	94.2	3.6	3.9	3	99.1	4.8	4.9	3	94.5	8.8	9.3	3
52	99.0	3.2	3.3	3	107.2	5.4	5.1	3	96.6	8.2	8.5	3
53	90.9	7.9	8.7	3	98.4	4.0	4.0	3	95.4	2.9	3.1	3
54	72.1	8.5	11.8	3	80.9	7.2	8.9	3	63.7	18.0	28.2	3
55	2.8	0.9	31.2	3	4.1	0.8	19.2	3	1.6	0.5	32.4	3
56	81.5	12.9	15.9	3	90.0	3.9	4.4	3	71.1	2.9	4.0	3
57	33.9	7.7	22.8	3	34.0	5.3	15.5	3	26.8	14.0	52.2	3
58	34.4	8.4	24.5	3	32.5	1.9	6.0	3	16.0	5.3	33.2	3
59	81.0	9.4	11.6	3	89.0	2.5	2.8	3	70.4	6.4	9.1	3
60	33.4	3.4	10.2	3	33.8	7.8	23.0	3	21.2	4.0	18.8	3
61	87.5	11.9	13.6	3	90.3	5.9	6.6	3	86.7	3.6	4.2	3
62	95.3	2.9	3.1	3	97.0	4.7	4.9	3	91.8	6.1	6.7	3
63	94.1	2.6	2.7	3	91.4	8.3	9.1	3	96.5	10.9	11.2	3
64	93.5	8.2	8.8	3	90.8	5.6	6.2	3	95.2	7.8	8.2	3
65	102.3	14.3	14.0	3	103.0	3.6	3.5	3	94.6	1.2	1.3	3
66	86.3	20.0	23.2	3	82.8	2.0	2.4	3	81.6	2.5	3.1	3
67	4.5	2.0	44.6	3	23.7	9.0	37.8	3	8.8	6.6	75.5	3
68	2.6	2.1	82.0	3	4.9	0.5	10.2	3	4.0	2.9	72.5	3
69	61.7	24.3	39.4	3	65.0	7.4	11.4	3	66.3	9.1	13.6	3
70	10.1	2.2	21.8	3	8.9	3.4	37.7	3	14.5	4.1	28.3	3
71	6.6	5.2	78.8	3	4.8	0.6	12.0	3	5.8	1.3	22.7	3
72	3.9	0.7	17.3	3	2.6	2.3	86.6	3	3.3	1.6	50.1	3
73	93.8	5.9	6.3	3	49.6	15.0	30.3	3	91.1	13.5	14.8	3
74	93.9	9.1	9.7	3	65.2	37.8	57.9	3	88.2	1.8	2.1	3
75	30.6	27.3	89.4	3	61.4	2.7	4.4	3	13.3	0.9	6.8	3
76	80.8	8.7	10.8	3	59.6	15.6	26.2	3	60.0	6.0	9.9	3
77	96.3	15.2	15.8	3	84.6	30.2	35.7	3	97.5	1.6	1.6	3
78	91.1	10.8	11.8	3	99.0	6.6	6.7	3	91.3	2.0	2.2	3
79	73.5	1.5	2.0	3	81.7	6.5	8.0	3	83.7	7.0	8.4	3
80	3.0	3.2	105.5	3	0.2	0.4	155.7	3	0.0	0.0	.	3
81	0.4	0.1	15.0	3	1.9	1.2	60.3	3	0.7	0.2	27.5	3
82	3.4	1.1	33.6	3	1.3	0.4	29.1	3	4.8	1.3	27.9	3
83	3.6	2.5	68.1	3	5.3	4.3	81.0	3	2.6	0.7	26.6	3
84	23.0	10.5	45.9	3	8.6	6.0	69.4	3	20.3	4.9	24.3	3
85	71.6	4.3	6.0	3	82.5	6.7	8.1	3	70.3	9.0	12.8	3
86	95.5	14.3	15.0	3	80.2	5.4	6.7	3	87.4	2.3	2.6	3
87	93.4	7.6	8.1	3	67.0	30.5	45.5	3	89.9	7.5	8.3	3
88	6.8	3.5	50.8	3	4.8	2.6	55.3	3	3.9	0.5	13.4	3
89	76.0	6.9	9.1	3	46.5	26.3	56.5	3	68.1	8.8	12.9	3
90	77.5	23.2	29.9	3	75.5	9.6	12.7	3	35.8	14.4	40.3	3
91	51.8	9.0	17.3	3	0.0	0.0	.	3	33.4	14.9	44.7	3
92	82.3	3.3	4.1	3	81.7	4.8	5.8	3	79.8	2.5	3.1	3
93	80.5	8.5	10.5	3	91.9	6.5	7.1	3	73.8	10.9	14.8	3
94	78.5	3.2	4.0	3	60.6	12.2	20.1	3	76.9	1.6	2.1	3
95	1.8	0.7	36.5	3	10.3	6.3	61.0	3	1.4	0.1	3.7	3
96	90.7	8.4	9.2	3	99.0	1.9	1.9	3	91.7	17.4	18.9	3
97	95.8	2.5	2.6	3	86.6	13.7	15.8	3	90.8	3.6	4.0	3

	laboratory											
	CARDAM				CEETOX				L'OREAL			
Chemical	mean	std	cv	n	mean	std	cv	n	mean	std	cv	n
98	92.8	13.6	14.7	3	75.2	6.4	8.5	3	82.8	4.9	5.9	3
99	22.0	4.6	21.0	3	8.1	5.5	68.6	3	23.3	5.1	21.8	3
100	36.8	15.9	43.3	3	30.6	12.0	39.2	3	51.3	21.3	41.6	3
101	91.7	8.3	9.1	3	91.0	6.3	6.9	3	79.2	1.6	2.0	3
102	111.6	3.8	3.4	3	99.5	2.8	2.8	3	92.0	5.1	5.5	3
103	7.6	2.2	29.6	3	4.2	2.1	50.8	3	5.1	0.4	7.7	3
104	96.4	13.3	13.8	3	89.0	6.5	7.3	3	90.8	6.5	7.2	3
105	9.2	1.6	17.1	3	5.9	0.5	7.7	3	7.9	0.8	10.2	3

Table 3.3.6 Standard deviation (std) and coefficient of variation (cv) from all available tests results (Q=qualified and NQ=non-qualified) per laboratory (n = number of tests that was used for the calculations)

	laboratory																	
	CARDAM						CEETOX						L'OREAL					
	Q			Q+NQ			Q			Q+NQ			Q			Q+NQ		
Chemical	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n
1	4.9	5.6	3	4.9	5.6	3	3.1	3.7	3	3.1	3.7	3	2.7	3.3	3	2.7	3.3	3
2	15.7	18.4	3	15.7	18.4	3	10.7	11.6	3	10.7	11.6	3	3.6	3.9	3	3.6	3.9	3
3	37.2	39.8	3	37.2	39.8	3	8.5	10.7	3	8.5	10.7	3	3.7	4.4	3	3.7	4.4	3
4	8.0	25.7	3	16.5	70.5	3	0.0	.	3	0.0	.	3	4.2	48.1	3	4.2	48.1	3
5	12.8	14.6	3	12.8	14.6	3	6.0	5.9	3	6.0	5.9	3	1.5	1.7	3	1.5	1.7	3
6	6.4	5.8	3	6.4	5.8	3	11.0	9.9	3	11.0	9.9	3	5.8	5.1	3	5.8	5.1	3
7	12.0	15.2	3	12.0	15.2	3	2.5	2.9	3	2.5	2.9	3	4.1	4.4	3	4.1	4.4	3
8	13.1	12.0	3	13.1	12.0	3	8.5	8.0	3	8.5	8.0	3	1.5	1.4	3	1.5	1.4	3
9	8.4	8.2	3	8.4	8.2	3	4.6	4.9	3	4.6	4.9	3	5.6	6.0	3	5.6	6.0	3
10	9.9	26.7	3	9.9	26.7	3	4.4	10.9	3	4.4	10.9	3	3.7	11.9	3	3.7	11.9	3
11	7.0	9.6	3	7.0	9.6	3	2.5	3.1	3	2.5	3.1	3	5.8	7.3	3	5.8	7.3	3
12	2.4	2.3	3	2.4	2.3	3	5.1	5.3	3	5.1	5.3	3	5.1	5.7	3	5.1	5.7	3
13	3.7	3.7	3	3.7	3.7	3	2.2	2.2	3	2.2	2.2	3	2.3	2.4	3	2.3	2.4	3
14	7.6	7.5	3	7.6	7.5	3	5.5	5.6	3	5.5	5.6	3	2.6	2.9	3	2.6	2.9	3
15	4.8	5.0	3	4.8	5.0	3	5.2	5.3	3	5.2	5.3	3	8.5	9.1	3	8.5	9.1	3
16	5.7	5.8	3	5.7	5.8	3	4.9	5.2	3	4.9	5.2	3	5.6	5.3	3	5.6	5.3	3
17	14.4	14.8	3	13.9	14.9	4	4.8	4.8	3	4.8	4.8	3	5.2	5.3	3	5.2	5.3	3
18	7.4	8.0	3	7.4	8.0	3	12.7	13.8	3	47.3	68.3	4	4.8	4.8	3	4.8	4.8	3
19	5.0	4.9	3	5.0	4.9	3	7.4	7.4	3	7.4	7.4	3	3.9	3.9	3	3.9	3.9	3
20	11.5	22.0	3	11.5	22.0	3	10.3	9.2	3	10.3	9.2	3	7.7	16.1	3	10.3	22.5	5
21	17.6	21.9	3	17.6	21.9	3	0.4	0.4	3	0.4	0.4	3	1.9	2.2	3	1.9	2.2	3
22	19.3	23.3	3	19.3	23.3	3	22.5	39.3	3	22.5	39.3	3	16.7	24.3	3	16.7	24.3	3
23	0.0	.	3	0.0	.	3	0.0	.	3	0.0	.	3	0.5	42.5	3	0.5	42.5	3
24	8.2	11.7	3	8.2	11.7	3	6.3	9.2	3	6.3	9.2	3	3.1	4.5	3	3.1	4.5	3
25	15.7	14.8	3	15.7	14.8	3	2.5	2.6	3	2.5	2.6	3	6.4	6.8	3	6.4	6.8	3
26	3.8	3.7	3	3.8	3.7	3	1.7	1.7	3	1.7	1.7	3	7.0	7.5	3	7.0	7.5	3
28	15.3	16.9	3	15.3	16.9	3	4.2	4.6	3	4.2	4.6	3	2.7	2.8	3	2.7	2.8	3
29	4.4	4.2	3	4.4	4.2	3	4.1	4.1	3	4.1	4.1	3	0.3	0.3	3	0.3	0.3	3
30	10.8	11.6	3	10.8	11.6	3	3.2	4.0	3	3.2	4.0	3	6.2	7.0	3	6.2	7.0	3
31	10.0	9.9	3	10.0	9.9	3	0.4	0.4	3	0.4	0.4	3	4.4	4.7	3	4.4	4.7	3
32	8.0	13.1	3	8.0	13.1	3	5.1	11.5	3	5.1	11.5	3	6.9	28.9	3	6.9	28.9	3
33	10.5	11.8	3	10.5	11.8	3	5.7	6.2	3	5.7	6.2	3	7.1	7.8	3	7.1	7.8	3
34	13.4	12.5	3	13.5	12.2	4	18.7	17.3	3	18.7	17.3	3	10.0	9.2	3	10.0	9.2	3
35	29.3	84.5	3	29.3	84.5	3	34.4	127.6	3	34.4	127.6	3	8.7	33.5	3	8.7	33.5	3
36	7.0	6.6	3	7.0	6.6	3	5.4	5.6	3	5.4	5.6	3	2.3	2.5	3	2.3	2.5	3
37	13.8	14.7	3	13.8	14.7	3	4.1	4.7	3	4.1	4.7	3	0.7	0.8	3	0.7	0.8	3
38	10.8	10.8	3	10.8	10.8	3	9.3	9.8	3	9.3	9.8	3	5.3	5.6	3	5.3	5.6	3
39	4.9	4.9	3	4.9	4.9	3	4.7	4.8	3	4.7	4.8	3	6.2	6.3	3	6.2	6.3	3
40	3.3	3.4	3	3.3	3.4	3	1.2	1.4	3	1.2	1.4	3	12.7	14.9	3	12.7	14.9	3
41	6.2	6.2	3	6.2	6.2	3	5.7	5.7	3	5.7	5.7	3	5.0	5.2	3	5.0	5.2	3
42	2.1	2.3	3	2.1	2.3	3	8.8	10.4	3	8.8	10.4	3	11.5	12.6	3	11.5	12.6	3
43	3.4	3.6	3	3.4	3.6	3	3.1	3.1	3	3.1	3.1	3	4.2	4.3	3	4.2	4.3	3
44	5.7	5.8	3	5.7	5.8	3	1.9	1.9	3	1.9	1.9	3	3.4	3.5	3	3.4	3.5	3
45	6.4	6.5	3	6.4	6.5	3	4.4	4.6	3	4.4	4.6	3	7.0	7.7	3	7.0	7.7	3
46	3.4	3.8	3	3.4	3.8	3	9.9	10.8	3	9.9	10.8	3	5.9	6.8	3	5.9	6.8	3
47	6.1	6.3	3	6.1	6.3	3	6.9	7.1	3	6.9	7.1	3	5.4	5.9	3	5.4	5.9	3

	laboratory																	
	CARDAM						CEETOX						L'OREAL					
	Q			Q+NQ			Q			Q+NQ			Q			Q+NQ		
Chemical	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n
48	7.4	16.1	3	7.4	16.1	3	10.7	37.8	3	10.7	37.8	3	5.5	13.9	3	5.5	13.9	3
49	4.1	3.9	3	4.1	3.9	3	7.5	7.1	3	7.5	7.1	3	4.7	4.7	3	4.7	4.7	3
50	8.4	9.0	3	8.4	9.0	3	4.6	5.1	3	4.6	5.1	3	5.4	6.0	3	5.4	6.0	3
51	3.6	3.9	3	3.6	3.9	3	4.8	4.9	3	4.8	4.9	3	8.8	9.3	3	8.8	9.3	3
52	3.2	3.3	3	3.2	3.3	3	5.4	5.1	3	5.4	5.1	3	8.2	8.5	3	8.2	8.5	3
53	7.9	8.7	3	7.9	8.7	3	4.0	4.0	3	4.0	4.0	3	2.9	3.1	3	2.9	3.1	3
54	8.5	11.8	3	8.5	11.8	3	7.2	8.9	3	7.2	8.9	3	18.0	28.2	3	18.0	28.2	3
55	0.9	31.2	3	0.9	31.2	3	0.8	19.2	3	0.8	19.2	3	0.5	32.4	3	0.5	32.4	3
56	12.9	15.9	3	12.9	15.9	3	3.9	4.4	3	3.9	4.4	3	2.9	4.0	3	2.9	4.0	3
57	7.7	22.8	3	7.7	22.8	3	5.3	15.5	3	5.3	15.5	3	14.0	52.2	3	14.0	52.2	3
58	8.4	24.5	3	8.4	24.5	3	1.9	6.0	3	1.9	6.0	3	5.3	33.2	3	5.3	33.2	3
59	9.4	11.6	3	9.4	11.6	3	2.5	2.8	3	2.5	2.8	3	6.4	9.1	3	6.4	9.1	3
60	3.4	10.2	3	3.4	10.2	3	7.8	23.0	3	7.8	23.0	3	4.0	18.8	3	4.0	18.8	3
61	11.9	13.6	3	11.9	13.6	3	5.9	6.6	3	5.9	6.6	3	3.6	4.2	3	3.6	4.2	3
62	2.9	3.1	3	2.9	3.1	3	4.7	4.9	3	4.7	4.9	3	6.1	6.7	3	6.1	6.7	3
63	2.6	2.7	3	2.6	2.7	3	8.3	9.1	3	8.3	9.1	3	10.9	11.2	3	10.9	11.2	3
64	8.2	8.8	3	8.2	8.8	3	5.6	6.2	3	5.6	6.2	3	7.8	8.2	3	7.8	8.2	3
65	14.3	14.0	3	14.3	14.0	3	3.6	3.5	3	3.6	3.5	3	1.2	1.3	3	1.2	1.3	3
66	20.0	23.2	3	20.0	23.2	3	2.0	2.4	3	2.0	2.4	3	2.5	3.1	3	2.5	3.1	3
67	2.0	44.6	3	2.0	44.6	3	9.0	37.8	3	9.0	37.8	3	6.6	75.5	3	6.6	75.5	3
68	2.1	82.0	3	2.1	82.0	3	0.5	10.2	3	0.5	10.2	3	2.9	72.5	3	2.9	72.5	3
69	24.3	39.4	3	24.3	39.4	3	7.4	11.4	3	7.4	11.4	3	9.1	13.6	3	9.1	13.6	3
70	2.2	21.8	3	2.2	21.8	3	3.4	37.7	3	3.4	37.7	3	4.1	28.3	3	4.1	28.3	3
71	5.2	78.8	3	5.2	78.8	3	0.6	12.0	3	0.6	12.0	3	1.3	22.7	3	1.3	22.7	3
72	0.7	17.3	3	0.7	17.3	3	2.3	86.6	3	2.3	86.6	3	1.6	50.1	3	1.6	50.1	3
73	5.9	6.3	3	5.9	6.3	3	15.0	30.3	3	15.0	30.3	3	13.5	14.8	3	13.5	14.8	3
74	9.1	9.7	3	9.1	9.7	3	37.8	57.9	3	37.8	57.9	3	1.8	2.1	3	1.8	2.1	3
75	27.3	89.4	3	22.3	73.0	4	2.7	4.4	3	2.7	4.4	3	0.9	6.8	3	8.9	45.7	5
76	8.7	10.8	3	8.7	10.8	3	15.6	26.2	3	15.6	26.2	3	6.0	9.9	3	6.0	9.9	3
77	15.2	15.8	3	15.2	15.8	3	30.2	35.7	3	30.2	35.7	3	1.6	1.6	3	1.6	1.6	3
78	10.8	11.8	3	10.8	11.8	3	6.6	6.7	3	6.6	6.7	3	2.0	2.2	3	2.0	2.2	3
79	1.5	2.0	3	1.5	2.0	3	6.5	8.0	3	6.5	8.0	3	7.0	8.4	3	7.0	8.4	3
80	3.2	105.5	3	3.2	105.5	3	0.4	155.7	3	0.4	155.7	3	0.0	.	3	0.0	.	3
81	0.1	15.0	3	0.1	15.0	3	1.2	60.3	3	1.2	60.3	3	0.2	27.5	3	0.2	27.5	3
82	1.1	33.6	3	1.1	33.6	3	0.4	29.1	3	0.4	29.1	3	1.3	27.9	3	1.3	27.9	3
83	2.5	68.1	3	2.5	68.1	3	4.3	81.0	3	4.3	81.0	3	0.7	26.6	3	0.7	26.6	3
84	10.5	45.9	3	10.5	45.9	3	6.0	69.4	3	6.0	69.4	3	4.9	24.3	3	4.9	24.3	3
85	4.3	6.0	3	4.3	6.0	3	6.7	8.1	3	6.7	8.1	3	9.0	12.8	3	9.0	12.8	3
86	14.3	15.0	3	14.3	15.0	3	5.4	6.7	3	5.4	6.7	3	2.3	2.6	3	2.3	2.6	3
87	7.6	8.1	3	7.6	8.1	3	30.5	45.5	3	30.5	45.5	3	7.5	8.3	3	7.5	8.3	3
88	3.5	50.8	3	3.5	50.8	3	2.6	55.3	3	2.6	55.3	3	0.5	13.4	3	0.5	13.4	3
89	6.9	9.1	3	6.9	9.1	3	26.3	56.5	3	26.3	56.5	3	8.8	12.9	3	8.8	12.9	3
90	23.2	29.9	3	23.2	29.9	3	9.6	12.7	3	9.6	12.7	3	14.4	40.3	3	14.4	40.3	3
91	9.0	17.3	3	9.0	17.3	3	0	.	3	0	.	3	14.9	44.7	3	14.9	44.7	3
92	3.3	4.1	3	3.3	4.1	3	4.8	5.8	3	4.8	5.8	3	2.5	3.1	3	2.5	3.1	3
93	8.5	10.5	3	8.5	10.5	3	6.5	7.1	3	6.5	7.1	3	10.9	14.8	3	10.9	14.8	3
94	3.2	4.0	3	3.2	4.0	3	12.2	20.1	3	12.2	20.1	3	1.6	2.1	3	1.6	2.1	3
95	0.7	36.5	3	0.7	36.5	3	6.3	61.0	3	6.3	61.0	3	0.1	3.7	3	0.1	3.7	3
96	8.4	9.2	3	8.4	9.2	3	1.9	1.9	3	1.9	1.9	3	17.4	18.9	3	17.4	18.9	3
97	2.5	2.6	3	2.5	2.6	3	13.7	15.8	3	13.7	15.8	3	3.6	4.0	3	3.6	4.0	3
98	13.6	14.7	3	13.6	14.7	3	6.4	8.5	3	6.4	8.5	3	4.9	5.9	3	4.9	5.9	3
99	4.6	21.0	3	4.6	21.0	3	5.5	68.6	3	5.5	68.6	3	5.1	21.8	3	5.1	21.8	3
100	15.9	43.3	3	15.9	43.3	3	12.0	39.2	3	12.0	39.2	3	21.3	41.6	3	21.3	41.6	3
101	8.3	9.1	3	8.3	9.1	3	6.3	6.9	3	6.3	6.9	3	1.6	2.0	3	1.6	2.0	3
102	3.8	3.4	3	3.8	3.4	3	2.8	2.8	3	2.8	2.8	3	5.1	5.5	3	5.1	5.5	3
103	2.2	29.6	3	2.2	29.6	3	2.1	50.8	3	2.1	50.8	3	0.4	7.7	3	0.4	7.7	3
104	13.3	13.8	3	13.3	13.8	3	6.5	7.3	3	6.5	7.3	3	6.5	7.2	3	6.5	7.2	3
105	1.6	17.1	3	1.6	17.1	3	0.5	7.7	3	0.5	7.7	3	0.8	10.2	3	0.8	10.2	3
Overall																		
Mean	8.4			8.4			6.8			7.2			5.4			5.5		
SD	6.5			6.4			7.0			8.0			4.3			4.3		

3.3.2 Between-laboratory variability

The arithmetic mean value of viability over the different qualified tests per laboratory was used to calculate the inter-laboratory variability. For calculation on the between-laboratory variability, only those chemicals are included for which at least one qualified test per laboratory was available. Table 3.3.7 gives the mean standard deviation as well as the standard deviation of the standard deviations

Table 3.3.7 Mean standard deviation and standard deviation per chemical considering the standard deviations as reported for each participating laboratory (Q=qualified and NQ=non-qualified).

	Q		Q+NQ	
Chemical	**mean SD**	**std SD**	**mean SD**	**std SD**
1	3.6	1.1	3.6	1.1
2	10.0	6.1	10	6.1
3	16.5	18.1	16.5	18.1
4	4.1	4.0	6.9	8.6
5	6.8	5.7	6.8	5.7
6	7.7	2.8	7.7	2.8
7	6.2	5.1	6.2	5.1
8	7.7	5.8	7.7	5.8
9	6.2	2.0	6.2	2
10	6.0	3.4	6	3.4
11	5.1	2.3	5.1	2.3
12	4.2	1.6	4.2	1.6
13	2.7	0.8	2.7	0.8
14	5.2	2.5	5.2	2.5
15	6.2	2.0	6.2	2
16	5.4	0.4	5.4	0.4
17	8.1	5.4	8	5.2
18	8.3	4.0	19.8	23.8
19	5.4	1.8	5.4	1.8
20	9.8	2.0	10.7	0.7
21	6.6	9.5	6.6	9.5
22	19.5	2.9	19.5	2.9
23	0.2	0.3	0.2	0.3
24	5.9	2.6	5.9	2.6
25	8.2	6.8	8.2	6.8
26	4.2	2.7	4.2	2.7
28	7.4	6.9	7.4	6.9
29	2.9	2.3	2.9	2.3
30	6.8	3.8	6.8	3.8
31	4.9	4.8	4.9	4.8
32	6.7	1.5	6.7	1.5
33	7.8	2.5	7.8	2.5
34	14.0	4.4	14.1	4.4
35	24.1	13.6	24.1	13.6
36	4.9	2.4	4.9	2.4
37	6.2	6.8	6.2	6.8
38	8.5	2.8	8.5	2.8
39	5.3	0.8	5.3	0.8
40	5.7	6.1	5.7	6.1
41	5.6	0.6	5.6	0.6
42	7.5	4.8	7.5	4.8
43	3.6	0.5	3.6	0.5
44	3.7	1.9	3.7	1.9
45	5.9	1.4	5.9	1.4
46	6.4	3.3	6.4	3.3
47	6.1	0.7	6.1	0.7
48	7.8	2.7	7.8	2.7
49	5.4	1.8	5.4	1.8
50	6.1	2.0	6.1	2
51	5.8	2.7	5.8	2.7
52	5.6	2.5	5.6	2.5

	Q		Q+NQ	
Chemical	**mean SD**	**std SD**	**mean SD**	**std SD**
53	4.9	2.6	4.9	2.6
54	11.2	5.9	11.2	5.9
55	0.7	0.2	0.7	0.2
56	6.6	5.5	6.6	5.5
57	9.0	4.5	9	4.5
58	5.2	3.2	5.2	3.2
59	6.1	3.5	6.1	3.5
60	5.1	2.4	5.1	2.4
61	7.2	4.3	7.2	4.3
62	4.6	1.6	4.6	1.6
63	7.3	4.3	7.3	4.3
64	7.2	1.4	7.2	1.4
65	6.4	7.0	6.4	7
66	8.2	10.3	8.2	10.3
67	5.9	3.5	5.9	3.5
68	1.8	1.2	1.8	1.2
69	13.6	9.3	13.6	9.3
70	3.2	1.0	3.2	1
71	2.4	2.5	2.4	2.5
72	1.5	0.8	1.5	0.8
73	11.5	4.9	11.5	4.9
74	16.2	19.0	16.2	19
75	10.3	14.8	11.3	10
76	10.1	5.0	10.1	5
77	15.7	14.3	15.7	14.3
78	6.5	4.4	6.5	4.4
79	5.0	3.1	5	3.1
80	1.2	1.7	1.2	1.7
81	0.5	0.6	0.5	0.6
82	1.0	0.5	1	0.5
83	2.5	1.8	2.5	1.8
84	7.2	3.0	7.2	3
85	6.7	2.4	6.7	2.4
86	7.3	6.2	7.3	6.2
87	15.2	13.2	15.2	13.2
88	2.2	1.5	2.2	1.5
89	14.0	10.7	14	10.7
90	15.7	6.9	15.7	6.9
91	8.0	7.5	8	7.5
92	3.5	1.2	3.5	1.2
93	8.6	2.2	8.6	2.2
94	5.6	5.7	5.6	5.7
95	2.3	3.4	2.3	3.4
96	9.2	7.8	9.2	7.8
97	6.6	6.2	6.6	6.2
98	8.3	4.7	8.3	4.7
99	5.1	0.5	5.1	0.5
100	16.4	4.7	16.4	4.7
101	5.4	3.5	5.4	3.5
102	3.9	1.2	3.9	1.2
103	1.6	1.0	1.6	1
104	8.8	3.9	8.8	3.9
105	0.9	0.6	0.9	0.6
Overall				
Mean	6.9		7.0	
SD	4.2		4.4	

Concordance of classification between laboratories was calculated based on qualified test from test chemicals for which at least one qualified test was available. In Table 3.3.8 the concordance between laboratories is given.

Table 3.3.8 Concordance between laboratories

BLV concordant	No.	Fraction(%)
NO	8	7.7
YES	96	92.3

Additional descriptive statistics can identify possible reasons for non-concordant results. These are presented in Table 3.3.9. For each non-concordant result the state (liquid/solid), the GHS classification, whether it is colouring or MTTreducer and the test results are given.

Table 3.3.9 Additional descriptive statistics on non-concordant results between laboratories

chemical	name	LS	coloring	MTT	GHS class	CEETOX	CARDAM	L'OREAL
20	Ricinoleic acid tin salt	Liquid	No	No	no cat	111.155	52.2596[2]	47.7012[2]
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	Solid	No	No	no cat	44.683	61.225[1]	23.762[2]
73	3,3'-dithiopropionic acid	Solid	No	No	cat 2A (ICCVAM:cat2B)	49.572	93.804	91.091
75	sodium benzoate INCI name: SODIUM BENZOATE	Solid	No	No	cat 2A	61.383	30.551	13.331
89	ethoxylated (5 EO) alkyl (C10-14) alcohol	Liquid	No	No	cat 1	46.479	75.962	68.120
90	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	Liquid	No	No	cat 1	75.471	77.506	35.800[3]
91	(ethylenediaminepropyl)trimethoxysilane	Liquid	No	Yes	Cat1	0	51.780	33.385
100	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	Solid	No	No	cat 1	30.575	36.760	51.292

[1] identified as colourant, [2] identified as colourant and MTT-reducer, [3] identified as MTT-reducer

The concordance for the set of chemicals tested during validation obtained by the different participating laboratories should ideally be equal or higher than 80%. As summarized in Table 3.3.10, this criteria was met.

Table 3.3.10 Statement whether the test method has fulfilled the performance criteria concerning the concordance of classifications between laboratories.

Fraction (%)	Statement: criteria is
92.3	fulfilled

A two-way ANOVA was applied to test for differences in mean viabilities between laboratories and chemicals. Five outlying observations (*(Ethylenediaminepropyl) trimethoxysilane, 3,3'-Dithiopropionic acid, Ricinoleic acid tin salt,* and *Sodium benzoate* from CEETOX and *alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE* from L'OREAL) were removed before analysis in order to fulfil the ANOVA-requirements. An outlier was defined as an observation with a residual > 3* residual error. The results from the two-way ANOVA are presented in Table 3.3.11. The null hypothesis of no difference was rejected at the 0.01 level of probability (α=0.01).

Table 3.3.11 Two-way ANOVA with factors laboratory and chemical, applied to the arithmetic mean value of the included test results

Effect	NumDF	DenDF	FValue	pvalue
laboratory	2	201	11.96	<.0001
chemical	103	201	83.98	<.0001

Table 3.3.12 Results of the Tukey post-hoc test on differences between laboratories

laboratory	vs	Estimate	Standard Error	DF	Tukey-corrected p-value
CARDAM	CEETOX	2.9826	0.9200	202	0.0040
CARDAM	L'OREAL	4.3373	0.9065	202	<.0001
CEETOX	L'OREAL	1.3547	0.9200	202	0.3063

The between-laboratory variability is described by the concordance of classifications between laboratories. Correlations coefficients between viability measurements give also information on this variability. Since the Pearson correlation coefficient is sensitive for outlying test results and high leverages, both the Pearson and the Spearman correlation coefficients (using ranks instead of the original test results) were calculated. These coefficients are presented in Table 3.3.13.

Table 3.3.13 Pearson and Spearman correlation coefficients between test results of the three participating laboratories.

laboratories	Pearson	Spearman
CARDAM-CEETOX	0.931	0.844
CARDAM-L'OREAL	0.970	0.894
CEETOX-L'OREAL	0.930	0.863

3.3.3 Predictive capacity (accuracy)

All qualified tests for each test chemical was used to calculate the predictive capacity values. The calculations were based on the individual predictions of each qualified test in each laboratory.

For each statistic of the prediction model, an acceptance rate was set by the VMG. These criteria are presented in Table 3.3.14. The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria are fulfilled are presented in Table 3.3.15.

Table 3.3.14 Acceptance criteria for the prediction model

	False Negatives[a] (%)	False Positives[b] (%)	Overall misclassifications[c] (%)
"Definitely acceptable" rates	≤ 10	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	40 < FP ≤ 50	25 < OM ≤ 35
"Definitely unacceptable" rates	> 20	> 50	> 35

[a] equal to (1-Sensitivity), [b] equal to (1-Specificity), [c] equal to (1-Overall accuracy)

Table 3.3.15 The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria for the prediction model are fulfilled.

laboratory	Characteristic	Number used for calculation	Value	95% lower limit	95% upper limit	Statement
CARDAM	Accuracy	204/312	0.654	0.598	0.707	further evaluation
	Sensitivity	63/156	0.404	0.326	0.485	definitely unacceptable
	Specificity	141/156	0.904	0.846	0.945	definitely acceptable
CEETOX	Accuracy	207/312	0.663	0.608	0.716	further evaluation
	Sensitivity	70/156	0.449	0.369	0.530	definitely unacceptable
	Specificity	137/156	0.878	0.816	0.925	definitely acceptable
L'OREAL	Accuracy	203/312	0.651	0.595	0.703	further evaluation
	Sensitivity	67/156	0.429	0.351	0.511	definitely unacceptable
	Specificity	136/156	0.872	0.809	0.920	definitely acceptable
Total	Accuracy	614/936	0.656	0.625	0.686	further evaluation
	Sensitivity	200/468	0.427	0.382	0.474	definitely unacceptable
	Specificity	414/468	0.885	0.852	0.912	definitely acceptable

In Table 3.3.16, the prediction for each qualified test result is given as well as the final classification based on the median of predictions.

Table 3.3.16 Final classification based on the median of all classifications for each chemical

		CARDAM			CEETOX			L'OREAL			Final classification based on median	Mispredicted tests/Total
chemical	GHS classification	1	2	3	1	2	3	1	2	3		
1	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
2	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
3	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
4	no cat	I	I	I	I	I	I	I	I	I	I	9/9
5	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
6	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
7	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
8	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
9	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
10	no cat	I	I	I	I	I	I	I	I	I	I	9/9
11	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
12	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
13	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
14	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
15	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
16	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
17	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
18	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
19	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
20	no cat	I	I	NI	NI	NI	NI	NI	I	I	NI	4/9
21	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
22	no cat	NI	NI	NI	NI	I	I	NI	NI	NI	NI	2/9
23	no cat	I	I	I	I	I	I	I	I	I	I	9/9
24	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
25	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
26	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
28	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
29	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
30	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
31	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
32	no cat	NI	NI	NI	I	I	I	I	I	I	I	6/9
33	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
34	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
35	no cat	I	NI	I	I	NI	I	I	I	I	I	7/9
36	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
37	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9

		CARDAM			CEETOX			L'OREAL			Final classification based on median	Mispredicted tests/Total
chemical	GHS classification	1	2	3	1	2	3	1	2	3		
38	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
39	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
40	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
41	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
42	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
43	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
44	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
45	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
46	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
47	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
48	no cat	I	I	NI	I	I	I	I	I	I	I	8/9
49	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
50	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
51	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
52	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
53	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
54	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	I	NI	8/9
55	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
56	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
57	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
58	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
59	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
60	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
61	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
62	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
63	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
64	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
65	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
66	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
67	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
68	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
69	cat 2A (ICCVAM:cat2B)	NI	I	NI	NI	NI	NI	NI	NI	NI	NI	8/9
70	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
71	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
72	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
73	cat 2A (ICCVAM:cat2B)	NI	NI	NI	NI	I	I	NI	NI	NI	NI	7/9
74	cat 2A	NI	NI	NI	NI	NI	I	NI	NI	NI	NI	8/9
75	cat 2A	NI	I	I	NI	NI	NI	I	I	I	I	4/9
76	cat 2A	NI	NI	NI	I	NI	NI	NI	NI	NI	NI	8/9
77	cat 2A	NI	NI	NI	I	NI	NI	NI	NI	NI	NI	8/9
78	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
79	cat 2A (ICCVAM:cat2B)	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
80	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
81	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
82	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
83	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
84	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
85	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
86	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
87	cat 1	NI	NI	NI	NI	NI	I	NI	NI	NI	NI	8/9
88	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
89	cat 1	NI	NI	NI	NI	NI	I	NI	NI	NI	NI	8/9
90	cat 1	NI	NI	NI	NI	NI	NI	NI	I	I	NI	7/9
91	cat 1	NI	I	NI	I	I	I	I	I	I	I	2/9
92	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9

chemical	GHS classification	CARDAM			CEETOX			L'OREAL			Final classification based on median	Mispredicted tests/Total
		1	2	3	1	2	3	1	2	3		
93	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
94	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
95	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
96	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
97	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
98	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
99	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
100	cat 1	I	NI	I	I	I	I	I	NI	NI	I	3/9
101	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
102	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
103	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
104	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
105	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

3.4 Reproducibility and accuracy using the LE protocol

In this section, a 50% cut-off was applied to determine the irritancy of the chemical based on the LE protocol. If the viability is above 50%, the chemical is considered to be non-irritant. If the viability is 50% or below, the chemical is considered to be irritant.

3.4.1 Within-laboratory variability

For each laboratory, concordance of classification was calculated based on qualified test from test chemicals for which at least two qualified tests were available. In Table 3.4.1 the concordance within each laboratory as well as in total is given.

Table 3.4.1 Concordance within laboratories and total

laboratory	WLV concordant	LE	
		No.	Fraction(%)
CARDAM	NO	5	4.8
	YES	99	95.2
CEETOX	NO	4	3.8
	YES	100	96.2
L'OREAL	NO	5	4.8
	YES	99	95.2
Total	NO	14	4.5
	YES	298	95.5

Additional descriptive statistics can identify possible reasons for non-concordant results. These are presented in Table 3.4.2. For each non-concordant result the reactivity, the GHS classification, whether it is colouring or MTTreducer and the test results are given.

Table 3.4.2 Additional descriptive statistics on non-concordant results within laboratories

laboratory	chemical & reactivity[1]	name	coloring	mtt	pGHS	Test 1	Test 2	Test 3
CARDAM	9 NR	1,9-decadiene	No	Yes	no cat	56.085	31.179	58.519
CARDAM	34 R	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	Yes	Yes	no cat	49.866	43.554	56.498
CARDAM	65 R	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	No	No	cat 2B	74.621	40.455	41.957

CARDAM	96 R	1-naphthalene acetic acid	No	No	cat 1	42.678	68.453	77.196
CARDAM	97 NR	sodium oxalate INCI name: SODIUM OXALATE	No	No	cat 1	65.493	49.507	73.543
CEETOX	47 R	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE	No	No	no cat	40.706	48.741	57.170
CEETOX	93 NR	2,5-dimethyl-2,5-hexanediol	No	No	cat 1	38.11	65.473	55.221
CEETOX	96 R	1-naphthalene acetic acid	No	No	cat 1	41.708	45.584	50.491
CEETOX	98 R	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	Yes	Yes	cat 1	75.025	74.437	40.963
L'OREAL	11 NR	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	No	Yes	no cat	74.860	69.280	49.103
L'OREAL	65 R	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	No	No	cat 2B	13.391	68.057	92.491
L'OREAL	66 R	sodium chloroacetate	No	No	cat 2B	62.220	18.556	3.315
L'OREAL	79 NR	ammonium nitrate INCI name: AMMONIUM NITRATE	No	No	cat 2A (ICCVAM:cat2B)	17.636	52.806	47.748
L'OREAL	101 NR	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31	Yes	No	cat 1	70.820	74.980	44.871

[1] Reactivity: R = reactive, NR = non-reactive

The concordance of classifications (irritant/non-irritant) for the set of chemicals tested during validation obtained in different, independent runs within a single laboratory should ideally be equal or higher than 85% for all participating laboratories. As summarized in Table 3.4.3, this criteria was met for each laboratory as well as in total.

Table 3.4.3 Statement whether the test method has fulfilled the performance criteria concerning the concordance of classifications within one laboratory.

	LE	
laboratory	**Fraction(%)**	**Statement: criteria is**
CARDAM	95.2	fulfilled
CEETOX	96.2	fulfilled
L'OREAL	95.2	fulfilled
Total	95.5	fulfilled

The intra-laboratory variability is described by the concordance of classifications. Correlation coefficients between viability measurements give also information on this variability. Since the Pearson correlation coefficient is sensitive to outlying test results and high leverages, both the Pearson and the Spearman correlation coefficients (using ranks instead of the original test results) were calculated. These coefficients are presented in Table 3.4.4.

Table 3.4.4 Pearson and Spearman correlation coefficients between tests results within each laboratory as well as in total.

Correlation	**laboratory**	**Qual1 - Qual2**	**Qual1 - Qual3**	**Qual2 - Qual3**
Pearson	L'OREAL	0.963	0.947	0.972
	CARDAM	0.930	0.970	0.947
	CEETOX	0.970	0.962	0.967
	Mean	0.954	0.960	0.962
Spearman	L'OREAL	0.926	0.912	0.901
	CARDAM	0.924	0.924	0.935
	CEETOX	0.927	0.929	0.938
	Mean	0.926	0.922	0.925

Finally, the arithmetic mean, standard deviation and coefficient of variation from the three valid tests are given per laboratory as well as in total (see Table 3.4.5). Note that the coefficient of variation is not a useful measure if the mean is close to zero.

Table 3.4.5 Arithmetic mean, standard deviation (std) and coefficient of variation (cv) from the three valid tests are given per laboratory as well as in total (n = number of qualified tests that was used for the calculation of the mean, std and cv)

	laboratory											
	CARDAM				CEETOX				L'OREAL			
Chemical	mean	std	cv	n	mean	std	cv	n	mean	std	cv	n
1	12.3	8.9	71.8	3	6.0	3.1	51.8	3	9.7	9.3	95.6	3
2	4.8	4.2	88.1	3	2.4	0.4	17.3	3	2.5	0.8	34.3	3
3	2.4	1.1	46.7	3	2.0	0.8	39.4	3	0.9	0.2	21.2	3
4	2.4	3.6	148.7	3	0.0	0.0	.	3	36.7	1.4	3.7	3
5	6.9	5.2	74.2	3	2.6	2.3	87.6	3	3.0	2.6	86.9	3
6	17.4	4.3	24.9	3	6.0	3.2	52.6	3	9.7	5.7	58.5	3
7	5.8	0.6	11.1	3	6.7	2.8	42.3	3	4.3	3.6	84.3	3
8	34.3	11.6	33.8	3	28.7	7.1	24.8	3	22.7	6.9	30.1	3
9	48.6	15.1	31.1	3	41.9	7.1	17.0	3	26.6	6.1	23.1	3
10	1.1	0.8	67.6	3	2.6	1.0	38.6	3	1.1	0.2	20.8	3
11	27.8	3.9	14.0	3	66.7	13.5	20.2	3	64.4	13.6	21.0	3
12	96.7	3.9	4.0	3	101.4	11.0	10.9	3	91.1	6.7	7.3	3
13	106.1	7.5	7.1	3	107.3	12.0	11.2	3	93.2	6.2	6.7	3
14	95.3	21.8	22.9	3	99.5	10.3	10.4	3	92.2	6.5	7.0	3
15	98.2	4.2	4.3	3	96.1	7.2	7.5	3	93.4	3.4	3.6	3
16	94.4	18.7	19.8	3	98.4	2.2	2.2	3	98.9	4.2	4.2	3
17	86.3	10.3	12.0	3	97.5	3.1	3.2	3	85.5	5.4	6.3	3
18	101.4	5.9	5.8	3	100.5	6.1	6.1	3	96.5	6.1	6.4	3
19	101.1	6.4	6.3	3	101.3	13.0	12.8	3	100.1	6.6	6.6	3
20	15.6	7.8	50.4	3	30.7	9.1	29.7	2	0.0	0.0	.	3
21	60.1	4.0	6.7	3	73.2	14.7	20.1	3	66.4	2.7	4.0	3
22	1.1	0.2	14.6	3	3.0	1.0	33.3	3	1.1	0.0	3.2	3
23	17.2	1.6	9.5	3	10.8	8.6	80.0	3	19.7	16.6	84.6	3
24	1.3	0.2	17.7	3	1.7	0.3	15.3	3	0.6	0.2	39.4	3
25	98.3	2.5	2.6	3	89.0	11.7	13.1	3	87.6	16.5	18.9	3
26	3.6	0.4	10.7	3	3.1	0.6	18.4	3	2.6	0.4	14.8	3
28	97.5	18.4	18.9	3	98.3	1.2	1.2	3	91.3	3.3	3.6	3
29	100.7	6.6	6.6	3	99.5	8.7	8.7	3	91.0	3.8	4.1	3
30	81.4	10.5	12.9	3	78.6	3.1	3.9	3	75.2	7.2	9.6	3
31	104.7	8.4	8.0	3	100.4	2.7	2.7	3	91.6	6.3	6.9	3
32	8.2	1.8	21.4	3	21.6	9.7	45.0	3	2.5	0.5	19.6	3
33	106.8	1.4	1.3	3	101.0	13.0	12.8	3	95.0	8.3	8.8	3
34	50.0	6.5	13.0	3	71.8	17.5	24.4	3	59.1	5.7	9.6	3
35	92.0	12.7	13.8	3	90.3	14.3	15.8	3	90.0	5.9	6.5	3
36	104.6	5.6	5.4	3	103.0	4.8	4.7	3	104.7	5.1	4.8	3
37	99.0	8.4	8.5	3	96.4	6.5	6.7	3	86.3	3.6	4.2	3
38	105.1	12.2	11.6	3	100.8	10.0	10.0	3	98.1	2.5	2.5	3
39	101.3	12.0	11.8	3	99.4	12.4	12.5	3	95.6	1.9	2.0	3
40	87.8	10.5	12.0	3	82.5	2.5	3.0	3	87.8	11.6	13.2	3
41	98.2	1.4	1.5	3	97.7	7.7	7.9	3	95.2	2.1	2.2	3
42	84.6	9.7	11.5	3	78.0	4.1	5.3	3	76.5	2.5	3.3	3
43	106.3	1.9	1.8	3	99.0	7.7	7.7	3	94.6	0.9	1.0	3
44	96.9	3.4	3.5	3	99.1	4.5	4.6	3	90.1	3.7	4.1	3
45	105.3	8.1	7.7	3	93.3	9.3	9.9	3	93.2	4.4	4.7	3
46	87.7	11.1	12.7	3	75.8	9.6	12.7	3	77.3	20.5	26.5	3
47	81.1	5.8	7.1	3	48.9	8.2	16.8	3	41.0	9.2	22.5	3
48	1.7	0.2	9.9	3	1.9	0.8	40.6	3	4.3	1.2	29.0	3
49	66.1	13.4	20.2	3	87.5	6.6	7.5	3	85.2	5.3	6.3	3
50	101.6	4.4	4.3	3	93.4	11.7	12.6	3	93.5	6.3	6.7	3
51	104.5	4.2	4.0	3	99.5	12.3	12.4	3	88.6	19.0	21.5	3
52	96.1	10.2	10.6	3	100.7	9.3	9.2	3	99.7	2.0	2.0	3
53	114.0	10.3	9.0	3	92.7	11.5	12.4	3	100.1	10.9	10.9	3
54	1.7	0.9	54.8	3	3.0	1.5	51.8	3	0.5	0.1	15.0	3
55	0.8	0.1	16.7	3	1.8	0.9	47.4	3	1.0	0.0	3.3	3
56	8.2	2.9	35.5	3	8.2	0.5	6.7	3	0.7	0.0	6.3	3
57	0.8	0.3	36.9	3	1.6	0.8	50.6	3	0.7	0.4	58.8	3
58	0.8	0.4	52.6	3	1.8	1.0	54.7	3	0.3	0.1	26.9	3
59	31.4	9.4	29.8	3	25.1	2.5	10.1	3	13.9	11.6	83.1	3
60	0.8	0.2	21.7	3	2.0	0.2	9.4	3	0.6	0.2	29.6	3
61	79.5	17.1	21.5	3	8.9	1.2	13.7	3	75.6	8.8	11.7	3

	laboratory											
	CARDAM				CEETOX				L'OREAL			
Chemical	mean	std	cv	n	mean	std	cv	n	mean	std	cv	n
62	92.8	12.6	13.5	3	96.7	2.5	2.6	3	89.2	3.6	4.0	3
63	84.4	11.2	13.3	3	83.5	9.5	11.4	3	87.8	1.3	1.5	3
64	70.7	7.6	10.8	3	77.6	8.5	11.0	3	73.4	4.9	6.7	3
65	52.3	19.3	36.9	3	76.1	12.6	16.5	3	58.0	40.5	69.9	3
66	3.7	4.1	112.0	3	18.0	24.8	137.8	3	28.0	30.6	109.1	3
67	0.9	0.2	16.8	3	12.4	8.5	68.6	3	1.5	0.6	41.6	3
68	0.9	0.3	36.8	3	1.3	0.3	20.3	3	0.6	0.3	55.6	3
69	0.4	0.4	91.7	3	0.9	0.3	33.8	3	1.0	0.8	82.8	3
70	1.1	0.4	33.4	3	1.8	0.4	21.5	3	0.9	0.1	12.3	3
71	0.7	0.2	27.4	3	1.2	0.2	16.8	3	0.8	0.3	37.0	3
72	0.8	0.1	14.8	3	0.9	0.1	7.8	3	1.9	1.3	67.7	3
73	87.4	17.9	20.5	3	91.8	7.7	8.4	3	93.7	4.7	5.0	3
74	134.0	65.3	48.7	3	84.0	7.9	9.4	3	91.1	13.3	14.6	3
75	0.9	0.1	13.1	3	1.3	0.1	4.2	3	1.1	0.2	23.0	3
76	86.0	12.1	14.0	3	65.8	12.2	18.6	3	71.1	9.7	13.6	3
77	94.1	11.5	12.2	3	86.9	8.3	9.6	3	89.9	2.3	2.6	3
78	87.8	12.7	14.5	3	82.5	5.8	7.0	3	86.0	1.6	1.8	3
79	63.9	4.0	6.2	3	39.1	8.4	21.5	3	39.4	19.0	48.3	3
80	1.4	1.6	115.7	3	0.0	0.0	.	3	0.4	0.7	173.2	3
81	0.4	0.1	14.0	3	0.5	0.1	20.5	3	0.7	0.3	36.3	3
82	0.7	0.3	48.1	3	0.9	0.4	40.6	3	0.3	0.1	25.9	3
83	0.3	0.1	47.9	3	0.9	0.2	22.7	3	0.6	0.3	54.2	3
84	0.5	0.2	30.2	3	1.5	0.5	34.7	3	0.5	0.1	26.4	3
85	0.6	0.3	50.8	3	0.7	0.1	20.1	3	0.4	0.1	32.5	3
86	8.2	6.1	73.8	3	2.7	1.3	46.4	3	7.7	3.5	45.6	3
87	0.4	0.1	25.1	3	1.5	0.5	34.9	3	1.6	0.5	34.3	3
88	0.7	0.3	37.3	3	1.2	1.0	88.3	3	0.8	0.2	21.3	3
89	1.3	0.1	9.5	3	2.1	0.3	16.4	3	1.4	0.2	15.3	3
90	9.6	3.9	40.3	3	2.8	1.0	34.6	3	10.9	12.4	113.3	3
91	4.1	4.4	109.2	3	11.6	6.1	52.3	3	8.3	3.9	46.7	3
92	6.2	1.1	17.1	3	7.6	3.1	40.4	3	3.9	3.2	83.6	3
93	28.4	5.4	18.9	3	52.9	13.8	26.1	3	24.5	10.5	42.9	3
94	18.5	4.8	26.0	3	12.7	12.7	100.0	3	14.8	2.8	19.2	3
95	0.4	0.3	66.1	3	1.2	0.2	16.0	3	0.7	0.3	47.7	3
96	62.8	17.9	28.6	3	45.9	4.4	9.6	3	41.0	7.6	18.6	3
97	62.8	12.2	19.5	3	62.2	2.8	4.6	3	63.6	3.7	5.9	3
98	74.1	9.0	12.1	3	63.5	19.5	30.7	3	32.3	12.4	38.3	3
99	1.9	0.4	18.5	3	1.4	0.3	19.3	3	1.3	0.1	4.4	3
100	1.6	0.2	13.1	3	2.1	0.3	16.1	3	1.1	0.3	27.8	3
101	67.0	9.4	14.0	3	72.8	9.8	13.4	3	63.6	16.3	25.7	3
102	95.0	5.0	5.3	3	85.0	20.0	23.5	3	83.0	4.9	6.0	3
103	1.3	0.2	15.5	3	0.6	0.6	108.4	3	0.9	0.2	19.4	3
104	84.0	12.9	15.3	3	76.9	11.0	14.3	3	87.4	8.9	10.2	3
105	1.7	0.7	39.7	3	0.4	0.4	87.5	3	1.6	0.5	28.6	3

Table 3.4.6 Standard deviation (std) and coefficient of variation (cv) from all available tests results (Q=qualified and NQ=non-qualified; non-qualified test results due to non-qualified PC results not included) per laboratory (n = number of tests that was used for the calculations)

	laboratory																	
	CARDAM						CEETOX						L'OREAL					
	Q			Q+NQ			Q			Q+NQ			Q			Q+NQ		
Chemical	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n
1	8.9	71.8	3	8.9	71.8	3	3.1	51.8	3	3.1	51.8	3	9.3	95.6	3	9.3	95.6	3
2	4.2	88.1	3	4.2	88.1	3	0.4	17.3	3	0.4	17.3	3	0.8	34.3	3	0.8	34.3	3
3	1.1	46.7	3	1.1	46.7	3	0.8	39.4	3	0.8	39.4	3	0.2	21.2	3	0.2	21.2	3
4	3.6	148.7	3	3.6	148.7	3	0.0	.	3	0.0	.	3	1.4	3.7	3	1.4	3.7	3
5	5.2	74.2	3	5.2	74.2	3	2.3	87.6	3	2.3	87.6	3	2.6	86.9	3	2.6	86.9	3
6	4.3	24.9	3	4.3	24.9	3	3.2	52.6	3	3.2	52.6	3	5.7	58.5	3	5.7	58.5	3
7	0.6	11.1	3	0.6	11.1	3	2.8	42.3	3	2.8	42.3	3	3.6	84.3	3	3.6	84.3	3
8	11.6	33.8	3	11.6	33.8	3	7.1	24.8	3	7.1	24.8	3	6.9	30.1	3	6.9	30.1	3
9	15.1	31.1	3	15.1	31.1	3	7.1	17.0	3	7.1	17.0	3	6.1	23.1	3	6.1	23.1	3

	laboratory																	
	CARDAM						CEETOX						L'OREAL					
	Q			Q+NQ			Q			Q+NQ			Q			Q+NQ		
Chemical	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n	std	cv	n
10	0.8	67.6	3	0.8	67.6	3	1.0	38.6	3	1.0	38.6	3	0.2	20.8	3	0.2	20.8	3
11	3.9	14.0	3	3.9	14.0	3	13.5	20.2	3	13.5	20.2	3	13.6	21.0	3	13.6	21.0	3
12	3.9	4.0	3	3.9	4.0	3	11.0	10.9	3	11.0	10.9	3	6.7	7.3	3	6.7	7.3	3
13	7.5	7.1	3	7.5	7.1	3	12.0	11.2	3	12.0	11.2	3	6.2	6.7	3	6.2	6.7	3
14	21.8	22.9	3	21.8	22.9	3	10.3	10.4	3	10.3	10.4	3	6.5	7.0	3	6.5	7.0	3
15	4.2	4.3	3	4.2	4.3	3	7.2	7.5	3	7.2	7.5	3	3.4	3.6	3	3.4	3.6	3
16	18.7	19.8	3	18.7	19.8	3	2.2	2.2	3	2.2	2.2	3	4.2	4.2	3	4.2	4.2	3
17	10.3	12.0	3	10.3	12.0	3	3.1	3.2	3	3.1	3.2	3	5.4	6.3	3	5.4	6.3	3
18	5.9	5.8	3	5.9	5.8	3	6.1	6.1	3	6.1	6.1	3	6.1	6.4	3	6.1	6.4	3
19	6.4	6.3	3	6.4	6.3	3	13.0	12.8	3	13.0	12.8	3	6.6	6.6	3	6.6	6.6	3
20	7.8	50.4	3	7.8	50.4	3	9.1	29.7	2	9.1	29.7	2	0.0	.	3	0.0	.	3
21	4.0	6.7	3	4.0	6.7	3	14.7	20.1	3	14.7	20.1	3	2.7	4.0	3	2.7	4.0	3
22	0.2	14.6	3	0.2	14.6	3	1.0	33.3	3	1.0	33.3	3	0.0	3.2	3	0.0	3.2	3
23	1.6	9.5	3	1.6	9.5	3	8.6	80.0	3	8.6	80.0	3	16.6	84.6	3	16.6	84.6	3
24	0.2	17.7	3	0.2	17.7	3	0.3	15.3	3	0.3	15.3	3	0.2	39.4	3	0.2	39.4	3
25	2.5	2.6	3	2.5	2.6	3	11.7	13.1	3	11.7	13.1	3	16.5	18.9	3	16.5	18.9	3
26	0.4	10.7	3	0.4	10.7	3	0.6	18.4	3	0.6	18.4	3	0.4	14.8	3	0.4	14.8	3
28	18.4	18.9	3	18.4	18.9	3	1.2	1.2	3	1.2	1.2	3	3.3	3.6	3	3.3	3.6	3
29	6.6	6.6	3	6.6	6.6	3	8.7	8.7	3	8.7	8.7	3	3.8	4.1	3	3.8	4.1	3
30	10.5	12.9	3	10.5	12.9	3	3.1	3.9	3	3.1	3.9	3	7.2	9.6	3	7.2	9.6	3
31	8.4	8.0	3	8.4	8.0	3	2.7	2.7	3	2.7	2.7	3	6.3	6.9	3	6.3	6.9	3
32	1.8	21.4	3	1.8	21.4	3	9.7	45.0	3	9.7	45.0	3	0.5	19.6	3	0.5	19.6	3
33	1.4	1.3	3	1.4	1.3	3	13.0	12.8	3	13.0	12.8	3	8.3	8.8	3	8.3	8.8	3
34	6.5	13.0	3	5.8	11.9	4	17.5	24.4	3	17.5	24.4	3	5.7	9.6	3	5.7	9.6	3
35	12.7	13.8	3	12.7	13.8	3	14.3	15.8	3	14.3	15.8	3	5.9	6.5	3	5.9	6.5	3
36	5.6	5.4	3	5.6	5.4	3	4.8	4.7	3	4.8	4.7	3	5.1	4.8	3	5.1	4.8	3
37	8.4	8.5	3	8.4	8.5	3	6.5	6.7	3	6.5	6.7	3	3.6	4.2	3	3.6	4.2	3
38	12.2	11.6	3	12.2	11.6	3	10.0	10.0	3	10.0	10.0	3	2.5	2.5	3	2.5	2.5	3
39	12.0	11.8	3	12.0	11.8	3	12.4	12.5	3	12.4	12.5	3	1.9	2.0	3	1.9	2.0	3
40	10.5	12.0	3	10.5	12.0	3	2.5	3.0	3	2.5	3.0	3	11.6	13.2	3	11.6	13.2	3
41	1.4	1.5	3	1.4	1.5	3	7.7	7.9	3	7.7	7.9	3	2.1	2.2	3	2.1	2.2	3
42	9.7	11.5	3	9.7	11.5	3	4.1	5.3	3	4.1	5.3	3	2.5	3.3	3	2.5	3.3	3
43	1.9	1.8	3	1.9	1.8	3	7.7	7.7	3	7.7	7.7	3	0.9	1.0	3	0.9	1.0	3
44	3.4	3.5	3	3.4	3.5	3	4.5	4.6	3	4.5	4.6	3	3.7	4.1	3	3.7	4.1	3
45	8.1	7.7	3	8.1	7.7	3	9.3	9.9	3	9.3	9.9	3	4.4	4.7	3	4.4	4.7	3
46	11.1	12.7	3	11.1	12.7	3	9.6	12.7	3	9.6	12.7	3	20.5	26.5	3	20.5	26.5	3
47	5.8	7.1	3	5.8	7.1	3	8.2	16.8	3	8.2	16.8	3	9.2	22.5	3	9.2	22.5	3
48	0.2	9.9	3	0.6	43.3	4	0.8	40.6	3	0.8	40.6	3	1.2	29.0	3	1.2	29.0	3
49	13.4	20.2	3	13.4	20.2	3	6.6	7.5	3	7.8	9.2	4	5.3	6.3	3	5.3	6.3	3
50	4.4	4.3	3	4.4	4.3	3	11.7	12.6	3	11.7	12.6	3	6.3	6.7	3	6.3	6.7	3
51	4.2	4.0	3	4.2	4.0	3	12.3	12.4	3	12.3	12.4	3	19.0	21.5	3	19.0	21.5	3
52	10.2	10.6	3	13.6	15.0	4	9.3	9.2	3	9.3	9.2	3	2.0	2.0	3	2.0	2.0	3
53	10.3	9.0	3	10.3	9.0	3	11.5	12.4	3	11.5	12.4	3	10.9	10.9	3	10.9	10.9	3
54	0.9	54.8	3	0.9	54.8	3	1.5	51.8	3	1.5	51.8	3	0.1	15.0	3	0.1	15.0	3
55	0.1	16.7	3	0.1	16.7	3	0.9	47.4	3	0.9	47.4	3	0.0	3.3	3	0.0	3.3	3
56	2.9	35.5	3	2.9	35.5	3	0.5	6.7	3	0.5	6.7	3	0.0	6.3	3	0.0	6.3	3
57	0.3	36.9	3	0.3	36.9	3	0.8	50.6	3	0.8	50.6	3	0.4	58.8	3	0.4	58.8	3
58	0.4	52.6	3	0.4	52.6	3	1.0	54.7	3	1.0	54.7	3	0.1	26.9	3	0.1	26.9	3
59	9.4	29.8	3	9.4	29.8	3	2.5	10.1	3	2.5	10.1	3	11.6	83.1	3	11.6	83.1	3
60	0.2	21.7	3	0.2	21.7	3	0.2	9.4	3	0.2	9.4	3	0.2	29.6	3	0.2	29.6	3
61	17.1	21.5	3	17.1	21.5	3	1.2	13.7	3	1.2	13.7	3	8.8	11.7	3	8.8	11.7	3
62	12.6	13.5	3	12.6	13.5	3	2.5	2.6	3	2.5	2.6	3	3.6	4.0	3	3.6	4.0	3
63	11.2	13.3	3	11.2	13.3	3	9.5	11.4	3	9.5	11.4	3	1.3	1.5	3	1.3	1.5	3
64	7.6	10.8	3	7.6	10.8	3	8.5	11.0	3	8.5	11.0	3	4.9	6.7	3	4.9	6.7	3
65	19.3	36.9	3	19.3	36.9	3	12.6	16.5	3	12.6	16.5	3	40.5	69.9	3	33.7	61.6	4
66	4.1	112.0	3	4.1	112.0	3	24.8	137.8	3	24.8	137.8	3	30.6	109.1	3	30.6	109.1	3
67	0.2	16.8	3	0.2	16.8	3	8.5	68.6	3	8.5	68.6	3	0.6	41.6	3	0.6	41.6	3
68	0.3	36.8	3	0.3	36.8	3	0.3	20.3	3	0.3	20.3	3	0.3	55.6	3	0.3	55.6	3
69	0.4	91.7	3	0.4	91.7	3	0.3	33.8	3	0.3	33.8	3	0.8	82.8	3	0.8	82.8	3
70	0.4	33.4	3	0.4	33.4	3	0.4	21.5	3	0.4	21.5	3	0.1	12.3	3	0.1	12.3	3
71	0.2	27.4	3	0.2	27.4	3	0.2	16.8	3	0.2	16.8	3	0.3	37.0	3	0.3	37.0	3
72	0.1	14.8	3	0.1	14.8	3	0.1	7.8	3	0.1	7.8	3	1.3	67.7	3	1.3	67.7	3
73	17.9	20.5	3	17.9	20.5	3	7.7	8.4	3	7.7	8.4	3	4.7	5.0	3	4.7	5.0	3

	laboratory																	
	CARDAM						CEETOX						L'OREAL					
	Q			Q+NQ			Q			Q+NQ			Q			Q+NQ		
Chemical	**std**	**cv**	**n**	**std**	**cv**	**n**	**std**	**cv**	**n**	**std**	**cv**	**n**	**std**	**cv**	**n**	**std**	**cv**	**n**
74	65.3	48.7	3	65.3	48.7	3	7.9	9.4	3	7.9	9.4	3	13.3	14.6	3	13.3	14.6	3
75	0.1	13.1	3	0.1	15.9	4	0.1	4.2	3	0.1	4.2	3	0.2	23.0	3	14.7	174.6	4
76	12.1	14.0	3	12.1	14.0	3	12.2	18.6	3	12.2	18.6	3	9.7	13.6	3	9.7	13.6	3
77	11.5	12.2	3	11.5	12.2	3	8.3	9.6	3	8.3	9.6	3	2.3	2.6	3	2.3	2.6	3
78	12.7	14.5	3	12.7	14.5	3	5.8	7.0	3	5.8	7.0	3	1.6	1.8	3	1.6	1.8	3
79	4.0	6.2	3	4.0	6.2	3	8.4	21.5	3	8.4	21.5	3	19.0	48.3	3	19.0	48.3	3
80	1.6	115.7	3	1.6	115.7	3	0.0	.	3	0.0	.	3	0.7	173.2	3	0.7	173.2	3
81	0.1	14.0	3	0.1	14.0	3	0.1	20.5	3	0.1	20.5	3	0.3	36.3	3	0.3	36.3	3
82	0.3	48.1	3	0.3	48.1	3	0.4	40.6	3	0.4	40.6	3	0.1	25.9	3	0.1	25.9	3
83	0.1	47.9	3	0.1	47.9	3	0.2	22.7	3	0.2	22.7	3	0.3	54.2	3	0.3	54.2	3
84	0.2	30.2	3	0.2	30.2	3	0.5	34.7	3	0.5	34.7	3	0.1	26.4	3	0.1	26.4	3
85	0.3	50.8	3	0.3	50.8	3	0.1	20.1	3	0.1	20.1	3	0.1	32.5	3	0.1	32.5	3
86	6.1	73.8	3	6.1	73.8	3	1.3	46.4	3	1.3	46.4	3	3.5	45.6	3	3.5	45.6	3
87	0.1	25.1	3	0.1	25.1	3	0.5	34.9	3	0.5	34.9	3	0.5	34.3	3	0.5	34.3	3
88	0.3	37.3	3	0.3	37.3	3	1.0	88.3	3	1.0	88.3	3	0.2	21.3	3	0.2	21.3	3
89	0.1	9.5	3	0.1	9.5	3	0.3	16.4	3	0.3	16.4	3	0.2	15.3	3	0.2	15.3	3
90	3.9	40.3	3	3.9	40.3	3	1.0	34.6	3	1.0	34.6	3	12.4	113.3	3	12.4	113.3	3
91	4.4	109.2	3	4.4	109.2	3	6.1	52.3	3	6.1	52.3	3	3.9	46.7	3	3.9	46.7	3
92	1.1	17.1	3	1.1	17.1	3	3.1	40.4	3	3.1	40.4	3	3.2	83.6	3	3.2	83.6	3
93	5.4	18.9	3	5.4	18.9	3	13.8	26.1	3	13.8	26.1	3	10.5	42.9	3	10.5	42.9	3
94	4.8	26.0	3	4.8	26.0	3	12.7	100.0	3	12.7	100.0	3	2.8	19.2	3	2.8	19.2	3
95	0.3	66.1	3	0.3	66.1	3	0.2	16.0	3	0.2	16.0	3	0.3	47.7	3	0.3	47.7	3
96	17.9	28.6	3	17.9	28.6	3	4.4	9.6	3	4.4	9.6	3	7.6	18.6	3	7.6	18.6	3
97	12.2	19.5	3	12.2	19.5	3	2.8	4.6	3	2.8	4.6	3	3.7	5.9	3	3.7	5.9	3
98	9.0	12.1	3	9.0	12.1	3	19.5	30.7	3	19.5	30.7	3	12.4	38.3	3	12.4	38.3	3
99	0.4	18.5	3	0.4	18.5	3	0.3	19.3	3	0.3	19.3	3	0.1	4.4	3	0.1	4.4	3
100	0.2	13.1	3	0.2	13.1	3	0.3	16.1	3	0.3	16.1	3	0.3	27.8	3	0.3	27.8	3
101	9.4	14.0	3	9.4	14.0	3	9.8	13.4	3	9.8	13.4	3	16.3	25.7	3	16.3	25.7	3
102	5.0	5.3	3	5.0	5.3	3	20.0	23.5	3	20.0	23.5	3	4.9	6.0	3	4.9	6.0	3
103	0.2	15.5	3	0.2	15.5	3	0.6	108.4	3	0.6	108.4	3	0.2	19.4	3	0.2	19.4	3
104	12.9	15.3	3	12.9	15.3	3	11.0	14.3	3	11.0	14.3	3	8.9	10.2	3	8.9	10.2	3
105	0.7	39.7	3	0.7	39.7	3	0.4	87.5	3	0.4	87.5	3	0.5	28.6	3	0.5	28.6	3
Overall																		
Mean	6.4			6.4			5.8			5.8			5.2			5.2		
SD	8.0			8.1			5.5			5.5			6.5			6.3		

3.4.2 Between-laboratory variability

The arithmetic mean value of viability over the different qualified tests per laboratory was used to calculate the inter-laboratory variability. For calculation on the between-laboratory variability, only those chemicals are included for which at least one qualified test per laboratory was available. Table 3.4.7 gives the mean standard deviation as well as the standard deviation of the standard deviations

Table 3.4.7 Mean standard deviation and standard deviation per chemical considering the standard deviations as reported for each participating laboratory (Q=qualified and NQ=non-qualified; non-qualified test results due to non-qualified PC results not included).[1].

	Q		Q+NQ	
Chemical	**mean SD**	**std SD**	**mean SD**	**std SD**
1	7.1	3.4	7.1	3.4
2	1.8	2.1	1.8	2.1
3	0.7	0.5	0.7	0.5
4	1.7	1.8	1.7	1.8
5	3.3	1.6	3.3	1.6
6	4.4	1.2	4.4	1.2
7	2.4	1.5	2.4	1.5
8	8.5	2.7	8.5	2.7
9	9.5	4.9	9.5	4.9

	Q		Q+NQ	
Chemical	**mean SD**	**std SD**	**mean SD**	**std SD**
10	0.7	0.4	0.7	0.4
11	10.3	5.6	10.3	5.6
12	7.2	3.6	7.2	3.6
13	8.6	3	8.6	3
14	12.9	8	12.9	8
15	4.9	2	4.9	2
16	8.3	9	8.3	9
17	6.3	3.7	6.3	3.7
18	6	0.1	6	0.1
19	8.7	3.7	8.7	3.7
20	5.7	4.9	5.7	4.9
21	7.1	6.6	7.1	6.6
22	0.4	0.5	0.4	0.5
23	9	7.5	9	7.5
24	0.2	0	0.2	0
25	10.2	7.1	10.2	7.1
26	0.4	0.1	0.4	0.1
28	7.6	9.4	7.6	9.4
29	6.3	2.5	6.3	2.5
30	6.9	3.7	6.9	3.7
31	5.8	2.9	5.8	2.9
32	4	5	4	5
33	7.6	5.8	7.6	5.8
34	9.9	6.6	9.6	6.8
35	11	4.5	11	4.5
36	5.2	0.4	5.2	0.4
37	6.2	2.4	6.2	2.4
38	8.2	5.1	8.2	5.1
39	8.8	6	8.8	6
40	8.2	5	8.2	5
41	3.8	3.4	3.8	3.4
42	5.5	3.8	5.5	3.8
43	3.5	3.6	3.5	3.6
44	3.9	0.6	3.9	0.6
45	7.3	2.6	7.3	2.6
46	13.8	5.9	13.8	5.9
47	7.7	1.8	7.7	1.8
48	0.7	0.5	0.9	0.3
49	8.4	4.3	8.8	4.1
50	7.5	3.8	7.5	3.8
51	11.8	7.4	11.8	7.4
52	7.2	4.5	8.3	5.9
53	10.9	0.6	10.9	0.6
54	0.8	0.7	0.8	0.7
55	0.3	0.5	0.3	0.5
56	1.2	1.5	1.2	1.5
57	0.5	0.3	0.5	0.3
58	0.5	0.5	0.5	0.5
59	7.8	4.7	7.8	4.7
60	0.2	0	0.2	0
61	9	7.9	9	7.9
62	6.2	5.5	6.2	5.5
63	7.4	5.3	7.4	5.3
64	7	1.9	7	1.9
65	24.1	14.6	21.9	10.8
66	19.8	13.9	19.8	13.9
67	3.1	4.7	3.1	4.7
68	0.3	0	0.3	0
69	0.5	0.3	0.5	0.3
70	0.3	0.1	0.3	0.1
71	0.2	0.1	0.2	0.1
72	0.5	0.7	0.5	0.7
73	10.1	6.9	10.1	6.9

	Q		Q+NQ	
Chemical	**mean SD**	**std SD**	**mean SD**	**std SD**
74	28.8	31.7	28.8	31.7
75	0.1	0.1	5	8.4
76	11.3	1.4	11.3	1.4
77	7.4	4.6	7.4	4.6
78	6.7	5.6	6.7	5.6
79	10.5	7.7	10.5	7.7
80	0.8	0.8	0.8	0.8
81	0.1	0.1	0.1	0.1
82	0.3	0.2	0.3	0.2
83	0.2	0.1	0.2	0.1
84	0.3	0.2	0.3	0.2
85	0.2	0.1	0.2	0.1
86	3.6	2.4	3.6	2.4
87	0.4	0.2	0.4	0.2
88	0.5	0.5	0.5	0.5
89	0.2	0.1	0.2	0.1
90	5.7	5.9	5.7	5.9
91	4.8	1.1	4.8	1.1
92	2.5	1.2	2.5	1.2
93	9.9	4.3	9.9	4.3
94	6.8	5.2	6.8	5.2
95	0.3	0.1	0.3	0.1
96	10	7.1	10	7.1
97	6.3	5.2	6.3	5.2
98	13.6	5.4	13.6	5.4
99	0.2	0.2	0.2	0.2
100	0.3	0.1	0.3	0.1
101	11.8	3.9	11.8	3.9
102	10	8.7	10	8.7
103	0.3	0.3	0.3	0.3
104	10.9	2	10.9	2
105	0.5	0.1	0.5	0.1
Overall				
mean	5.8		5.8	
SD	5.1		5.0	

Concordance of classification between laboratories was calculated based on qualified test from test chemicals for which at least one qualified test was available. In Table 3.4.8 the concordance between laboratories is given.

Table 3.4.8 Concordance between laboratories

BLV concordant	**No.**	**Fraction(%)**
NO	8	7.7
YES	96	92.3

Additional descriptive statistics can identify possible reasons for non-concordant results. These are presented in Table 3.4.9. For each non-concordant result the state (liquid/solid), the GHS classification, whether it is colouring or MTTreducer and the test results are given.

Table 3.4.9 Additional descriptive statistics on non-concordant results between laboratories

Chemical	**name**	**LS**	**coloring**	**mtt**	**GHS**	**CEETOX**	**CARDAM**	**L_OREAL**
11	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	Liquid	No	No	no cat	66.728	27.848	64.415[3]

Chemical	name	LS	coloring	mtt	GHS	CEETOX	CARDAM	L_OREAL
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	Solid	Yes	Yes	no cat	71.761	49.973	59.120
47	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE	Solid	No	No	no cat	48.872	81.105	41.011
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	Solid	No	No	cat 2B	8.854	79.461[1]	75.605[1]
79	ammonium nitrate INCI name: AMMONIUM NITRATE	Solid	No	No	cat 2A (ICCVAM:cat2B)	39.138	63.890	39.396
93	2,5-dimethyl-2,5-hexanediol	Solid	No	No	cat 1	52.935	28.438	24.543
96	1-naphthalene acetic acid	Solid	No	No	cat 1	45.928	62.776	41.016
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	Solid	Yes	No	cat 1	63.475[2]	74.064	32.346

[1] identified as colourant, [2] identified as colourant and MTT-reducer, [3] identified as MTT-reducer

The concordance for the set of chemicals tested during validation obtained by the different participating laboratories should ideally be equal or higher than 80%. As summarized in Table 3.4.10, this criteria was met.

Table 3.4.10 Statement whether the test method has fulfilled the performance criteria concerning the concordance of classifications between laboratories.

Fraction (%)	Statement: criteria is
92.3	fulfilled

A two-way ANOVA was applied to test for differences in mean viabilities between laboratories and chemicals. Data were log-transformed before analysis. Five outlying observations (*2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE* and *gamma-butyrolactone INCI name: BUTYROLACTONE* for CEETOX and *isopropyl acetoacetate* and *iso-octylthioglycolate* for L'OREAL and *iso-octylthioglycolate* for CARDAM*)* were removed before analysis in order to fulfil the ANOVA-requirements. An outlier was defined as an observation with a residual > 3* residual error. The results from the two-way ANOVA are presented in Table 3.4.11. The null hypothesis of no difference was rejected at the 0.01 level of probability (α=0.01).

Table 3.4.11 Two-way ANOVA with factors laboratory and chemical, applied to the arithmetic mean value of the included test results (based on log-transformation)

Effect	NumDF	DenDF	FValue	pvalue
laboratory	2	201	8.62	0.0003
chemical	103	201	112.85	<.0001

Table 3.4.12 Results of the Tukey post-hoc test on differences between laboratories (after log-transformation)

laboratory	vs	Estimate	Standard Error	DF	Tukey-corrected p-value
CARDAM	CEETOX	1.0371	0.9571	201	0.5253
CARDAM	L'OREAL	3.8322	0.9535	201	0.0002
CEETOX	L'OREAL	2.7951	0.9606	201	0.0112

There was no statistically significant difference between CARDAM and CEETOX (p-value = 0.5253) nor between CEETOX and L'OREAL (p-value = 0.0112).
The between-laboratory variability is described by the concordance of classifications between laboratories. Correlations coefficients between viability measurements give also information on this variability. Since the Pearson

correlation coefficient is sensitive for outlying test results and high leverages, both the Pearson and the Spearman correlation coefficients (using ranks instead of the original test results) were calculated. These coefficients are presented in Table 3.4.13.

Table 3.4.13 Pearson and Spearman correlation coefficients between test results of the three participating laboratories.

laboratories	Pearson	Spearman
CARDAM-CEETOX	0.958	0.942
CARDAM-L'OREAL	0.968	0.937
CEETOX-L'OREAL	0.968	0.920

3.4.3 Predictive capacity (accuracy)

All qualified tests for each test chemical was used to calculate the predictive capacity values. The calculations were based on the individual predictions of each qualified test in each laboratory.

For each statistic of the prediction model, an acceptance rate was set by the VMG. These criteria are presented in Table 3.4.14. The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria are fulfilled are presented in Table 3.4.15.

Table 3.4.14 Acceptance criteria for the prediction model

	False Negatives[a] (%)	False Positives[b] (%)	Overall misclassifications[c] (%)
"Definitely acceptable" rates	≤ 10	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	40 < FP ≤ 50	25 < OM ≤ 35
"Definitely unacceptable" rates	> 20	> 50	> 35

[a] equal to (1-Sensitivity), [b] equal to (1-Specificity), [c] equal to (1-Overall accuracy)

Table 3.4.15 The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria for the prediction model are fulfilled.

laboratory	Characteristic	Number used for calculation	Value	95% lower limit	95% upper limit	Statement
CARDAM	Accuracy	211/312	0.676	0.621	0.728	further evaluation
	Sensitivity	109/156	0.699	0.620	0.769	definitely unacceptable
	Specificity	102/156	0.654	0.574	0.728	definitely acceptable
CEETOX	Accuracy	215/311	0.691	0.637	0.742	further evaluation
	Sensitivity	112/156	0.718	0.640	0.787	definitely unacceptable
	Specificity	103/155	0.665	0.584	0.738	definitely acceptable
L'OREAL	Accuracy	215/312	0.689	0.635	0.740	further evaluation
	Sensitivity	114/156	0.731	0.654	0.799	definitely unacceptable
	Specificity	101/156	0.647	0.567	0.722	definitely acceptable
Total	Accuracy	641/935	0.686	0.655	0.715	further evaluation
	Sensitivity	335/468	0.716	0.673	0.756	definitely unacceptable
	Specificity	306/467	0.655	0.610	0.698	definitely acceptable

In Table 3.4.16, the prediction for each qualified test result is given as well as the final classification based on the median of predictions.

Table 3.4.16 Final classification based on the median of all classifications for each chemical

		CARDAM			CEETOX			L'OREAL			Final classification based on	Mispredicted tests/Total
Chemical	GHS	1	2	3	1	2	3	1	2	3	median	
1	no cat	I	I	I	I	I	I	I	I	I	I	9/9
2	no cat	I	I	I	I	I	I	I	I	I	I	9/9
3	no cat	I	I	I	I	I	I	I	I	I	I	9/9
4	no cat	I	I	I	I	I	I	I	I	I	I	9/9
5	no cat	I	I	I	I	I	I	I	I	I	I	9/9
6	no cat	I	I	I	I	I	I	I	I	I	I	9/9
7	no cat	I	I	I	I	I	I	I	I	I	I	9/9
8	no cat	I	I	I	I	I	I	I	I	I	I	9/9
9	no cat	NI	I	NI	I	I	I	I	I	I	I	7/9
10	no cat	I	I	I	I	I	I	I	I	I	I	9/9
11	no cat	I	I	I	NI	NI	NI	NI	NI	I	NI	4/9
12	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
13	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
14	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
15	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
16	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
17	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
18	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
19	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
20	no cat	I	I	I	I	I	.	I	I	I	I	8/8
21	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
22	no cat	I	I	I	I	I	I	I	I	I	I	9/9
23	no cat	I	I	I	I	I	I	I	I	I	I	9/9
24	no cat	I	I	I	I	I	I	I	I	I	I	9/9
25	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
26	no cat	I	I	I	I	I	I	I	I	I	I	9/9
28	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
29	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
30	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
31	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
32	no cat	I	I	I	I	I	I	I	I	I	I	9/9
33	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
34	no cat	I	I	NI	NI	NI	NI	NI	NI	NI	NI	2/9
35	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
36	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
37	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
38	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
39	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
40	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
41	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
42	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
43	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
44	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
45	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
46	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
47	no cat	NI	NI	NI	I	I	NI	I	I	I	I	5/9
48	no cat	I	I	I	I	I	I	I	I	I	I	9/9
49	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
50	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
51	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
52	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
53	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
54	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
55	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
56	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
57	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
58	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
59	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
60	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9

		CARDAM			CEETOX			L'OREAL			Final classification based on median	Mispredicted tests/Total
Chemical	GHS	1	2	3	1	2	3	1	2	3		
61	cat 2B	NI	NI	NI	I	I	I	NI	NI	NI	NI	6/9
62	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
63	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
64	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
65	cat 2B	NI	I	I	NI	NI	NI	I	NI	NI	NI	6/9
66	cat 2B	I	I	I	I	I	I	NI	I	I	I	1/9
67	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
68	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
69	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
70	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
71	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
72	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
73	cat 2A (ICCVAM:cat2B)	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
74	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
75	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
76	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
77	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
78	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
79	cat 2A (ICCVAM:cat2B)	NI	NI	NI	I	I	I	I	NI	I	I	4/9
80	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
81	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
82	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
83	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
84	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
85	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
86	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
87	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
88	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
89	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
90	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
91	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
92	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
93	cat 1	I	I	I	I	NI	NI	I	I	I	I	2/9
94	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
95	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
96	cat 1	I	NI	NI	I	I	NI	I	I	I	I	3/9
97	cat 1	NI	I	NI	NI	NI	NI	NI	NI	NI	NI	8/9
98	cat 1	NI	NI	NI	NI	NI	I	I	I	I	NI	5/9
99	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
100	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
101	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	I	NI	8/9
102	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
103	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
104	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
105	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

3.5 Reproducibility and accuracy using the test strategy

In this section, a 50% cut-off was applied to determine the irritancy of the chemical based on the test strategy: results for reactive chemicals are based on the SE protocol and results for non-reactive chemicals are based on the LE protocol. If the

viability is above 50%, the chemical is considered to be non-irritant. If the viability is 50% or below, the chemical is considered to be irritant.

The selection of the protocol for each chemical is given in Table 3.5.1.The EPRA results that are used to determine the protocol are presented in Appendix X.

Table 3.5.1. Selection of protocol for each chemical

Chemical	name	Protocol
1	1-bromohexane	SE
2	1-methylpropyl benzene	LE
3	2-ethoxyethyl methacrylate	SE
4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	SE
5	4-(methylthio)-benzaldehyde	SE
6	dipropyl disulphide	SE
7	1-bromo-4-chlorobutane	SE
8	1-bromo-octane	LE
9	1,9-decadiene	LE
10	2,2-dimethyl-3-pentanol	LE
11	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL	LE
12	bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated (53-57% aqueousemulsion)	SE
13	bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated (56% aqueous emulsion)	SE
14	dioctyl ether INCI name: DICAPRYLYL ETHER	LE
15	dioctyl carbonate INCI name: DICAPRYLYL CARBONATE	LE
16	2-propylheptyl octanoate INCI name: PROPYLHEPTYL CAPRYLATE	LE
17	polyglyceryl-3 diisooctadecanoate INCI name: POLYGLYCERYL-3 DIISOSTEARATE	LE
18	steareth-10 allyl ether/acrylates copolymer (30% aqueous) INCI name: STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	SE
19	dimethyl siloxane, mono dimethylvinylsiloxy- and mono trimethoxysiloxy-terminated (95%)	LE
20	ricinoleic acid tin salt	LE
21	1-ethyl-3-methylimidazolium ethylsulphate	LE
22	3-phenoxybenzyl alcohol	LE
23	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE	LE
24	glycidyl methacrylate	SE
25	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE	LE
26	propiconazole	LE
28	4,4'-methylene bis-(2,6-di-tert-butylphenol)	LE
29	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE	LE
30	1,1-dimethylguanidine sulphate	LE
31	potassium tetrafluoroborate	SE
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	SE
33	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11	SE
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	SE
35	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	SE
36	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN	LE
37	polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL	SE
38	2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-	LE

Chemical	name	Protocol
	tetramethylbutyl)phenol) INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYLBUTYLPHENOL	
39	2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol] INCI name: BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE	LE
40	acrylamidopropyltrimonium chloride/acrylamide copolymer	LE
41	tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate INCI name: ETHYLHEXYL TRIAZONE	LE
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	SE
43	hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE	SE
44	[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine	LE
45	1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol	LE
46	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10	LE
47	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE	SE
48	sodium hydrogensulphite INCI name: SODIUM BISULFITE	LE
49	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN	LE
50	iodosulfuron-methyl-sodium	SE
51	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz	SE
52	2-anilino-4,6-dimethylpyrimidine common name: Pyrimethanil	LE
53	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam	SE
54	3-chloropropionitrile	SE
55	2-methylpropanal INCI name: 2-METHYLPROPANAL	SE
56	isopropyl acetoacetate	SE
57	2-methyl-1-pentanol	LE
58	1-(1-methyl-2-propoxyethoxy)propan-2-ol INCI name: PPG-2 PROPYL ETHER	SE
59	ethyl-2-methyl acetoacetate	LE
60	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET	LE
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	SE
62	1,4-dibutoxy benzene	SE
63	4-nitrobenzoic acid	SE
64	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate	SE
65	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE	SE
66	sodium chloroacetate	SE
67	gamma-butyrolactone INCI name: BUTYROLACTONE	LE
68	cyclopentanol	LE
69	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL C10-16 ALKYL GLUCOSIDE	SE
70	methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-	SE

Chemical	name	Protocol
	oxobicyclo[2.2.1]hept-2-ylidene)methyl]anilinium sulphate (30% aqueous) INCI name: CAMPHOR BENZALKONIUM METHOSULFATE	
71	1-propoxy-2-propanol INCI name: PROPYLENE GLYCOL PROPYL ETHER	LE
72	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE	SE
73	3,3'-dithiopropionic acid	SE
74	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	SE
75	sodium benzoate INCI name: SODIUM BENZOATE	LE
76	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one	LE
77	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate	SE
78	(2R,3R)-3-((R)-1-(tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate	SE
79	ammonium nitrate INCI name: AMMONIUM NITRATE	LE
80	methylthioglycolate INCI name: METHYL THIOGLYCOLATE	SE
81	3-diethylaminopropionitrile	SE
82	coco alkyl dimethyl betaine (~ 30% aqueous) INCI name: COCO-BETAINE	LE
83	coco amidopropyl betaine (~ 30% aqueous) INCI name: COCAMIDOPROPYL BETAINE	LE
84	sodium coco amphoacetate (~ 30% aqueous)	LE
85	triethanol ammonium alkyl sulphate (~ 40% aqueous) INCI name: TEA-C12-14 ALKYL SULFATE	SE
86	di-sodium alkyl ether sulfosuccinate (~ 30% aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE	SE
87	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE	SE
88	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)	LE
89	ethoxylated (5 EO) alkyl (C10-14) alcohol	LE
90	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE	LE
91	(ethylenediaminepropyl)trimethoxysilane	LE
92	tetraethylene glycol diacrylate	SE
93	2,5-dimethyl-2,5-hexanediol	LE
94	dodecanoic acid INCI name: LAURIC ACID	LE
95	1,2,4-triazole sodium salt	LE
96	1-naphthalene acetic acid	SE
97	sodium oxalate INCI name: SODIUM OXALATE	LE
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	SE
99	1,2-benzisothiazol-3(2H)-one INCI name: BENZISOTHIAZOLINONE	SE
100	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL	LE
101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride	LE

Chemical	name	Protocol
	INCI name: BASIC ORANGE 31	
102	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE	LE
103	3,4-dimethyl-1H-pyrazole	LE
104	N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide	SE
105	1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate	SE

3.5.1 Predictive capacity (accuracy)

All qualified tests for each test chemical was used to calculate the predictive capacity values. The calculations were based on the individual predictions of each qualified test in each laboratory.

For each statistic of the prediction model, an acceptance rate was set by the VMG. These criteria are presented in Table 3.5.2. The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria are fulfilled are presented in Table 3.5.3.

Table 3.5.2 Acceptance criteria for the prediction model

	False Negatives[a] (%)	False Positives[b] (%)	Overall misclassifications[c] (%)
"Definitely acceptable" rates	≤ 10	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	40 < FP ≤ 50	25 < OM ≤ 35
"Definitely unacceptable" rates	> 20	> 50	> 35

[a] equal to (1-Sensitivity), [b] equal to (1-Specificity), [c] equal to (1-Overall accuracy)

Table 3.5.3 The sensitivity, specificity and overall accuracy, subdivided into laboratories and total, including the 95% confidence intervals as well as a statement whether the acceptance criteria for the prediction model are fulfilled.

laboratory	Characteristic	Number used for calculation	Value	95% lower limit	95% upper limit	Statement
CARDAM	Accuracy	206/312	0.660	0.605	0.713	further evaluation
	Sensitivity	83/156	0.532	0.451	0.612	definitely unacceptable
	Specificity	123/156	0.788	0.716	0.850	definitely acceptable
CEETOX	Accuracy	208/311	0.669	0.613	0.721	further evaluation
	Sensitivity	87/156	0.558	0.476	0.637	definitely unacceptable
	Specificity	121/155	0.781	0.707	0.843	definitely acceptable
L'Oreal	Accuracy	204/312	0.654	0.598	0.707	further evaluation
	Sensitivity	85/156	0.545	0.463	0.625	definitely unacceptable
	Specificity	119/156	0.763	0.688	0.827	definitely acceptable
Total	Accuracy	618/935	0.661	0.630	0.691	further evaluation
	Sensitivity	255/468	0.545	0.499	0.591	definitely unacceptable
	Specificity	363/467	0.777	0.737	0.814	definitely acceptable

In Table 3.5.4, the prediction for each qualified test result is given as well as the final classification based on the median of predictions.

Table 3.5.4 Final classification based on the median of all classifications for each chemical

		CARDAM			CEETOX			L'OREAL			Final classification based on median	Mispredicted tests/Total
Chemical	GHS	1	2	3	1	2	3	1	2	3		
1	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
2	no cat	I	I	I	I	I	I	I	I	I	I	9/9
3	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
4	no cat	I	I	I	I	I	I	I	I	I	I	9/9
5	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
6	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
7	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
8	no cat	I	I	I	I	I	I	I	I	I	I	9/9
9	no cat	NI	I	NI	I	I	I	I	I	I	I	7/9
10	no cat	I	I	I	I	I	I	I	I	I	I	9/9
11	no cat	I	I	I	NI	NI	NI	NI	NI	I	NI	4/9
12	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
13	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
14	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
15	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
16	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
17	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
18	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
19	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
20	no cat	I	I	I	I	I	.	I	I	I	I	8/8
21	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
22	no cat	I	I	I	I	I	I	I	I	I	I	9/9
23	no cat	I	I	I	I	I	I	I	I	I	I	9/9
24	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
25	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
26	no cat	I	I	I	I	I	I	I	I	I	I	9/9
28	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
29	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
30	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
31	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
32	no cat	NI	NI	NI	I	I	I	I	I	I	I	6/9
33	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
34	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
35	no cat	I	NI	I	I	NI	I	I	I	I	I	7/9
36	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
37	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
38	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
39	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
40	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
41	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
42	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
43	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
44	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
45	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
46	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
47	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
48	no cat	I	I	I	I	I	I	I	I	I	I	9/9
49	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
50	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
51	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
52	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
53	no cat	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	0/9
54	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	I	NI	8/9
55	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
56	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
57	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
58	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
59	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9
60	cat 2B	I	I	I	I	I	I	I	I	I	I	0/9

		CARDAM			CEETOX			L'OREAL			Final classification based on median	Mispredicted tests/Total
Chemical	GHS	1	2	3	1	2	3	1	2	3		
61	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
62	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
63	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
64	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
65	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
66	cat 2B	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
67	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
68	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
69	cat 2A (ICCVAM:cat2B)	NI	I	NI	NI	NI	NI	NI	NI	NI	NI	8/9
70	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
71	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
72	cat 2A (ICCVAM:cat2B)	I	I	I	I	I	I	I	I	I	I	0/9
73	cat 2A (ICCVAM:cat2B)	NI	NI	NI	NI	I	I	NI	NI	NI	NI	7/9
74	cat 2A	NI	NI	NI	NI	NI	I	NI	NI	NI	NI	8/9
75	cat 2A	I	I	I	I	I	I	I	I	I	I	0/9
76	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
77	cat 2A	NI	NI	NI	I	NI	NI	NI	NI	NI	NI	8/9
78	cat 2A	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
79	cat 2A (ICCVAM:cat2B)	NI	NI	NI	I	I	I	I	NI	I	I	4/9
80	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
81	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
82	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
83	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
84	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
85	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
86	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
87	cat 1	NI	NI	NI	NI	NI	I	NI	NI	NI	NI	8/9
88	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
89	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
90	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
91	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
92	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
93	cat 1	I	I	I	I	NI	NI	I	I	I	I	2/9
94	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
95	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
96	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
97	cat 1	NI	I	NI	NI	NI	NI	NI	NI	NI	NI	8/9
98	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
99	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
100	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
101	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	I	NI	8/9
102	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
103	cat 1	I	I	I	I	I	I	I	I	I	I	0/9
104	cat 1	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	9/9
105	cat 1	I	I	I	I	I	I	I	I	I	I	0/9

4 Overall summary and recommendations

The validation study is considered of high quality due to a very complete dataset. The test method is highly reproducible. The within-laboratory reproducibility (WLR) and between-laboratory reproducibility (BLR) was well above the acceptance criteria set by the VMG (i.e. WLR ≥ 85% and BLR ≥ 80%).

The concordance of classifications within a single laboratory was above 90% for all participating laboratories. The concordance of final classifications obtained between the different participating laboratories was greater than 90%.

A cut-off value of 50% was applied, meaning that a chemical for which the mean viabililty was below 50% is classified as irritant and non-irritant otherwise. The specificity of the prediction model was ‘definitely acceptable’ according to the acceptance criteria as defined by the VMG, regardless the protocol that was used (SE: 0.885; LE: 0.655; test strategy: 0.777). Further evaluation is needed regarding the accuracy (SE: 0.656; LE: 0.686; test strategy: 0.661). The results for the sensitivity are ‘definitely unaccaptable’ according to the acceptance criteria as defined by the VMG (SE: 0.427; LE: 0.716; test strategy: 0.545).

5 Signature

Zeist, March 14, 2014 Placeholder

Han van de Sandt, PhD Carina Rubingh, PhD

Head of department Author

Appendix I MTT reducers and colourants

Note that some chemicals are treated differently by the three laboratories, as is mentioned in section 3.2.1. If a chemical is treated as an MTT-reducer or a colorant in at least one of the laboratories, it is listed in appendix I.

Chemical	name	coloring	MTT
4	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE	No	Yes
5	4-(methylthio)-benzaldehyde	No	Yes
9	1,9-decadiene	No	Yes
20	ricinoleic acid tin salt	No	Yes
23	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE	No	Yes
25	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE	No	Yes
32	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE	Yes	No
33	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11	Yes	Yes
34	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17	Yes	Yes
35	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE	No	Yes
42	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE	No	Yes
48	sodium hydrogensulphite INCI name: SODIUM BISULFITE	No	Yes
49	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN	No	Yes
61	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE	Yes	No
74	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE	Yes	Yes
80	methylthioglycolate INCI name: METHYL THIOGLYCOLATE	No	Yes
81	3-diethylaminopropionitrile	No	Yes
88	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)	No	Yes
91	(ethylenediaminepropyl)trimethoxysilane	No	Yes
92	tetraethylene glycol diacrylate	No	Yes
95	1,2,4-triazole sodium salt	No	Yes
98	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE	Yes	No
101	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31	Yes	No

Appendix II SAS-code for statistical analysis

```
/* ============================== */
/* STEP5_SkinEthic_SAP.sas         */
/*                                 */
/* Data analysis according to SAP  */
/* 10-01-2012 Intial CdJ           */
/*                                 */
/* ============================== */

LIBNAME RhT '\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis';
OPTIONS fmtsearch=(RhT.formats work.formats) NOCENTER;

PROC FORMAT;
   VALUE fmtconcl 0 = 'Qualified and included'
                  1 = 'Non-Qualified'
                2 = 'Excluded';
   VALUE fmtc 0 = 'NQ'
              1 = 'Ex'
              . = ' ';
   VALUE FMTINI 0 = 'NI'
                1 = 'I';
RUN;

/* Merge locked data with chemical information */

DATA chemorder;
   INFILE '\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\chemorder_skinethic.txt'
           DSD DELIMITER='09'x MISSOVER FIRSTOBS=2;
   INFORMAT name $200. tnocode $20. DPRA $40.;
   FORMAT name $200. tnocode $20. DPRA $40.;
   INPUT order (tnocode state name predGHS predEPA Loreal   Cardam Ceetox DPRA) ($);   IF order = .
THEN DELETE;
   IF tnocode IN ('chemical102' 'chemical68' 'chemical49') THEN DELETE; * deselected chemicals;
     LS = SCAN(state,1);
   /* Hardened castor oil with approx. 40 mol EO (INCI name: PEG-40 Hydrogenated Castor Oil) */
   /* is listed as solid, but treated as liquid */
   /* decision by the VMG NOV10 2011 */
   IF order = 37 THEN LS = 'Solid';
   IF order < 54 THEN trueINI = "NI";
   ELSE trueINI = "I";
RUN;

DATA chemorder2;
   SET chemorder(keep = name order LS predGHS loreal DPRA rename=(loreal = chemical_code))
       chemorder(keep = name order LS predGHS cardam DPRA rename=(cardam = chemical_code))
       chemorder(keep = name order LS predGHS ceetox DPRA rename=(ceetox = chemical_code));
RUN;
PROC SORT data= RhT.SE_meanviabilities_locked; BY chemical_code; RUN;
PROC SORT data= RhT.LE_meanviabilities_locked; BY chemical_code; RUN;
PROC SORT data= chemorder2; BY chemical_code; RUN;
DATA pre_all_SE;
   MERGE RhT.SE_meanviabilities_locked(in=ok2) chemorder2 (in=ok);
   BY chemical_code;
   IF ok and ok2;
   tmp=chemical_code;
   SUBSTR(tmp,1,1)='';
   tmp2=PUT(INPUT(tmp,best12.),z3.);
   *IF test >3 then delete;
   IF order < 54 THEN trueINI = "NI";
   ELSE trueINI = "I";
   runN = INPUT(run,best12.);
   IF mean_NSC NE . THEN coloring = 'Yes';
   ELSE coloring = 'No';
   mean_NSMTT = mean_MTT;
   IF mean_NSMTT NE . THEN MTT = 'Yes';
   ELSE MTT = 'No';
   RETAIN test 0;
   test = test+1;
   IF first.chemical_code THEN test=1;
   IF (UPCASE(SUBSTR(DPRA,1,8)) IN ('REACTIVE' '"REACTIV') AND UPCASE(SUBSTR(DPRA,1,15)) NE 'NON-
REACTIVE AT') THEN keuze = 'SE';
   IF chemical_code = 'X13' and laboratory = '' then delete; * technical;
   /* exclude runs with technical issues */
   IF run = -1 THEN DELETE;
RUN;
DATA pre_all_LE;
   MERGE RhT.LE_meanviabilities_locked(in=ok2) chemorder2 (in=ok);
   BY chemical_code;
   IF ok and ok2;
   tmp=chemical_code;
   SUBSTR(tmp,1,1)='';
   tmp2=PUT(INPUT(tmp,best12.),z3.);
   *IF test >3 then delete;
   IF order < 54 THEN trueINI = "NI";
   ELSE trueINI = "I";
   runN = INPUT(run,best12.);
   IF mean_NSC NE . THEN coloring = 'Yes';
   ELSE coloring = 'No';
   mean_NSMTT = mean_MTT;
   IF mean_NSMTT NE . THEN MTT = 'Yes';
   ELSE MTT = 'No';
   RETAIN test 0;
```

```
   test = test+1;
   IF first.chemical_code THEN test=1;
   IF (UPCASE(SUBSTR(DPRA,1,8)) NOT IN ('REACTIVE' '"REACTIV') OR UPCASE(SUBSTR(DPRA,1,15)) EQ 'NON-
REACTIVE AT') THEN keuze = 'LE';
   IF PCqual = 1 OR NCqual = 1 OR qual_sd = 1 THEN conclusion = 1;
   /* exclude runs with technical issues */
   IF run = -1 THEN DELETE;
RUN;
DATA pre_all;
   SET pre_all_SE (in=se) pre_all_LE (in=LE);
   IF SE THEN select = 'SE';
   IF LE THEN select = 'LE';
   /* exclude runs with technical issues */
   IF run = -1 THEN DELETE;
   *IF run = . THEN DELETE;
RUN;
PROC SORT data=pre_all; BY laboratory tmp2; RUN;

/* check wheter selection was made for SE or LE, not for both */
PROC SORT data=pre_all_SE out=tmp1 nodupkey; BY laboratory chemical_code; RUN;
PROC SORT data=pre_all_LE out=tmp2 nodupkey; BY laboratory chemical_code; RUN;
DATA niegoe;
   SET tmp1(in=se) tmp2(in=le);
   IF se AND le THEN OUTPUT niegoe; * empty;
RUN;

/* 09082012 CdJ Revision */

DATA pre_106107;
   SET pre_all;
   /* remove chemical 106 and 107 for statistical analysis */
   IF chemical_code IN ('L6' 'C52' 'X95' 'L100' 'C56''X32') THEN OUTPUT;
RUN;
DATA pre_all;
   SET pre_all;
   /* remove chemical 106 and 107 for statistical analysis */
   IF chemical_code IN ('L6' 'C52' 'X95') THEN DELETE; * 106;
   IF chemical_code IN ('L100'   'C56''X32') THEN DELETE; * 107;
   /* for some chemicals the VMG overrode the 50% rule regarding NSMTT */
   IF select = 'LE' THEN DO;
      IF chemical_code IN ('C6' 'X31') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then conclusion
= 0; * 80;
     IF chemical_code IN ('C6' 'X31') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then conclusion
= 1; * 80;
      IF chemical_code IN ('X62' 'C53') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 4;
      IF chemical_code IN ('X62' 'C53') and  (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 4;
      IF chemical_code IN ('L58' 'C58') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 20;
      IF chemical_code IN ('L58' 'C58') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 20;
   END;
   IF select = 'SE' THEN DO;
      IF chemical_code = 'C53' AND run = 1 THEN qual_sd = 1;
   /* for some chemicals the VMG overrode the 50% rule regarding NSMTT */
      IF chemical_code IN ('X139') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then conclusion =
0; * 23;
      IF chemical_code IN ('X139') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then conclusion =
1; * 23;
      IF chemical_code IN ('X62' 'C53' 'L7') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 4;
      IF chemical_code IN ('X62' 'C53' 'L7') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 4;
      IF chemical_code IN ('L58' 'C58') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 20;
      IF chemical_code IN ('L58' 'C58') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 20;
      IF chemical_code IN ('X81') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then conclusion = 0;
* 91;
      IF chemical_code IN ('X81') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then conclusion = 1;
* 91;
   /* conclusion for chemical 20 L'oreal is not correct */
   END;
RUN;

DATA pre_all_LE;
   SET pre_all_LE;
   /* remove chemical 106 and 107 for statistical analysis */
   IF chemical_code IN ('L6' 'C52' 'X95') THEN DELETE; * 106;
   IF chemical_code IN ('L100'   'C56''X32') THEN DELETE; * 107;
   /* for some chemicals the VMG overrode the 50% rule regarding NSMTT */
      IF chemical_code IN ('C6' 'X31') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then conclusion
= 0; * 80;
     IF chemical_code IN ('C6' 'X31') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then conclusion
= 1; * 80;
      IF chemical_code IN ('X62' 'C53') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 4;
      IF chemical_code IN ('X62' 'C53') and  (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 4;
      IF chemical_code IN ('L58' 'C58') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 20;
      IF chemical_code IN ('L58' 'C58') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 20;
RUN;


/* === */
```

```
/* SE   */
/* === */

PROC SORT data=pre_all_SE; BY chemical_code; RUN;
DATA rules;
   SET pre_all_SE;
   BY chemical_code;
   if conclusion = 1 /* non-qual */ then delete;
   IF mean_viability >50 THEN pred50=0;
   ELSE pred50 = 1;
   IF mean_TA >50 THEN pred50raw=0;
   ELSE pred50raw = 1;
   FORMAT pred50  pred50raw  fmtpred.;
RUN;
DATA rules2;
    SET rules;
   BY chemical_code;
   RETAIN t 0;
   t = t+1;
   IF first.chemical_code THEN t=1;
   IF t>3 then delete;
RUN;
PROC SORT data=rules2; BY order  laboratory  ; RUN;
PROC TRANSPOSE data=rules2 out=allT1 prefix=p50_;
   VAR pred50;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT1raw prefix=p50r_;
   VAR pred50raw;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT3 prefix=v_;
   VAR mean_viability;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT4 prefix=TA_;
   VAR mean_TA;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT5 prefix=CC_;
   VAR mean_NSC;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT6 prefix=KC_;
   VAR mean_NSMTT;
   BY order  laboratory  ;
   ID t;
RUN;
DATA overall (drop=_name_);
   MERGE allT1  allT1raw allT3 allT4 allT5 allT6;
   BY order  laboratory  ;
RUN;
PROC SORT data=overall; BY laboratory order; RUN;
DATA rules3_no rules3_yes;
   SET overall;
   mean_nsc=mean(CC_1,CC_2,CC_3);
   mean_mtt=mean(KC_1,KC_2,KC_3);
   * rule 1 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory
is less than or equal to (=) 50%,
   THEN this chemical is considered to be compatible with the test method. The chemical should be
included in the overview tables,
   and included in all statistical calculations of reproducibility and predictive capacity.;
  IF mean_nsc <= 50 THEN DO; inclusion50_nsc = 'yes'; inclusion60_nsc = 'yes'; END;
  IF mean_mtt<=50 THEN DO; inclusion50_mtt = 'yes'; inclusion60_mtt = 'yes'; END;
  * rule 2 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory
is greater than (>) 50% AND
  their classification (I or NI) remains the same upon correction, THEN this chemical is considered to
be compatible with the test
  method. The chemical should be included in the overview tables, and included in all statistical
calculations of reproducibility and
  predictive capacity.;
  IF mean_nsc > 50 AND p50_1=p50r_1 AND  p50_2=p50r_2 AND p50_3=p50r_3 THEN inclusion50_nsc = 'yes';
  IF mean_mtt > 50 AND p50_1=p50r_1 AND  p50_2=p50r_2 AND p50_3=p50r_3 THEN inclusion50_mtt = 'yes';
* rule 3 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory is
greater than (>) 50% AND
  the classification of at least one of the qualified tests changes upon correction, THEN this chemical
is considered to be
  incompatible with the test method. The chemical should be included in the overview tables, but
excluded from all statistical
  calculations of reproducibility and predictive capacity.;
  IF mean_nsc > 50 AND (p50_1 NE p50r_1 OR  p50_2 NE p50r_2 OR p50_3 NE p50r_3) THEN inclusion50_nsc =
'no';
  IF mean_mtt > 50 AND (p50_1 NE p50r_1 OR  p50_2 NE p50r_2 OR p50_3 NE p50r_3) THEN inclusion50_mtt =
'no';
  * output;
  IF inclusion50_nsc = 'no' OR inclusion50_mtt = 'no' OR inclusion60_nsc = 'no' OR inclusion60_mtt =
'no' THEN OUTPUT rules3_no;
  ELSE OUTPUT rules3_yes;
RUN;
/* CONCLUSION */
/* new rules give selection : chemical 4, 20 (Cardam only), 91 (Ceetox only) */

DATA select /*(keep = order laboratory run conclusion NCqual PCqual qual_sd)*/;
   SET pre_all_SE;
```

```
   IF order IN (4 20 91)  THEN OUTPUT;
RUN;

DATA pre_all_SE;
   SET pre_all_SE;
   /* remove chemical 106 and 107 for statistical analysis */
   IF chemical_code IN ('L6' 'C52' 'X95') THEN DELETE; * 106;
   IF chemical_code IN ('L100'   'C56' 'X32') THEN DELETE; * 107;
   /* for some chemicals the VMG overrode the 50% rule regarding NSMTT */
      IF chemical_code = 'C53' AND run = 1 THEN qual_sd = 1;
   /* for some chemicals the VMG overrode the 50% rule regarding NSMTT */
      IF chemical_code IN ('X139') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then conclusion =
0; * 23;
      IF chemical_code IN ('X139') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then conclusion =
1; * 23;
      IF chemical_code IN ('X62' 'C53' 'L7') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 4;
      IF chemical_code IN ('X62' 'C53' 'L7') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 4;
      IF chemical_code IN ('L58' 'C58') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 20;
      IF chemical_code IN ('L58' 'C58') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 20;
      IF chemical_code IN ('X81') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then conclusion = 0;
* 91;
      IF chemical_code IN ('X81') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then conclusion = 1;
* 91;
RUN;
PROC SORT data=RhT.SE2 out=ODnc(keep = laboratory run chemical_code meanODnc) nodupkey;
   BY laboratory run chemical_code;
   where chemical_code NE 'PC';
RUN;
PROC SORT data=pre_all_SE; BY laboratory run chemical_code; RUN;
DATA pre_all_SE;
   MERGE pre_all_SE (in=ok) ODnc;
   BY laboratory run chemical_code;
   IF ok;
RUN;

* Table 3.2.2 - MTT and colouring differences
* some chemicals are treated differently by the labs concerning the coloring or mtt;
PROC SORT data=pre_all_SE out=extra0s (keep = order name laboratory mtt coloring where=(laboratory NE
'')) nodupkey;
   BY order laboratory mtt coloring;
RUN;
PROC TRANSPOSE data=extra0s out=extra0a;
   VAR mtt;
   BY order name;
   ID laboratory;
RUN;
DATA extra0_mtt(keep = order name L_oreal ceetox cardam mttcheck) ;
   SET extra0a ;
   BY order;
   mttcheck = 'not ok';
   IF l_oreal = ceetox AND L_oreal = cardam and cardam = ceetox THEN mttcheck = ' ';
   ELSE mttcheck = '#';
   *IF mttcheck = 'not ok' THEN OUTPUT;
RUN;
PROC TRANSPOSE data=extra0s out=extra0b;
   VAR coloring;
   BY order name;
   ID laboratory;
RUN;
DATA extra0_color( keep = order name L_oreal ceetox cardam colorcheck);
   SET  extra0b;
   BY order;
   colorcheck = 'not ok';
   IF l_oreal = ceetox AND L_oreal = cardam and cardam = ceetox THEN colorcheck = ' ';
   ELSE colorcheck = '#';
   *IF colorcheck = 'not ok' THEN OUTPUT;
RUN;

/* non-qual NC and PC */
PROC SORT data=pre_all_SE out=pre412 nodupkey; BY filename; RUN;
PROC FREQ data=pre412 ;
   TABLE laboratory*NCqual/out=table412_NC NOCOL NOPERCENT;
   TABLE laboratory*PCqual/out=table412_PC NOCOL NOPERCENT;
RUN;
PROC TRANSPOSE data=table412_NC out=table412NCt;
   VAR count;
   ID NCqual;
   BY laboratory;
RUN;
PROC TRANSPOSE data=table412_PC out=table412PCt;
   VAR count;
   ID PCqual;
   BY laboratory;
RUN;
DATA table412;
   SET table412NCt(in=nc) table412PCt(in=pc);
   BY laboratory;
   IF nc THEN var = 'NC';
   IF pc THEN var = 'PC';
   IF non_qualified = . THEN non_qualified = 0;
   fraction_nq = 100* non_qualified/(non_qualified+qualified);
   fraction_q = 100*qualified/(non_qualified+qualified);
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table412.doc' notoc_data;
```

```
PROC REPORT data = table412 NOWINDOWS HEADLINE HEADSKIP;
   COLUMN laboratory var qualified fraction_q non_qualified fraction_nq;
   DEFINE laboratory/GROUP;
   DEFINE var/DISPLAY ' ';
   DEFINE qualified/DISPLAY 'No.Qualified' width = 12 CENTER;
   DEFINE fraction_q/DISPLAY '%' width = 5 format=8.1 CENTER;
   DEFINE non_qualified/DISPLAY 'No.Non-Qualified' width = 16 CENTER;
   DEFINE fraction_nq/DISPLAY '%' width = 5 format=8.1 CENTER;
RUN; QUIT;
ODS rtf close;


/* 5.2 Table with number and fraction of qualified and non_qualified runs */
PROC SORT data=pre_all_SE; BY laboratory; RUN;
PROC FREQ data=pre_all_SE noprint;
   TABLES conclusion/out=table5_2LAB;
   BY laboratory;
RUN;
PROC FREQ data=pre_all_SE noprint;
   TABLES conclusion/out=table5_2TOTAL;
RUN;
DATA table5_2;
   SET table5_2LAB table5_2TOTAL (in=ok);
   IF ok THEN laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthic_Table5_2.doc' notoc_data;
PROC REPORT data = table5_2 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory conclusion count percent;
   DEFINE laboratory/GROUP;
   DEFINE conclusion /DISPLAY 'Call';
   DEFINE count/ DISPLAY 'No.';
   DEFINE percent/DISPLAY width = 15 format=8.1 'Fraction (%)';
RUN;QUIT;
ODS RTF close;

OPTIONS PS=42 LS=120;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthic_Table5_2LIST.doc' notoc_data;
PROC REPORT data=pre_all_SE (where=(conclusion IN (1 2)) keep = run order conclusion laboratory name
qual_sd PCqual NCqual NSCcall NSMTTcall)
            NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS conclusion laboratory order run NCqual PCqual qual_sd  NSCcall NSMTTcall;
   DEFINE conclusion / GROUP width = 15;
   DEFINE laboratory / GROUP width = 15;
   DEFINE order/DISPLAY width = 4 'Chemical';
   DEFINE NSCcall/DISPLAY width = 12;
   BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

/* 5.4 Table with number of tests within each test sequence */
OPTIONS PS=55 LS=80;
PROC SORT data=pre_all_SE; BY laboratory tmp2 run; RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthic_Table5_4.doc' notoc_data;
PROC FREQ data=pre_all_SE ;
   TABLES order*laboratory/out=table5_4 NOROW NOCOL NOPERCENT;
RUN;
ODS RTF close;

/* 5.5 Table with list, no and fraction of NQ tests */
PROC SORT data=pre_all_SE; BY laboratory order; RUN;
PROC FREQ data=pre_all_SE NOPRINT;
   TABLES conclusion/out=table5_5;
   BY laboratory order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthic_Table5_5.doc' notoc_data;
PROC PRINT data=table5_5(WHERE=(CONCLUSION IN (1 2))); RUN;
ODS RTF close;

/* 5.6 Table with list and fraction of complete test sequences */
DATA pre5_6;
   SET pre_all_SE;
   IF conclusion IN (1 2) THEN DELETE;
RUN;
PROC FREQ data=pre5_6 noprint;
   TABLES laboratory * order/out=pre5_6b;
RUN;
DATA table5_6LIST;
   SET pre5_6b;
   IF count >=3 THEN OUTPUT;
RUN;
PROC SORT data=pre5_6b; BY order; RUN;
PROC TRANSPOSE data=pre5_6b out=table5_6LIST;
   VAR COUNT;
   ID laboratory;
   BY order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthic_Table5_6LIST.doc' notoc_data;
PROC PRINT data=table5_6LIST; RUN;
ODS RTF close;
/*switched off by Rinke*/
/*PROC FREQ data=table5_6LIST noprint;*/
/*   TABLES laboratory/out=table5_6B;*/
/*RUN;*/
/* Above proc Freq statement doesn't work! adaption below gives desired results, it seems. */
```

```
/*adaption by rinke to test*/

PROC FREQ data=pre5_6b noprint;
   TABLES laboratory/out=table5_6B;
RUN;
/*  end adaption by rinke to test*/

DATA table5_6LAB;
   SET table5_6B;
   fraction_complete = 100*count/104;
   test_sequence_criteria = 'not fulfilled';
   IF fraction_complete > 85 THEN test_sequence_criteria = 'fulfilled';
RUN;
PROC MEANS data=table5_6LAB NOPRINT;
   VAR count;
   OUTPUT out=table5_6D sum=sumcount;
RUN;
DATA table5_6OVERALL;
   SET table5_6D;
   fraction_complete = 100*sumcount/(3*104);
   test_sequence_criteria = 'not fulfilled';
   IF fraction_complete >= 85 THEN test_sequence_criteria = 'fulfilled';
RUN;
DATA table5_6;
   SET table5_6LAB table5_6OVERALL(in=ok);
   IF ok then laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table5_6.doc' notoc_data;
PROC REPORT data = table5_6 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory fraction_complete;
   DEFINE laboratory/DISPLAY;
   DEFINE fraction_complete/DISPLAY format=8.1 'Fraction';
RUN; QUIT;
ODS rtf close;
PROC DATASETS library = work;
   DELETE pre5_6 pre5_6b table5_6B table5_6D;
RUN;QUIT;

/* 5.7 Table with list and fraction of incomplete test sequences */

DATA pre5_7a pre5_7b;
   SET pre_all_SE;
   IF conclusion IN (1 2) THEN output pre5_7a;
   IF conclusion NOT IN (1 2) THEN output pre5_7b;
RUN;
PROC FREQ data=pre5_7a noprint;
   TABLES laboratory * order/out=pre5_7a2;
RUN;
PROC FREQ data=pre5_7b noprint;
   TABLES laboratory * order/out=pre5_7b2;
RUN;
DATA pre5_7;
   MERGE pre5_7a2(rename=(count=OUT)) pre5_7b2(rename=(count=IN));
   BY laboratory order;
   IF IN NOT IN (. 0 1 2) THEN complete = 'Yes';
   IF IN IN (. 0 1 2) THEN complete = 'No';
RUN;
DATA table5_7LIST;
   SET pre5_7;
   IF IN = . THEN IN = 0;
   IF complete = 'No' THEN OUTPUT;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table5_7LIST.doc' notoc_data;
PROC REPORT data = table5_7LIST NOWINDOWS HEADLINE HEADSKIP;
   COLUMN laboratory order IN OUT;
   DEFINE laboratory/GROUP;
   DEFINE order /DISPLAY ;
   DEFINE IN/DISPLAY 'Qualified' width = 10 CENTER;
   DEFINE OUT/DISPLAY 'Non-Qual or Excluded' width = 20 CENTER;
RUN; QUIT;
ODS RTF close;
PROC FREQ data=table5_7LIST noprint;
   TABLES laboratory/out=table5_7b;
RUN;
DATA table5_7LAB;
   SET table5_7B;
   fraction_incomplete = 100*count/104;
   test_sequence_criteria = 'fulfilled';
   IF fraction_incomplete > 15 THEN test_sequence_criteria = 'not fulfilled';
RUN;
PROC MEANS data=table5_7LAB NOPRINT;
   VAR count;
   OUTPUT out=table5_7D sum=sumcount;
RUN;
DATA table5_7OVERALL;
   SET table5_7D;
   fraction_incomplete = 100*sumcount/(3*104);
   test_sequence_criteria = 'fulfilled';
   IF fraction_incomplete > 15 THEN test_sequence_criteria = 'not fulfilled';
RUN;
DATA table5_7;
   SET table5_7LAB table5_7OVERALL(in=ok);
   IF ok then laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table5_7.doc' notoc_data;
PROC REPORT data = table5_7 NOWINDOWS HEADLINE HEADSKIP;
```

```
   COLUMNS laboratory fraction_incomplete;
   DEFINE laboratory/DISPLAY;
   DEFINE fraction_incomplete/DISPLAY format=8.1 'Fraction';
RUN; QUIT;
ODS rtf close;
PROC DATASETS library = work;
   DELETE pre5_7 pre5_7b table5_7B table5_7D;
RUN;QUIT;

/* 5.8 statement whether test method has fulfilled the performance criteria */
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\SkinEthic_Table5_8.doc' notoc_data;
PROC REPORT data = table5_6 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory fraction_complete test_sequence_criteria;
   DEFINE laboratory/DISPLAY;
   DEFINE fraction_complete/DISPLAY format=8.1 'Fraction';
   DEFINE test_sequence_criteria/DISPLAY 'Statement: criteria is ' CENTER;
RUN; QUIT;
ODS rtf close;



/* 5.10 summarise results of all tests (including NQ and excl) */
DATA appVI (keep=laboratory order predGHS MTT coloring test meanODnc stdNC NCqual meanPC sdPC PCqual
          mean_TA std_TA qual_sd mean_NSC mean_NSMTT mean_viability conclusion pred50);
   RETAIN laboratory order predGHS MTT coloring test meanODnc stdNC NCqual meanPC sdPC PCqual
          mean_TA std_TA qual_sd mean_NSC mean_NSMTT mean_viability conclusion pred50;
   SET pre_all_SE;
   IF mean_viability > 50 THEN pred50 = 'NI';
   ELSE pred50 = 'I';
RUN;
PROC SORT data=appVI; BY laboratory order test; RUN;


/* ---------------------------------------------- */
/* Section 6 of SAP: Intralaboratory variability */
/* ---------------------------------------------- */

/* at least two qualified tests */
PROC SORT data=pre_all_SE; BY laboratory name; RUN;
PROC FREQ data=pre_all_SE noprint;
   TABLES conclusion/out=pre_WLV;
   BY laboratory name;
RUN;
DATA pre_WLV2;
   SET pre_WLV (where=(conclusion = 0 AND count >=2));
RUN;
DATA pre_WLV3;
   MERGE pre_all_SE(drop=test where=(conclusion NOT IN (1 2))) pre_WLV2 (in=ok);
   BY laboratory name;
   IF ok;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
RUN;
DATA WLV;
   SET pre_WLV3;
   BY laboratory name;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
   IF test > 3 THEN DELETE;
/* check mean viability dataset op excluded chemicals, pas daarop nummers hieronder aan */
   /* exclude chemicals */
/*   IF order IN (6 7 17 52 53 58 62 81 95 100) THEN DELETE;*/
   IF order IN ( 106 107) THEN DELETE;
RUN;

/* 6.1 Table with concordance of classifications */
PROC SORT data=WLV; BY laboratory name; RUN;
PROC TRANSPOSE data=WLV out=pre6_1;
   BY laboratory name order;
   ID test;
   VAR predINI;
RUN;
PROC FREQ data=WLV noprint;
   TABLES predINI/out=pre6_1;
   BY laboratory name order;
RUN;
DATA pre6_1b;
   SET pre6_1;
   IF percent NE 100 THEN WLV_concordant = 'NO ';
   ELSE WLV_concordant = 'YES';
RUN;
PROC SORT data=pre6_1b out=pre6_1c nodupkey;
   BY laboratory name order;
RUN;
PROC FREQ data=pre6_1c noprint;
   TABLES WLV_concordant/out=table6_1LAB;
   BY laboratory;
RUN;
PROC FREQ data=pre6_1c noprint;
   TABLES WLV_concordant/out=table6_1TOTAL;
RUN;
DATA table6_1;
   SET table6_1LAB table6_1TOTAL(in=ok);
   IF ok THEN laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table6_1.doc' notoc_data;
```

```
PROC REPORT data=table6_1 NOWINDOWS HEADLINE HEADSKIP ;
   COLUMNS laboratory WLV_concordant count percent;
   DEFINE laboratory / GROUP width = 10;
   DEFINE WLV_concordant / DISPLAY width=15 'WLV concordant';
   DEFINE count / DISPLAY FLOW 'No.';
   DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
   BREAK after laboratory/SKIP;
RUN;
ODS RTF close;

/* 6.2 Additional descriptives of non-concordant results */
DATA pre6_2;
   MERGE WLV pre6_1c(keep = laboratory name order WLV_concordant);
   BY laboratory name order;
RUN;
/* 16082012 CdJ revision */
DATA pre6_2b;
   SET pre6_2(where=(WLV_concordant = 'NO '));
   KEEP laboratory order name LS coloring MTT predGHS mean_viability test;
RUN;
PROC SORT data=pre6_2b; BY laboratory order name test;
PROC TRANSPOSE data=pre6_2b out=pre6_2t(drop=_name_);
   BY laboratory order name LS coloring mTT predGHS;
   VAR mean_viability;
   ID test;
RUN;
DATA table6_2;
   RETAIN laboratory order name LS coloring mtt predGHS _1 _2 _3;
   SET pre6_2t;
RUN;
* view in excel to create table for report;

/* 6.3 Statement per laboratory regarding WLV */
DATA table6_3 ;
   SET table6_1LAB table6_1TOTAL(in=total);
   IF total THEN laboratory = 'Total';
   WHERE WLV_concordant = 'YES';
   WLV_criteria = 'not fulfilled';
   IF percent >= 85 THEN WLV_criteria = 'fulfilled';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthic_Table6_3.doc' notoc_data;
PROC REPORT data=table6_3 NOWINDOWS HEADLINE HEADSKIP ;
   COLUMNS laboratory percent WLV_criteria;
   DEFINE laboratory / GROUP width = 10;
   DEFINE WLV_criteria / DISPLAY width=15 'Statement: criteria is ';
   DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
RUN;
ODS RTF close;

/* 6.4 Pearson Correlations */
PROC SORT data=WLV; BY laboratory name; RUN;
PROC TRANSPOSE data=WLV out=WLVt;
   BY laboratory name;
   ID test;
   VAR mean_viability;
RUN;
PROC CORR data=WLVt noprint outp=pearson outs=spearman;
   VAR _1 _2 _3;
   BY laboratory;
RUN;
/*PROC GPLOT data=WLVt; */
/*   PLOT _1 * _2 _1 * _3 _2 * _3;*/
/*   BY laboratory;*/
/*RUN; QUIT;*/
DATA set1 (keep=laboratory _name_ _1 where=(_name_ NE '_1'))
     set2 (keep=laboratory _name_ _2 where=(_name_ NE '_2'))  ;
   SET pearson;
   WHERE _TYPE_ = 'CORR';
RUN;
PROC TRANSPOSE data=set1 out=set1T(drop=_name_) prefix = _1;
   VAR _1;
   BY laboratory;
   ID _name_;
RUN;
PROC TRANSPOSE data=set2 out=set2T(drop=_name_) prefix = _2;
   VAR _2;
   BY laboratory;
   ID _name_;
RUN;
DATA pre_pearson(drop=_2_1);
   MERGE set1T set2T;
   BY laboratory;
   FORMAT _1_2 _1_3 _2_3 8.3;
RUN;

DATA set1 (keep=laboratory _name_ _1 where=(_name_ NE '_1'))
     set2 (keep=laboratory _name_ _2 where=(_name_ NE '_2'))  ;
   SET spearman;
   WHERE _TYPE_ = 'CORR';
RUN;
PROC TRANSPOSE data=set1 out=set1T(drop=_name_) prefix = _1;
   VAR _1;
   BY laboratory;
   ID _name_;
RUN;
PROC TRANSPOSE data=set2 out=set2T(drop=_name_) prefix = _2;
   VAR _2;
   BY laboratory;
```

```
   ID _name_;
RUN;
DATA pre_spearman(drop=_2_1);
   MERGE set1T set2T;
   BY laboratory;
   FORMAT _1_2 _1_3 _2_3 8.3;
RUN;

DATA pre6_4;
   SET pre_pearson (in=p) pre_spearman (in=s);
   BY laboratory;
   IF s THEN corr = 'spearman';
   IF p THEN corr = 'pearson';
RUN;
PROC SORT data=pre6_4; BY corr; RUN;
PROC MEANS data=pre6_4 noprint;
   VAR _1_2 _1_3 _2_3;
   BY corr;
   OUTPUT out=pre6_4b mean = _1_2 _1_3 _2_3;
RUN;

DATA pretable6_4;
/*LABNAMES AANPASSEN*/
SET pre6_4 pre6_4b(in=m);
   IF m THEN laboratory = 'Mean';
   IF laboratory = 'CARDAM' THEN tmp1 = 1;
   IF laboratory = 'CEETOX' THEN tmp1 = 2;
   IF laboratory = 'LOREAL' THEN tmp1 = 3;
   IF laboratory = 'Mean' THEN tmp1 = 4;
RUN;
PROC SORT data=pretable6_4 out=table6_4(drop=tmp1 _type_ _freq_); BY corr tmp1; RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthic_Table6_4.doc' notoc_data;
PROC REPORT data=table6_4 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS corr laboratory _1_2 _1_3 _2_3;
   DEFINE corr / GROUP;
   DEFINE laboratory/DISPLAY width = 15;
   DEFINE _1_2/ DISPLAY 'Qual1 - Qual2' format=8.3 width = 15 CENTER;
   DEFINE _1_3/ DISPLAY 'Qual1 - Qual3' format=8.3 width = 15 CENTER;
   DEFINE _2_3/ DISPLAY 'Qual2 - Qual3' format=8.3 width = 15 CENTER;
   BREAK after corr/SKIP;
RUN; QUIT;
ODS RTF close;

/* 6.5 mean and mean diff */
PROC MEANS data=WLV noprint;
   VAR mean_viability;
   CLASS laboratory name order;
   OUTPUT out=table6_5(where=(_type_=7)) mean=means std=stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table6_5.doc' notoc_data;
PROC REPORT data=table6_5 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS order laboratory,(means stds cvs ns);
   DEFINE order / GROUP width = 5 'Chemical';
   DEFINE laboratory/ACROSS "_laboratory_";
   DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean';
   DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std';
   DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv';
   DEFINE ns/ANALYSIS mean width=3 CENTER 'n';
RUN; QUIT;
ODS RTF close;

* also with non-qualified tests included;
DATA inclnonqual;
   SET pre_all_SE(where=(conclusion NE 2));
RUN;
PROC MEANS data=inclnonqual noprint;
   VAR mean_viability;
   CLASS laboratory name order;
   OUTPUT out=table6_5b(where=(_type_=7)) mean=meansnq std=stdsnq cv=cvsnq n=nsnq;
RUN;
DATA table6_5c;
   MERGE table6_5 table6_5b;
   BY laboratory name order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table6_5b.doc' notoc_data;
PROC REPORT data=table6_5c NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS order laboratory,(("_Q_" stds cvs ns) ("_Q+NQ_" stdsnq cvsnq nsnq));
   DEFINE order / GROUP width = 5 'Chemical';
   DEFINE laboratory/ACROSS "_laboratory_";
   DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std';
   DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv';
   DEFINE ns/ANALYSIS mean width=3 CENTER 'n';
   DEFINE stdsnq/ANALYSIS mean format=8.1 CENTER 'std';
   DEFINE cvsnq/ANALYSIS mean format=8.1 CENTER 'cv';
   DEFINE nsnq/ANALYSIS mean width=3 CENTER 'n';
RUN; QUIT;
ODS RTF close;
/* ---------------------------------------------- */
/* Section 7 of SAP: Interlaboratory variability */
/* ---------------------------------------------- */

/* at least one qualified tests per laboratory*/
PROC SORT data=pre_all_SE; BY laboratory name; RUN;
PROC FREQ data=pre_all_SE noprint;
   TABLES conclusion/out=pre_BLV;
   BY laboratory name;
```

```
RUN;
DATA pre_BLV2;
   SET pre_BLV (where=(conclusion IN (0 /*1*/) AND count >=1));
RUN;
PROC SORT data=pre_BLV2 nodupkey; BY name laboratory; RUN:
PROC TRANSPOSE data=pre_BLV2 out=pre_BLV2t;
   VAR count;
   ID laboratory;
   BY name;
RUN;
DATA pre_BLV2t2;
   SET pre_BLV2t;
/*LABNAMES AANPASSEN*/
IF CARDAM IN (0 .) OR CEETOX IN (0 .) OR L_OREAL IN (0 .) THEN DELETE;
RUN;
PROC SORT data=pre_all_SE; BY name; RUN;
DATA pre_BLV3;
   MERGE pre_all_SE(drop=test where=(conclusion NOT IN (1 2) /*(2)*/)) pre_BLV2t2 (in=ok);
   BY name;
   IF ok;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
RUN;
PROC SORT data=pre_BLV3; BY laboratory name; RUN;
DATA BLV;
   SET pre_BLV3;
   BY laboratory name;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
   IF test > 3 THEN DELETE;
/*CHECK EXCLUDED CHEMS MET BOVEN*/
    IF order IN (106 107) THEN DELETE;
RUN;

/* 7.1 Table with means, std, cv and pred */
PROC MEANS data=BLV noprint;
   CLASS laboratory name order;
   VAR mean_viability;
   OUTPUT out=pre7_1(where=(_type_ = 7)) mean = meanlab std = stdlab cv=cvlab n=nlab;
RUN;
PROC MEANS data=pre7_1 noprint;
   CLASS name order;
   VAR stdlab;
   OUTPUT out=table7_1(where=(_type_ = 3)) mean = means std = stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table7_1.doc' notoc_data;
PROC REPORT data=table7_1 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS order  means stds cvs;
   DEFINE order / GROUP width = 5 'Chemical';
   DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean SD';
   DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std SD';
   DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv SD';
RUN; QUIT;
ODS RTF close;
DATA table7_1b;
   SET pre7_1;
   IF meanlab > 50 THEN finalINI = 0;
   ELSE finalINI = 1;
   FORMAT finalINI fmtINI.;
RUN;

/* with NQ */
DATA pre_BLV3;
   MERGE pre_all_SE(drop=test where=(conclusion NOT IN (2))) pre_BLV2t2 (in=ok);
   BY name;
   IF ok;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
RUN;
PROC SORT data=pre_BLV3; BY laboratory name; RUN;
DATA BLVnq;
   SET pre_BLV3;
   BY laboratory name;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
/*CHECK EXCLUDED CHEMS MET BOVEN*/
    IF order IN (106 107) THEN DELETE;
RUN;

/* 7.1 Table with means, std, cv and pred with NQ*/
PROC MEANS data=BLVnq noprint;
   CLASS laboratory name order;
   VAR mean_viability;
   OUTPUT out=pre7_1(where=(_type_ = 7)) mean = meanlab std = stdlab cv=cvlab n=nlab;
RUN;
PROC MEANS data=pre7_1 noprint;
   CLASS name order;
   VAR stdlab;
   OUTPUT out=table7_1(where=(_type_ = 3)) mean = means std = stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table7_1b.doc' notoc_data;
PROC REPORT data=table7_1 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS order  means stds cvs;
   DEFINE order / GROUP width = 5 'Chemical';
   DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean SD';
```

```
   DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std SD';
   DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv SD';
RUN; QUIT;
ODS RTF close;

/* 7.2 concordance final classifications */
PROC SORT data=table7_1b out=pre7_2; BY name order; RUN;
PROC FREQ data=pre7_2 noprint;
   TABLES finalINI/out=pre7_2b;
   BY name order;
RUN;
DATA pre7_2c;
   SET pre7_2b;
   IF percent NE 100 THEN BLV_concordant = 'NO ';
   ELSE BLV_concordant = 'YES';
RUN;
PROC SORT data=pre7_2c out=pre7_2d nodupkey;
   BY name order;
RUN;
DATA pre7_2e;
   MERGE pre7_2d pre7_2;
   BY name order;
RUN;
PROC SORT data=BLV; BY laboratory name order; RUN;
PROC SORT data=pre7_2e; BY laboratory name order; RUN;
DATA pre7_2f;
   MERGE BLV(where=(test=1)) pre7_2e(keep = laboratory name order BLV_concordant meanlab);
   BY laboratory name order;
RUN;
DATA pre7_2g;
   SET pre7_2f(where=(BLV_concordant = 'NO '));
   KEEP laboratory order name LS coloring MTT predGHS meanlab;
RUN;
PROC SORT data=pre7_2g; BY order name order name LS coloring mTT predGHS; RUN;
PROC TRANSPOSE data=pre7_2g out=pre7_2t(drop=_name_);
   BY order name LS coloring mTT predGHS;
   VAR meanlab;
   ID laboratory;
RUN;
DATA table7_2;
   RETAIN order name LS coloring mtt predGHS CEETOX CARDAM L_OREAL;
   SET pre7_2t;
RUN;

/* 7.3 descriptive statistics non-concordant results */
* see 7.2 ;


/* 7.4 statement regarding BLV */
PROC FREQ data=pre7_2d;
   TABLES BLV_concordant/out=tmp;
RUN;
DATA table7_4 ;
   SET tmp;
   WHERE BLV_concordant = 'YES';
   BLV_criteria = 'not fulfilled';
   IF percent >= 80 THEN BLV_criteria = 'fulfilled';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table7_4.doc' notoc_data;
PROC REPORT data=table7_4 NOWINDOWS HEADLINE HEADSKIP ;
   COLUMNS percent BLV_criteria;
   DEFINE BLV_criteria / DISPLAY width=15 'Statement: criteria is ';
   DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
RUN;
ODS RTF close;

/* 7.5&7.6  Two-way ANOVA with laboratory and chemicals as factor */
DATA pre7_5;
   SET pre7_1 (keep = laboratory name order meanlab);
   IF meanlab NE 0 THEN meanlog = log(meanlab); * but analysed on original scale;
RUN;
ODS trace off;
ODS listing close;
PROC MIXED data=pre7_5;
   CLASS laboratory name;
   MODEL meanlab = laboratory name /outp=tmp1;
   LSMEANS laboratory/pdiff cl adjust=tukey;
   ODS OUTPUT tests3 = table7_5;
   ODS OUTPUT lsmeans = table7_5partial;
   ODS OUTPUT diffs = table7_6;
   ODS OUTPUT covparms = covparms;
RUN;
ODS listing;
PROC GPLOT data=tmp1;
   PLOT resid * pred;
RUN;QUIT;
DATA pre7_5_nooutlier (drop=tmp0) table7_5_outliers(drop=tmp0);
   MERGE tmp1 covparms;
   RETAIN tmp0;
   IF estimate NE . THEN tmp0 = estimate; ELSE estimate = tmp0;
   IF abs(resid) <= 3*sqrt(estimate) THEN OUTPUT pre7_5_nooutlier;
   ELSE OUTPUT table7_5_outliers;
RUN;
proc print data=table7_5_outliers; run;
ODS listing close;
PROC MIXED data=pre7_5_nooutlier;
   CLASS laboratory name;
   MODEL meanlab = laboratory name /outp=tmp1 ;
```

```
   LSMEANS laboratory/pdiff cl adjust=tukey alpha = 0.01;
   ODS OUTPUT tests3 = table7_5;
   ODS OUTPUT lsmeans = table7_5partial;
   ODS OUTPUT diffs = table7_6;
   ODS OUTPUT covparms = covparms;
RUN;
ODS listing;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table7_5residualplot.doc' notoc_data;
PROC GPLOT data=tmp1;
   PLOT resid * pred;
RUN;QUIT;
ODS RTF close;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table7_5.doc' notoc_data;
PROC PRINT data=table7_5 NOOBS; RUN;
ODS RTF close;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table7_6.doc' notoc_data;
PROC REPORT data=table7_6 NOWINDOWS HEADLINE HEADSKIP ;
   COLUMNS laboratory _laboratory estimate stderr DF adjP;
   DEFINE laboratory / DISPLAY;
   DEFINE _laboratory /DISPLAY 'vs';
   DEFINE estimate/DISPLAY;
   DEFINE stderr/DISPLAY;
   DEFINE DF/DISPLAY;
   DEFINE adjP/DISPLAY 'Tukey-corrected p-value' width=15;
RUN;
ODS RTF close;

/* 7.7 Pearson correlations */
/* check labnames enzo hier beneden;*/
PROC SORT data=pre7_1; BY name; RUN;
PROC TRANSPOSE data=pre7_1 out=pre7_7;
   BY name;
   ID laboratory;
   VAR meanlab;
RUN;
PROC CORR data=pre7_7 noprint outp=pearson outs=spearman;
VAR CEETOX CARDAM L_OREAL;
RUN;
/*PROC GPLOT data=pre7_7; */
/*   PLOT Beiersdorf * Harlan Beiersdorf * IIVS Harlan * IIVS;*/
/*RUN; QUIT;*/
DATA set1p (keep= _name_ CARDAM where=(_name_ NE 'CARDAM'))
     set2p (keep= _name_ CEETOX where=(_name_ NE 'CEETOX'))  ;
   SET pearson;
   WHERE _TYPE_ = 'CORR';
RUN;
DATA pre_pearson7_7(keep = laboratories pearson);
   SET set1p(in=s1 rename=(CARDAM = pearson)) set2p(in=s2 rename=(CEETOX = pearson));
   IF s1 THEN with = 'CARDAM';
   IF s2 THEN with = 'CEETOX';
   IF _name_ = 'CARDAM' THEN DELETE;
   Laboratories = TRIM(LEFT(with))||'-'||TRIM(LEFT(_name_));
RUN;
DATA set1s (keep= _name_ CARDAM where=(_name_ NE 'CARDAM'))
     set2s (keep= _name_ CEETOX where=(_name_ NE 'CEETOX'))  ;
   SET spearman;
   WHERE _TYPE_ = 'CORR';
RUN;
DATA pre_spearman7_7(keep = laboratories spearman);
   SET set1s(in=s1 rename=(CARDAM = spearman)) set2s(in=s2 rename=(CEETOX = spearman));
   IF s1 THEN with = 'CARDAM';
   IF s2 THEN with = 'CEETOX';
   IF _name_ = 'CARDAM' THEN DELETE;
   Laboratories = TRIM(LEFT(with))||'-'||TRIM(LEFT(_name_));
RUN;
DATA table7_7;
   RETAIN laboratories pearson spearman;
   MERGE pre_pearson7_7 pre_spearman7_7;
   BY laboratories;
   FORMAT pearson spearman 8.3;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table7_7.doc' notoc_data;
PROC REPORT data=table7_7 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratories pearson spearman;
   DEFINE laboratories / DISPLAY;
   DEFINE pearson/ DISPLAY  format=8.3 width = 15 CENTER;
   DEFINE spearman/ DISPLAY format=8.3 width = 15 CENTER;
RUN; QUIT;
ODS RTF close;

/* ------------------------------------ */
/* Section 8 of SAP: Predictive capacity */
/* ------------------------------------ */

PROC SORT data= pre_all_SE; BY laboratory name; RUN;
DATA PCA;
   SET pre_all_SE (drop=test);
   BY laboratory name;
   WHERE conclusion = 0;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
   IF test>3 THEN DELETE;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
```

```
RUN;
/* 8.1 sens, spec, acc */
%MACRO predmodel(lab=, output=);
DATA pre8_1;
   SET PCA;
   %IF &lab NE %THEN %DO;
      WHERE laboratory = &lab;
   %END;
   IF trueINI = 'I' THEN DO;
      IF predINI = 'I' THEN result = 'TP';
     ELSE IF predINI = 'NI' THEN result = 'FN';
   END;
   ELSE IF trueINI = 'NI' THEN DO;
      IF predINI = 'NI' THEN result = 'TN';
     ELSE IF predINI = 'I' THEN result = 'FP';
   END;
RUN;
PROC SORT data=pre8_1;
   BY trueINI predINI;
RUN;
DATA pre8_1b (drop=result);
   SET pre8_1;
   BY trueINI;
   retain tp tn fp fn;
   if (first.trueINI) then do;
      tp=0; tn=0; fp=0; fn=0;
   end;
   if (result in ("TP")) then tp=tp+1;
   if (result in ("TN")) then tn=tn+1;
   if (result in ("FN")) then fn=fn+1;
   if (result in ("FP")) then fp=fp+1;
   else ;
   if (last.trueINI) then output;
run;
DATA pre8_1C;
   SET pre8_1B;
   tntp=tn+tp;
   fnfp=fn+fp;
RUN;
PROC SQL;
   CREATE TABLE pre8_1D as
   select sum(tp) as tp, sum(tn) as tn, sum(fp)as fp, sum(fn) as fn, sum(tntp) as
          tntp, sum(fnfp) as fnfp
   from pre8_1C;
QUIT;
PROC SQL;
   CREATE TABLE pre8_1E as
   select tp/(tp+fn) as sensitivity, tn/(tn+fp) as specificity,
         (tn+tp)/(tn+tp+fn+fp) as accuracy
    from pre8_1D;
QUIT;
PROC TRANSPOSE data=pre8_1D out=pre8_1F;
   VAR tp tn fn fp tntp fnfp;
RUN;
DATA pre8_1G (drop=_name_ col1);
   LENGTH group $20;
   SET pre8_1F;
   count=col1;
   if _name_="tp" then do;
      group="Sensitivity";
      response=0;
      output;
   end;
   else if _name_="fn" then do;
      group="Sensitivity";
      response=1;
      output;
   end;
   else if _name_="tn" then do;
      group="Specificity";
      response=0;
      output;
   end;
   else if _name_="fp" then do;
      group="Specificity";
      response=1;
      output;
   end;
   else if _name_="tntp" then do;
      group="Accuracy";
      response=0;
      output;
   end;
   else if _name_="fnfp" then do;
      group="Accuracy";
      response=1;
      output;
   end;
RUN;
PROC SORT data=pre8_1G; BY group; RUN;
ODS trace off;
ODS listing close;
PROC FREQ data= pre8_1G;
   WEIGHT count;
   BY group;
   TABLES response/alpha=0.05 binomial(p=0.5);
   exact binomial;
   ODS OUTPUT BinomialProp = pre8_1CI;
RUN;
```

```
ODS listing;
DATA pre8_1TOTAL;
   SET pre8_1CI;
   WHERE name1 IN ('_BIN_' 'XL_BIN' 'XU_BIN');
RUN;
PROC TRANSPOSE data=pre8_1TOTAL out=pre8_1TOTALt;
   VAR nvalue1;
   ID name1;
   BY group;
RUN;
PROC TRANSPOSE data=pre8_1G out=pre8_1H;
   VAR count;
   ID response;
   BY group;
RUN;
DATA &output;
   MERGE pre8_1TOTALt pre8_1H;
   BY group;
RUN;
%MEND;
%predmodel(lab=,output=table8_1TOTAL);
%predmodel(lab='CEETOX',output=table8_1ceetox);
%predmodel(lab='CARDAM',output=table8_1cardam);
%predmodel(lab="L'OREAL",output=table8_1loreal);

DATA table8_1 (keep = group laboratory _BIN_ XL_BIN XU_BIN abs abs2);
   SET table8_1ceetox (in=set1) table8_1cardam (in=set2)
       table8_1loreal (in=set3) table8_1TOTAL (in=set4);
   IF set1 THEN laboratory = 'CEETOX';
   IF set2 THEN laboratory = 'CARDAM';
   IF set3 THEN laboratory = "L'Oreal";
   IF set4 THEN laboratory = 'Total';
   x = PUT(_1,$3.);
   y = PUT(_0+_1,$3.);
   z = PUT(_0,$3.);
   abs = x||'/'||y;
   abs2 = z||'/'||y;
RUN;
* report @8.2;

/* 8.2 statement regarding predictive capacity */
DATA table8_2;
   SET table8_1;
   LENGTH PC_criteria $25;
   IF group = 'Sensitivity' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.90 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.80 THEN PC_criteria = 'definitely unacceptable';
   END;
   IF group = 'Specificity' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.60 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.50 THEN PC_criteria = 'definitely unacceptable';
   END;
   IF group = 'Accuracy' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.75 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.65 THEN PC_criteria = 'definitely unacceptable';
   END;
RUN;

ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthic_Table8_1.doc' notoc_data;
PROC REPORT data=table8_2 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory group abs2 _BIN_ XL_BIN XU_BIN PC_criteria;
   DEFINE laboratory/GROUP;
   DEFINE group/DISPLAY 'Characteristic' width = 15;
   DEFINE abs2/DISPLAY 'No.';
   DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
   DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
   DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
   DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
   BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

 * falsepos/falseneg;
PROC SORT data=PCA; BY order predGHS; RUN;
DATA PCA2;
   SET PCA;
   IF predINI = 'NI' THEN value = 0;
   ELSE value = 1;
   IF trueINI = 'NI' THEN true = 0;
   ELSE true = 1;
   mis=0;
   IF value = 1 AND true = 0 THEN mis = 1;
   IF value = 0 AND true = 1 THEN mis = 1;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CARDAM')) out=extra1a prefix=B;
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CEETOX')) out=extra1b prefix=H;
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = "L'OREAL")) out=extra1c prefix=V;
```

```
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CARDAM')) out=extra1d prefix=misB;
   VAR mis;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CEETOX')) out=extra1e prefix=misH;
   VAR mis;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = "L'OREAL")) out=extra1f prefix=misV;
   VAR mis;
   BY order name predGHS LS;
   ID test;
RUN;
PROC SORT data=PCA2 out=PCA2b nodupkey; BY order; RUN;
PROC TRANSPOSE data=PCA2b out=extra1g;
   VAR true;
   BY order name;
RUN;
DATA extra1;
   MERGE extra1a extra1b extra1c extra1d extra1e extra1f extra1g;
   BY order name;
   med = MEDIAN(B1,B2,B3,H1,H2,H3,V1,V2,V3);
   summis = SUM(misB1,misB2,misB3,misH1,misH2,misH3,misV1,misV2,misV3);
   mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/9';
   IF order = 20 THEN DO;
         med = MEDIAN(H1,H2,H3,V1,V2,V3);
         summis = SUM(misH1,misH2,misH3,misV1,misV2,misV3);
         mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/6';
   END;
   IF order = 91 THEN DO;
         med = MEDIAN(B1,B2,B3,V1,V2,V3);
         summis = SUM(misB1,misB2,misB3,misV1,misV2,misV3);
         mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/6';
   END;
   FORMAT B1--V3 med fmtini.;
   label mis = 'Mispredicted tests/Total'
          med = 'Final classification based on median';
RUN;
PROC SORT data=extra1;
   BY order;
RUN;

/* === */
/* LE  */
/* === */

PROC SORT data=pre_all_LE; BY chemical_code; RUN;
DATA rules;
   SET pre_all_LE;
   BY chemical_code;
   if conclusion = 1 /* non-qual */ then delete;
   IF mean_viability >50 THEN pred50=0;
   ELSE pred50 = 1;
   IF mean_TA >50 THEN pred50raw=0;
   ELSE pred50raw = 1;
   FORMAT pred50  pred50raw  fmtpred.;
   IF filename = '' then delete;
RUN;
DATA rules2;
    SET rules;
   BY chemical_code;
   RETAIN t 0;
   t = t+1;
   IF first.chemical_code THEN t=1;
   IF t>3 then delete;
RUN;
PROC SORT data=rules2; BY order  laboratory  ; RUN;
PROC TRANSPOSE data=rules2 out=allT1 prefix=p50_;
   VAR pred50;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT1raw prefix=p50r_;
   VAR pred50raw;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT3 prefix=v_;
   VAR mean_viability;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT4 prefix=TA_;
   VAR mean_TA;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT5 prefix=CC_;
   VAR mean_NSC;
   BY order  laboratory  ;
   ID t;
RUN;
PROC TRANSPOSE data=rules2 out=allT6 prefix=KC_;
```

```
   VAR mean_NSMTT;
   BY order  laboratory  ;
   ID t;
RUN;
DATA overall (drop=_name_);
   MERGE allT1  allT1raw allT3 allT4 allT5 allT6;
   BY order  laboratory  ;
RUN;
PROC SORT data=overall; BY laboratory order; RUN;
DATA rules3_no rules3_yes;
   SET overall;
   mean_nsc=mean(CC_1,CC_2,CC_3);
   mean_mtt=mean(KC_1,KC_2,KC_3);
   * rule 1 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory
is less than or equal to (=) 50%,
   THEN this chemical is considered to be compatible with the test method. The chemical should be
included in the overview tables,
   and included in all statistical calculations of reproducibility and predictive capacity.;
   if mean_nsc NE . then do;
  IF mean_nsc <= 50 THEN DO; inclusion50_nsc = 'yes'; inclusion60_nsc = 'yes'; END;
   end;
   if mean_mtt NE . then do;
  IF mean_mtt<=50 THEN DO; inclusion50_mtt = 'yes'; inclusion60_mtt = 'yes'; END;
   end;
  * rule 2 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory
is greater than (>) 50% AND
  their classification (I or NI) remains the same upon correction, THEN this chemical is considered to
be compatible with the test
  method. The chemical should be included in the overview tables, and included in all statistical
calculations of reproducibility and
  predictive capacity.;
   if mean_nsc NE . then do;
  IF mean_nsc > 50 AND p50_1=p50r_1 AND  p50_2=p50r_2 AND p50_3=p50r_3 THEN inclusion50_nsc = 'yes';
   end;
   if mean_mtt NE . then do;
  IF mean_mtt > 50 AND p50_1=p50r_1 AND  p50_2=p50r_2 AND p50_3=p50r_3 THEN inclusion50_mtt = 'yes';
   end;
  * rule 3 - IF mean (%NSC or %NSMTT) of all qualified tests obtained for a chemical in one laboratory
is greater than (>) 50% AND
  the classification of at least one of the qualified tests changes upon correction, THEN this chemical
is considered to be
  incompatible with the test method. The chemical should be included in the overview tables, but
excluded from all statistical
  calculations of reproducibility and predictive capacity.;
   if mean_nsc NE . then do;
  IF mean_nsc > 50 AND (p50_1 NE p50r_1 OR  p50_2 NE p50r_2 OR p50_3 NE p50r_3) THEN inclusion50_nsc =
'no';
   end;
   if mean_mtt NE . then do;
  IF mean_mtt > 50 AND (p50_1 NE p50r_1 OR  p50_2 NE p50r_2 OR p50_3 NE p50r_3) THEN inclusion50_mtt =
'no';
   end;
  * output;
  IF inclusion50_nsc = 'no' OR inclusion50_mtt = 'no' OR inclusion60_nsc = 'no' OR inclusion60_mtt =
'no' THEN OUTPUT rules3_no;
  ELSE OUTPUT rules3_yes;
RUN;
/* CONCLUSION */
/* new rules give selection : chemical 4 (cardam and ceetox) and 80 (ceetox) */

DATA select (keep = order laboratory run conclusion);
   SET pre_all_LE;
   IF order IN (4 80) OR conclusion IN (1 2) THEN OUTPUT;
RUN;
DATA pre_all_LE;
   SET pre_all_LE;
   /* remove chemical 106 and 107 for statistical analysis */
   IF chemical_code IN ('L6' 'C52' 'X95') THEN DELETE; * 106;
   IF chemical_code IN ('L100'   'C56' 'X32') THEN DELETE; * 107;
   IF laboratory = '' THEN DELETE;
   IF pcqual = 1 THEN conclusion = 1;
   IF ncqual = 1 then conclusion = 1;
   if qual_sd = 1 then conclusion = 1;
   /* for some chemicals the VMG overrode the 50% rule regarding NSMTT */
   *IF chemical_code IN ('L140' 'C128' 'X139') then conclusion = 0; * 23;
      IF chemical_code IN ('C6' 'X31') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then conclusion
= 0; * 80;
     IF chemical_code IN ('C6' 'X31') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then conclusion
= 1; * 80;
      IF chemical_code IN ('X62' 'C53') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 4;
      IF chemical_code IN ('X62' 'C53') and  (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 4;
      IF chemical_code IN ('L58' 'C58') and NCqual NE 1 AND PCqual NE 1 AND qual_sd NE 1 then
conclusion = 0; * 20;
      IF chemical_code IN ('L58' 'C58') and (NCqual EQ 1 OR PCqual EQ 1 OR qual_sd EQ 1) then
conclusion = 1; * 20;
RUN;
data select;
   set pre_all_le;
*   where chemical_code = 'X31';
    where conclusion = 2;
run;
PROC SORT data=RhT.LE2 out=ODnc(keep = laboratory run chemical_code meanODnc) nodupkey;
   BY laboratory run chemical_code;
   where chemical_code NE 'PC';
RUN;
PROC SORT data=pre_all_LE; BY laboratory run chemical_code; RUN;
DATA pre_all_LE;
```

```
   MERGE pre_all_LE (in=ok) ODnc;
   BY laboratory run chemical_code;
   IF ok;
RUN;
PROC SORT data=pre_all_LE; BY chemical_code; RUN;

* Table 3.2.2 - MTT and colouring differences
* some chemicals are treated differently by the labs concerning the coloring or mtt;
PROC SORT data=pre_all_LE out=extra0s (keep = order name laboratory mtt coloring where=(laboratory NE
'')) nodupkey;
   BY order laboratory mtt coloring;
RUN;
PROC TRANSPOSE data=extra0s out=extra0a;
   VAR mtt;
   BY order name;
   ID laboratory;
RUN;
DATA extra0_mtt(keep = order name L_oreal ceetox cardam mttcheck) ;
   SET extra0a ;
   BY order;
   mttcheck = 'not ok';
   IF l_oreal = ceetox AND L_oreal = cardam and cardam = ceetox THEN mttcheck = ' ';
   ELSE mttcheck = '#';
   *IF mttcheck = 'not ok' THEN OUTPUT;
RUN;
PROC TRANSPOSE data=extra0s out=extra0b;
   VAR coloring;
   BY order name;
   ID laboratory;
RUN;
DATA extra0_color( keep = order name L_oreal ceetox cardam colorcheck);
   SET  extra0b;
   BY order;
   colorcheck = 'not ok';
   IF l_oreal = ceetox AND L_oreal = cardam and cardam = ceetox THEN colorcheck = ' ';
   ELSE colorcheck = '#';
   *IF colorcheck = 'not ok' THEN OUTPUT;
RUN;

/* non-qual NC and PC */
PROC SORT data=pre_all_LE out=pre412 nodupkey; BY filename; RUN;
PROC FREQ data=pre412 ;
   TABLE laboratory*NCqual/out=table412_NC NOCOL NOPERCENT;
   TABLE laboratory*PCqual/out=table412_PC NOCOL NOPERCENT;
RUN;
PROC TRANSPOSE data=table412_NC out=table412NCt;
   VAR count;
   ID NCqual;
   BY laboratory;
RUN;
PROC TRANSPOSE data=table412_PC out=table412PCt;
   VAR count;
   ID PCqual;
   BY laboratory;
RUN;
DATA table412;
   SET table412NCt(in=nc) table412PCt(in=pc);
   BY laboratory;
   IF nc THEN var = 'NC';
   IF pc THEN var = 'PC';
   IF non_qualified = . THEN non_qualified = 0;
   fraction_nq = 100* non_qualified/(non_qualified+qualified);
   fraction_q = 100*qualified/(non_qualified+qualified);
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table412.doc' notoc_data;
PROC REPORT data = table412 NOWINDOWS HEADLINE HEADSKIP;
   COLUMN laboratory var qualified fraction_q non_qualified fraction_nq;
   DEFINE laboratory/GROUP;
   DEFINE var/DISPLAY ' ';
   DEFINE qualified/DISPLAY 'No.Qualified' width = 12 CENTER;
   DEFINE fraction_q/DISPLAY '%' width = 5 format=8.1 CENTER;
   DEFINE non_qualified/DISPLAY 'No.Non-Qualified' width = 16 CENTER;
   DEFINE fraction_nq/DISPLAY '%' width = 5 format=8.1 CENTER;
RUN; QUIT;
ODS rtf close;

/* 5.2 Table with number and fraction of qualified and non_qualified runs */
PROC SORT data=pre_all_LE; BY laboratory; RUN;
PROC FREQ data=pre_all_LE noprint;
   TABLES conclusion/out=table5_2LAB;
   BY laboratory;
RUN;
PROC FREQ data=pre_all_LE noprint;
   TABLES conclusion/out=table5_2TOTAL;
RUN;
DATA table5_2;
   SET table5_2LAB table5_2TOTAL (in=ok);
   IF ok THEN laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthicLE_Table5_2.doc' notoc_data;
PROC REPORT data = table5_2 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory conclusion count percent;
   DEFINE laboratory/GROUP;
   DEFINE conclusion /DISPLAY 'Call';
   DEFINE count/ DISPLAY 'No.';
   DEFINE percent/DISPLAY width = 15 format=8.1 'Fraction (%)';
RUN;QUIT;
```

```
ODS RTF close;

OPTIONS PS=42 LS=120;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthicLE_Table5_2LIST.doc' notoc_data;
PROC REPORT data=pre_all_LE (where=(conclusion IN (1 2)) keep = run order conclusion laboratory name
qual_sd PCqual NCqual NSCcall NSMTTcall)
            NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS conclusion laboratory order run NCqual PCqual qual_sd  NSCcall NSMTTcall;
   DEFINE conclusion / GROUP width = 15;
   DEFINE laboratory / GROUP width = 15;
   DEFINE order/DISPLAY width = 4 'Chemical';
   DEFINE NSCcall/DISPLAY width = 12;
   BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

/* 5.4 Table with number of tests within each test sequence */
OPTIONS PS=55 LS=80;
PROC SORT data=pre_all_LE; BY laboratory tmp2 run; RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthicLE_Table5_4.doc' notoc_data;
PROC FREQ data=pre_all_LE ;
   TABLES order*laboratory/out=table5_4 NOROW NOCOL NOPERCENT;
RUN;
ODS RTF close;
* 106 en 107;
data chem106_107;
   set rht.LE_meanviabilities_locked;
   IF chemical_code IN ('L6' 'C52' 'X95' 'L100'  'C56''X32') THEN output;
run;
data chem106_107;
   set rht.SE_meanviabilities_locked;
   IF chemical_code IN ('L6' 'C52' 'X95' 'L100'  'C56''X32') THEN output;
run;
/* 5.5 Table with list, no and fraction of NQ tests */
PROC SORT data=pre_all_LE; BY laboratory order; RUN;
PROC FREQ data=pre_all_LE NOPRINT;
   TABLES conclusion/out=table5_5;
   BY laboratory order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthicLE_Table5_5.doc' notoc_data;
PROC PRINT data=table5_5(WHERE=(CONCLUSION IN (1 2))); RUN;
ODS RTF close;

/* 5.6 Table with list and fraction of complete test sequences */
DATA pre5_6;
   SET pre_all_LE;
   IF conclusion IN (1 2) THEN DELETE;
RUN;
PROC FREQ data=pre5_6 noprint;
   TABLES laboratory * order/out=pre5_6b;
RUN;
DATA table5_6LIST;
   SET pre5_6b;
   IF count >=3 THEN OUTPUT;
RUN;
PROC SORT data=pre5_6b; BY order; RUN;
PROC TRANSPOSE data=pre5_6b out=table5_6LIST;
   VAR COUNT;
   ID laboratory;
   BY order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthicLE_Table5_6LIST.doc' notoc_data;
PROC PRINT data=table5_6LIST; RUN;
ODS RTF close;

PROC FREQ data=table5_6LIST noprint;   TABLES CARDAM /out=table5_6B1; RUN;
PROC FREQ data=table5_6LIST noprint;   TABLES CEETOX /out=table5_6B2; RUN;
PROC FREQ data=table5_6LIST noprint;   TABLES L_OREAL /out=table5_6B3; RUN;
DATA table5_6C;
   SET table5_6B1 (in=s1 rename=(cardam = aantal))
       table5_6B2  (in=s2 rename=(ceetox = aantal))
       table5_6B3  (in=s3 rename=(l_oreal = aantal));
   if s1 then lab = 'CARDAM';
   if s2 then lab = 'CEETOX';
   if s3 then lab = 'LOREAL';
   IF aantal >2 THEN OUTPUT;
RUN;
PROC MEANS data=table5_6C noprint;
   VAR count;
   BY lab;
   OUTPUT out=table5_6D sum=sums;
RUN;
DATA table5_6LAB;
   SET table5_6D;
   fraction_complete = 100*sums/104;
   test_sequence_criteria = 'not fulfilled';
   IF fraction_complete > 85 THEN test_sequence_criteria = 'fulfilled';
RUN;
PROC MEANS data=table5_6LAB NOPRINT;
   VAR sums;
   OUTPUT out=table5_6D sum=sumcount;
RUN;
DATA table5_6OVERALL;
   SET table5_6D;
   fraction_complete = 100*sumcount/(3*104);
```

```
   test_sequence_criteria = 'not fulfilled';
   IF fraction_complete >= 85 THEN test_sequence_criteria = 'fulfilled';
RUN;
DATA table5_6;
   SET table5_6LAB table5_6OVERALL(in=ok);
   IF ok then laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table5_6.doc' notoc_data;
PROC REPORT data = table5_6 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory fraction_complete;
   DEFINE laboratory/DISPLAY;
   DEFINE fraction_complete/DISPLAY format=8.1 'Fraction';
RUN; QUIT;
ODS rtf close;
PROC DATASETS library = work;
   DELETE pre5_6 pre5_6b table5_6B table5_6D;
RUN;QUIT;

/* 5.7 Table with list and fraction of incomplete test sequences */

DATA pre5_7a pre5_7b;
   SET pre_all_LE;
   IF conclusion IN (1 2) THEN output pre5_7a;
   IF conclusion NOT IN (1 2) THEN output pre5_7b;
RUN;
PROC FREQ data=pre5_7a noprint;
   TABLES laboratory * order/out=pre5_7a2;
RUN;
PROC FREQ data=pre5_7b noprint;
   TABLES laboratory * order/out=pre5_7b2;
RUN;
DATA pre5_7;
   MERGE pre5_7a2(rename=(count=OUT)) pre5_7b2(rename=(count=IN));
   BY laboratory order;
   IF IN NOT IN (. 0 1 2) THEN complete = 'Yes';
   IF IN IN (. 0 1 2) THEN complete = 'No';
RUN;
DATA table5_7LIST;
   SET pre5_7;
   IF IN = . THEN IN = 0;
   IF complete = 'No' THEN OUTPUT;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table5_7LIST.doc' notoc_data;
PROC REPORT data = table5_7LIST NOWINDOWS HEADLINE HEADSKIP;
   COLUMN laboratory order IN OUT;
   DEFINE laboratory/GROUP;
   DEFINE order /DISPLAY ;
   DEFINE IN/DISPLAY 'Qualified' width = 10 CENTER;
   DEFINE OUT/DISPLAY 'Non-Qual or Excluded' width = 20 CENTER;
RUN; QUIT;
ODS RTF close;
PROC FREQ data=table5_7LIST noprint;
   TABLES laboratory/out=table5_7b;
RUN;
DATA table5_7LAB;
   SET table5_7B;
   fraction_incomplete = 100*count/104;
   test_sequence_criteria = 'fulfilled';
   IF fraction_incomplete > 15 THEN test_sequence_criteria = 'not fulfilled';
RUN;
PROC MEANS data=table5_7LAB NOPRINT;
   VAR count;
   OUTPUT out=table5_7D sum=sumcount;
RUN;
DATA table5_7OVERALL;
   SET table5_7D;
   fraction_incomplete = 100*sumcount/(3*104);
   test_sequence_criteria = 'fulfilled';
   IF fraction_incomplete > 15 THEN test_sequence_criteria = 'not fulfilled';
RUN;
DATA table5_7;
   SET table5_7LAB table5_7OVERALL(in=ok);
   IF ok then laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table5_7.doc' notoc_data;
PROC REPORT data = table5_7 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory fraction_incomplete;
   DEFINE laboratory/DISPLAY;
   DEFINE fraction_incomplete/DISPLAY format=8.1 'Fraction';
RUN; QUIT;
ODS rtf close;
PROC DATASETS library = work;
   DELETE pre5_7 pre5_7b table5_7B table5_7D;
RUN;QUIT;

/* 5.8 statement whether test method has fulfilled the performance criteria */
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\SkinEthicLE_Table5_8.doc' notoc_data;
PROC REPORT data = table5_6 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory fraction_complete test_sequence_criteria;
   DEFINE laboratory/DISPLAY;
   DEFINE fraction_complete/DISPLAY format=8.1 'Fraction';
   DEFINE test_sequence_criteria/DISPLAY 'Statement: criteria is ' CENTER;
RUN; QUIT;
ODS rtf close;
```

```
/* 5.10 summarise results of all tests (including NQ and excl) */
DATA appVI (keep=laboratory order predGHS MTT coloring test meanODnc stdNC NCqual meanPC sdPC PCqual
          mean_TA std_TA qual_sd mean_NSC mean_NSMTT mean_viability conclusion pred50);
   RETAIN laboratory order predGHS MTT coloring test meanODnc stdNC NCqual meanPC sdPC PCqual
          mean_TA std_TA qual_sd mean_NSC mean_NSMTT mean_viability conclusion pred50;
   SET pre_all_LE;
   IF mean_viability > 50 THEN pred50 = 'NI';
   ELSE pred50 = 'I';
RUN;
PROC SORT data=appVI; BY laboratory order test; RUN;


/* ---------------------------------------------- */
/* Section 6 of SAP: Intralaboratory variability */
/* ---------------------------------------------- */

/* at least two qualified tests */
PROC SORT data=pre_all_LE; BY laboratory name; RUN;
PROC FREQ data=pre_all_LE noprint;
   TABLES conclusion/out=pre_WLV;
   BY laboratory name;
RUN;
DATA pre_WLV2;
   SET pre_WLV (where=(conclusion = 0 AND count >=2));
RUN;
DATA pre_WLV3;
   MERGE pre_all_LE(drop=test where=(conclusion NOT IN (1 2))) pre_WLV2 (in=ok);
   BY laboratory name;
   IF ok;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
RUN;
DATA WLV;
   SET pre_WLV3;
   BY laboratory name;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
   IF test > 3 THEN DELETE;
/* check mean viability dataset op excluded chemicals, pas daarop nummers hieronder aan */
   /* exclude chemicals */
/*   IF order IN (6 7 17 52 53 58 62 81 95 100) THEN DELETE;*/
   IF order IN (106 107) THEN DELETE;
RUN;
/* 6.1 Table with concordance of classifications */
PROC SORT data=WLV; BY laboratory name; RUN;
PROC TRANSPOSE data=WLV out=pre6_1;
   BY laboratory name order;
   ID test;
   VAR predINI;
RUN;
PROC FREQ data=WLV noprint;
   TABLES predINI/out=pre6_1;
   BY laboratory name order;
RUN;
DATA pre6_1b;
   SET pre6_1;
   IF percent NE 100 THEN WLV_concordant = 'NO ';
   ELSE WLV_concordant = 'YES';
RUN;
PROC SORT data=pre6_1b out=pre6_1c nodupkey;
   BY laboratory name order;
RUN;
PROC FREQ data=pre6_1c noprint;
   TABLES WLV_concordant/out=table6_1LAB;
   BY laboratory;
RUN;
PROC FREQ data=pre6_1c noprint;
   TABLES WLV_concordant/out=table6_1TOTAL;
RUN;
DATA table6_1;
   SET table6_1LAB table6_1TOTAL(in=ok);
   IF ok THEN laboratory = 'Total';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table6_1.doc' notoc_data;
PROC REPORT data=table6_1 NOWINDOWS HEADLINE HEADSKIP ;
   COLUMNS laboratory WLV_concordant count percent;
   DEFINE laboratory / GROUP width = 10;
   DEFINE WLV_concordant / DISPLAY width=15 'WLV concordant';
   DEFINE count / DISPLAY FLOW 'No.';
   DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
   BREAK after laboratory/SKIP;
RUN;
ODS RTF close;

/* 6.2 Additional descriptives of non-concordant results */
DATA pre6_2;
   MERGE WLV pre6_1c(keep = laboratory name order WLV_concordant);
   BY laboratory name order;
RUN;
/* 16082012 CdJ revision */
DATA pre6_2b;
   SET pre6_2(where=(WLV_concordant = 'NO '));
   KEEP laboratory order name LS coloring MTT predGHS mean_viability test;
RUN;
PROC SORT data=pre6_2b; BY laboratory order name test;
PROC TRANSPOSE data=pre6_2b out=pre6_2t(drop=_name_);
   BY laboratory order name LS coloring mTT predGHS;
```

```
   VAR mean_viability;
   ID test;
RUN;
DATA table6_2;
   RETAIN laboratory order name LS coloring mtt predGHS _1 _2 _3;
   SET pre6_2t;
RUN;
* view in excel to create table for report;

/* 6.3 Statement per laboratory regarding WLV */
DATA table6_3 ;
   SET table6_1LAB table6_1TOTAL(in=total);
   IF total THEN laboratory = 'Total';
   WHERE WLV_concordant = 'YES';
   WLV_criteria = 'not fulfilled';
   IF percent >= 85 THEN WLV_criteria = 'fulfilled';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthicLE_Table6_3.doc' notoc_data;
PROC REPORT data=table6_3 NOWINDOWS HEADLINE HEADSKIP ;
   COLUMNS laboratory percent WLV_criteria;
   DEFINE laboratory / GROUP width = 10;
   DEFINE WLV_criteria / DISPLAY width=15 'Statement: criteria is ';
   DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
RUN;
ODS RTF close;

/* 6.4 Pearson Correlations */
PROC SORT data=WLV; BY laboratory name; RUN;
PROC TRANSPOSE data=WLV out=WLVt;
   BY laboratory name;
   ID test;
   VAR mean_viability;
RUN;
PROC CORR data=WLVt noprint outp=pearson outs=spearman;
   VAR _1 _2 _3;
   BY laboratory;
RUN;
/*PROC GPLOT data=WLVt; */
/*   PLOT _1 * _2 _1 * _3 _2 * _3;*/
/*   BY laboratory;*/
/*RUN; QUIT;*/
DATA set1 (keep=laboratory _name_ _1 where=(_name_ NE '_1'))
     set2 (keep=laboratory _name_ _2 where=(_name_ NE '_2'))  ;
   SET pearson;
   WHERE _TYPE_ = 'CORR';
RUN;
PROC TRANSPOSE data=set1 out=set1T(drop=_name_) prefix = _1;
   VAR _1;
   BY laboratory;
   ID _name_;
RUN;
PROC TRANSPOSE data=set2 out=set2T(drop=_name_) prefix = _2;
   VAR _2;
   BY laboratory;
   ID _name_;
RUN;
DATA pre_pearson(drop=_2_1);
   MERGE set1T set2T;
   BY laboratory;
   FORMAT _1_2 _1_3 _2_3 8.3;
RUN;

DATA set1 (keep=laboratory _name_ _1 where=(_name_ NE '_1'))
     set2 (keep=laboratory _name_ _2 where=(_name_ NE '_2'))  ;
   SET spearman;
   WHERE _TYPE_ = 'CORR';
RUN;
PROC TRANSPOSE data=set1 out=set1T(drop=_name_) prefix = _1;
   VAR _1;
   BY laboratory;
   ID _name_;
RUN;
PROC TRANSPOSE data=set2 out=set2T(drop=_name_) prefix = _2;
   VAR _2;
   BY laboratory;
   ID _name_;
RUN;
DATA pre_spearman(drop=_2_1);
   MERGE set1T set2T;
   BY laboratory;
   FORMAT _1_2 _1_3 _2_3 8.3;
RUN;

DATA pre6_4;
   SET pre_pearson (in=p) pre_spearman (in=s);
   BY laboratory;
   IF s THEN corr = 'spearman';
   IF p THEN corr = 'pearson';
RUN;
PROC SORT data=pre6_4; BY corr; RUN;
PROC MEANS data=pre6_4 noprint;
   VAR _1_2 _1_3 _2_3;
   BY corr;
   OUTPUT out=pre6_4b mean = _1_2 _1_3 _2_3;
RUN;

DATA pretable6_4;
/*LABNAMES AANPASSEN*/
```

```
SET pre6_4 pre6_4b(in=m);
   IF m THEN laboratory = 'Mean';
   IF laboratory = 'CARDAM' THEN tmp1 = 1;
   IF laboratory = 'CEETOX' THEN tmp1 = 2;
   IF laboratory = 'LOREAL' THEN tmp1 = 3;
   IF laboratory = 'Mean' THEN tmp1 = 4;
RUN;
PROC SORT data=pretable6_4 out=table6_4(drop=tmp1 _type_ _freq_); BY corr tmp1; RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\REVISION\SkinEthicLE_Table6_4.doc' notoc_data;
PROC REPORT data=table6_4 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS corr laboratory _1_2 _1_3 _2_3;
   DEFINE corr / GROUP;
   DEFINE laboratory/DISPLAY width = 15;
   DEFINE _1_2/ DISPLAY 'Qual1 - Qual2' format=8.3 width = 15 CENTER;
   DEFINE _1_3/ DISPLAY 'Qual1 - Qual3' format=8.3 width = 15 CENTER;
   DEFINE _2_3/ DISPLAY 'Qual2 - Qual3' format=8.3 width = 15 CENTER;
   BREAK after corr/SKIP;
RUN; QUIT;
ODS RTF close;

/* 6.5 mean and mean diff */
PROC MEANS data=WLV noprint;
   VAR mean_viability;
   CLASS laboratory name order;
   OUTPUT out=table6_5(where=(_type_=7)) mean=means std=stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table6_5.doc' notoc_data;
PROC REPORT data=table6_5 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS order laboratory,(means stds cvs ns);
   DEFINE order / GROUP width = 5 'Chemical';
   DEFINE laboratory/ACROSS "_laboratory_";
   DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean';
   DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std';
   DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv';
   DEFINE ns/ANALYSIS mean width=3 CENTER 'n';
RUN; QUIT;
ODS RTF close;

* also with non-qualified tests included;
DATA inclnonqual;
   SET pre_all_LE(where=(conclusion NE 2));
   IF conclusion = 1 and mean_viability = 0 and std_viability = 0 THEN DO;
      IF mean_TA NE 0 THEN mean_viability = mean_TA;
     IF std_TA NE 0 THEN std_viability = std_TA;
     IF mean_MTT ne 0 THEN mean_viability = mean_TA - mean_MTT;
     IF mean_TA = . THEN mean_viability = . ;
     IF std_TA = . THEN std_viability = .;
   END;
   IF mean_viability = 0 AND std_viability = . THEN DELETE;
   IF mean_viability = . THEN DELETE;
RUN;
PROC MEANS data=inclnonqual noprint;
   VAR mean_viability;
   CLASS laboratory name order;
   OUTPUT out=table6_5b(where=(_type_=7)) mean=meansnq std=stdsnq cv=cvsnq n=nsnq;
RUN;
DATA table6_5c;
   MERGE table6_5 table6_5b;
   BY laboratory name order;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table6_5b.doc' notoc_data;
PROC REPORT data=table6_5c NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS order laboratory,(("_Q_" stds cvs ns) ("_Q+NQ_" stdsnq cvsnq nsnq));
   DEFINE order / GROUP width = 5 'Chemical';
   DEFINE laboratory/ACROSS "_laboratory_";
   DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std';
   DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv';
   DEFINE ns/ANALYSIS mean width=3 CENTER 'n';
   DEFINE stdsnq/ANALYSIS mean format=8.1 CENTER 'std';
   DEFINE cvsnq/ANALYSIS mean format=8.1 CENTER 'cv';
   DEFINE nsnq/ANALYSIS mean width=3 CENTER 'n';
RUN; QUIT;
ODS RTF close;
/* ------------------------------------------- */
/* Section 7 of SAP: Interlaboratory variability */
/* ------------------------------------------- */

/* at least one qualified tests per laboratory*/
PROC SORT data=pre_all_LE; BY laboratory name; RUN;
PROC FREQ data=pre_all_LE noprint;
   TABLES conclusion/out=pre_BLV;
   BY laboratory name;
RUN;
DATA pre_BLV2;
   SET pre_BLV (where=(conclusion = 0 AND count >=1));
RUN;
PROC SORT data=pre_BLV2; BY name; RUN:
PROC TRANSPOSE data=pre_BLV2 out=pre_BLV2t;
   VAR count;
   ID laboratory;
   BY name;
RUN;
DATA pre_BLV2t2;
   SET pre_BLV2t;
/*LABNAMES AANPASSEN*/
IF CARDAM IN (0 .) OR CEETOX IN (0 .) OR L_OREAL IN (0 .) THEN DELETE;
```

```
RUN;
PROC SORT data=pre_all_LE; BY name; RUN;
DATA pre_BLV3;
   MERGE pre_all_LE(drop=test where=(conclusion NOT IN (1 2))) pre_BLV2t2 (in=ok);
   BY name;
   IF ok;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
RUN;
PROC SORT data=pre_BLV3; BY laboratory name; RUN;
DATA BLV;
   SET pre_BLV3;
   BY laboratory name;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
   IF test > 3 THEN DELETE;
/*CHECK EXCLUDED CHEMS MET BOVEN*/
    IF order IN (106 107) THEN DELETE;
RUN;

/* 7.1 Table with means, std, cv and pred */
PROC MEANS data=BLV noprint;
   CLASS laboratory name order;
   VAR mean_viability;
   OUTPUT out=pre7_1(where=(_type_ = 7)) mean = meanlab std = stdlab cv=cvlab n=nlab;
RUN;
PROC MEANS data=pre7_1 noprint;
   CLASS name order;
   VAR stdlab;
   OUTPUT out=table7_1(where=(_type_ = 3)) mean = means std = stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table7_1.doc' notoc_data;
PROC REPORT data=table7_1 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS order  means stds cvs;
   DEFINE order / GROUP width = 5 'Chemical';
   DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean SD';
   DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std SD';
   DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv SD';
RUN; QUIT;
ODS RTF close;
DATA table7_1b;
   SET pre7_1;
   IF meanlab > 50 THEN finalINI = 0;
   ELSE finalINI = 1;
   FORMAT finalINI fmtINI.;
RUN;


/* with NQ */
PROC SORT data=pre_all_LE; BY laboratory name; RUN;
PROC FREQ data=pre_all_LE noprint;
   TABLES conclusion/out=pre_BLV;
   BY laboratory name;
RUN;
DATA pre_BLV2;
   SET pre_BLV (where=(conclusion = 0 AND count >=1));
RUN;
PROC SORT data=pre_BLV2; BY name; RUN:
PROC TRANSPOSE data=pre_BLV2 out=pre_BLV2t;
   VAR count;
   ID laboratory;
   BY name;
RUN;
DATA pre_BLV2t2;
   SET pre_BLV2t;
/*LABNAMES AANPASSEN*/
IF CARDAM IN (0 .) OR CEETOX IN (0 .) OR L_OREAL IN (0 .) THEN DELETE;
RUN;
PROC SORT data=pre_all_LE; BY name; RUN;
DATA pre_BLV3;
   MERGE pre_all_LE(drop=test where=(conclusion NOT IN ( 2))) pre_BLV2t2 (in=ok);
   BY name;
   IF ok;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
RUN;
PROC SORT data=pre_BLV3; BY laboratory name; RUN;
DATA BLVnq;
   SET pre_BLV3;
   BY laboratory name;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
 *  IF test > 3 THEN DELETE;
/*CHECK EXCLUDED CHEMS MET BOVEN*/
    IF order IN (106 107) THEN DELETE;
   IF conclusion = 1 and mean_viability = 0 and std_viability = 0 THEN DO;
      IF mean_TA NE 0 THEN mean_viability = mean_TA;
     IF std_TA NE 0 THEN std_viability = std_TA;
     IF mean_MTT ne 0 THEN mean_viability = mean_TA - mean_MTT;
     IF mean_TA = . THEN mean_viability = . ;
     IF std_TA = . THEN std_viability = .;
   END;
   IF mean_viability = 0 AND std_viability = . THEN DELETE;
   IF mean_viability = . THEN DELETE;
RUN;
```

```
/* 7.1 Table with means, std, cv and pred */
PROC MEANS data=BLVnq noprint;
   CLASS laboratory name order;
   VAR mean_viability;
   OUTPUT out=pre7_1(where=(_type_ = 7)) mean = meanlab std = stdlab cv=cvlab n=nlab;
RUN;
PROC MEANS data=pre7_1 noprint;
   CLASS name order;
   VAR stdlab;
   OUTPUT out=table7_1(where=(_type_ = 3)) mean = means std = stds cv=cvs n=ns;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table7_1b.doc' notoc_data;
PROC REPORT data=table7_1 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS order  means stds cvs;
   DEFINE order / GROUP width = 5 'Chemical';
   DEFINE means/ANALYSIS mean format=8.1 CENTER 'mean SD';
   DEFINE stds/ANALYSIS mean format=8.1 CENTER 'std SD';
   DEFINE cvs/ANALYSIS mean format=8.1 CENTER 'cv SD';
RUN; QUIT;
ODS RTF close;

/* 7.2 concordance final classifications */
PROC SORT data=table7_1b out=pre7_2; BY name order; RUN;
PROC FREQ data=pre7_2 noprint;
   TABLES finalINI/out=pre7_2b;
   BY name order;
RUN;
DATA pre7_2c;
   SET pre7_2b;
   IF percent NE 100 THEN BLV_concordant = 'NO ';
   ELSE BLV_concordant = 'YES';
RUN;
PROC SORT data=pre7_2c out=pre7_2d nodupkey;
   BY name order;
RUN;
DATA pre7_2e;
   MERGE pre7_2d pre7_2;
   BY name order;
RUN;
PROC SORT data=BLV; BY laboratory name order; RUN;
PROC SORT data=pre7_2e; BY laboratory name order; RUN;
DATA pre7_2f;
   MERGE BLV(where=(test=1)) pre7_2e(keep = laboratory name order BLV_concordant meanlab);
   BY laboratory name order;
RUN;
DATA pre7_2g;
   SET pre7_2f(where=(BLV_concordant = 'NO '));
   KEEP laboratory order name LS coloring MTT predGHS meanlab;
RUN;
PROC SORT data=pre7_2g; BY order name order name LS coloring mTT predGHS; RUN;
PROC TRANSPOSE data=pre7_2g out=pre7_2t(drop=_name_);
   BY order name LS coloring mTT predGHS;
   VAR meanlab;
   ID laboratory;
RUN;
DATA table7_2;
   RETAIN order name LS coloring mtt predGHS CEETOX CARDAM L_OREAL;
   SET pre7_2t;
RUN;

/* 7.3 descriptive statistics non-concordant results */
* see 7.2 ;

/* 7.4 statement regarding BLV */
PROC FREQ data=pre7_2d;
   TABLES BLV_concordant/out=tmp;
RUN;
DATA table7_4 ;
   SET tmp;
   WHERE BLV_concordant = 'YES';
   BLV_criteria = 'not fulfilled';
   IF percent >= 80 THEN BLV_criteria = 'fulfilled';
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table7_4.doc' notoc_data;
PROC REPORT data=table7_4 NOWINDOWS HEADLINE HEADSKIP ;
   COLUMNS percent BLV_criteria;
   DEFINE BLV_criteria / DISPLAY width=15 'Statement: criteria is ';
   DEFINE percent / DISPLAY format=8.1 'Fraction(%)' width = 12;
RUN;
ODS RTF close;

/* 7.5&7.6  Two-way ANOVA with laboratory and chemicals as factor */
DATA pre7_5;
   SET pre7_1 (keep = laboratory name order meanlab);
   IF meanlab NE 0 THEN meanlog = log(meanlab);
RUN;
ODS trace off;
ODS listing close;
PROC MIXED data=pre7_5;
   CLASS laboratory name;
   MODEL meanlog = laboratory name /outp=tmp1;
   LSMEANS laboratory/pdiff cl adjust=tukey;
   ODS OUTPUT tests3 = table7_5;
   ODS OUTPUT lsmeans = table7_5partial;
   ODS OUTPUT diffs = table7_6;
   ODS OUTPUT covparms = covparms;
RUN;
```

```
ODS listing;
PROC GPLOT data=tmp1;
   PLOT resid * pred;
RUN;QUIT;
DATA pre7_5_nooutlier (drop=tmp0) table7_5_outliers(drop=tmp0);
   MERGE tmp1 covparms;
   RETAIN tmp0;
   IF estimate NE . THEN tmp0 = estimate; ELSE estimate = tmp0;
   IF abs(resid) <= 3*sqrt(estimate) THEN OUTPUT pre7_5_nooutlier;
   ELSE OUTPUT table7_5_outliers;
RUN;

proc print data=table7_5_outliers; run;
ODS listing close;
PROC MIXED data=pre7_5_nooutlier;
   CLASS laboratory name;
   MODEL meanlab = laboratory name /outp=tmp1 ;
   LSMEANS laboratory/pdiff cl adjust=tukey alpha = 0.01;
   ODS OUTPUT tests3 = table7_5;
   ODS OUTPUT lsmeans = table7_5partial;
   ODS OUTPUT diffs = table7_6;
   ODS OUTPUT covparms = covparms;
RUN;
ODS listing;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table7_5residualplot.doc' notoc_data;
PROC GPLOT data=tmp1;
   PLOT resid * pred;
RUN;QUIT;
ODS RTF close;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table7_5.doc' notoc_data;
PROC PRINT data=table7_5 NOOBS; RUN;
ODS RTF close;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table7_6.doc' notoc_data;
PROC REPORT data=table7_6 NOWINDOWS HEADLINE HEADSKIP ;
   COLUMNS laboratory _laboratory estimate stderr DF adjP;
   DEFINE laboratory / DISPLAY;
   DEFINE _laboratory /DISPLAY 'vs';
   DEFINE estimate/DISPLAY;
   DEFINE stderr/DISPLAY;
   DEFINE DF/DISPLAY;
   DEFINE adjP/DISPLAY 'Tukey-corrected p-value' width=15;
RUN;
ODS RTF close;

/* 7.7 Pearson correlations */
/* check labnames enzo hier beneden;*/
PROC SORT data=pre7_1; BY name; RUN;
PROC TRANSPOSE data=pre7_1 out=pre7_7;
   BY name;
   ID laboratory;
   VAR meanlab;
RUN;
PROC CORR data=pre7_7 noprint outp=pearson outs=spearman;
VAR CEETOX CARDAM L_OREAL;
RUN;
/*PROC GPLOT data=pre7_7; */
/*   PLOT Beiersdorf * Harlan Beiersdorf * IIVS Harlan * IIVS;*/
/*RUN; QUIT;*/
DATA set1p (keep= _name_ CARDAM where=(_name_ NE 'CARDAM'))
     set2p (keep= _name_ CEETOX where=(_name_ NE 'CEETOX'))  ;
   SET pearson;
   WHERE _TYPE_ = 'CORR';
RUN;
DATA pre_pearson7_7(keep = laboratories pearson);
   SET set1p(in=s1 rename=(CARDAM = pearson)) set2p(in=s2 rename=(CEETOX = pearson));
   IF s1 THEN with = 'CARDAM';
   IF s2 THEN with = 'CEETOX';
   IF _name_ = 'CARDAM' THEN DELETE;
   Laboratories = TRIM(LEFT(with))||'-'||TRIM(LEFT(_name_));
RUN;
DATA set1s (keep= _name_ CARDAM where=(_name_ NE 'CARDAM'))
     set2s (keep= _name_ CEETOX where=(_name_ NE 'CEETOX'))  ;
   SET spearman;
   WHERE _TYPE_ = 'CORR';
RUN;
DATA pre_spearman7_7(keep = laboratories spearman);
   SET set1s(in=s1 rename=(CARDAM = spearman)) set2s(in=s2 rename=(CEETOX = spearman));
   IF s1 THEN with = 'CARDAM';
   IF s2 THEN with = 'CEETOX';
   IF _name_ = 'CARDAM' THEN DELETE;
   Laboratories = TRIM(LEFT(with))||'-'||TRIM(LEFT(_name_));
RUN;
DATA table7_7;
   RETAIN laboratories pearson spearman;
   MERGE pre_pearson7_7 pre_spearman7_7;
   BY laboratories;
   FORMAT pearson spearman 8.3;
RUN;
ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table7_7.doc' notoc_data;
PROC REPORT data=table7_7 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratories pearson spearman;
   DEFINE laboratories / DISPLAY;
   DEFINE pearson/ DISPLAY  format=8.3 width = 15 CENTER;
   DEFINE spearman/ DISPLAY format=8.3 width = 15 CENTER;
RUN; QUIT;
```

```
ODS RTF close;

/* ------------------------------------ */
/* Section 8 of SAP: Predictive capacity */
/* ------------------------------------ */

PROC SORT data= pre_all_LE; BY laboratory name; RUN;
DATA PCA;
   SET pre_all_LE (drop=test);
   BY laboratory name;
   WHERE conclusion = 0;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
   IF test>3 THEN DELETE;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
RUN;
/* 8.1 sens, spec, acc */
%MACRO predmodel(lab=, output=);
DATA pre8_1;
   SET PCA;
   %IF &lab NE %THEN %DO;
      WHERE laboratory = &lab;
   %END;
   IF trueINI = 'I' THEN DO;
      IF predINI = 'I' THEN result = 'TP';
     ELSE IF predINI = 'NI' THEN result = 'FN';
   END;
   ELSE IF trueINI = 'NI' THEN DO;
      IF predINI = 'NI' THEN result = 'TN';
     ELSE IF predINI = 'I' THEN result = 'FP';
   END;
RUN;
PROC SORT data=pre8_1;
   BY trueINI predINI;
RUN;
DATA pre8_1b (drop=result);
   SET pre8_1;
   BY trueINI;
   retain tp tn fp fn;
   if (first.trueINI) then do;
      tp=0; tn=0; fp=0; fn=0;
   end;
   if (result in ("TP")) then tp=tp+1;
   if (result in ("TN")) then tn=tn+1;
   if (result in ("FN")) then fn=fn+1;
   if (result in ("FP")) then fp=fp+1;
   else ;
   if (last.trueINI) then output;
run;
DATA pre8_1C;
   SET pre8_1B;
   tntp=tn+tp;
   fnfp=fn+fp;
RUN;
PROC SQL;
   CREATE TABLE pre8_1D as
   select sum(tp) as tp, sum(tn) as tn, sum(fp)as fp, sum(fn) as fn, sum(tntp) as
          tntp, sum(fnfp) as fnfp
   from pre8_1C;
QUIT;
PROC SQL;
   CREATE TABLE pre8_1E as
   select tp/(tp+fn) as sensitivity, tn/(tn+fp) as specificity,
         (tn+tp)/(tn+tp+fn+fp) as accuracy
    from pre8_1D;
QUIT;
PROC TRANSPOSE data=pre8_1D out=pre8_1F;
   VAR tp tn fn fp tntp fnfp;
RUN;
DATA pre8_1G (drop=_name_ col1);
   LENGTH group $20;
   SET pre8_1F;
   count=col1;
   if _name_="tp" then do;
      group="Sensitivity";
      response=0;
      output;
   end;
   else if _name_="fn" then do;
      group="Sensitivity";
      response=1;
      output;
   end;
   else if _name_="tn" then do;
      group="Specificity";
      response=0;
      output;
   end;
   else if _name_="fp" then do;
      group="Specificity";
      response=1;
      output;
   end;
   else if _name_="tntp" then do;
      group="Accuracy";
      response=0;
      output;
```

```
   end;
   else if _name_="fnfp" then do;
      group="Accuracy";
      response=1;
      output;
   end;
RUN;
PROC SORT data=pre8_1G; BY group; RUN;
ODS trace off;
ODS listing close;
PROC FREQ data= pre8_1G;
   WEIGHT count;
   BY group;
   TABLES response/alpha=0.05 binomial(p=0.5);
   exact binomial;
   ODS OUTPUT BinomialProp = pre8_1CI;
RUN;
ODS listing;
DATA pre8_1TOTAL;
   SET pre8_1CI;
   WHERE name1 IN ('_BIN_' 'XL_BIN' 'XU_BIN');
RUN;
PROC TRANSPOSE data=pre8_1TOTAL out=pre8_1TOTALt;
   VAR nvalue1;
   ID name1;
   BY group;
RUN;
PROC TRANSPOSE data=pre8_1G out=pre8_1H;
   VAR count;
   ID response;
   BY group;
RUN;
DATA &output;
   MERGE pre8_1TOTALt pre8_1H;
   BY group;
RUN;
%MEND;
%predmodel(lab=,output=table8_1TOTAL);
%predmodel(lab='CEETOX',output=table8_1ceetox);
%predmodel(lab='CARDAM',output=table8_1cardam);
%predmodel(lab="L'OREAL",output=table8_1loreal);

DATA table8_1 (keep = group laboratory _BIN_ XL_BIN XU_BIN abs abs2);
   SET table8_1ceetox (in=set1) table8_1cardam (in=set2)
       table8_1loreal (in=set3) table8_1TOTAL (in=set4);
   IF set1 THEN laboratory = 'CEETOX';
   IF set2 THEN laboratory = 'CARDAM';
   IF set3 THEN laboratory = "L'Oreal";
   IF set4 THEN laboratory = 'Total';
   z = PUT(_0,$3.);
   x = PUT(_1,$3.);
   y = PUT(_0+_1,$3.);
   abs = x||'/'||y;
   abs2 = z||'/'||y;
RUN;
* report @8.2;

/* 8.2 statement regarding predictive capacity */
DATA table8_2;
   SET table8_1;
   LENGTH PC_criteria $25;
   IF group = 'Sensitivity' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.90 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.80 THEN PC_criteria = 'definitely unacceptable';
   END;
   IF group = 'Specificity' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.60 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.50 THEN PC_criteria = 'definitely unacceptable';
   END;
   IF group = 'Accuracy' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.75 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.65 THEN PC_criteria = 'definitely unacceptable';
   END;
RUN;

ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicLE_Table8_1.doc' notoc_data;
PROC REPORT data=table8_2 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory group abs2 _BIN_ XL_BIN XU_BIN PC_criteria;
   DEFINE laboratory/GROUP;
   DEFINE group/DISPLAY 'Characteristic' width = 15;
   DEFINE abs2/DISPLAY 'No.';
   DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
   DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
   DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
   DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
   BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

 * falsepos/falseneg;
PROC SORT data=PCA; BY order predGHS; RUN;
DATA PCA2;
   SET PCA;
   IF predINI = 'NI' THEN value = 0;
   ELSE value = 1;
```

```
   IF trueINI = 'NI' THEN true = 0;
   ELSE true = 1;
   mis=0;
   IF value = 1 AND true = 0 THEN mis = 1;
   IF value = 0 AND true = 1 THEN mis = 1;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CARDAM')) out=extra1a prefix=B;
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CEETOX')) out=extra1b prefix=H;
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = "L'OREAL")) out=extra1c prefix=V;
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CARDAM')) out=extra1d prefix=misB;
   VAR mis;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CEETOX')) out=extra1e prefix=misH;
   VAR mis;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = "L'OREAL")) out=extra1f prefix=misV;
   VAR mis;
   BY order name predGHS LS;
   ID test;
RUN;
PROC SORT data=PCA2 out=PCA2b nodupkey; BY order; RUN;
PROC TRANSPOSE data=PCA2b out=extra1g;
   VAR true;
   BY order name;
RUN;
DATA extra1;
   MERGE extra1a extra1b extra1c extra1d extra1e extra1f extra1g;
   BY order name;
   med = MEDIAN(B1,B2,B3,H1,H2,H3,V1,V2,V3);
   summis = SUM(misB1,misB2,misB3,misH1,misH2,misH3,misV1,misV2,misV3);
   mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/9';
   FORMAT B1--V3 med fmtini.;
   label mis = 'Mispredicted tests/Total'
         med = 'Final classification based on median';
RUN;
PROC SORT data=extra1;
   BY order;
RUN;


/* ------------------------------------ */
/* Section 8 of SAP: Predictive capacity */
/* Based on test strategy               */
/* ------------------------------------ */

PROC SORT data= pre_all_LE; BY laboratory name; RUN;
PROC SORT data= pre_all_SE; BY laboratory name; RUN;
DATA pre_all_test;
   SET pre_all_LE pre_all_SE;
   IF keuze = '' THEN DELETE;
RUN;

PROC SORT data=pre_all_test nodupkey out=sele(keep = order keuze trueINI); BY order; RUN;
PROC FREQ data=sele(where=(order NOT IN (106 107)));
tables trueINI*keuze;
run;
PROC SORT data=pre_all_test; BY laboratory name; RUN;
DATA PCA(where=(order NOT IN (106 107)));
   SET pre_all_test (drop=test);
   BY laboratory name;
   WHERE conclusion = 0;
   RETAIN test 0;
   test = test+1;
   IF first.name THEN test=1;
   IF test>3 THEN DELETE;
   IF mean_viability > 50 THEN predINI = 'NI';
   ELSE predINI = 'I';
RUN;
/* 8.1 sens, spec, acc */
%MACRO predmodel(lab=, output=);
DATA pre8_1;
   SET PCA;
   %IF &lab NE %THEN %DO;
      WHERE laboratory = &lab;
   %END;
   IF trueINI = 'I' THEN DO;
      IF predINI = 'I' THEN result = 'TP';
     ELSE IF predINI = 'NI' THEN result = 'FN';
   END;
   ELSE IF trueINI = 'NI' THEN DO;
      IF predINI = 'NI' THEN result = 'TN';
     ELSE IF predINI = 'I' THEN result = 'FP';
   END;
```

```
RUN;
PROC SORT data=pre8_1;
   BY trueINI predINI;
RUN;
DATA pre8_1b (drop=result);
   SET pre8_1;
   BY trueINI;
   retain tp tn fp fn;
   if (first.trueINI) then do;
      tp=0; tn=0; fp=0; fn=0;
   end;
   if (result in ("TP")) then tp=tp+1;
   if (result in ("TN")) then tn=tn+1;
   if (result in ("FN")) then fn=fn+1;
   if (result in ("FP")) then fp=fp+1;
   else ;
   if (last.trueINI) then output;
run;
DATA pre8_1C;
   SET pre8_1B;
   tntp=tn+tp;
   fnfp=fn+fp;
RUN;
PROC SQL;
   CREATE TABLE pre8_1D as
   select sum(tp) as tp, sum(tn) as tn, sum(fp)as fp, sum(fn) as fn, sum(tntp) as
          tntp, sum(fnfp) as fnfp
   from pre8_1C;
QUIT;
PROC SQL;
   CREATE TABLE pre8_1E as
   select tp/(tp+fn) as sensitivity, tn/(tn+fp) as specificity,
         (tn+tp)/(tn+tp+fn+fp) as accuracy
    from pre8_1D;
QUIT;
PROC TRANSPOSE data=pre8_1D out=pre8_1F;
   VAR tp tn fn fp tntp fnfp;
RUN;
DATA pre8_1G (drop=_name_ col1);
   LENGTH group $20;
   SET pre8_1F;
   count=col1;
   if _name_="tp" then do;
      group="Sensitivity";
      response=0;
      output;
   end;
   else if _name_="fn" then do;
      group="Sensitivity";
      response=1;
      output;
   end;
   else if _name_="tn" then do;
      group="Specificity";
      response=0;
      output;
   end;
   else if _name_="fp" then do;
      group="Specificity";
      response=1;
      output;
   end;
   else if _name_="tntp" then do;
      group="Accuracy";
      response=0;
      output;
   end;
   else if _name_="fnfp" then do;
      group="Accuracy";
      response=1;
      output;
   end;
RUN;
PROC SORT data=pre8_1G; BY group; RUN;
ODS trace off;
ODS listing close;
PROC FREQ data= pre8_1G;
   WEIGHT count;
   BY group;
   TABLES response/alpha=0.05 binomial(p=0.5);
   exact binomial;
   ODS OUTPUT BinomialProp = pre8_1CI;
RUN;
ODS listing;
DATA pre8_1TOTAL;
   SET pre8_1CI;
   WHERE name1 IN ('_BIN_' 'XL_BIN' 'XU_BIN');
RUN;
PROC TRANSPOSE data=pre8_1TOTAL out=pre8_1TOTALt;
   VAR nvalue1;
   ID name1;
   BY group;
RUN;
PROC TRANSPOSE data=pre8_1G out=pre8_1H;
   VAR count;
   ID response;
   BY group;
RUN;
DATA &output;
```

```
   MERGE pre8_1TOTALt pre8_1H;
   BY group;
RUN;
%MEND;
%predmodel(lab=,output=table8_1TOTAL);
%predmodel(lab='CEETOX',output=table8_1ceetox);
%predmodel(lab='CARDAM',output=table8_1cardam);
%predmodel(lab="L'OREAL",output=table8_1loreal);

DATA table8_1 (keep = group laboratory _BIN_ XL_BIN XU_BIN abs abs2);
   SET table8_1ceetox (in=set1) table8_1cardam (in=set2)
       table8_1loreal (in=set3) table8_1TOTAL (in=set4);
   IF set1 THEN laboratory = 'CEETOX';
   IF set2 THEN laboratory = 'CARDAM';
   IF set3 THEN laboratory = "L'Oreal";
   IF set4 THEN laboratory = 'Total';
   x = PUT(_1,$3.);
   z = PUT(_0,$3.);
   y = PUT(_0+_1,$3.);
   abs = x||'/'||y;
   abs2 = z||'/'||y;
RUN;
* report @8.2;

/* 8.2 statement regarding predictive capacity */
DATA table8_2;
   SET table8_1;
   LENGTH PC_criteria $25;
   IF group = 'Sensitivity' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.90 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.80 THEN PC_criteria = 'definitely unacceptable';
   END;
   IF group = 'Specificity' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.60 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.50 THEN PC_criteria = 'definitely unacceptable';
   END;
   IF group = 'Accuracy' THEN DO;
      PC_criteria = 'further evaluation';
      IF _BIN_ >= 0.75 THEN PC_criteria = 'definitely acceptable';
      IF _BIN_ <= 0.65 THEN PC_criteria = 'definitely unacceptable';
   END;
RUN;

ODS RTF body='\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data
analysis\Reports\Revision\SkinEthicTEST_Table8_1.doc' notoc_data;
PROC REPORT data=table8_2 NOWINDOWS HEADLINE HEADSKIP;
   COLUMNS laboratory group abs2 _BIN_ XL_BIN XU_BIN PC_criteria;
   DEFINE laboratory/GROUP;
   DEFINE group/DISPLAY 'Characteristic' width = 15;
   DEFINE abs2/DISPLAY 'No.';
   DEFINE _BIN_/DISPLAY 'Value' format=8.3 CENTER;
   DEFINE XL_BIN/DISPLAY '95% lower limit'  format=8.3 width=15 CENTER;
   DEFINE XU_BIN/DISPLAY '95% upper limit' format=8.3 width=15 CENTER;
   DEFINE PC_criteria/DISPLAY 'Statement' width = 25;
   BREAK after laboratory/SKIP;
RUN; QUIT;
ODS RTF close;

 * falsepos/falseneg;
PROC SORT data=PCA; BY order predGHS; RUN;
DATA PCA2;
   SET PCA;
   IF predINI = 'NI' THEN value = 0;
   ELSE value = 1;
   IF trueINI = 'NI' THEN true = 0;
   ELSE true = 1;
   mis=0;
   IF value = 1 AND true = 0 THEN mis = 1;
   IF value = 0 AND true = 1 THEN mis = 1;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CARDAM')) out=extra1a prefix=B;
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CEETOX')) out=extra1b prefix=H;
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = "L'OREAL")) out=extra1c prefix=V;
   VAR value;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CARDAM')) out=extra1d prefix=misB;
   VAR mis;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = 'CEETOX')) out=extra1e prefix=misH;
   VAR mis;
   BY order name predGHS LS;
   ID test;
RUN;
PROC TRANSPOSE data=PCA2(where=(laboratory = "L'OREAL")) out=extra1f prefix=misV;
   VAR mis;
```

```
   BY order name predGHS LS;
   ID test;
RUN;
PROC SORT data=PCA2 out=PCA2b nodupkey; BY order; RUN;
PROC TRANSPOSE data=PCA2b out=extra1g;
   VAR true;
   BY order name;
RUN;
DATA extra1;
   MERGE extra1a extra1b extra1c extra1d extra1e extra1f extra1g;
   BY order name;
   med = MEDIAN(B1,B2,B3,H1,H2,H3,V1,V2,V3);
   summis = SUM(misB1,misB2,misB3,misH1,misH2,misH3,misV1,misV2,misV3);
   mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/9';
   IF order = 20 THEN DO;
         med = MEDIAN(H1,H2,V1,V2,V3);
         summis = SUM(misV1,misV2,misV3);
         mis = '*'||TRIM(LEFT(PUT(summis,best12.)))||'/3';
   END;
   FORMAT B1--V3 med fmtini.;
   label mis = 'Mispredicted tests/Total'
          med = 'Final classification based on median';
RUN;
PROC SORT data=extra1;
   BY order;
RUN;

* overview of protocol selection;
PROC SORT data=pre_all_test out=test (keep = order name keuze) nodupkey;
   BY order;
RUN;



*****************************;
*** NOG DOEN (combi met LE) ***;
*****************************;
/* 5.9 Summarise results for  NC and PC */

/*DEZE FILE PRE5_9 MOET JE NAAR EXCEL DOEN EN DAN INLEZEN IN R EN PLOTS MAKEN*/

PROC SORT data=RhT.SE2 out=ODnc(keep = laboratory run tissue chemical_code meanODnc) nodupkey;
   BY laboratory run chemical_code;
   where chemical_code NE 'PC';
RUN;
PROC SORT data=pre_all_SE out=all_SE(keep = laboratory StdNC meanPC sdPC std_TA chemical_code run
filename conclusion);
   BY laboratory run chemical_code;
RUN;
DATA all_SE2;
   MERGE all_SE(in=ok) ODnc;
   BY laboratory run chemical_code;
   IF ok;
RUN;
PROC SORT data=all_SE2 out=pre5_9(keep = laboratory meanODnc StdNC meanPC sdPC std_TA chemical_code run
conclusion) nodupkey;
BY laboratory filename;
RUN;
DATA pre5_9b;
   SET pre5_9 pre5_9(in=set2);
   IF set2 THEN laboratory = 'Total';
RUN;
DATA pre5_9c;
   RETAIN labstate StdNC meanPC sdPC;
   SET pre5_9b;
   labstate = TRIM(LEFT(laboratory)) || TRIM(LEFT('(SE)'));
RUN;
PROC SORT data=RhT.LE2 out=ODnc(keep = laboratory run tissue chemical_code meanODnc) nodupkey;
   BY laboratory run chemical_code;
   where chemical_code NE 'PC';
RUN;
PROC SORT data=pre_all_LE out=all_LE(keep = laboratory StdNC meanPC sdPC std_TA chemical_code run
filename conclusion);
   BY laboratory run chemical_code;
RUN;
DATA all_LE2;
   MERGE all_LE(in=ok) ODnc;
   BY laboratory run chemical_code;
   IF ok;
RUN;
PROC SORT data=all_LE2 out=pre5_9(keep = laboratory meanODnc StdNC meanPC sdPC std_TA chemical_code run
conclusion) nodupkey;
BY laboratory filename;
RUN;
DATA pre5_9b;
   SET pre5_9 pre5_9(in=set2);
   IF set2 THEN laboratory = 'Total';
RUN;
DATA pre5_9e;
   RETAIN labstate StdNC meanPC sdPC std_TA;
   SET pre5_9b;
   labstate = TRIM(LEFT(laboratory)) || TRIM(LEFT('(LE)'));
RUN;
DATA pre5_9f;
   SET pre5_9c (in=se) pre5_9e (in=le);
   IF se THEN protocol = 'SE';
   IF le THEN protocol = 'LE';
RUN;
PROC SORT data=pre5_9f out=pre5_9g; BY labstate; RUN;
```

```
DATA _NULL_;
   SET pre5_9f;
   FILE '\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Plots in
R\skinethic.txt';
   PUT labstate meanODnc StdNC  meanPC sdPC  laboratory     protocol;
RUN;
* voor std van uncorr viab;
PROC SORT data=RhT.SE2 out=ODnc(keep = laboratory run tissue chemical_code meanODnc) nodupkey;
   BY laboratory run chemical_code;
   where chemical_code NE 'PC';
RUN;
PROC SORT data=pre_all_SE out=all_SE(keep = laboratory StdNC meanPC sdPC std_TA chemical_code run
filename conclusion);
   BY laboratory run chemical_code;
RUN;
DATA all_SE2;
   MERGE all_SE(in=ok) ODnc;
   BY laboratory run chemical_code;
   IF ok;
RUN;
PROC SORT data=all_SE2 out=pre5_9(keep = laboratory meanODnc StdNC meanPC sdPC std_TA chemical_code run
conclusion);
BY laboratory filename;
RUN;
DATA pre5_9b;
   SET pre5_9 pre5_9(in=set2);
   IF set2 THEN laboratory = 'Total';
RUN;
DATA pre5_9c;
   RETAIN labstate StdNC meanPC sdPC;
   SET pre5_9b;
   labstate = TRIM(LEFT(laboratory)) || TRIM(LEFT('(SE)'));
RUN;
PROC SORT data=RhT.LE2 out=ODnc(keep = laboratory run tissue chemical_code meanODnc) nodupkey;
   BY laboratory run chemical_code;
   where chemical_code NE 'PC';
RUN;
PROC SORT data=pre_all_LE out=all_LE(keep = laboratory StdNC meanPC sdPC std_TA chemical_code run
filename conclusion);
   BY laboratory run chemical_code;
RUN;
DATA all_LE2;
   MERGE all_LE(in=ok) ODnc;
   BY laboratory run chemical_code;
   IF ok;
RUN;
PROC SORT data=all_LE2 out=pre5_9(keep = laboratory meanODnc StdNC meanPC sdPC std_TA chemical_code run
conclusion);
BY laboratory filename;
RUN;
DATA pre5_9b;
   SET pre5_9 pre5_9(in=set2);
   IF set2 THEN laboratory = 'Total';
RUN;
DATA pre5_9e;
   RETAIN labstate StdNC meanPC sdPC std_TA;
   SET pre5_9b;
   labstate = TRIM(LEFT(laboratory)) || TRIM(LEFT('(LE)'));
RUN;
DATA pre5_9f;
   SET pre5_9c (in=se) pre5_9e (in=le);
   IF se THEN protocol = 'SE';
   IF le THEN protocol = 'LE';
RUN;
PROC SORT data=pre5_9f out=pre5_9g; BY labstate; RUN;
DATA _NULL_;
   SET pre5_9f (where=(conclusion IN (0 1) AND std_TA NE .));
   FILE '\\tsn.tno.nl\Data\Projects\031\1\14497\Kluis\Biostatistiek\Data analysis\Plots in
R\skinethic_TA.txt';
   PUT labstate std_TA laboratory     protocol;
RUN;
data select;
   set pre5_9f (where=(conclusion IN (0 1) AND std_TA NE .));
run;
* Plots and statistics in R;

/* ---------- */
/* appendix I */
/* ---------- */
PROC sort data=pre_all_SE out=appendix1 (keep = order name mtt coloring
                                                                                    where=(UPCASE(MTT) NE 'NO'
OR UPCASE(coloring) NE 'NO')) nodupkey ;
   BY order name;
RUN;
/* ----------- */
/* Appendix IV */
/* ----------- */
PROC SORT data=rht.se_remarks out=remarks_se (keep = filename laboratory remark);
by filename;
RUN;
PROC SORT data=rht.le_remarks out=remarks_le (keep = filename laboratory remark);
by filename;
RUN;
/* ---------------- */
/* Appendix VI */
/* ----------------*/
DATA appVI_SE/*(keep=order  laboratory  predGHS  MTTcoloring test  meanODnc stdNC NCqual meanPC sdPC
   PCqual mean_TA  std_TA qual_sd  mean_NSC mean_MTT mean_viability conclusion  pred50)*/;
```

```
   RETAIN order laboratory  predGHS  MTTcoloring test  meanODnc stdNC NCqualmeanPC sdPC  PCqual
   mean_TA  std_TA qual_sd  mean_NSC mean_MTT mean_viability conclusion  pred50;
   SET pre_all_SE;
   IF mean_viability > 50 THEN pred50 = 'NI';
   ELSE pred50 = 'I';
RUN;
PROC SORT data=appVI_SE; BY laboratory order test; RUN;
* add std en call tav nsc en mtt;
proc sort data=RhT.SE_extra out=sort nodupkey;
   BY laboratory chemical_code run;
RUN;
DATA sort2;
   SET sort;
   KEEP chemical_code MTT coloring run laboratory NSMTTcall NSMTT_pct stdNSMTT_pct NSC_pct stdNSC_pct
NSCcall;
   IF chemical_code = 'PC' THEN DELETE;
   IF SUBSTR(run,1,14) NE 'Chemical : Run' THEN DELETE;
RUN;
DATA sort3;
   SET sort2;
   runs = INPUT(SUBSTR(run,16,1),best12.);
   DROP run;
RUN;
PROC SORT data=appVI_SE; BY laboratory chemical_code run; RUN;
PROC SORT data=sort3(rename=(runs=run)); BY laboratory chemical_code run; RUN;
DATA mergen /*(keep=SMTTcall NSMTT_pct stdNSMTT_pct NSC_pct stdNSC_pct NSCcall chemical_name run order
   laboratory  predGHS  MTTcoloring test  meanODnc stdNC NCqualmeanPC sdPC  PCqualmean_TA  std_TA
   qual_sd  mean_NSC mean_MTT mean_viability conclusion  pred50)*/;
   MERGE appVI_SE sort3;
   BY laboratory chemical_code run;
   IF mean_MTT EQ . AND mean_NSC EQ . THEN DELETE;
RUN;
PROC SORT data=mergen; BY laboratory order test; RUN;
DATA mergen (keep=flag SMTTcall NSMTT_pct stdNSMTT_pct NSC_pct stdNSC_pct NSCcall chemical_name run
order laboratory  predGHS  MTTcoloring test  meanODnc stdNC NCqualmeanPC sdPC  PCqualmean_TA
   std_TA qual_sd  mean_NSC mean_MTT mean_viability conclusion  pred50);
   MERGE appVI_SE(in=set1) sort3;
   BY laboratory chemical_code run;
   IF set1 then flag = 1;
RUN;
PROC SORT data=mergen; BY laboratory order test; RUN;
* 106 en 107;
DATA chem106107;
   SET RhT.SE_extra;
   IF chemical_code IN ('L6' 'C52' 'X95' 'L100' 'C56''X32') THEN OUTPUT;
RUN;
proc sort data=chem106107 out=sortb nodupkey;
   BY laboratory chemical_code run;
RUN;

DATA appVI_LE /*(keep=order laboratory  predGHS  MTTcoloring test  meanODnc stdNC NCqualmeanPC sdPC
   PCqualmean_TA  std_TA qual_sd  mean_NSC mean_MTT mean_viability conclusion  pred50)*/;
   RETAIN order laboratory  predGHS  MTTcoloring test  meanODnc stdNC NCqualmeanPC sdPC  PCqual
   mean_TA  std_TA qual_sd  mean_NSC mean_MTT mean_viability conclusion  pred50;
   SET pre_all_LE;
   IF mean_viability > 50 THEN pred50 = 'NI';
   ELSE pred50 = 'I';
RUN;
PROC SORT data=appVI_LE; BY laboratory order test; RUN;
* add std en call tav nsc en mtt;
proc sort data=RhT.LE_extra out=sortc nodupkey;
   BY laboratory chemical_code run;
RUN;
DATA sortc2;
   SET sortc;
   KEEP chemical_code MTT coloring run laboratory NSMTTcall NSMTT_pct stdNSMTT_pct NSC_pct stdNSC_pct
NSCcall;
   IF chemical_code = 'PC' THEN DELETE;
   IF SUBSTR(run,1,14) NE 'Chemical : Run' THEN DELETE;
RUN;
DATA sortc3;
   SET sortc2;
   runs = INPUT(SUBSTR(run,16,1),best12.);
   DROP run;
RUN;
PROC SORT data=appVI_LE; BY laboratory chemical_code run; RUN;
PROC SORT data=sortc3(rename=(runs=run)); BY laboratory chemical_code run; RUN;
DATA mergenC /*(keep=SMTTcall NSMTT_pct stdNSMTT_pct NSC_pct stdNSC_pct NSCcall chemical_name run order
   laboratory  predGHS  MTTcoloring test  meanODnc stdNC NCqualmeanPC sdPC  PCqualmean_TA  std_TA
   qual_sd  mean_NSC mean_MTT mean_viability conclusion  pred50)*/;
   MERGE appVI_LE sortc3;
   BY laboratory chemical_code run;
   IF mean_MTT EQ . AND mean_NSC EQ . THEN DELETE;
RUN;
PROC SORT data=mergenC; BY laboratory order test; RUN;
DATA mergenC (keep=flag SMTTcall NSMTT_pct stdNSMTT_pct NSC_pct stdNSC_pct NSCcall chemical_name run
order laboratory  predGHS  MTTcoloring test  meanODnc stdNC NCqualmeanPC sdPC  PCqualmean_TA
   std_TA qual_sd  mean_NSC mean_MTT mean_viability conclusion  pred50);
   MERGE appVI_LE(in=set1) sortc3;
   BY laboratory chemical_code run;
   IF set1 then flag = 1;
RUN;
PROC SORT data=mergenC; BY laboratory order test; RUN;

* 106 107;
data od_LE (keep = chemical_code run meanODnc stdNC);
   set rht.LE2;
   WHERE chemical_code IN ('L6' 'C52' 'X95' 'L100' 'C56''X32');
RUN;
```

```
proc sort data=od_LE nodupkey; BY chemical_code run; RUN;
data od_SE (keep = chemical_code run meanODnc stdNC);
   set rht.SE2;
   WHERE chemical_code IN ('L6' 'C52' 'X95' 'L100'  'C56''X32');
RUN;
proc sort data=od_SE nodupkey; BY chemical_code run; RUN;
```

Appendix III Receipt of data

Se

No	Remark	Used	Filename	saved as	LAB	v	date of receipt											
1		YES	EIVS_CARDAM_SE_10HCE029_35.xls		CARDAM_SE	1	Jan-11	C1(1)	C2(1)	C17(1)	C19(1)	C26(1)	C30(1)	C33(1)	C34(1)	C35(1)		
2		YES	EIVS_CARDAM_SE_10HCE031_37.xls		CARDAM_SE	1	Jan-11	C1(2)	C2(2)	C17(2)	C19(2)	C26(2)	C30(2)	C33(2)	C34(2)	C35(2)		
3		YES	EIVS_CARDAM_SE_10HCE032_38.xls		CARDAM_SE	1	Jan-11	C1(3)	C2(3)	C17(3)	C19(3)	C26(3)	C30(3)	C77(1)	C34(3)	C35(3)		
4		YES	EIVS_CARDAM_SE_10HCE033_39(C77).xls		CARDAM_SE	1	Jan-11	C77(2)										
5		YES	EIVS_CARDAM_SE_10HCE033_39.xls		CARDAM_SE	1	Jan-11	C33(3)	C35(4)	C36(1)	C37(1)	C49(1)	C51(1)	C54(1)	C60(1)	C63(1)	C65(1)	C66(1)
6		YES	EIVS_CARDAM_SE_10HCE034_40(C79).xls		CARDAM_SE	1	Jan-11	C79(1)										
7		YES	EIVS_CARDAM_SE_10HCE034_40.xls		CARDAM_SE	1	Jan-11	C36(2)	C37(2)	C49(2)	C51(2)	C54(2)	C60(2)	C63(2)	C65(2)	C66(2)	C75(2)	C76(2)
8		NO	EIVS_CARDAM_SE_10HCE033Kt_40.xlsx		CARDAM_SE	1	Jan-11	C6(Kt)	C30(Kt)	C34(Kt)	C54(Kt)	C75(Kt)	C87(Kt)	C90(Kt)	C104(Kt)			
9		NO	EIVS_CARDAM_SE_10HCE044_50.xlsx		CARDAM_SE	1	Jan-11	C45(4)	C53(4)	C98(3)	C101(3)	C119(3)	C123(3)	C127(3)	C132(3)	C83(4)	C6(3)	
10		YES	EIVS_CARDAM_SE1_10HCE035_41.xls		CARDAM_SE	1	Jan-11	C36(3)	C37(3)	C49(3)	C51(3)	C54(3)	C60(3)	C63(3)	C65(3)	C66(3)	C75(3)	C76(3)
11		NO	EIVS_CARDAM_SE1_10HCE036_42.xls		CARDAM_SE	1	Jan-11	C104(1)	C78(3)	C79(3)	C82(2)	C85(2)	C87(2)	C88(2)	C90(2)	C91(2)	C94(2)	C96(2)
12		NO	EIVS_CARDAM_SE1_10HCE037_43.xls		CARDAM_SE	1	Jan-11	C82(3)	C85(3)	C87(3)	C88(3)	C90(3)	C91(3)	C94(3)	C96(3)	C99(2)	C104(2)	C3(2)
13		NO	EIVS_CARDAM_SE1_10HCE040_46.xls		CARDAM_SE	1	Jan-11	C99(3)	C104(3)	C3(3)	C11(3)	C12(3)	C13(3)	C15(3)	C16(3)	C21(3)	C25(3)	C27(3)
14		YES	EIVS_CARDAM_SE2_10HCE035_41.xls		CARDAM_SE	1	Jan-11	C82(1)	C85(1)	C87(1)	C88(1)	C90(1)	C91(1)	C94(1)	C96(1)			
15		NO	EIVS_CARDAM_SE2_10HCE041_47.xls		CARDAM_SE	1	Jan-11	C123(1)	C127(1)	C132(1)	C134(1)	C6(1)						
16		NO	EIVS_CARDAM_SE2_10HCE042_48.xls		CARDAM_SE	1	Jan-11	C127(2)	C132(2)	C134(2)	C135(1)	C136(1)	C138(1)	C6(2)				
17	replaced by 123	NO	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls		CEETOX_SE	1	09/02/2011	x1(1)	x2(1)	x5(1)	x6(1)	x7(1)	x16(1)	x22(1)	x28(1)	x36(1)	x38(1)	
18	replaced by 124	NO	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls		CEETOX_SE	1	09/02/2011	x1(2)	x2(2)	x5(2)	x6(2)	x7(2)	x16(2)	x22(2)	x28(2)	x36(2)	x38(2)	
19	replaced by 125	NO	EIVS_CEETOX_SE_10HCE025_27_FUSION.XLS	EIVS_CEETOX_SE_10HCE025_27_v1.0.XLS	CEETOX_SE	1	09/02/2011	x1(3)	x2(3)	x5(3)	x6(3)	x7(3)	x16(3)	x22(3)	x28(3)	x36(3)	x38(3)	
20	replaced by 126	NO	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls		CEETOX_SE	1	09/02/2011	x63(1)	x72(1)	x73(1)	x83(1)	x86(1)	x89(1)	x93(1)	x98(1)	x99(1)	x103(1)	
21	replaced by 127	NO	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls		CEETOX_SE	1	09/02/2011	x63(2)	x72(2)	x73(2)	x83(2)	x86(2)	x89(2)	x93(2)	x98(2)	x99(2)	x103(2)	
22	replaced by 128	NO	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls		CEETOX_SE	1	09/02/2011	x63(3)	x72(3)	x73(3)	x83(3)	x86(3)	x89(3)	x93(3)	x98(3)	x99(3)	x103(3)	
23	replaced by 129	NO	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls		CEETOX_SE	1	09/02/2011	x45(1)	x47(1)	x49(1)	x51(1)	x52(1)	x59(1)	x68(1)				
24	replaced by 130	NO	EIVS_CEETOX_SE_10HCE044_50_v1.0.xls		CEETOX_SE	1	09/02/2011	x45(2)	x47(2)	x49(2)	x51(2)	x52(2)	x59(2)	x68(2)				
25	replaced by 131	NO	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.XLS		CEETOX_SE	1	09/02/2011	x45(3)	x47(3)	x49(3)	x51(3)	x52(3)	x59(3)	x68(3)				
26	replaced by 132	NO	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls		CEETOX_SE	1	09/02/2011	x41(1)	x17(1)	x31(1)	x91(1)	x121(1)	x3(1)	x25(1)	x30(1)	x33(1)		
27		NO	EIVS_LOREAL_SE_10HCE023_25.xls		LOREAL_SE	1	02/03/2011	L5(1)	L9(1)	L11(1)	L12(1)	L17(1)	L18(1)	L20(1)	L23(1)	L24(1)	L27(1)	L28(1)
28		NO	EIVS_LOREAL_SE_10HCE024_26.xls		LOREAL_SE	1	02/03/2011	L5(2)	L9(2)	L11(2)	L12(2)	L17(2)	L18(2)	L20(2)	L23(2)	L24(2)	L27(2)	L28(2)
29		NO	EIVS_LOREAL_SE_10HCE025_27.xls		LOREAL_SE	1	02/03/2011	L30(1)	L39(1)	L43(1)	L45(1)	L48(1)	L51(1)	L55(1)	L59(1)	L60(1)	L66(1)	L68(1)
30		NO	EIVS_LOREAL_SE_10HCE026_28.xls		LOREAL_SE	1	02/03/2011	L9(3)	L12(3)	L17(3)	L20(3)	L27(3)	L43(2)					
31		NO	EIVS_LOREAL_SE_10HCE027_29.xls		LOREAL_SE	1	02/03/2011	L30(1)	L39(1)	L43(1)	L45(1)	L48(1)	L51(1)	L55(1)	L59(1)	L60(1)	L66(1)	L68(1)
32		NO	EIVS_LOREAL_SE_10HCE028_30.xls		LOREAL_SE	1	02/03/2011	L5(2)	L11(2)	L23(2)	L24(2)	L30(2)	L39(2)	L48(2)	L51(2)	L55(2)	L60(2)	L68(2)
33		NO	EIVS_LOREAL_SE_10HCE029_35.xls		LOREAL_SE	1	02/03/2011	L74(1)	L75(1)	L78(1)	L81(1)	L82(1)	L85(1)	L91(1)	L94(1)	L97(1)	L98(1)	L102(1)
34		NO	EIVS_LOREAL_SE_10HCE031_37.xls		LOREAL_SE	1	02/03/2011	L45(3)	L59(3)	L66(3)	L74(2)	L82(2)	L94(1)					
35		NO	EIVS_LOREAL_SE_10HCE032_38.xls		LOREAL_SE	1	02/03/2011	L74(3)	L75(2)	L78(2)	L81(2)	L82(3)	L85(2)	L91(2)	L94(3)	L97(2)	L98(2)	L102(2)
36		NO	EIVS_LOREAL_SE_10HCE033_39.xls		LOREAL_SE	1	02/03/2011	L11(5)	L18(3)	L28(3)	L73(2)	L75(3)	L78(3)	L81(3)	L85(3)	L91(3)	L97(3)	
37		NO	EIVS_LOREAL_SE_10HCE034_40.xls		LOREAL_SE	1	02/03/2011	L73(3)	L98(3)	L4(1)	L7(1)	L8(1)						

38		NO	EIVS_LOREAL_SE_10HCE035_41.xls		LOREAL_SE	1	02/03/2011	L4(2)	L7(2)	L8(2)	L29(1)	L42(1)	L56(1)	L57(1)	L61(1)	L63(1)	L64(1)	
39		NO	EIVS_LOREAL_SE_10HCE036_42.xls		LOREAL_SE	1	02/03/2011	L102(3)	L7(3)	L29(2)	L57(2)							
40		NO	EIVS_LOREAL_SE_10HCE037_43.xls		LOREAL_SE	1	02/03/2011	L4(3)	L8(3)	L29(3)	L42(2)	L56(2)	L61(2)	L57(3)	L63(2)	L64(2)	L67(1)	L70(1)
41		NO	EIVS_LOREAL_SE_10HCE040_46.xls		LOREAL_SE	1	02/03/2011	L30(4)	L42(3)	L56(3)	L61(3)	L63(3)	L64(3)	L67(2)	L70(2)	L72(1)	L79(1)	L83(1)
42		NO	EIVS_LOREAL_SE_10HCE041_47.xls		LOREAL_SE	1	02/03/2011	L67(3)	L72(2)	L79(2)	L83(2)	L87(2)	L90(1)	L92(2)	L96(1)	L101(1)	L99(1)	
43		NO	EIVS_LOREAL_SE_10HCE042_48.xls		LOREAL_SE	1	02/03/2011	L87(3)	L90(2)	L92(2)	L99(2)	L104(1)	L119(1)	L120(1)	L130(1)	L131(1)	L132(1)	
44		NO	EIVS_LOREAL_SE_10HCE043_49.xls		LOREAL_SE	1	02/03/2011	L83(3)	L96(2)	L101(2)	L104(2)	L106(1)	L107(1)	L108(1)	L109(1)	L112(1)	L113(1)	
45		NO	EIVS_LOREAL_SE_10HCE044_50.xls		LOREAL_SE	1	02/03/2011	L79(3)	L96(3)	L101(3)	L106(2)	L107(2)	L108(2)	L109(2)	L112(2)	L113(2)	L114(1)	L115(1)
46		NO	EIVS_LOREAL_SE_11HCE005_5.xls		LOREAL_SE	1	02/03/2011	Kt-L70	Kt-L72	Kt-L90	Kt-L99	Kt-L104	Kt-L107	Kt-L119	Kt-L120	Kt-L132	Kt-L133	
47	replacement of 27	YES	EIVS_LOREAL_SE_10HCE023_25.xls		LOREAL_SE	1	16/03/2011	L5(1)	L9(1)	L11(1)	L12(1)	L17(1)	L18(1)	L20(1)	L23(1)	L24(1)	L27(1)	L28(1)
48	replacement of 28	YES	EIVS_LOREAL_SE_10HCE024_26.xls		LOREAL_SE	1	16/03/2011	L5(2)	L9(2)	L11(2)	L12(2)	L17(2)	L18(2)	L20(2)	L23(2)	L24(2)	L27(2)	L28(2)
49	replacement of 29	YES	EIVS_LOREAL_SE_10HCE025_27.xls		LOREAL_SE	1	16/03/2011	L30(1)	L39(1)	L43(1)	L45(1)	L48(1)	L51(1)	L55(1)	L59(1)	L60(1)	L66(1)	L68(1)
50	replacement of 30	YES	EIVS_LOREAL_SE_10HCE026_28.xls		LOREAL_SE	1	16/03/2011	L9(3)	L12(3)	L17(3)	L20(3)	L27(3)	L43(2)					
51	replacement of 31	YES	EIVS_LOREAL_SE_10HCE027_29.xls		LOREAL_SE	1	16/03/2011	L30(2)	L39(2)	L43(3)	L45(2)	L48(2)	L51(2)	L55(2)	L59(2)	L60(2)	L66(2)	L68(2)
52	replacement of 32	YES	EIVS_LOREAL_SE_10HCE028_30.xls		LOREAL_SE	1	16/03/2011	L5(3)	L11(4)	L23(3)		L24(3)	L30(3)	L39(3)	L48(3)	L51(3)	L55(3)	L60(3)
53	replacement of 33	YES	EIVS_LOREAL_SE_10HCE029_35.xls		LOREAL_SE	1	16/03/2011	L74(1)	L75(1)	L78(1)	L81(1)	L82(1)	L85(1)	L91(1)	L94(1)	L97(1)	L98(1)	L102(1)
54	replacement of 34	YES	EIVS_LOREAL_SE_10HCE031_37.xls		LOREAL_SE	1	16/03/2011	L45(3)	L59(3)	L66(3)	L74(2)	L82(2)	L94(2)					
55	replacement of 35	YES	EIVS_LOREAL_SE_10HCE032_38.xls		LOREAL_SE	1	16/03/2011	L74(3)	L75(2)	L78(2)	L81(2)	L82(3)	L85(2)	L91(2)	L94(3)	L97(2)	L98(2)	L102(2)
56	replacement of 36	YES	EIVS_LOREAL_SE_10HCE033_39.xls		LOREAL_SE	1	16/03/2011	L11(5)	L18(3)	L28(3)	L73(2)	L75(3)	L78(3)	L81(3)	L85(3)	L91(3)	L97(3)	
57	replacement of 37	YES	EIVS_LOREAL_SE_10HCE034_40.xls		LOREAL_SE	1	16/03/2011	L73(3)	L98(3)	L4(1)	L7(1)	L8(1)						
58	replacement of 38	YES	EIVS_LOREAL_SE_10HCE035_41.xls		LOREAL_SE	1	16/03/2011	L4(2)	L7(2)	L8(2)	L29(1)	L42(1)	L56(1)	L57(1)	L61(1)	L63(1)	L64(1)	
59	replacement of 39	YES	EIVS_LOREAL_SE_10HCE036_42.xls		LOREAL_SE	1	16/03/2011	L102(3)	L7(3)	L29(2)	L57(2)							
60	replacement of 40	YES	EIVS_LOREAL_SE_10HCE037_43.xls		LOREAL_SE	1	16/03/2011	L4(3)	L8(3)	L29(3)	L42(2)	L56(2)	L61(2)	L57(3)	L63(2)	L64(2)	L67(1)	L70(1)
61	replacement of 41	YES	EIVS_LOREAL_SE_10HCE040_46.xls		LOREAL_SE	1	16/03/2011	L30(4)	L42(3)	L56(3)	L61(3)	L63(3)	L64(3)	L67(2)	L70(2)	L72(1)	L79(1)	L83(1)
62	replacement of 42	YES	EIVS_LOREAL_SE_10HCE041_47.xls		LOREAL_SE	1	16/03/2011	L67(3)	L72(2)	L79(2)	L83(2)	L87(2)	L90(1)	L92(1)	L96(1)	L101(1)	L99(1)	
63	replacement of 43	YES	EIVS_LOREAL_SE_10HCE042_48.xls		LOREAL_SE	1	16/03/2011	L87(3)	L90(2)	L92(2)	L99(2)	L104(1)	L119(1)	L120(1)	L130(1)	L131(1)	L132(1)	
64	replacement of 44	YES	EIVS_LOREAL_SE_10HCE043_49.xls		LOREAL_SE	1	16/03/2011	L83(3)	L96(2)	L101(2)	L104(1)	L106(1)	L107(1)	L108(1)	L109(1)	L112(1)	L113(1)	
65	replacement of 45	YES	EIVS_LOREAL_SE_10HCE044_50.xls		LOREAL_SE	1	16/03/2011	L79(3)	L96(3)	L101(3)	L106(2)	L107(2)	L108(2)	L109(2)	L112(2)	L113(2)	L114(1)	L115(1)
66	replacement of 46	YES	EIVS_LOREAL_SE_11HCE005_5.xls		LOREAL_SE	1	16/03/2011	Kt-L70	Kt-L72	Kt-L90	Kt-L99	Kt-L104	Kt-L107	Kt-L119	Kt-L120	Kt-L132	Kt-L133	
67	replaced by 133	NO	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls		CEETOX_SE	1	04/05/2011	x41(2)	x17(2)	x31(2)	x91(2)	x121(2)	x3(2)	x25(2)	x30(2)	x33(2)		

68	replaced by 134	NO	EIVS_CEETOX_SE_11HCE007_7_v1.0.xls		CEETOX_SE	1	04/05/2011	x41(3)	x17(3)	x31(3)	x91(3)	x121(3)	x3(3)	x25(3)	x30(3)	x33(3)		
69	replacement of 11	YES	EIVS_CARDAM_SE1_10HCE036_42.xls		CARDAM_SE	1	12/05/2011	C78(3)	C79(3)	C82(2)	C85(2)	C87(2)	C88(2)	C90(2)	C91(2)	C94(2)	C96(2)	C99(1)
70	replacement of 12	YES	EIVS_CARDAM_SE1_10HCE037_43.xls		CARDAM_SE	1	12/05/2011	C82(3)	C85(3)	C87(3)	C88(3)	C90(3)	C91(3)	C94(3)	C96(3)	C99(2)	C104(2)	C3(2)
71	replacement of 13	YES	EIVS_CARDAM_SE1_10HCE040_46.xls		CARDAM_SE	1	12/05/2011	C99(3)	C104(3)	C3(3)	C11(3)	C12(3)	C13(3)	C15(3)	C16(3)	C21(3)	C25(3)	C27(3)
72		YES	EIVS_CARDAM_SE1_10HCE041_47.xls		CARDAM_SE	1	12/05/2011	C38(3)	C45(2)	C46(2)	C47(2)	C50(2)	C53(2)	C62(2)	C70(2)	C83(2)	C84(2)	C98(1)
73		YES	EIVS_CARDAM_SE1_10HCE042_48.xls		CARDAM_SE	1	12/05/2011	C45(3)	C46(3)	C47(3)	C50(3)	C53(3)	C62(3)	C70(3)	C83(3)	C84(3)	C98(2)	C101(2)
74		YES	EIVS_CARDAM_SE2_10HCE036_42.xls		CARDAM_SE	1	12/05/2011	C11(1)	C12(1)	C13(1)	C15(1)	C16(1)	C21(1)	C25(1)	C27(1)			
75		YES	EIVS_CARDAM_SE2_10HCE037_43.xls		CARDAM_SE	1	12/05/2011	C13(2)	C15(2)	C16(2)	C21(2)	C25(2)	C27(2)	C38(1)				
76		YES	EIVS_CARDAM_SE2_10HCE040_46.xls		CARDAM_SE	1	12/05/2011	C46(1)	C47(1)	C50(1)	C53(1)	C62(1)	C70(1)	C83(1)	C84(1)			
77	replacement of 15	YES	EIVS_CARDAM_SE2_10HCE041_47.xls		CARDAM_SE	1	12/05/2011	C123(1)	C127(1)	C132(1)	C134(1)	C6(1)						
78	replacement of 16	YES	EIVS_CARDAM_SE2_10HCE042_48.xls		CARDAM_SE	1	12/05/2011	C127(2)	C132(2)	C134(2)	C135(1)	C136(1)	C138(1)	C6(2)				
79	replacement of 8	YES	EIVS_CARDAM_SE_10HCE033Kt_40.xlsx		CARDAM_SE	1	12/05/2011	C6(Kt)	C30(Kt)	C34(Kt)	C54(Kt)	C75(Kt)	C87(Kt)	C90(Kt)	C104(Kt)			
80		YES	EIVS_CARDAM_SE_10HCE033kt_45.xls		CARDAM_SE	1	12/05/2011	C3(Kt)										
81	replacement of 9	YES	EIVS_CARDAM_SE_10HCE044_50.xls		CARDAM_SE	1	12/05/2011	C45(4)	C53(4)	C98(3)	C101(3)	C119(3)	C123(3)	C127(3)	C132(3)	C83(4)	C6(3)	
82		YES	EIVS_CARDAM_SE_11HCE001_Kt_2.xls		CARDAM_SE	1	12/05/2011	C45(Kt)	C53(Kt)	C101(Kt)	C113(Kt)	C135(Kt)	C128(Kt)					
83		YES	EIVS_CARDAM_SE_11HCE003_3.xls		CARDAM_SE	1	12/05/2011	C105(1)	C106(1)	C107(1)	C108(1)	C139(1)	C110(1)	C112(1)	C134(3)	C135(2)	C136(2)	C138(2)
84		YES	EIVS_CARDAM_SE_11HCE005_5.xls		CARDAM_SE	1	12/05/2011	C105(2)	C106(2)	C107(2)	C108(2)	C139(2)	C110(2)	C112(2)	C113(1)	C135(3)	C136(3)	C138(3)
85		YES	EIVS_CARDAM_SE_11HCE006_6.xls		CARDAM_SE	1	12/05/2011	C105(3)	C106(3)	C107(3)	C108(3)	C139(3)	C110(3)	C112(3)	C113(2)	C116(1)	C120(1)	C124(1)
86		YES	EIVS_CARDAM_SE_11HCE007_7.xls		CARDAM_SE	1	12/05/2011	C113(3)	C109(1)	C116(2)	C120(2)	C125(1)	C129(1)	C131(1)				
87		YES	EIVS_CARDAM_SE_11HCE008_8.xls		CARDAM_SE	1	12/05/2011	C124(2)	C109(2)	C125(2)	C129(2)	C131(2)						
88		YES	EIVS_CARDAM_SE_11HCE009_9.xls		CARDAM_SE	1	12/05/2011	C124(3)	C109(3)	C125(3)	C129(3)	C131(3)	C116(3)	C120(3)				
89	replaced by 135	NO	EIVS_CEETOX_SE_11HCE008_8_v1.0 JOEY.xls		CEETOX_SE	1	16/06/2011	x13(1)	x39(1)	x8(1)	x128(1)							
90	replaced by 136	NO	EIVS_CEETOX_SE_11HCE008_8_v1.0 LISA.xls		CEETOX_SE	1	16/06/2011	x62(1)	x64(1)	x65(1)	x81(1)	x82(1)	x117(1)	x43(1)	x44(1)			
91	MTT data needed	NO	EIVS_CEETOX_SE_11HCE010 FK_16_v1.0 Set 1.xls	CEETOX_SE	1	16/06/2011		X39(1)	X8(1)	X27(1)	X46(1)	X87(1)	X109(1)	X110(1)	X119(1)	X133(1)	X136(1)	
92		YES	EIVS_CEETOX_SE_11HCE010 FK_16_v1.0 Set 2.xls	CEETOX_SE	1	16/06/2011		x139(1)										
93	replaced by 137	NO	EIVS_CEETOX_SE_11HCE013_13_v1.0 Set 1.xls		CEETOX_SE	1	16/06/2011	x13(3)	x39(3)	x8(3)	x128(3)	x43(3)	x62(3)	x64(3)				
94	replaced by 138	NO	EIVS_CEETOX_SE_11HCE013_13_v1.0 Set 2.xls		CEETOX_SE	1	16/06/2011	x65(3)	x81(3)	x82(3)	x117(3)	x112(1)	x126(1)	x21(1)				
95		YES	EIVS_CARDAM_SE_11HCE020 Killed_22.xls		CARDAM_SE	1	19/07/2011	C48(Kt)	C58(Kt)	C141(Kt)	C170(Kt)	C195(Kt)						
96		YES	EIVS_CARDAM_SE_11HCE020_18.xls		CARDAM_SE	1	19/07/2011	C4(1)	C9(1)	C20(1)	C39(1)	C28(1)	C48(1)	C52(1)	C55(1)	C58(1)		
97		YES	EIVS_CARDAM_SE_11HCE022_19.xls		CARDAM_SE	1	19/07/2011	C4(2)	C9(2)	C14(1)	C20(2)	C28(2)	C29(1)	C39(2)	C48(2)	C52(2)		
98		YES	EIVS_CARDAM_SE_11HCE024_20.xls		CARDAM_SE	1	19/07/2011	C4(3)	C9(3)	C14(2)	C28(3)	C29(2)	C52(3)	C56(1)	C58(2)			
99		YES	EIVS_CARDAM_SE_11HCE026_21.xls		CARDAM_SE	1	19/07/2011	C14(3)	C20(3)	C29(3)	C52(4)	C56(2)	C64(1)	C67(1)	C71(1)	C97(1)	C114(1)	
100		YES	EIVS_CARDAM_SE_11HCE029_23.xls		CARDAM_SE	1	19/07/2011	C39(3)	C48(3)	C55(2)	C52(5)	C56(3)	C58(3)	C103(1)	C137(1)	C140(1)	C141(1)	
101		YES	EIVS_CARDAM_SE_11HCE032_25.xls		CARDAM_SE	1	19/07/2011	C55(3)	C64(2)	C67(2)	C163(1)	C164(1)	C166(1)	C170(1)	C185(1)	C193(1)	C195(1)	C196(1)
102		YES	EIVS_CARDAM_SE_11HCE034_26.xls		CARDAM_SE	1	19/07/2011	C97(2)	C103(2)	C114(2)	C137(2)	C140(2)	C141(2)	C163(2)	C164(2)	C166(2)	C170(2)	C185(2)
103		YES	EIVS_CARDAM_SE_11HCE036_27.xls		CARDAM_SE	1	19/07/2011	C64(3)	C67(3)	C71(3)	C97(3)	C103(3)	C114(3)	C137(3)	C140(3)	C141(3)	C163(3)	C195(2)
104		YES	EIVS_CARDAM_SE_11HCE038_28.xls		CARDAM_SE	1	19/07/2011	C164(3)	C166(3)	C170(3)	C185(3)	C193(3)	C195(3)	C196(3)				

105	replaced by 139	NO	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls		CEETOX_SE	1	08/08/2011	X21(3)	X112(3)	X126(3)	X14(1)	X46(1)	X27(1)					
106	MTT data needed	NO	EIVS_CEETOX_SE_11HCE029_30_v1.0.xls		CEETOX_SE	1	11/08/2011	X24(1)	X32(1)	X42(1)	X95(1)	X143(1)	X165(1)	X173(1)				
107		YES	EIVS_LOREAL_SE_11HCE020_18.xls		LOREAL_SE	1	12/08/2011	L1(1)	L6(1)	L13(1)	L15(1)	L16(1)	L32(1)	L33(1)	L36(1)	L37(1)		
108		NO	EIVS_LOREAL_SE_11HCE022_19.xls		LOREAL_SE	1	12/08/2011	L50(1)	L53(1)	L58(1)	L62(1)	L65(1)	L76(1)	L80(1)	L100(1)	L111(1)	L125(1)	L127(1)
109		YES	EIVS_LOREAL_SE_11HCE024_20.xls		LOREAL_SE	1	12/08/2011	L144(1)	L148(1)	L156(1)	L161(1)	L164(1)	L169(1)	L174(1)	L185(1)	L200(1)	L15(2)	L6(2)
110		YES	EIVS_LOREAL_SE_11HCE026_21.xls		LOREAL_SE	1	12/08/2011	L1(2)	L13(2)	L16(2)	L32(2)	L33(2)	L36(2)	L37(2)	L50(2)	L53(2)		
111		NO	EIVS_LOREAL_SE_11HCE029_23.xls		LOREAL_SE	1	12/08/2011	L33(3)	L58(2)	L62(2)	L65(2)	L76(2)	L80(2)	L100(2)	L111(2)	L161(2)	L169(2)	L174(2)
112		NO	EIVS_LOREAL_SE_11HCE032_25(1).xls		LOREAL_SE	1	12/08/2011	L125(2)	L127(2)	L144(2)	L148(2)	L156(2)	L164(2)	L185(2)	L200(2)	L1(3)	L6(3)	L13(3)
113		YES	EIVS_LOREAL_SE_11HCE032_25(2).xls		LOREAL_SE	1	12/08/2011	L100(3)										
114		NO	EIVS_LOREAL_SE_11HCE034_26(1).xls		LOREAL_SE	1	12/08/2011	L6(4)	L15(3)	L32(3)	L36(3)	L37(3)	L50(3)	L53(3)	L58(4)	L62(3)	L65(3)	L76(3)
115		YES	EIVS_LOREAL_SE_11HCE034_26(2).xls		LOREAL_SE	1	12/08/2011	L111(3)	L125(3)	L127(3)	L144(3)	L148(3)	L156(3)	L161(3)				
116		NO	EIVS_LOREAL_SE_11HCE036_27.xls		LOREAL_SE	1	12/08/2011	L6(5)	L58(5)	L164(3)	L100(5)	L169(3)	L174(3)	L185(3)	L200(3)			
117		YES	EIVS_LOREAL_SE_11HCE002_2.xls		LOREAL_SE	1	18/08/2011	L122(1)	L123(1)	L126(1)	L129(1)	L133(1)	L134(1)	L136(1)	L137(1)	L139(1)	L140(1)	L114(2)
118		YES	EIVS_LOREAL_SE_11HCE006_6.xls		LOREAL_SE	1	18/08/2011	L70(3)	L72(3)	L90(3)	L99(3)	L104(2)	L106(3)	L107(3)	L108(3)			
119		YES	EIVS_LOREAL_SE_11HCE007_7.xls		LOREAL_SE	1	18/08/2011	L109(3)	L112(3)	L113(3)	L114(3)	L115(3)	L118(2)	L119(2)	L120(2)	L122(2)	L123(2)	
120		YES	EIVS_LOREAL_SE_11HCE008_8.xls		LOREAL_SE	1	18/08/2011	L118(3)	L119(3)	L120(3)	L122(3)	L123(3)	L126(2)	L129(2)	L130(2)	L131(2)	L132(2)	L133(2)
121		YES	EIVS_LOREAL_SE_11HCE009_9.xls		LOREAL_SE	1	18/08/2011	L126(3)	L129(3)	L130(3)	L131(3)	L132(3)	L133(3)	L134(3)	L136(2)	L137(2)	L139(2)	L140(2)
122		YES	EIVS_LOREAL_SE_11HCE014_14.xls		LOREAL_SE	1	18/08/2011	L136(3)	L137(3)	L139(3)	L140(3)							
123	replacement of 17	YES	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls		CEETOX_SE	2	31/10/2011	x1(1)	x2(1)	x5(1)	x6(1)	x7(1)	x16(1)	x22(1)	x28(1)	x36(1)	x38(1)	
124	replacement of 18	YES	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls		CEETOX_SE	2	31/10/2011	x1(2)	x2(2)	x5(2)	x6(2)	x7(2)	x16(2)	x22(2)	x28(2)	x36(2)	x38(2)	
125	replacement of 19	YES	EIVS_CEETOX_SE_10HCE025_27_v1.0.XLS		CEETOX_SE	2	31/10/2011	x1(3)	x2(3)	x5(3)	x6(3)	x7(3)	x16(3)	x22(3)	x28(3)	x36(3)	x38(3)	
126	replacement of 20	YES	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls		CEETOX_SE	2	31/10/2011	x63(1)	x72(1)	x73(1)	x83(1)	x86(1)	x89(1)	x93(1)	x98(1)	x99(1)	x103(1)	
127	replacement of 21	YES	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls		CEETOX_SE	2	31/10/2011	x63(2)	x72(2)	x73(2)	x83(2)	x86(2)	x89(2)	x93(2)	x98(2)	x99(2)	x103(2)	
128	replacement of 22	YES	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls		CEETOX_SE	2	31/10/2011	x63(3)	x72(3)	x73(3)	x83(3)	x86(3)	x89(3)	x93(3)	x98(3)	x99(3)	x103(3)	
129	replacement of 23	YES	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls		CEETOX_SE	2	31/10/2011	x45(1)	x47(1)	x49(1)	x51(1)	x52(1)	x59(1)	x68(1)				
130	replacement of 24	YES	EIVS_CEETOX_SE_10HCE044_50_v1.0.xls		CEETOX_SE	2	31/10/2011	x45(2)	x47(2)	x49(2)	x51(2)	x52(2)	x59(2)	x68(2)				
131	replacement of 25	YES	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.XLS		CEETOX_SE	2	31/10/2011	x45(3)	x47(3)	x49(3)	x51(3)	x52(3)	x59(3)	x68(3)				
132	replacement of 26	YES	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls		CEETOX_SE	2	31/10/2011	x41(1)	x17(1)	x31(1)	x91(1)	x121(1)	x3(1)	x25(1)	x30(1)	x33(1)		
133	replacement of 67	YES	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls		CEETOX_SE	2	31/10/2011	x41(2)	x17(2)	x31(2)	x91(2)	x121(2)	x3(2)	x25(2)	x30(2)	x33(2)		
134	replacement of 68	YES	EIVS_CEETOX_SE_11HCE007_7_v1.0.xls		CEETOX_SE	2	31/10/2011	x41(3)	x17(3)	x31(3)	x91(3)	x121(3)	x3(3)	x25(3)	x30(3)	x33(3)		
135	replacement of 89	YES	EIVS_CEETOX_SE_11HCE008_8_v1.0 JOEY.xls		CEETOX_SE	2	31/10/2011	x13(1)	x39(1)	x8(1)	x128(1)							
136	replacement of 90	YES	EIVS_CEETOX_SE_11HCE008_8_v1.0 LISA.xls		CEETOX_SE	2	31/10/2011	x62(1)	x64(1)	x65(1)	x81(1)	x82(1)	x117(1)	x43(1)	x44(1)			
137	replacement of 93	YES	EIVS_CEETOX_SE_11HCE013_13_v1.0 Set 1.xls		CEETOX_SE	2	31/10/2011	x13(3)	x39(3)	x8(3)	x128(3)	x43(3)	x62(3)	x64(3)				
138	replacement	YES	EIVS_CEETOX_SE_11HCE013_13_v1.0 Set		CEETOX_SE	2	31/10/2011	x65(3)	x81(3)	x82(3)	x117(3)	x112(1)	x126(1)	x21(1)				

	of 94		2.xls																
139	replacement of 105	YES	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls		CEETOX_SE	2	11/11/2011	X21(3)	X112(3)	X126(3)	X14(1)	X46(1)	X27(1)						
140		YES	EIVS_CEETOX_SE_11HCE009_9_v1.0 LISA.xls		CEETOX_SE	1	31/10/2011	x62(2)	x65(2)	x81(2)	x82(2)	x117(2)	#REF!	#REF!					
141		YES	EIVS_CEETOX_SE_11HCE009_9_v1.0.xls		CEETOX_SE	1	31/10/2011	x13(1)	x39(2)	x8(2)	x128(2)	x64(2)	x43(2)	x44(2)					
142		YES	EIVS_CEETOX_SE_11HCE020_18_v1.0.xls		CEETOX_SE	1	11/11/2011	X13(4)	X21(2)	X112(2)	X126(2)	X81 FK(2)	X108 FK(1)	X118 FK(1)					
143		YES	EIVS_CEETOX_SE_11HCE047_37_v1.0 UPDATED.xls	CEETOX_SE	1	31/01/2012		X27(2)	X46(2)	X50(1)	X53(1)	X70(1)	X84(1)	X87(1)	X102(1)	X107(1)	X108(1)	X109(1)	
144		YES	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls		CEETOX_SE	1	11/11/2011	X14(3)	X27(3)	X46(3)	X50(2)	X53(2)	X70(2)	X84(2)	X87(2)	X102(2)	X107(2)	X108(2)	
145		YES	EIVS_CEETOX_SE_11HCE051_39_v1.0 SET 1.xls		CEETOX_SE	1	11/11/2011	X50(3)	X53(3)	X70(3)	X84(3)	X87(3)	X102(3)	X107(3)					
146		YES	EIVS_CEETOX_SE_11HCE051_39_v1.0 SET 2.xls		CEETOX_SE	1	11/11/2011	X108(3)	X109(3)	X110(1)	X111(1)	X114(1)	X115(1)	X116(1)					
147		YES	EIVS_CEETOX_SE_11HCE053_40_v1.0 SET 1.xls		CEETOX_SE	1	11/11/2011	X110(2)	X111(2)	X114(2)	X115(2)	X116(2)	X118(1)	X119(1)					
148		YES	EIVS_CEETOX_SE_11HCE053_40_v1.0 SET 2.xls		CEETOX_SE	1	11/11/2011	X123(1)	X125(1)	X129(1)	X131(1)	X133(1)	X134(1)	X136(1)					
149		YES	EIVS_CEETOX_SE_11HCE055_41_v1.0 SET 1.xls		CEETOX_SE	1	11/11/2011	X37(1)	X143(1)	X190(1)	X131(2)	X119(2)	X173(1)	X169(1)					
150		YES	EIVS_CEETOX_SE_11HCE055_41_v1.0 SET 2.xls		CEETOX_SE	1	11/11/2011	X133(2)	X127(1)	X139(1)	X40(1)	X111(3)	X138(1)						
151		YES	EIVS_CEETOX_SE_11HCE057_42_v1.0 SET 1.xls		CEETOX_SE	1	11/11/2011	X37(2)	X143(2)	X190(2)	X131(3)	X119(3)	X173(2)	X169(2)					
152		YES	EIVS_CEETOX_SE_11HCE057_42_v1.0 SET 2.xls		CEETOX_SE	1	11/11/2011	X133(3)	X127(2)	X139(2)	X40(2)	X138(2)							
153		YES	EIVS_CEETOX_SE_11HCE059_43_v1.0 SET 1.xls		CEETOX_SE	1	16/12/2011	X37(3)	X143(3)	X190(3)	X173(3)	X169(3)	X127(3)	X139(3)					
154		YES	EIVS_CEETOX_SE_11HCE059_43_v1.0 SET 2.xls		CEETOX_SE	1	16/12/2011	X40(3)	X138(3)	X118(2)	X125(2)	X123(2)	X134(2)	X129(2)					
155		YES	EIVS_CEETOX_SE_11HCE061_44_v1.0 SET 1.xls		CEETOX_SE	1	16/12/2011	X118(3)	X125(3)	X123(3)	X134(3)	X129(3)	X196(1)	X110(3)					
156		YES	EIVS_CEETOX_SE_11HCE061_44_v1.0 SET 2.xls		CEETOX_SE	1	16/12/2011	X114(3)	X115(3)	X116(3)	X136(2)	X11(1)	X19(1)	X29(1)					
157		YES	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls		CEETOX_SE	1	16/12/2011	X11(2)	X19(2)	X29(2)	X196(2)	X136(3)	X24(1)	X32(1)	X42(1)	X55(1)	X56(1)		
158		YES	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls		CEETOX_SE	1	04/01/2012	X19(3)	X196(3)	X24(2)	X32(2)	X42(2)	X55(2)	X56(2)	X61(1)	X66(1)	X75(1)	X77(1)	
159		YES	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls		CEETOX_SE	1	04/01/2012	X61(2)	X66(2)	X75(2)	X77(2)	X80(2)	X94(1)	X95(1)	X113(1)	X120(1)	X157(1)	X158(1)	
160		YES	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls		CEETOX_SE	1	04/01/2012	X11(3)	X19(4)	X24(3)	X29(3)	X94(2)	X95(2)	X113(2)	X120(2)	X157(2)	X158(2)	X160(2)	
161		YES	EIVS_CEETOX_SE_12HCE002_2_v1.0.xls		CEETOX_SE	1	24/01/2012	X32(3)	X42(3)	X55(3)	X56(3)								
162		YES	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls		CEETOX_SE	1	24/01/2012	X61(3)	X66(3)	X75(3)	X77(3)	X80(3)	X94(3)	X95(3)	X113(3)	X120(3)	X157(3)	X158(3)	
163	replacement of 108	YES	EIVS_LOREAL_SE_11HCE022_19 (L58 retested on killed tissues oct2012).xlsx	EIVS_LOREAL_SE_11HCE022_19	LOREAL_SE	2	16/11/2012	L50(1)	L53(1)	L58(1)	L62(1)	L65(1)	L76(1)	L80(1)	L100(1)	L111(1)	L125(1)	L127(1)	
164	replacement of 111	YES	EIVS_LOREAL_SE_11HCE029_23 (L58 retested on killed tissues Oct2012).xlsx	EIVS_LOREAL_SE_11HCE029_23	LOREAL_SE	2	16/11/2012	L33(3)	L58(2)	L62(2)	L65(2)	L76(2)	L80(2)	L100(2)	L111(2)	L161(2)	L169(2)	L174(2)	
165	replacement of 112	YES	EIVS_LOREAL_SE_11HCE032_25(1) (L58 retested on killed tissues Oct2012).xlsx	EIVS_LOREAL_SE_11HCE032_25(1)	LOREAL_SE	2	16/11/2012	L125(2)	L127(2)	L144(2)	L148(2)	L156(2)	L164(2)	L185(2)	L200(2)	L1(3)	L6(3)	L13(3)	
166	replacement of 114	YES	EIVS_LOREAL_SE_11HCE034_26(1) (L58 retested on killed tissues Oct2012).xlsx	EIVS_LOREAL_SE_11HCE034_26(1)	LOREAL_SE	2	16/11/2012	L6(4)	L15(3)	L32(3)	L36(3)	L37(3)	L50(3)	L53(3)	L58(4)	L62(3)	L65(3)	L76(3)	
167	replacement of 116	YES	EIVS_LOREAL_SE_11HCE036_27 (L58 retested on killed tissues Oct2012).xlsx	EIVS_LOREAL_SE_11HCE036_27	LOREAL_SE	2	16/11/2012	L6(5)	L58(5)	L164(3)	L100(5)	L169(3)	L174(3)	L185(3)	L200(3)				

LE

No	Remark	Used	Filename	Saved as	LAB	v	date of receipt	content												
1		YES	EIVS_CARDAM_LE_10HCE029_35.xls		CARDAM_LE	1	01/01/2011	C1(1)	C2(1)	C17(1)	C19(1)	C26(1)	C30(1)	C33(1)	C34(1)	C35(1)				
2		YES	EIVS_CARDAM_LE_10HCE031_37.xls		CARDAM_LE	1	01/01/2011	C1(2)	C2(2)	C17(2)	C19(2)	C26(2)	C30(2)	C33(2)	C34(2)	C35(2)				
3		YES	EIVS_CARDAM_LE_10HCE032_38.xls		CARDAM_LE	1	01/01/2011	C1(3)	C2(3)	C17(3)	C19(3)	C26(3)	C30(3)	C77(1)	C34(3)	C35(3)				
4	Opening file failed	NO	EIVS_CARDAM_LE_10HCE033_W39.xls		CARDAM_LE	1	01/01/2011													
5		YES	EIVS_CARDAM_LE_10HCE033_W39_(C77).xls		CARDAM_LE	1	01/01/2011	C77(2)												
6		NO	EIVS_CARDAM_LE_10HCE033Kt_40.xlsx		CARDAM_LE	1	01/01/2011	C6(Kt)	C30(Kt)	C34(Kt)	C54(Kt)	C75(Kt)	C87(Kt)	C90(Kt)	C104(Kt)					
7		NO	EIVS_CARDAM_LE_10HCE033kt_45.xlsx		CARDAM_LE	1	01/01/2011	C3(Kt)	C87(Kt)											
8	Wrong file name	NO	EIVS_LABNAME_LE_10HCE034_40.xls		LABNAME_LE	1	01/01/2011	C36(1)	C37(1)	C49(1)	C51(1)	C54(1)	C60(1)	C63(1)	C65(1)	C66(1)	C75(1)	C76(1)	C77(1)	C78(1)
9		NO	EIVS_CARDAM_LE_10HCE044_50.xlsx		CARDAM_LE	1	01/01/2011	C45(4)	C84(2)	C98(2)	C101(2)	C119(3)	C123(2)	C127(2)	C132(2)	C135(2)	C6(3)			
10	incorrect run numbers	NO	EIVS_CARDAM_LE1_10HCE035_41.xls		CARDAM_LE	1	01/01/2011	C36(3)	C37(3)	C49(3)	C51(3)	C54(3)	C60(3)	C63(3)	C65(3)	C66(3)	C75(3)	C76(3)	C77(2)	C78(2)
11		YES	EIVS_CARDAM_LE1_10HCE036_42.xls		CARDAM_LE	1	01/01/2011	C36(3)	C37(3)	C49(3)	C51(3)	C54(3)	C60(3)	C63(3)	C65(3)	C66(3)	C75(3)	C76(3)	C78(2)	C79(2)
12		NO	EIVS_CARDAM_LE1_10HCE037_43.xlsx		CARDAM_LE	1	01/01/2011	C78(3)	C79(3)	C82(3)	C85(3)	C87(3)	C88(3)	C90(3)	C91(3)	C94(2)	C96(3)	C99(1)	C104(1)	C3(1)
13		NO	EIVS_CARDAM_LE1_10HCE040_46.xls		CARDAM_LE	1	01/01/2011	C94(3)	C99(2)	C104(2)	C3(2)	C11(2)	C12(2)	C13(2)	C15(2)	C16(2)	C21(2)	C25(2)	C27(2)	C38(1)
14		NO	EIVS_CARDAM_LE1_10HCE041_47.xls		CARDAM_LE	1	01/01/2011	C99(3)	C104(3)	C3(3)	C11(3)	C12(3)	C13(3)	C15(3)	C16(3)	C21(3)	C25(3)	C27(3)	C38(2)	C45(2)
15	wrong run number C79	NO	EIVS_CARDAM_LE2_10HCE035_41.xlsx		CARDAM_LE	1	01/01/2011	C79(2)	C82(1)	C85(1)	C87(1)	C88(1)	C90(1)	C91(1)	C96(1)					
16		NO	EIVS_CARDAM_LE2_10HCE041_47.xls		CARDAM_LE	1	01/01/2011	C46(2)	C47(2)	C50(2)	C53(2)	C62(2)	C70(2)	C83(2)	C119(1)	C6(1)				
17		NO	EIVS_CARDAM_LE2_10HCE042_48.xls		CARDAM_LE	1	01/01/2011	C123(1)	C127(1)	C132(1)	C134(1)	C135(1)	C6(2)							
18	Wrong file name	NO	EIVS_LABNAME_LE_10HCE034_40(C79).xls		LABNAME_LE	1	01/01/2011	C79(1)												
19		YES	EIVS_CARDAM_LE2_10HCE036_42.xls		CARDAM_LE	1	01/01/2011	C82(2)	C85(2)	C87(2)	C88(2)	C90(2)	C91(2)	C94(1)	C96(2)					
20		NO	EIVS_CEETOX_LE_10HCE023_25_v1.0.xls		CEETOX_LE	1	09/02/2011	x1(1)	x2(1)	x5(1)	x6(1)	x7(1)	x16(1)	x22(1)	x28(1)	x36(1)	x38(1)			
21		NO	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls		CEETOX_LE	1	09/02/2011	x1(2)	x2(2)	x5(2)	x6(2)	x7(2)	x16(2)	x22(2)	x28(2)	x36(2)	x38(2)			
22		NO	EIVS_CEETOX_LE_10HCE042_48_v1.0.xls		CEETOX_LE	1	09/02/2011	x1(3)	x2(3)	x5(3)	x6(3)	x7(3)	x16(3)	x22(3)	x28(3)	x36(3)	x38(3)			
23		NO	EIVS_CEETOX_LE_10HCE043_49_v1.0.xls		CEETOX_LE	1	09/02/2011	x1(4)	x2(4)	x5(4)	x6(4)	x7(4)	x16(4)	x22(4)	x28(4)	x36(4)	x38(4)			
24		NO	EIVS_CEETOX_LE_10HCE044_50_v1.0.xls		CEETOX_LE	1	09/02/2011	x1(5)	x2(5)	x5(5)	x6(5)	x7(5)	x16(5)	x22(5)	x28(5)	x36(5)	x38(5)			
25		NO	EIVS_CEETOX_LE_11HCE003_3_v1.0 .xls		CEETOX_LE	1	09/02/2011	x63(1)	x72(1)	x73(1)	x83(1)	x86(1)	x89(1)	x93(1)	x98(1)	x99(1)	x103(1)			
26	equal to 25	NO	EIVS_CEETOX_LE_11HCE003_3_v1.0 SET 1.xls		CEETOX_LE	1	26/01/2011	x63(1)	x72(1)	x73(1)	x83(1)	x86(1)	x89(1)	x93(1)	x98(1)	x99(1)	x103(1)			
27		NO	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY.XLS		CEETOX_LE	1	09/02/2011	x45(2)	x47(2)	x49(1)	x51(2)	x52(2)	x59(2)	x68(2)						
28		NO	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls		CEETOX_LE	1	09/02/2011	x41(1)	x17(1)	x31(1)	x91(1)	x121(1)	x3(1)	x25(1)	x30(1)	x33(1)				
29	replacement of 4	YES	EIVS_CARDAM_LE_10HCE033_W39.xls		CARDAM_LE	2	25/02/2011	C33(3)	C35(4)	C36(1)	C37(1)	C49(1)	C51(1)	C54(1)	C60(1)	C63(1)	C65(1)	C66(1)	C75(1)	C76(1)
30	replacement of 8; non-qual NC/PC	YES	EIVS_CARDAM_LE_10HCE034_40.xls		CARDAM_LE	2	25/02/2011	C36(1)	C37(1)	C49(1)	C51(1)	C54(1)	C60(1)	C63(1)	C65(1)	C66(1)	C75(1)	C76(1)	C77(1)	C78(1)
31	replacement of 18; non-qual NC/PC	YES	EIVS_CARDAM_LE_10HCE034_40(C79).xls		CARDAM_LE	1	25/02/2011	C79(1)												
32	replacement of 10	YES	Corrected of EIVS_CARDAM_LE1_10HCE035_41.xls	EIVS_CARDAM_LE1_10HCE035_41.xls	CARDAM_LE	2	25/02/2011	C36(2)	C37(2)	C49(2)	C51(2)	C54(2)	C60(2)	C63(2)	C65(2)	C66(2)	C75(2)	C76(2)	C77(3)	C78(1)
33		NO	EIVS_LOREAL_LE_10HCE023_25.xls		LOREAL_LE	1	02/03/2011	L5(1)	L9(1)	L11(1)	L12(1)	L17(1)	L18(1)	L20(1)	L23(1)	L24(1)	L27(1)	L28(1)		
34		NO	EIVS_LOREAL_LE_10HCE024_26.xls		LOREAL_LE	1	02/03/2011	L5(2)	L9(2)	L11(2)	L12(2)	L17(2)	L18(2)	L20(2)	L23(2)	L24(2)	L27(2)	L28(2)		
35		NO	EIVS_LOREAL_LE_10HCE025_27.xls		LOREAL_LE	1	02/03/2011	L30(1)	L39(1)	L43(1)	L45(1)	L48(1)	L51(1)	L55(1)	L59(1)	L60(1)	L66(1)	L68(1)	L11(3)	
36		NO	EIVS_LOREAL_LE_10HCE026_28.xls		LOREAL_LE	1	02/03/2011	L9(3)	L12(3)	L17(3)	L20(3)	L27(3)	L43(2)							
37		NO	EIVS_LOREAL_LE_10HCE027_29.xls		LOREAL_LE	1	02/03/2011	L30(1)	L39(1)	L43(1)	L45(1)	L48(1)	L51(1)	L55(1)	L59(1)	L60(1)	L66(1)	L68(1)	L73(3)	

38		NO	EIVS_LOREAL_LE_10HCE028_30.xls		LOREAL_LE	1	02/03/2011	L5(2)	L11(2)	L23(2)	L24(2)	L30(2)	L39(2)	L48(2)	L51(2)	L55(2)	L60(2)	L68(2)		
39		NO	EIVS_LOREAL_LE_10HCE029_35.xls		LOREAL_LE	1	02/03/2011	L74(1)	L75(1)	L78(1)	L81(1)	L82(1)	L85(1)	L91(1)	L94(1)	L97(1)	L98(1)	L102(1)		
40		NO	EIVS_LOREAL_LE_10HCE031_37.xls		LOREAL_LE	1	02/03/2011	L45(3)	L59(3)	L66(3)	L74(2)	L82(2)	L94(2)							
41		NO	EIVS_LOREAL_LE_10HCE032_38.xls		LOREAL_LE	1	02/03/2011	L74(3)	L75(2)	L78(2)	L81(2)	L82(3)	L85(2)	L91(2)	L94(3)	L97(2)	L98(2)	L102(2)		
42		NO	EIVS_LOREAL_LE_10HCE033_39.xls		LOREAL_LE	1	02/03/2011	L18(3)	L28(3)	L39(3)	L73(2)	L75(3)	L78(3)	L81(3)	L85(3)	L91(3)	L97(3)			
43		NO	EIVS_LOREAL_LE_10HCE034_40(1).xls		LOREAL_LE	1	02/03/2011	L73(3)	L74(4)	L75(4)	L78(4)	L81(4)	L82(4)	L91(4)	L94(4)	L97(4)	L98(3)	L102(3)		
44		NO	EIVS_LOREAL_LE_10HCE034_40(2).xls		LOREAL_LE	1	02/03/2011	L4(1)	L7(1)	L8(1)										
45		NO	EIVS_LOREAL_LE_10HCE035_41.xls		LOREAL_LE	1	02/03/2011	L85(4)	L98(4)	L4(2)	L7(2)	L8(2)	L29(1)	L42(1)	L56(1)	L57(1)	L61(1)	L63(1)	L64(1)	
46		NO	EIVS_LOREAL_LE_10HCE036_42.xls		LOREAL_LE	1	02/03/2011	L102(4)	L7(3)	L29(2)	L57(2)									
47		NO	EIVS_LOREAL_LE_10HCE037_43.xls		LOREAL_LE	1	02/03/2011	L4(3)	L8(3)	L29(3)	L42(2)	L56(2)	L61(2)	L57(2)	L63(2)	L64(2)	L67(1)	L70(1)		
48		NO	EIVS_LOREAL_LE_10HCE040_46.xls		LOREAL_LE	1	02/03/2011	L42(3)	L56(3)	L61(3)	L63(3)	L64(3)	L67(2)	L70(2)	L72(1)	L79(1)	L83(1)	L87(1)	L92(1)	
49		NO	EIVS_LOREAL_LE_10HCE041_47.xls		LOREAL_LE	1	02/03/2011	L67(3)	L72(2)	L79(2)	L83(2)	L87(2)	L90(1)	L92(2)	L96(1)	L99(1)	L101(1)			
50		NO	EIVS_LOREAL_LE_10HCE042_48.xls		LOREAL_LE	1	02/03/2011	L87(3)	L90(2)	L92(3)	L99(2)	L104(1)	L119(1)	L120(1)	L130(1)	L131(1)	L132(1)			
51		NO	EIVS_LOREAL_LE_10HCE043_49.xls		LOREAL_LE	1	02/03/2011	L83(3)	L96(2)	L101(2)	L104(2)	L106(1)	L107(1)	L108(1)	L109(1)	L112(1)	L113(1)			
52		NO	EIVS_LOREAL_LE_10HCE044_50.xls		LOREAL_LE	1	02/03/2011	L79(3)	L96(3)	L101(3)	L106(2)	L107(2)	L108(2)	L109(2)	L112(2)	L113(2)	L114(1)	L115(1)	L118(1)	
53		NO	EIVS_LOREAL_LE_11HCE005_5.xls		LOREAL_LE	1	02/03/2011	Kt-L70	Kt-L72	Kt-L90	Kt-L99	Kt-L104	Kt-L107	Kt-L119	Kt-L120	Kt-L132	Kt-L133			
54	replacement of 33	YES	EIVS_LOREAL_LE_10HCE023_25.xls		LOREAL_LE	2	16/03/2011	L5(1)	L9(1)	L11(1)	L12(1)	L17(1)	L18(1)	L20(1)	L23(1)	L24(1)	L27(1)	L28(1)		
55	replacement of 34	YES	EIVS_LOREAL_LE_10HCE024_26.xls		LOREAL_LE	2	16/03/2011	L5(2)	L9(2)	L11(2)	L12(2)	L17(2)	L18(2)	L20(2)	L23(2)	L24(2)	L27(2)	L28(2)		
56	replacement of 35	YES	EIVS_LOREAL_LE_10HCE025_27.xls		LOREAL_LE	2	16/03/2011	L30(1)	L39(1)	L43(1)	L45(1)	L48(1)	L51(1)	L55(1)	L59(1)	L60(1)	L66(1)	L68(1)	L11(3)	
57	replacement of 36	YES	EIVS_LOREAL_LE_10HCE026_28.xls		LOREAL_LE	2	16/03/2011	L9(3)	L12(3)	L17(3)	L20(3)	L27(3)	L43(2)							
58	replacement of 37	YES	EIVS_LOREAL_LE_10HCE027_29.xls		LOREAL_LE	2	16/03/2011	L30(2)	L39(1)	L43(3)	L45(2)	L48(2)	L51(2)	L55(2)	L59(2)	L60(2)	L66(2)	L68(2)	L73(1)	
59	replacement of 38	YES	EIVS_LOREAL_LE_10HCE028_30.xls		LOREAL_LE	2	16/03/2011	L5(3)	L11(4)	L23(3)		L24(3)	L30(3)	L39(2)	L48(3)	L51(3)	L55(3)	L60(3)	L68(3)	
	replacement of 39;							L74(1)	L75(1)	L78(1)	L81(1)	L82(1)	L85(1)	L91(1)	L94(1)	L97(1)	L98(1)	L102(1)		
60	non-qual NC/PC	NO	EIVS_LOREAL_LE_10HCE029_35.xls		LOREAL_LE	2	16/03/2011													
61	replacement of 40	YES	EIVS_LOREAL_LE_10HCE031_37.xls		LOREAL_LE	2	16/03/2011	L45(3)	L59(3)	L66(3)	L74(1)	L82(1)	L94(1)							
62	replacement of 41	YES	EIVS_LOREAL_LE_10HCE032_38.xls		LOREAL_LE	2	16/03/2011	L74(2)	L75(1)	L78(1)	L81(1)	L82(2)	L85(1)	L91(1)	L94(2)	L97(1)	L98(1)	L102(1)		
63	replacement of 42	YES	EIVS_LOREAL_LE_10HCE033_39.xls		LOREAL_LE	2	16/03/2011	L18(3)	L28(3)	L39(3)	L73(2)	L75(2)	L78(2)	L81(2)	L85(2)	L91(2)	L97(2)			
64	replacement of 43	YES	EIVS_LOREAL_LE_10HCE034_40(1).xls		LOREAL_LE	2	16/03/2011	L73(3)	L74(3)	L75(3)	L78(3)	L81(3)	L82(3)	L91(3)	L94(3)	L97(3)	L98(2)	L102(2)		
65	replacement of 44	YES	EIVS_LOREAL_LE_10HCE034_40(2).xls		LOREAL_LE	2	16/03/2011	L4(1)	L7(1)	L8(1)										
66	replacement of 45	YES	EIVS_LOREAL_LE_10HCE035_41.xls		LOREAL_LE	2	16/03/2011	L85(3)	L98(3)	L4(2)	L7(2)	L8(2)	L29(1)	L42(1)	L56(1)	L57(1)	L61(1)	L63(1)	L64(1)	
67	replacement of 46	YES	EIVS_LOREAL_LE_10HCE036_42.xls		LOREAL_LE	2	16/03/2011	L102(3)	L7(3)	L29(2)	L57(2)									
68	replacement of 47	YES	EIVS_LOREAL_LE_10HCE037_43.xls		LOREAL_LE	2	16/03/2011	L4(3)	L8(3)	L29(3)	L42(2)	L56(2)	L61(2)	L57(3)	L63(2)	L64(2)	L67(1)	L70(1)		
69	replacement of 48	YES	EIVS_LOREAL_LE_10HCE040_46.xls		LOREAL_LE	2	16/03/2011	L42(3)	L56(3)	L61(3)	L63(3)	L64(3)	L67(2)	L70(2)	L72(1)	L79(1)	L83(1)	L87(1)	L92(1)	
70	replacement of 49	YES	EIVS_LOREAL_LE_10HCE041_47.xls		LOREAL_LE	2	16/03/2011	L67(3)	L72(2)	L79(2)	L83(2)	L87(2)	L90(1)	L92(2)	L96(1)	L99(1)	L101(1)			
71	replacement of 50	YES	EIVS_LOREAL_LE_10HCE042_48.xls		LOREAL_LE	2	16/03/2011	L87(3)	L90(2)	L92(3)	L99(2)	L104(1)	L119(1)	L120(1)	L130(1)	L131(1)	L132(1)			
72	replacement of 51	YES	EIVS_LOREAL_LE_10HCE043_49.xls		LOREAL_LE	2	16/03/2011	L83(3)	L96(2)	L101(2)	L104(2)	L106(1)	L107(1)	L108(1)	L109(1)	L112(1)	L113(1)			
73	replacement of 52	YES	EIVS_LOREAL_LE_10HCE044_50.xls		LOREAL_LE	2	16/03/2011	L79(3)	L96(3)	L101(3)	L106(2)	L107(2)	L108(2)	L109(2)	L112(2)	L113(2)	L114(1)	L115(1)	L118(1)	
74	replacement of 53	YES	EIVS_LOREAL_LE_11HCE005_5.xls		LOREAL_LE	2	16/03/2011	Kt-L70	Kt-L72	Kt-L90	Kt-L99	Kt-L104	Kt-L107	Kt-L119	Kt-L120	Kt-L132	Kt-L133			
75	replacement of 15	YES	EIVS_CARDAM_LE2_10HCE035_41-Corr C79.xls	EIVS_CARDAM_LE2_10HCE035_41.xls	CARDAM_LE	1	14/03/2011	C79(1)	C82(1)	C85(1)	C87(1)	C88(1)	C90(1)	C91(1)	C96(1)					
76	replacement of 27	NO	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY Updated.xls		CEETOX_LE	1	04/05/2011	x45(1)	x47(1)	x49(1)	x51(1)	x52(1)	x59(1)	x68(1)						
77		NO	EIVS_CEETOX_LE_11HCE009_9_v1.0 Joey FAILED RUN.XLS		CEETOX_LE	1	04/05/2011	x13(2)	x39(2)	x8(2)	x128(2)	x64(2)	x43(2)	x44(2)	x103(3)	x63(3)				
78		NO	EIVS_CEETOX_LE_11HCE009_9_v1.0 LISA FAILED RUN.XLS		CEETOX_LE	1	04/05/2011	x62(2)	x65(2)	x81(2)	x82(2)	x117(2)								
79		NO	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.XLS		CEETOX_LE	1	04/05/2011	x72(2)	x73(2)	x83(2)	x86(2)	x89(2)	x93(2)	x98(2)	x99(2)					
80		NO	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.XLS		CEETOX_LE	1	04/05/2011	x45(2)	x47(2)	x49(2)	x51(2)	x52(2)	x59(2)	x68(2)						
81		NO	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls		CEETOX_LE	1	04/05/2011	x41(2)	x17(2)	x31(2)	x91(2)	x121(2)	x3(2)	x25(2)	x30(2)	x33(2)				

82		NO	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 1.xls	CEETOX_LE	1	04/05/2011	x63(2)	x72(3)	x73(3)	x83(3)	x86(3)	x89(3)	x93(3)	x98(3)	x99(3)								
83		NO	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 Joey.xls	CEETOX_LE	1	04/05/2011	x45(3)	x47(3)	x49(3)	x51(3)	x52(3)												
84		NO	EIVS_CEETOX_LE_11HCE007_7_v1.0.xls	CEETOX_LE	1	04/05/2011	x41(3)	x17(3)	x31(3)	x91(3)	x121(3)	x3(3)	x25(3)	x30(3)	x33(3)								
85		NO	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.XLS	CEETOX_LE	1	04/05/2011	x62(1)	x64(1)	x65(1)	x81(1)	x82(1)	x117(1)	x43(1)	x44(1)									
86	replacement of 12	YES	EIVS_CARDAM_LE1_10HCE037_43.xlsx	CARDAM_LE	1	12/05/2011	C78(3)	C79(3)	C82(3)	C85(3)	C87(3)	C88(3)	C90(3)	C91(3)	C94(2)	C96(3)	C99(1)	C104(1)	C3(1)				
87	replacement of 13	YES	EIVS_CARDAM_LE1_10HCE040_46.xls	CARDAM_LE	1	12/05/2011	C94(3)	C99(2)	C104(2)	C3(2)	C11(2)	C12(2)	C13(2)	C15(2)	C16(2)	C21(2)	C25(2)	C27(2)	C38(1)				
88	replacement of 14	YES	EIVS_CARDAM_LE1_10HCE041_47.xls	CARDAM_LE	1	12/05/2011	C99(3)	C104(3)	C3(3)	C11(3)	C12(3)	C13(3)	C15(3)	C16(3)	C21(3)	C25(3)	C27(3)	C38(2)	C45(2)				
89		YES	EIVS_CARDAM_LE1_10HCE042_48.xls	CARDAM_LE	1	12/05/2011	C38(3)	C45(3)	C46(3)	C47(3)	C50(3)	C53(3)	C62(3)	C70(3)	C83(3)	C84(1)	C98(1)	C101(1)	C119(2)				
90		YES	EIVS_CARDAM_LE2_10HCE037_43.xlsx	CARDAM_LE	1	12/05/2011	C11(1)	C12(1)	C13(1)	C15(1)	C16(1)	C21(1)	C25(1)	C27(1)									
91		YES	EIVS_CARDAM_LE2_10HCE040_46.xls	CARDAM_LE	1	12/05/2011	C45(1)	C46(1)	C47(1)	C50(1)	C53(1)	C62(1)	C70(1)	C83(1)									
92	replacement of 16	YES	EIVS_CARDAM_LE2_10HCE041_47.xls	CARDAM_LE	1	12/05/2011	C46(2)	C47(2)	C50(2)	C53(2)	C62(2)	C70(2)	C83(2)	C119(1)	C6(1)								
93	replacement of 17	YES	EIVS_CARDAM_LE2_10HCE042_48.xls	CARDAM_LE	1	12/05/2011	C123(1)	C127(1)	C132(1)	C134(1)	C135(1)	C6(2)											
94	replacement of 6	YES	EIVS_CARDAM_LE_10HCE033Kt_40.xlsx	CARDAM_LE	1	12/05/2011	C6(Kt)	C30(Kt)	C34(Kt)	C54(Kt)	C75(Kt)	C87(Kt)	C90(Kt)	C104(Kt)									
95	replacement of 7	YES	EIVS_CARDAM_LE_10HCE033kt_45.xlsx	CARDAM_LE	1	12/05/2011	C3(Kt)	C87(Kt)															
96	replacement of 9	YES	EIVS_CARDAM_LE_10HCE044_50.xls	CARDAM_LE	1	12/05/2011	C45(4)	C84(2)	C98(2)	C101(2)	C119(3)	C123(2)	C127(2)	C132(2)	C135(2)	C6(3)							
97		YES	EIVS_CARDAM_LE_11HCE001_Kt_2.xls	CARDAM_LE	1	12/05/2011	C45(Kt)	C53(Kt)	C101(Kt)	C113(Kt)	C135(Kt)	C128(Kt)											
98		YES	EIVS_CARDAM_LE_11HCE003_3.xls	CARDAM_LE	1	12/05/2011	C84(3)	C98(3)	C101(3)	C123(3)	C127(3)	C132(3)	C134(2)	C135(3)	C106(1)	C107(1)	C128(1)						
99		YES	EIVS_CARDAM_LE_11HCE005_5.xls	CARDAM_LE	1	12/05/2011	C105(1)	C106(2)	C107(2)	C108(1)	C110(1)	C112(1)	C134(3)	C135(4)	C136(1)	C138(1)	C139(1)	C128(2)					
100		YES	EIVS_CARDAM_LE_11HCE006_6.xls	CARDAM_LE	1	12/05/2011	C105(2)	C106(3)	C107(3)	C108(2)	C110(2)	C112(2)	C113(1)	C116(1)	C136(2)	C138(2)	C139(2)	C128(3)					
101		YES	EIVS_CARDAM_LE_11HCE007_7.xls	CARDAM_LE	1	12/05/2011	C105(3)	C109(1)	C120(1)	C108(3)	C125(1)	C129(1)	C113(2)	C116(2)	C131(1)								
102		YES	EIVS_CARDAM_LE_11HCE008_8.xls	CARDAM_LE	1	12/05/2011	C110(3)	C109(2)	C120(2)	C124(1)	C125(2)	C129(2)	C131(2)										
103		YES	EIVS_CARDAM_LE_11HCE009_9.xls	CARDAM_LE	1	12/05/2011	C136(3)	C109(3)	C120(3)	C124(2)	C138(3)	C112(3)	C113(3)	C116(3)	C139(3)								
104	MTT needed	NO	EIVS_CARDAM_LE_11HCE020_18.0.xls	CARDAM_LE	1	12/05/2011	C124(3)	C125(3)	C129(3)	C131(3)	C4(1)	C9(1)	C20(1)	C28(1)	C48(1)	C58(1)							
105		NO	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls	CEETOX_LE	1	16/06/2011	x13(1)	x39(1)	x8(1)	x128(1)	x103(2)	x49(4)											
106	same as 85	NO	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls	CEETOX_LE	1	16/06/2011	x62(1)	x64(1)	x65(1)	x81(1)	x82(1)	x117(1)	x43(1)	x44(1)									
107		YES	EIVS_CEETOX_LE_11HCE012 FK_16_v1.0 Set 1.xls	CEETOX_LE	1	16/06/2011	X39(Kt)	X8(Kt)	X27(Kt)	X46(Kt)	X87(Kt)	X108(Kt)	X109(Kt)	X110(Kt)	X119(Kt)	X133(Kt)	X136(Kt)						
108		YES	EIVS_CEETOX_LE_11HCE012 FK_16_v1.0 Set 2.xls	CEETOX_LE	1	16/06/2011	x138(Kt)	x139(Kt)															
109		NO	EIVS_CEETOX_LE_11HCE013_13_v1.0 Set 1.xls	CEETOX_LE	1	16/06/2011	x13(2)	x39(1)	x8(2)	x128(2)	x43(2)	x62(2)	x64(2)										
110		NO	EIVS_CEETOX_LE_11HCE013_13_v1.0 Set 2.xls	CEETOX_LE	1	16/06/2011	x65(2)	x81(2)	x82(2)	x117(2)	x112(1)	x126(1)	x21(1)	x103(3)	x63(3)	x47(4)	x17(4)						
111		YES	EIVS_CARDAM_LE_11HCE020 Killed_22.xls	CARDAM_LE	1	19/07/2011	C48(Kt)	C58(Kt)	C141(Kt)	C170(Kt)	C195(Kt)												
112	replacement of 104	YES	EIVS_CARDAM_LE_11HCE020_18.xls	CARDAM_LE	1	19/07/2011	C124(3)	C125(3)	C129(3)	C131(3)	C4(1)	C9(1)	C20(1)	C28(1)	C48(1)	C58(1)							
113		YES	EIVS_CARDAM_LE_11HCE022_19.xls	CARDAM_LE	1	19/07/2011	C4(2)	C9(2)	C14(1)	C20(2)	C28(2)	C29(1)	C39(1)	C48(2)	C52(1)								
114		YES	EIVS_CARDAM_LE_11HCE024_20.xls	CARDAM_LE	1	19/07/2011	C4(3)	C9(3)	C14(2)	C28(3)	C29(2)	C52(2)	C56(1)	C58(2)									
115		YES	EIVS_CARDAM_LE_11HCE026_21.xls	CARDAM_LE	1	19/07/2011	C14(3)	C20(3)	C29(3)	C52(3)	C56(2)	C64(1)	C67(1)	C71(1)	C97(1)	C114(1)							
116		YES	EIVS_CARDAM_LE_11HCE029_23.xls	CARDAM_LE	1	19/07/2011	C39(2)	C48(3)	C55(1)	C52(4)	C56(3)	C58(3)	C103(1)	C137(1)	C140(1)	C141(1)							
117		YES	EIVS_CARDAM_LE_11HCE032_25.xls	CARDAM_LE	1	19/07/2011	C39(3)	C55(2)	C64(2)	C67(2)	C163(1)	C164(1)	C166(1)	C185(1)	C170(1)	C193(1)	C195(1)	C196(1)					
118		YES	EIVS_CARDAM_LE_11HCE034_26.xls	CARDAM_LE	1	19/07/2011	C55(3)	C71(2)	C97(2)	C103(2)	C114(2)	C137(2)	C140(2)	C141(2)	C163(2)	C164(2)	C166(2)	C170(2)					
119		YES	EIVS_CARDAM_LE_11HCE036_27.xls	CARDAM_LE	1	19/07/2011	C64(3)	C67(3)	C71(3)	C97(3)	C103(3)	C114(3)	C137(3)	C166(3)	C185(2)	C193(2)	C195(2)	C196(2)					
120		YES	EIVS_CARDAM_LE_11HCE038_28.xls	CARDAM_LE	1	19/07/2011	C140(3)	C141(3)	C163(3)	C164(3)	C166(4)	C170(3)	C185(3)	C193(3)	C195(3)	C196(3)							
121		NO	EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 1.xls	CEETOX_LE	1	08/08/2011	X21(2)	X112(2)	X126(2)	X14(1)	X46(1)	X27(1)	X50(1)	X53(1)	X70(1)	X84(1)	X87(1)	X102(1)	X107(1)				
122		NO	EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 2.xls	CEETOX_LE	1	08/08/2011	X108(1)	X109(1)	X110(1)	X118(1)	X136(1)	X138(1)	X139(1)	X13(3)	X43(3)	X47(5)	X59(3)	X68(3)	X8(3)				
123		NO	EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 3.xls	CEETOX_LE	1	08/08/2011	X62(3)	X64(3)	X65(3)	X81(3)	X82(3)	X117(3)	X128(3)	X39(3)	PC2(1)	PC3(1)							
124	MTT needed	NO	EIVS_CEETOX_LE_11HCE029_30_v1.0.xls	CEETOX_LE	1	11/08/2011	X24(1)	X32(1)	X42(1)	X95(1)	X143(1)	X165(1)	X173(1)										
125		NO	EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 1.xls	CEETOX_LE	1	11/08/2011	X14(2)	X46(2)	X27(2)	X50(2)	X53(2)	X70(2)	X84(2)	X87(2)	X102(2)	X107(2)							
126		NO	EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 2.xls	CEETOX_LE	1	11/08/2011	X108(2)	X109(2)	X110(2)	X118(2)	X136(2)	X138(2)	X139(2)	X39(4)	X21(3)	X112(3)	X126(3)						

127		NO	EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 3.xls	CEETOX_LE	1	11/08/2011	X111(1)	X114(1)	X115(1)	X116(1)	X119(1)	X123(1)	X125(1)	X129(1)	X131(1)	X133(1)	X134(1)				
128		NO	EIVS_CEETOX_LE_11HCE040_29_v1.0 SET 1.xls	CEETOX_LE	1	11/08/2011	X14(3)	X46(3)	X27(3)	X50(3)	X53(3)	X70(3)	X84(3)	X87(3)	X102(3)	X107(3)						
129		NO	EIVS_CEETOX_LE_11HCE040_29_v1.0 SET 2.xls	CEETOX_LE	1	11/08/2011	X108(3)	X109(3)	X110(3)	X118(3)	X136(3)	X138(3)	X139(3)	X111(2)	X114(2)	X115(2)	X116(2)				
130		YES	EIVS_LOREAL_LE_11HCE020_18.xls	LOREAL_LE	1	12/08/2011	L1(1)	L6(1)	L13(1)	L15(1)	L16(1)	L32(1)	L33(1)	L36(1)	L37(1)						
131		YES	EIVS_LOREAL_LE_11HCE022_19.xls	LOREAL_LE	1	12/08/2011	L50(1)	L53(1)	L58(1)	L62(1)	L65(1)	L76(1)	L80(1)	L100(1)	L111(1)	L125(1)	L127(1)				
132		YES	EIVS_LOREAL_LE_11HCE024_20.xls	LOREAL_LE	1	12/08/2011	L144(1)	L148(1)	L156(1)	L161(1)	L164(1)	L169(1)	L174(1)	L185(1)	L200(1)	L137(4)	L6(2)				
133		YES	EIVS_LOREAL_LE_11HCE026_21.xls	LOREAL_LE	1	12/08/2011	L1(2)	L13(2)	L15(2)	L16(2)	L32(2)	L33(2)	L36(2)	L37(2)	L50(2)	L53(2)	L148(1)				
134		YES	EIVS_LOREAL_LE_11HCE029_23.xls	LOREAL_LE	1	12/08/2011	L33(3)	L58(2)	L62(2)	L65(2)	L76(2)	L80(2)	L100(2)	L161(2)	L169(2)	L174(2)	L111(2)	L6			
135		YES	EIVS_LOREAL_LE_11HCE032_25(1).xls	LOREAL_LE	1	12/08/2011	L125(2)	L127(2)	L144(2)	L148(2)	L156(2)	L164(2)	L185(2)	L200(2)	L1(3)	L6(3)	L13(3)	L16(3)	L58(3)		
136		YES	EIVS_LOREAL_LE_11HCE032_25(2).xls	LOREAL_LE	1	12/08/2011	L100(3)														
137		YES	EIVS_LOREAL_LE_11HCE034_26.xls	LOREAL_LE	1	12/08/2011	L6(4)	L15(3)	L32(3)	L36(3)	L37(3)	L50(3)	L53(3)	L62(3)	L65(3)	L76(3)	L80(3)	L111(3)	L125(3)		
138		YES	EIVS_LOREAL_LE_11HCE036_27.xls	LOREAL_LE	1	12/08/2011	L6(5)	L127(3)	L144(3)	L148(3)	L156(3)	L161(3)	L164(3)	L169(3)	L174(3)	L185(3)	L200(3)				
139		YES	EIVS_LOREAL_LE_11HCE002_2.xls	LOREAL_LE	1	18/08/2011	L122(1)	L123(1)	L126(1)	L129(1)	L133(1)	L134(1)	L136(1)	L137(1)	L139(1)	L140(1)	L114(2)	L115(2)			
140		YES	EIVS_LOREAL_LE_11HCE006_6.xls	LOREAL_LE	1	18/08/2011	L70(3)	L72(3)	L90(3)	L99(3)	L104(3)	L106(3)	L107(3)	L108(3)							
141		YES	EIVS_LOREAL_LE_11HCE007_7.xls	LOREAL_LE	1	18/08/2011	L109(3)	L112(3)	L113(3)	L114(3)	L115(3)	L118(2)	L119(2)	L120(2)	L122(2)	L123(2)					
142		YES	EIVS_LOREAL_LE_11HCE008_8.xls	LOREAL_LE	1	18/08/2011	L118(3)	L119(3)	L120(3)	L122(3)	L123(3)	L126(2)	L129(2)	L130(2)	L131(2)	L132(2)	L133(2)	L134(2)			
143		YES	EIVS_LOREAL_LE_11HCE009_9.xls	LOREAL_LE	1	18/08/2011	L126(3)	L129(3)	L130(3)	L131(3)	L132(3)	L133(3)	L134(3)	L136(2)	L137(2)	L139(2)	L140(2)				
144		YES	EIVS_LOREAL_LE_11HCE014_14.xls	LOREAL_LE	1	18/08/2011	L136(3)	L137(3)	L139(3)	L140(3)											
145	replacement of 20	YES	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls	CEETOX_LE	2	31/10/2011	x1(1)	x2(1)	x5(1)	x6(1)	x7(1)	x16(1)	x22(1)	x28(1)	x36(1)	x38(1)					
146	replacement of 21	YES	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls	CEETOX_LE	2	31/10/2011	x1(2)	x2(2)	x5(2)	x6(2)	x7(2)	x16(2)	x22(2)	x28(2)	x36(2)	x38(2)					
147	replacement of 22	YES	EIVS_CEETOX_LE_10HCE042_48_v1.0 UPDATED.xls	CEETOX_LE	2	31/10/2011	x1(3)	x2(3)	x5(3)	x6(3)	x7(3)	x16(3)	x22(3)	x28(3)	x36(3)	x38(3)					
148	replacement of 23	YES	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls	CEETOX_LE	2	31/10/2011	x1(4)	x2(4)	x5(4)	x6(4)	x7(4)	x16(4)	x22(4)	x28(4)	x36(4)	x38(4)					
149	replacement of 24	YES	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls	CEETOX_LE	2	31/10/2011	x1(5)	x2(5)	x5(5)	x6(5)	x7(5)	x16(5)	x22(5)	x28(5)	x36(5)	x38(5)					
150	replacement of 25	YES	EIVS_CEETOX_LE_11HCE003_3_v1.0 .xls	CEETOX_LE	2	31/10/2011	x63(1)	x72(1)	x73(1)	x83(1)	x86(1)	x89(1)	x93(1)	x98(1)	x99(1)	x103(1)					
151	replacement of 28	YES	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls	CEETOX_LE	2	31/10/2011	x41(1)	x17(1)	x31(1)	x91(1)	x121(1)	x3(1)	x25(1)	x30(1)	x33(1)						
152	replacement of 76	YES	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY Updated.xls	CEETOX_LE	2	31/10/2011	x45(1)	x47(1)	x49(1)	x51(1)	x52(1)	x59(1)	x68(1)								
153	replacement of 77	YES	EIVS_CEETOX_LE_11HCE009_9_v1.0 Joey FAILED RUN UPDATED.XLS	CEETOX_LE	2	31/10/2011	x13(2)	x39(2)	x8(2)	x128(2)	x64(2)	x43(2)	x44(2)	x103(3)	x63(3)						
154	replacement of 78	YES	EIVS_CEETOX_LE_11HCE009_9_v1.0 LISA FAILED RUN UPDATED.XLS	CEETOX_LE	2	31/10/2011	x62(2)	x65(2)	x81(2)	x82(2)	x117(2)										
155	replacement of 79	YES	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.XLS	CEETOX_LE	2	31/10/2011	x72(2)	x73(2)	x83(2)	x86(2)	x89(2)	x93(2)	x98(2)	x99(2)							
156	replacement of 80	YES	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.XLS	CEETOX_LE	2	31/10/2011	x45(2)	x47(2)	x49(2)	x51(2)	x52(2)	x59(2)	x68(2)								
157	replacement of 81	YES	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls	CEETOX_LE	2	31/10/2011	x41(2)	x17(2)	x31(2)	x91(2)	x121(2)	x3(2)	x25(2)	x30(2)	x33(2)						
158	replacement of 82	YES	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 1.xls	CEETOX_LE	2	31/10/2011	x63(2)	x72(3)	x73(3)	x83(3)	x86(3)	x89(3)	x93(3)	x98(3)	x99(3)						
159	replacement of 83	YES	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 Joey.xls	CEETOX_LE	2	31/10/2011	x45(3)	x47(3)	x49(3)	x51(3)	x52(3)										
160	replacement of 84	YES	EIVS_CEETOX_LE_11HCE007_7_v1.0.xls	CEETOX_LE	2	31/10/2011	x41(3)	x17(3)	x31(3)	x91(3)	x121(3)	x3(3)	x25(3)	x30(3)	x33(3)						
161	replacement of 85	YES	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.XLS	CEETOX_LE	2	31/10/2011	x62(1)	x64(1)	x65(1)	x81(1)	x82(1)	x117(1)	x43(1)	x44(1)							
162	replacement of 105	YES	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls	CEETOX_LE	2	31/10/2011	x13(1)	x39(1)	x8(1)	x128(1)	x103(2)	x49(4)									
163	replacement of 109	YES	EIVS_CEETOX_LE_11HCE013_13_v1.0 Set 1.xls	CEETOX_LE	2	31/10/2011	x13(2)	x39(1)	x8(2)	x128(2)	x43(2)	x62(2)	x64(2)								
164	replacement of 110	YES	EIVS_CEETOX_LE_11HCE013_13_v1.0 Set 2.xls	CEETOX_LE	2	31/10/2011	x65(2)	x81(2)	x82(2)	x117(2)	x112(1)	x126(1)	x21(1)	x103(3)	x63(3)	x47(4)	x17(4)				
165	replacement of 121	YES	EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 1.xls	CEETOX_LE	2	11/11/2011	X21(2)	X112(2)	X126(2)	X14(1)	X46(1)	X27(1)	X50(1)	X53(1)	X70(1)	X84(1)	X87(1)	X102(1)			
166	replacement of 122	NO	EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 2.xls	CEETOX_LE	2	11/11/2011	X108(1)	X109(1)	X110(1)	X118(1)	X136(1)	X138(1)	X139(1)	X13(3)	X43(3)	X47(5)	X59(3)	X68(3)			
167	replacement of 123	YES	EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 3.xls	CEETOX_LE	2	11/11/2011	X62(3)	X64(3)	X65(3)	X81(3)	X82(3)	X117(3)	X128(3)	X39(3)	PC2(1)	PC3(1)			X107(1)		
168	replacement of 125	YES	EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 1.xls	CEETOX_LE	2	11/11/2011	X14(2)	X46(2)	X27(2)	X50(2)	X53(2)	X70(2)	X84(2)	X87(2)	X102(2)	X107(2)			X8(3)		
169	replacement of 126	NO	EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 2.xls	CEETOX_LE	2	11/11/2011	X108(2)	X109(2)	X110(2)	X118(2)	X136(2)	X138(2)	X139(2)	X39(4)	X21(3)	X112(3)	X126(3)				

170	replacement of 127	YES	EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 3.xls		CEETOX_LE	2	11/11/2011	X111(1)	X114(1)	X115(1)	X116(1)	X119(1)	X123(1)	X125(1)	X129(1)	X131(1)	X133(1)	X134(1)		
171	replacement of 128	YES	EIVS_CEETOX_LE_11HCE040_29_v1.0 SET 1.xls		CEETOX_LE	2	11/11/2011	X14(3)	X46(3)	X27(3)	X50(3)	X53(3)	X70(3)	X84(3)	X87(3)	X102(3)	X107(3)					
172	replacement of 129	YES	EIVS_CEETOX_LE_11HCE040_29_v1.0 SET 2.xls		CEETOX_LE	2	11/11/2011	X108(3)	X109(3)	X110(3)	X118(3)	X136(3)	X138(3)	X139(3)	X111(2)	X114(2)	X115(2)	X116(2)				
173			EIVS_CEETOX_LE_11HCE020_18_v1.0 SET 1.xls		CEETOX_LE	1	11/11/2011	#REF!	#REF!	#REF!	#REF!	#REF!	#REF!	#REF!	#REF!							
174			EIVS_CEETOX_LE_11HCE020_18_v1.0 SET 2.xls		CEETOX_LE	1	11/11/2011	X62(5)	X64(5)	X65(5)	X81(5)	X82(5)	X117(5)	X128(5)	X39(5)	X118 FK(1)	X68(5)					
175			EIVS_CEETOX_LE_11HCE047_37_v1.0.xls		CEETOX_LE	1	11/11/2011	X111(6)	X114(6)	X115(6)	X116(6)	X50(6)	X119(6)	X123(6)	X125(6)	X129(6)	X131(6)					
176			EIVS_CEETOX_LE_11HCE049_38_v1.0.xls		CEETOX_LE	1	11/11/2011	X111(4)	X114(4)	X115(4)	X116(4)	X50(5)	X119(3)	X123(3)	X125(3)	X129(3)	X131(3)					
177			EIVS_CEETOX_LE_11HCE051_39_v1.0.xls		CEETOX_LE	1	11/11/2011	X133(2)	X134(2)	X119(4)	X123(4)	X125(4)	X129(4)	X131(4)	X11(1)	X19(1)	X29(1)					
178			EIVS_CEETOX_LE_11HCE053_40_v1.0.xls		CEETOX_LE	1	11/11/2011	X133(1)	X134(1)	X11(1)	X19(1)	X29(1)	X24(1)	X32(1)	X37(1)							
179			EIVS_CEETOX_LE_11HCE055_41_v1.0.xls		CEETOX_LE	1	11/11/2011	X37(2)	X143(1)	X190(1)	X173(1)	X169(1)	X133(4)	X127(1)								
180			EIVS_CEETOX_LE_11HCE057_42_v1.0.xls		CEETOX_LE	1	11/11/2011	X37(1)	X143(2)	X190(2)	X173(2)	X169(2)	X127(2)	X40(1)								
181			EIVS_CEETOX_LE_11HCE059_43_v1.0.xls		CEETOX_LE	1	16/12/2011	X37(2)	X143(3)	X190(3)	X173(1)	X169(3)	X127(3)	X40(2)	X134(4)	X196(1)	X11(3)	X19(3)				
182			EIVS_CEETOX_LE_11HCE061_44_v1.0.xls		CEETOX_LE	1	16/12/2011	X37(5)	X173(4)	X40(3)	X196(2)	X11(4)	X19(4)	X24(2)	X32(2)							
183			EIVS_CEETOX_LE_11HCE063_45_v1.0.xls		CEETOX_LE	1	16/12/2011	X173(5)	X24(3)	X29(3)	X196(3)	X42(1)	X55(1)	X56(1)	X61(1)	X66(1)	X75(1)					
184			EIVS_CEETOX_LE_11HCE065_46_v1.0.xls		CEETOX_LE	1	04/01/2012	X24(2)	X42(2)	X55(2)	X95(2)	X113(2)	X120(2)	X157(2)	X158(2)	X160(2)	X165(2)					
185			EIVS_CEETOX_LE_11HCE068_48_v1.0.xls		CEETOX_LE	1	04/01/2012	X29(4)	X77(2)	X80(2)	X94(2)	X95(1)	X113(1)	X120(1)	X157(1)	X158(1)	X160(1)	X165(1)				
186			EIVS_CEETOX_LE_11HCE070_49_v1.0.xls		CEETOX_LE	1	04/01/2012	X24(2)	X42(2)	X55(2)	X95(2)	X113(2)	X120(2)	X157(2)	X158(2)	X160(2)	X165(2)					
187			EIVS_CEETOX_LE_12HCE002_2_v1.0 - Set 1.xls		CEETOX_LE	1	24/01/2012	X24(5)	X32(4)	X42(4)	X55(4)	X56(3)	X165(3)	X66(3)								
188			EIVS_CEETOX_LE_12HCE002_2_v1.0 - Set 2.xls		CEETOX_LE	1	24/01/2012	X75(3)	X77(3)	X80(3)	X94(3)	X95(1)	X113(3)	X120(3)	X157(3)	X158(3)	X160(3)	X61(1)				
189			EIVS_CEETOX_LE_12HCE004_3_v1.0.xls		CEETOX_LE	1	24/01/2012	X95(4)	X113(4)	X120(4)	X157(4)	X158(4)	X160(4)	X165(4)	X61(4)							
190			EIVS_CEETOX_LE_12HCE009_7_v1.0.xls		CEETOX_LE	1	06/03/2012	x95(2)														
191	replacement of 151		EIVS_CEETOX_LE_11HCE004_4_v1.0 UPDATE X17FK.XLS		CEETOX_LE	2	21/12/2013	x17(1)														
192	replacement of 157		EIVS_CEETOX_LE_11HCE006_6_v1.0 UPDATED X17FK.XLS		CEETOX_LE	2	21/12/2013	x17(2)														
193	replacement of 160		EIVS_CEETOX_LE_11HCE007_7_v1.0 UPDATE X17FK.XLS		CEETOX_LE	2	21/12/2013	x17(3)														
194	replacement of 164		EIVS_CEETOX_LE_11HCE013_13_v1.0 Set 2 UPDATE X17FK.XLS		CEETOX_LE	2	21/12/2013	x17(4)														
195			EIVS_CEETOX_LE_12HCE0 FK_48_v1.0 run 1.xls		CEETOX_LE	2	21/12/2013															
196	replacement of 169		EIVS_CEETOX_LE_11HCE034_26_v1.0 SET 2_revised19Sept2012ct.xls	EIVS_CEETOX_LE_11HCE034_26_v1.0 Set 2.xls	CEETOX_LE	2	19/09/2012	X108(2)	X109(2)	X110(2)	X118(2)	X136(2)	X138(2)	X139(2)	X39(6)	X21(3)	X112(3)	X126(3)				
197	replacement of 166		EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 2_revised19Sept2012ct.xls	EIVS_CEETOX_LE_11HCE022_19_v1.0 SET 2.xls	CEETOX_LE	2	19/09/2012	X108(1)	X109(1)	X110(1)	X118(1)	X136(1)	X138(1)	X139(1)	X13(3)	X43(3)	X47(6)	X59(3)	X68(3)			

Appendix IV Remarks and special observations by the study personal

CARDAM in an email to TNO:
I understand that the VMG still wants the freedom to decide what to do with the data were %NSC or %NSMTT > 50 %; but I would be very carefully using these mean viability and std viability, so I wrote that in my comment column. Maybe an idea is to make a separate table with this kind of data, or maybe already when >30 % ...

SE

laboratory	remark	filename
CARDAM	In the first and second tissue of C78, the test item was pulling towards the edges	EIVS_CARDAM_SE1_10HCE035_41.xls
CARDAM	C76 has created a hole in the tissues	EIVS_CARDAM_SE1_10HCE035_41.xls
CARDAM	Test item C78 was pulling towards the edges	EIVS_CARDAM_SE1_10HCE036_42.xls
CARDAM	C96 this time the test item was not washed with a cotton bud (as in 10HCE035),	EIVS_CARDAM_SE1_10HCE036_42.xls
CARDAM	however minimal damage in the middle of the tissue was observed, so must be test item specific	EIVS_CARDAM_SE1_10HCE036_42.xls
CARDAM	C104 tissue are broken	EIVS_CARDAM_SE1_10HCE037_43.xls
CARDAM	C11 and C12: tissues are partially or completely damaged by the test item after wash step	EIVS_CARDAM_SE1_10HCE037_43.xls
CARDAM	C90 tissue eaten away	EIVS_CARDAM_SE1_10HCE037_43.xls
CARDAM	C45 tissue 2 test item still a little present on plastic cup after washing	EIVS_CARDAM_SE1_10HCE040_46.xls
CARDAM	C45 tissues are still colored after washing step	EIVS_CARDAM_SE1_10HCE041_47.xls
CARDAM	C62 test item melts after application on tissues	EIVS_CARDAM_SE1_10HCE041_47.xls
CARDAM	C53: %NSMTT is unqualified because >50%; condition 2! (see e-mail from Nathalie 5th Nov 2010!)	EIVS_CARDAM_SE1_10HCE041_47.xls
CARDAM	SD >18% for killed tissue C53 but this is not the case in run SE from week 48. Not repeat killed tissue because test	EIVS_CARDAM_SE1_10HCE041_47.xls
CARDAM	item is not compatible for HCE test	EIVS_CARDAM_SE1_10HCE041_47.xls
CARDAM	C45 tissues are still colored after washing step	EIVS_CARDAM_SE1_10HCE042_48.xls

laboratory	remark	filename
CARDAM	C62 test item melts after application on tissues	EIVS_CARDAM_SE1_10HCE042_48.xls
CARDAM	C6: no picture taken after 3h MTT because can not leave Biohazard in lab L0210 because of strong smell	EIVS_CARDAM_SE1_10HCE042_48.xls
CARDAM	C53: %NSMTT is unqualified because >50%; condition 2! (see e-mail from Nathalie 5th Nov 2010!)	EIVS_CARDAM_SE1_10HCE042_48.xls
CARDAM	C96 tissue has small black dot= pigment	EIVS_CARDAM_SE2_10HCE035_41.xls
CARDAM	C96 very sticky so for washing needed to use cotton swab and after MTT incubation saw that all 3 tissues damaged	EIVS_CARDAM_SE2_10HCE035_41.xls
CARDAM	C11 tissue 3 has come loose during washing step, but was not washed away	EIVS_CARDAM_SE2_10HCE036_42.xls
CARDAM	/	EIVS_CARDAM_SE2_10HCE037_43.xls
CARDAM	C62 test item melts after application on tissues	EIVS_CARDAM_SE2_10HCE040_46.xls
CARDAM	C123 test item is ,not completely dissolved, suspension	EIVS_CARDAM_SE2_10HCE041_47.xls
CARDAM	C134 test item reacts with the plastic cup, cup became white	EIVS_CARDAM_SE2_10HCE041_47.xls
CARDAM	C6, no pictures, test item can not leave lab L0210, terrible smell.	EIVS_CARDAM_SE2_10HCE041_47.xls
CARDAM	C138: Tissue 3 has a small hole after washing	EIVS_CARDAM_SE2_10HCE042_48.xls
CARDAM	C134 test item reacts with the plastic cup	EIVS_CARDAM_SE2_10HCE042_48.xls
CARDAM	C6, no pictures, test item can not leave lab L0210, terrible smell.	EIVS_CARDAM_SE2_10HCE042_48.xls
CARDAM	No pictures from C30 en C33, short exposure. Observation done without pictures	EIVS_CARDAM_SE_10HCE029_35.xls
CARDAM	Test item C17 sticks to tissue, wash off with cotton bud.	EIVS_CARDAM_SE_10HCE029_35.xls
CARDAM	Test item C17and test item C30, MTT solution beneath tissue is purple after 3H incubation and not just tissue	EIVS_CARDAM_SE_10HCE029_35.xls
CARDAM	PBS without Ca and Mg is used from set 4 short exposure untill positive controle long exposure	EIVS_CARDAM_SE_10HCE029_35.xls
CARDAM	for C26, after 3 h MTT: 2 tissues white and 1 light purple (AVR)	EIVS_CARDAM_SE_10HCE029_35.xls
CARDAM	First tissue of c17 was not fully covered + because the test item was hard to remove there can be	EIVS_CARDAM_SE_10HCE031_37.xls
CARDAM	a possible damage of the tissues after washing	EIVS_CARDAM_SE_10HCE031_37.xls
CARDAM	first tissue of c19 was damaged in the middle, after	EIVS_CARDAM_SE_10HCE031_37.xls

laboratory	remark	filename
	10min all tissue were damaged	
CARDAM	second tissue of c35 was not fully covered, a part of the tissue from tissue 1 and 2 was gone after washing	EIVS_CARDAM_SE_10HCE031_37.xls
CARDAM	c35 was spread with a regular pipette	EIVS_CARDAM_SE_10HCE031_37.xls
CARDAM	Test item C17 sticks to tissue, wash off with cotton bud.	EIVS_CARDAM_SE_10HCE031_37.xls
CARDAM	Test item C17and testitem C30, MTT solution beneath tissue is purple after 3H incubation and not just tissue	EIVS_CARDAM_SE_10HCE031_37.xls
CARDAM	C1, C2, C17, C19, C26 and C77 were applied with normal pipette	EIVS_CARDAM_SE_10HCE032_38.xls
CARDAM	MTT stock solution was not completely dissolved	EIVS_CARDAM_SE_10HCE032_38.xls
CARDAM	Test item C17 sticks to tissue, wash off with cotton bud.	EIVS_CARDAM_SE_10HCE032_38.xls
CARDAM	Test item C17and test item C30, MTT solution beneath tissue is purple after 3H incubation and not just tissue	EIVS_CARDAM_SE_10HCE032_38.xls
CARDAM	/	EIVS_CARDAM_SE_10HCE033_39(C77).xls
CARDAM	C76 difficult to spread, liquid sticks together	EIVS_CARDAM_SE_10HCE033_39.xls
CARDAM	/	EIVS_CARDAM_SE_10HCE034_40(C79).xls
CARDAM	C78 tissue 1, air bubble was present during MTT incubation	EIVS_CARDAM_SE_10HCE034_40.xls
CARDAM	C65 tissue 1, air bubble was present during MTT incubation	EIVS_CARDAM_SE_10HCE034_40.xls
CARDAM	C76 has created a hole in the tissues	EIVS_CARDAM_SE_10HCE034_40.xls
CARDAM	C45 and C101 tissues are still colored after washing step	EIVS_CARDAM_SE_10HCE044_50.xls
CARDAM	C6 no picture taken because needs to stay in Biohazard because of smell	EIVS_CARDAM_SE_10HCE044_50.xls
CARDAM	C53: %NSMTT is unqualified because >50%; condition 2! (see e-mail from Nathalie 5th Nov 2010!)	EIVS_CARDAM_SE_10HCE044_50.xls
CARDAM	SD >18% for killed tissue C53 but this is not the case in run SE from week 48. Not repeat killed tissue because test	EIVS_CARDAM_SE_10HCE044_50.xls
CARDAM	item is not compatible for HCE test	EIVS_CARDAM_SE_10HCE044_50.xls
CARDAM	C134 and C138: It looks like a white precipitate is formed on the tissues. Reaction of test item with the tissue???	EIVS_CARDAM_SE_11HCE003_3.xls
CARDAM	Tissues might have had extra stress, Since the delivery by courier went first wrongly to UK and then to CARDAM	EIVS_CARDAM_SE_11HCE003_3.xls
CARDAM	C138: It looks like a white precipitate is formed on the	EIVS_CARDAM_SE_11HCE005_5.xls

laboratory	remark	filename
	tissues. Reaction of test item with the tissue???	
CARDAM	C113, solid that sticks together, difficult to spread.	EIVS_CARDAM_SE_11HCE005_5.xls
CARDAM	C113, solid that sticks together, spreading was OK this time	EIVS_CARDAM_SE_11HCE006_6.xls
CARDAM	C124 is a solid resin. You have to weigh 1 piece of +-30mg. It can not be spread on the tissue. On tissue 1 I tried to	EIVS_CARDAM_SE_11HCE006_6.xls
CARDAM	use a mesh but it doesn't help.	EIVS_CARDAM_SE_11HCE006_6.xls
CARDAM	C116, looks like glass pieces.	EIVS_CARDAM_SE_11HCE006_6.xls
CARDAM	C109, sticky but with positive placement pipette it is OK	EIVS_CARDAM_SE_11HCE007_7.xls
CARDAM	Wash with cotton tip	EIVS_CARDAM_SE_11HCE007_7.xls
CARDAM	C109, sticky but with positive placement pipette it is OK	EIVS_CARDAM_SE_11HCE008_8.xls
CARDAM	Wash with cotton tip	EIVS_CARDAM_SE_11HCE008_8.xls
CARDAM	C124, resin, difficult to cover whole tissue.	EIVS_CARDAM_SE_11HCE008_8.xls
CARDAM	C109, sticky but with positive placement pipette it is OK	EIVS_CARDAM_SE_11HCE009_9.xls
CARDAM	Wash with cotton tip	EIVS_CARDAM_SE_11HCE009_9.xls
CARDAM	C124, resin, difficult to cover whole tissue.	EIVS_CARDAM_SE_11HCE009_9.xls
CARDAM	C28, first tissue damaged by cotton tip	EIVS_CARDAM_SE_11HCE020_18.xls
CARDAM	C28 and C52, washed once more after MTT incubation, before isopropanol incubation	EIVS_CARDAM_SE_11HCE020_18.xls
CARDAM	C28 and C52, washed once more after MTT incubation, before isopropanol incubation	EIVS_CARDAM_SE_11HCE022_19.xls
CARDAM	C28 and C52, washed once more after MTT incubation, before isopropanol incubation	EIVS_CARDAM_SE_11HCE024_20.xls
CARDAM	C52, washed once more after MTT incubation, before isopropanol incubation	EIVS_CARDAM_SE_11HCE026_21.xls
CARDAM	C52, washed once more after MTT incubation, before isopropanol incubation	EIVS_CARDAM_SE_11HCE029_23.xls
CARDAM	C55, wash with cotton tip, forms a mucus layer	EIVS_CARDAM_SE_11HCE029_23.xls
CARDAM	C55, wash with cotton tip, forms a mucus layer	EIVS_CARDAM_SE_11HCE032_25.xls
CARDAM	C163, viscous, difficult to spread	EIVS_CARDAM_SE_11HCE032_25.xls
CARDAM	C163, viscous, difficult to spread	EIVS_CARDAM_SE_11HCE034_26.xls
CARDAM	C163, viscous, difficult to spread	EIVS_CARDAM_SE_11HCE036_27.xls
CEETOX	C1a -- clump in center of tissue, powder is spread evenly around it.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls

laboratory	remark	filename
CEETOX	C1c -- it felt like I scratched the tissue, there may be a small mark.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C2a -- 10 seconds late rinsing.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C2 -- plastic of the insert looks etched around the top.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C3a -- touched the tip to the tissue during the application.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C3 -- compound is very thin and difficult to spread.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C4 -- tissue looks rippled.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C5 -- compound spread at first, but then pulled to the sides and became harder to spread	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C6a -- chunks of the compounds, most of the tissue is covered	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C6b -- compound is still chunky, however there is better coverage; some compound was left in the glass weigh boat.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	There was not enough time to tap it out.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C6c -- same as above, some compound left in plastic weigh boat as well.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C7 -- like C5 very difficult to spread. C7b looked better, but pulled to sides again later	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C9a -- some compound fell out into the plastic weigh boat during application, and seemed to stick to the sides of the insert.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C9c -- lost some compound in the plastic weigh boat.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	C9 -- during rinsing of a the compound looked like some had dissolved.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	in b there was a bubbled on the tissue.	EIVS_CEETOX_SE_10HCE023_25_v1.0.xls
CEETOX	PCb - dropped in funnel during rinsing. Tissue looks fine.	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C1 - a little compound left in each glass weigh boat	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C3 - liquid is thin, a little difficulty spreading, but it looks like good coverage	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C4 - same as C3	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C3 - plastic looks degraded during rinsing	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C4a - dropped tissues in funnel during rinsing tissue looks wrinkled	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls

laboratory	remark	filename
CEETOX	C4b - tissue looks wrinkled	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C5 - compound pulled to sides, or looked like it evaporated	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C5 rinsing - plastic degraded	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C6 - clumpy, a little left in glass weigh boat in each	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C7 - a little difficulty spreading; tissue is mostly covered	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	rinsing - plastic degraded	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C9 - some compound left in glass weigh boat	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C10 - a little difficulty spreading	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	C9 rinsing - middle of tissue looks like compound melted	EIVS_CEETOX_SE_10HCE024_26_v1.0.xls
CEETOX	NC c -- may have scratched the tissue, does not look scratched	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	PC a -- bubbles around the rim of the tissue	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	C1 -- some clumps, good coverage, a little compound stuck on the sides	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	C3 -- compound not staying spread on earlier tissues (a and b).	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	C4 -- a looks like it has good coverage, but b is not spreading well, c had good coverage	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	C6 -- large clumps of compound in the middle, but tissue is mostly covered	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	C7 -- Rinsing - plastic degraded	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	b -- rinsed 10 seconds late	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	C9 -- a some up on sides of insert; a little left in the glass weigh boat for all three	EIVS_CEETOX_SE_10HCE025_27_v1.0.xls
CEETOX	C1 -- a would not spread, worked better after I went back to it	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	C2 -- lots stuck in wht weigh boats; it was caked on and would not tap out.	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	clumpy compound; broke up gently using the pipette	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	Rinsing -- a dropped in funnel	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	C3 -- clumpy compound; spread out with tip	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	b -- lost some from the glass weigh boat while tapping	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	C4 -- tissues looked slightly ripped during rinsing	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	C5 -- residual compound left in the glass weigh boats	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls

laboratory	remark	filename
CEETOX	C6 -- compound was very difficult to spread because it was so thin	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	C7 -- thin compound, some difficulty spreading	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	Rinsing -- a ripped, c had small tear	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	C9 -- some compound stuck to glass weigh boat	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	clumpy compound; spread with pipette tip	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	C10 -- compound appears to spread well, but after 10 seconds it seems to pull away to the sides	EIVS_CEETOX_SE_10HCE027_29_v1.0.xls
CEETOX	C1 -- difficult to spread; thin compound; c spread better than a and b	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	C2 -- a coated on the glass weigh boat; some compound fell out of the weigh boat as well	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	b same as a, some compound left on the outside of the glass weigh boat	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	c less compound stuck in the glass weigh boat, spread better	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	Rinsing -- plastic degraded	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	C3 -- a stuck to glass weigh boat, difficult to tap out	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	b came out better, but still some compound stuck	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	c tapped some out of weigh boat, not all added to tissue (only a very small amount)	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	Used pipette on all of these to move the compound around. Powder still on the tissue at rinsing, but clumped up	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	C6 -- difficult to spread; rippled tissue at rinsing	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	C7 -- slightly thin, but compound seemed to spread well	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	c compound splashed a little out of insert	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	Rinsing -- a had a small rip; c tissue folded up some	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	C9 -- compound clumpy, some stuck on the glass weigh boat; good coverage	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	C10 -- b spread better than a	EIVS_CEETOX_SE_10HCE028_30_v1.0.xls
CEETOX	C1 -- thin liquid, pulled to sides, hard to spread	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls
CEETOX	C2 -- some compound stuck in weigh boat	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls
CEETOX	C3b -- a little clumpy, but seemed to spread ok	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls
CEETOX	C5 -- compound left in weigh boat; tissues stained	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls

laboratory	remark	filename
CEETOX	C6 -- a little difficulty spreading; tissues are rippled after rinsing	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls
CEETOX	C7c -- tissue doesn't look good, ripped on the bottom during rinsing	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls
CEETOX	C9b -- large clump, but the tissue is still covered	EIVS_CEETOX_SE_10HCE042_48_v1.0.xls
CEETOX	C1 -- difficult to spread; tissues looked like they were peeling after they were rinsed	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C1 a -- tissue torn a little	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C2 a -- compound in weigh boat, some compound left in glass weigh boat	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C2 b and c -- some compound left in glass weigh boat	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C3 a -- could not spread well, used tip	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C3 b -- spread better, dosed 30 seconds late	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C4 a -- tissue came off (it appears)	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C4 b -- tissue degraded	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C6 -- hard to spread well and did not stay spread over the tissues	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C7 b -- dosed 30 seconds late	EIVS_CEETOX_SE_10HCE043_49_v1.0.xls
CEETOX	C1 a -- tissue looked very smooth after rinsing; cannot tell if tissue was lost	EIVS_CEETOX_SE_10HCE044_50_v1.0.xls
CEETOX	C2 -- compound left in all three glass weigh boats	EIVS_CEETOX_SE_10HCE044_50_v1.0.xls
CEETOX	C3 -- compound left in all three glass weigh boats, not too much	EIVS_CEETOX_SE_10HCE044_50_v1.0.xls
CEETOX	C4 -- tissue may have dissolved; cannot tell	EIVS_CEETOX_SE_10HCE044_50_v1.0.xls
CEETOX	C7 FK a -- tissue cracked after rinsing	EIVS_CEETOX_SE_10HCE044_50_v1.0.xls
CEETOX	C7 FK b -- dosed 30 seconds late	EIVS_CEETOX_SE_10HCE044_50_v1.0.xls
CEETOX	NC c -- dropped in funnel	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.xls
CEETOX	PC c -- dropped in funnel	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.xls
CEETOX	C2 -- used tip to spread compound; some compound left in all weigh boats	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.xls
CEETOX	C1 -- tissue looks like it has bubbles underneath it after rinsing	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.xls
CEETOX	C3 -- dropped tissue a after compound dosed; had better coverage on tissues b and c	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.xls
CEETOX	C4 -- tissues disintegrated during rinsing	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.xls

laboratory	remark	filename
CEETOX	C6 -- compound is thin and difficult to spread	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.xls
CEETOX	C7 - thin; difficult to spread	EIVS_CEETOX_SE_11HCE004_4_v1.0 JOEY.xls
CEETOX	C1- precipitate in compound bottle	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C1a- 15 seconds late on rinse	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C2b- dropped rinsed tissue	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C3a- 15 seconds late on rinse	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C4- not all compound removed from tissue with extra rinse	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C4a- compound remaining in weigh boat	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C4b- clump of compound on tissue	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C4c- compound remaining in weigh boat	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C5b - late rinse	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C5c- dropped tissue in flask while rinsing	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C6a- dropped tissue in flask while rinsing	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C7b- nicked tissue	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	C4 - After incubation the compound stained the media and tissue a dark color see pictures in 11HCE007 Lisa	EIVS_CEETOX_SE_11HCE004_4_v1.0.xls
CEETOX	PC - extra rinse	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls
CEETOX	C2 - spread with tip	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls
CEETOX	C4 - not all compound removed after extra rinse	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls
CEETOX	C7a - 30 sec late rinsing	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls
CEETOX	C7c - extra rinse	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls
CEETOX	C8 - spread with tip	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls
CEETOX	C4 - After incubation the compound stained the media and tissue a dark color see pictures in 11HCE007 Lisa	EIVS_CEETOX_SE_11HCE006_6_v1.0.xls
CEETOX	C1 - extra rinse	EIVS_CEETOX_SE_11HCE007_7_v1.0.xls
CEETOX	C4b and c - compound left in weigh boat	EIVS_CEETOX_SE_11HCE007_7_v1.0.xls
CEETOX	C4b - spread compound with tip	EIVS_CEETOX_SE_11HCE007_7_v1.0.xls
CEETOX	C4 - not all compound removed after extra rinse	EIVS_CEETOX_SE_11HCE007_7_v1.0.xls
CEETOX	C7 - extra rinse	EIVS_CEETOX_SE_11HCE007_7_v1.0.xls
CEETOX	C4 - After incubation the compound stained the media and tissue a dark color see pictures in 11HCE007 Lisa	EIVS_CEETOX_SE_11HCE007_7_v1.0.xls
CEETOX	x13 C1 -- used tip, some compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE008_8_v1.0 JOEY.xls
CEETOX	x39 C2 -- some compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE008_8_v1.0 JOEY.xls

laboratory	remark	filename
CEETOX	X8 C3 -- used tip; some compound left in both glass and plastic weigh boats (compound very fluttery)	EIVS_CEETOX_SE_11HCE008_8_v1.0 JOEY.xls
CEETOX	x128 c C4c -- tissue looks ripped	EIVS_CEETOX_SE_11HCE008_8_v1.0 JOEY.xls
CEETOX	C2 - spread with tip	EIVS_CEETOX_SE_11HCE008_8_v1.0 LISA.xls
CEETOX	C2 - extra rinse	EIVS_CEETOX_SE_11HCE008_8_v1.0 LISA.xls
CEETOX	C8 - not all compound removed after extra rinsing	EIVS_CEETOX_SE_11HCE008_8_v1.0 LISA.xls
CEETOX	PC a - dropped tissue in flask	EIVS_CEETOX_SE_11HCE009_9_v1.0 LISA.xls
CEETOX	C4 - spread with tip	EIVS_CEETOX_SE_11HCE009_9_v1.0 LISA.xls
CEETOX	C4 FK a - dropped tissue in flask	EIVS_CEETOX_SE_11HCE009_9_v1.0 LISA.xls
CEETOX	C1 x13 -- used tip; compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE009_9_v1.0.xls
CEETOX	C1b x13b -- very wet compounds	EIVS_CEETOX_SE_11HCE009_9_v1.0.xls
CEETOX	C3 x8 -- used tip; color came off in post rinsing	EIVS_CEETOX_SE_11HCE009_9_v1.0.xls
CEETOX	C3-MTT x8-MTT -- used tip	EIVS_CEETOX_SE_11HCE009_9_v1.0.xls
CEETOX	C8 x44 b -- used tip to spread	EIVS_CEETOX_SE_11HCE009_9_v1.0.xls
CEETOX	C7 x43 -- used tip	EIVS_CEETOX_SE_11HCE009_9_v1.0.xls
CEETOX	C4 x128 -- tissues cracked after rinsing	EIVS_CEETOX_SE_11HCE009_9_v1.0.xls
CEETOX	C1 X13 -- used tip to spread	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 1.xls
CEETOX	C3 X8 -- compound is staticy; used tip	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 1.xls
CEETOX	C5 X43 -- compound is staticy; all over the glass weigh boat; used tip to spread	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 1.xls
CEETOX	C4 X128 -- extra rinse, tissues cracked	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 1.xls
CEETOX	C7 X64 -- not a solution; settled out on the bottom; all tissues received extra rinse	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 1.xls
CEETOX	C6 c X62c -- dropped tissue in funnel	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 1.xls
CEETOX	C9 X81 -- precipitate in vial; cracked tissues	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 2.xls
CEETOX	C8b X65b -- dropped in funnel	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 2.xls
CEETOX	C13 X126 -- very small amount, difficult to cover the tissues	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 2.xls
CEETOX	C14 b and c X21 b and c -- tissues dropped in funnel	EIVS_CEETOX_SE_11HCE013_13_v1.0 set 2.xls
CEETOX	NC b -- dosed 10 seconds late; dropped in funnel	EIVS_CEETOX_SE_11HCE020_18_v1.0.xls
CEETOX	C1 X13 -- used tip to spread compound	EIVS_CEETOX_SE_11HCE020_18_v1.0.xls
CEETOX	PC c -- dropped in funnel	EIVS_CEETOX_SE_11HCE020_18_v1.0.xls
CEETOX	C4 X126 -- did not spread well on tissue; used tip, but clumps were too large	EIVS_CEETOX_SE_11HCE020_18_v1.0.xls
CEETOX	Solid compounds left in all weigh boats.	EIVS_CEETOX_SE_11HCE020_18_v1.0.xls

laboratory	remark	filename
CEETOX	NC b -- bubble on apical surface	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls
CEETOX	C2 X112 c -- compound remaining in weigh boat	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls
CEETOX	C4 X14 -- Spread with tip	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls
CEETOX	C4-MTT X14-MTT -- spread with tip	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls
CEETOX	C6-MTT X27-MTT b -- nicked tissue	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls
CEETOX	C6 X27 -- extra rinse and swab	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls
CEETOX	C6-MTT X27-MTT -- extra rinse and swab	EIVS_CEETOX_SE_11HCE022_19_v1.0.xls
CEETOX	C1 X14 -- used tip to spread compound; compound left in glass weigh boat; compound did not fully cover the tissue	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C1-MTT X14-MTT -- used tip to spread compound; compound left in glass weigh boat; compound did not fully cover the tissue	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C2 X27 -- compound left in glass weigh boat and plastic weigh boats, the compound was very staticy	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C2-MTT X27-MTT -- compound left in glass weigh boat and plastic weigh boats, the compound was very staticy	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C3 X46 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C4 X50 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C6 X70 -- compound left in glass weigh boat; compound would not spread when wet	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C7 X84 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C8 X87 -- compound left in glass weigh boat; used tip to spread; compound dissolved on tissue	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C9 X102 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C10 X107 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C11 X108 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	C12 X109 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE047_37_v1.0.xls
CEETOX	NC a -- dropped in funnel	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C1 X14 -- used tip to spread compound: compound did not cover the tissues well; compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C1-MTT X14-MTT -- used tip to spread compound; compound did not cover the tissues well;	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C2 X27 -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls

laboratory	remark	filename
	on tissues	
CEETOX	C2-MTT X27-MTT -- compound left in glass weigh boat; extra swab on tissues	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C3 X46 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C4 X50 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C6 X70 -- compound left in glass weigh boat; had to scrape off of the tissues because it stuck to them after dosing	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C7 X84 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C8 X71 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C9 X102 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C11 X108 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C10 X107 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C12 X109 -- compound left in glass weigh boat; had to scrape the compound out of the weigh boat	EIVS_CEETOX_SE_11HCE049_38_v1.0.xls
CEETOX	C1 X50 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 1.xls
CEETOX	C3 X70 -- compound left in glass weigh boat; compound stuck to all tissues during rinsings	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 1.xls
CEETOX	C4 X84 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 1.xls
CEETOX	C5 X87 -- compound left in glass weigh boat; not covering tissue totally; used tip to spread	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 1.xls
CEETOX	C6 X102 -- compound left in weigh boat	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 1.xls
CEETOX	C7 X107 -- compound left in weigh boat	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 1.xls
CEETOX	C8 X108 -- compound left in glass weigh boat; compound did not cover well	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 2.xls
CEETOX	C9 X109 -- compound left in glass weigh boat; compound stuck in glass weigh boat	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 2.xls
CEETOX	C10 X110 -- needed extra swabs to rinse the tissue	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 2.xls
CEETOX	C11 X111 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 2.xls
CEETOX	C12 X114 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 2.xls
CEETOX	C13 X115 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 2.xls
CEETOX	C14 X116 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_SE_11HCE051_39_v1.0 set 2.xls

laboratory	remark	filename
CEETOX	C2 X111 -- used tip to spread compound; compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 1.xls
CEETOX	C1 X110 -- used 2 extra swabs while rinsing	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 1.xls
CEETOX	C3 X114 -- used tip to spread compound; compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 1.xls
CEETOX	C4 X115 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 1.xls
CEETOX	C5 X116 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 1.xls
CEETOX	C6 X118 -- tissue c cracked	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 1.xls
CEETOX	C7 X119 -- compound left in glass weigh boat; compound dissolved on tissue	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 1.xls
CEETOX	C8 X123 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 2.xls
CEETOX	C9 X125 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 2.xls
CEETOX	C10 X129 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 2.xls
CEETOX	C11 X131 -- compound left in glass weigh boat; used tip to spread compound; compound dissolved on tissue	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 2.xls
CEETOX	C13 X134 -- compound disappeared from weigh boat; it seems a much smaller amount than what I weighed out	EIVS_CEETOX_SE_11HCE053_40_v1.0 set 2.xls
CEETOX	C3 X190 -- tissues were wet prior to dosing; needed to be swabbed	EIVS_CEETOX_SE_11HCE055_41_v1.0 set 1.xls
CEETOX	C4 X131 -- used tip to spread compound; compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE055_41_v1.0 set 1.xls
CEETOX	C5 X119 -- compound dissolved on tissues; compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE055_41_v1.0 set 1.xls
CEETOX	C6 X173 -- used tip to spread compound; compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE055_41_v1.0 set 1.xls
CEETOX	C7 X169 -- used tip to spread compound; compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE055_41_v1.0 set 1.xls
CEETOX	C11 X40 -- compound left in glass weigh boat; extra swab; difficult to remove from the tissue	EIVS_CEETOX_SE_11HCE055_41_v1.0 set 2.xls
CEETOX	C12 X108 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_SE_11HCE055_41_v1.0 set 2.xls
CEETOX	C13 X111 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_SE_11HCE055_41_v1.0 set 2.xls

laboratory	remark	filename
CEETOX	C4 X131 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_SE_11HCE057_42_v1.0 set 1.xls
CEETOX	C6 X173 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE057_42_v1.0 set 1.xls
CEETOX	C5 X119 -- compound dissolved on tissue	EIVS_CEETOX_SE_11HCE057_42_v1.0 set 1.xls
CEETOX	C7 X169 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_SE_11HCE057_42_v1.0 set 1.xls
CEETOX	C11 X40 -- compound left in glass weigh boat; used extra swabs; compound was difficult to get off tissue	EIVS_CEETOX_SE_11HCE057_42_v1.0 set 2.xls
CEETOX	C12 X108 -- compound left in glass weigh boat; used tip to spread compound on tissue a - this removed some of the compound	EIVS_CEETOX_SE_11HCE057_42_v1.0 set 2.xls
CEETOX	C13 X111 -- compound left in glass weigh boat; a little compound spilled from tissue a - but there was good coverage	EIVS_CEETOX_SE_11HCE057_42_v1.0 set 2.xls
CEETOX	C4 X173 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 1.xls
CEETOX	C5 X169 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 1.xls
CEETOX	C8 X40 -- compound left in glass weigh boat; hard to scrape off	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 2.xls
CEETOX	C9 X138 -- b cracked; c as well	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 2.xls
CEETOX	C10 X118 -- tissues a, b, and c cracked	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 2.xls
CEETOX	C11 X125 -- compound left in glass weigh boat; used tip to spread the compound	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 2.xls
CEETOX	C12 X123 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 2.xls
CEETOX	C13 X134 -- compound disappeared over time; small rock on the tissue; used tip to spread; sticky	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 2.xls
CEETOX	C14 X129 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE059_43_v1.0 set 2.xls
CEETOX	C1 X118 -- thin, poor coverage; tissues cracked	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 1.xls
CEETOX	C2 X125 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 1.xls
CEETOX	C3 X123 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 1.xls
CEETOX	C4 X134 -- compound left in glass weigh boat; smaller than when weighed out; sticky; rock in middle of the tissue	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 1.xls
CEETOX	C5 X129 -- compound left in glass weigh boat; compound wet around edges at rinse	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 1.xls
CEETOX	C6 X196 -- compound left in glass weigh boat; needed	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 1.xls

laboratory	remark	filename
	extra swab	
CEETOX	C7 X110 -- required extra swab	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 1.xls
CEETOX	C8 X114 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 2.xls
CEETOX	C9 X115 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 2.xls
CEETOX	C10 X116 -- compound left in glass weigh boat; very thin, covering on tissue	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 2.xls
CEETOX	C12 X11 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE061_44_v1.0 set 2.xls
CEETOX	C1 X11 -- compound left in glass weigh boat; compound staticy	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C4 X196 -- compound left in glass weigh boat; used extra swab	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C6 X24 -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C6-MTT X24-MTT -- compound left in glass weigh boat; used extra swab	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C7 X32 -- compound left in glass and plastic weigh boats; staticy	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C7-MTT X32-MTT -- compound left in glass and plastic weigh boats; staticy	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C7 FK X32 FK -- compound left in glass weigh boat; staticy; tissues stained more than the live tissues	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C8 X42 -- lost tissues, dissolved	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C9 X55 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C10 X56 -- looks as though the tissue dissolved	EIVS_CEETOX_SE_11HCE063_45_v1.0.xls
CEETOX	C2 X196 -- compound left in glass weigh boat; used extra swab	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C1 X19 -- used extra swab	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C3 X24 -- compound left in glass weigh boat; used extra swab	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C3-MTT X24-MTT -- compound left in glass weigh boat; used extra swab	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C4 X32 -- compound left in glass weigh boat; staticy; compound left in plastic weigh boat; extra swab	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C4-MTT X32-MTT -- compound left in glass weigh boat; staticy; compound left in plastic weigh boat; extra swab	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C6 X55 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls

laboratory	remark	filename
CEETOX	C5 X42 -- only half of tissue left on tissue a	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C7 X56 -- lost tissues	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C8 X61 -- extra rinse and swab	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C10 X75 -- compound left in glass and plastic weigh boats; staticy	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C12 X80 -- compound left in glass weigh boat; extra swab; compound clumped; used tip to spread	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	C11 X77 -- used extra swab	EIVS_CEETOX_SE_11HCE065_46_v1.0.xls
CEETOX	NC -- tissue c dropped in funnel	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C1 X61 -- compound was very thick, could not spread; tissue C had very little compound dosed, tissue C dropped in funnel	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C3 X75 -- compound left in glass weigh boat; compound staticy; extra swab used	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C4 X77 -- extra swab used	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C5 X80 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C7 X95 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C7-MTT X95-MTT -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C9 X120 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C10 X157 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C11 X158 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C12 X160 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_SE_11HCE068_48_v1.0.xls
CEETOX	C1 X11 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C2 X19 -- compound hard to spread, extra swab used	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C3 X24 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C3-MTT X24-MTT -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C6 X95 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C6-MTT X95-MTT -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C8 X120 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C9 X157 -- compound left in glass weigh boat, used tip to spread	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C10 X158 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls

laboratory	remark	filename
CEETOX	C11 X160 -- compound left in glass weigh boat	EIVS_CEETOX_SE_11HCE070_49_v1.0.xls
CEETOX	C1 X32 -- compound left in glass weigh boat	EIVS_CEETOX_SE_12HCE002_2_v1.0.xls
CEETOX	C1-MTT X32-MTT -- compound left in glass weigh boat	EIVS_CEETOX_SE_12HCE002_2_v1.0.xls
CEETOX	C1 FK X32 FK -- compound left in glass weigh boat; compound did not wash off as well as the live tissues did	EIVS_CEETOX_SE_12HCE002_2_v1.0.xls
CEETOX	C2 X42 -- lost tissues	EIVS_CEETOX_SE_12HCE002_2_v1.0.xls
CEETOX	C3 X55 -- compound left in glass weigh boat	EIVS_CEETOX_SE_12HCE002_2_v1.0.xls
CEETOX	C4 X56 -- lost tissues	EIVS_CEETOX_SE_12HCE002_2_v1.0.xls
CEETOX	C1 X61 -- very sticky; could not consistently pipette or dose; very difficult to manipulate	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C3 X75 -- compound left in glass weigh boat; very staticy; tissue b dropped in funnel	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C4 X77 -- used extra swab	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C5 X80 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C7 X95 -- compound left in glass weigh boat	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C7-MTT X95-MTT -- compound left in glass weigh boat	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C9 X120 -- compound left in glass weigh boat	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C8 X113 -- tissue a dropped in funnel	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C10 X157 -- used tip to spread compound	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C11 X158 -- compound left in glass weigh boat	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
CEETOX	C12 X160 -- compound left in glass weigh boat	EIVS_CEETOX_SE_12HCE004_3_v1.0.xls
L'OREAL	TEST SUBSTANCE L11:	EIVS_LOREAL_SE_10HCE023_25.xls
L'OREAL	Discrepancy observed between the three tissues : UNQUALIFIED run	EIVS_LOREAL_SE_10HCE023_25.xls
L'OREAL	Substances L9 and L20: The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE023_25.xls
L'OREAL	The rinsing procedure was very difficult. The test substances might be not completely removed from the tissues.	EIVS_LOREAL_SE_10HCE023_25.xls
L'OREAL	TEST SUBSTANCES L9 and L20:	EIVS_LOREAL_SE_10HCE024_26.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE024_26.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_SE_10HCE024_26.xls

laboratory	remark	filename
L'OREAL	TEST SUBSTANCE L11:	EIVS_LOREAL_SE_10HCE024_26.xls
L'OREAL	Discrepancy observed between the three tissues : UNQUALIFIED run	EIVS_LOREAL_SE_10HCE024_26.xls
L'OREAL	TEST SUBSTANCE L66	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	The membrane was melted.	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCE L30	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface.	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) were scratched to facilitate its removal.	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	SD > 18% UNQUALIFIED TEST	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCE L11:	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	In the SOP, 30 ?L PBS are applied onto the tissue in order to improve the contact between the powder and the epithelium.	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	To improve such contact, the PBS was not aspirate before applying the powder L11.	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	The tissue should be well pre-wetting	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	This technical aspect might explain that the 2 first runs were invalids.	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	A SD > 18% and contradictorily classification were observed for the 3 tissues (high intra-run variability).	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCE L43:	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_SE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCES L9 and L43:	EIVS_LOREAL_SE_10HCE026_28.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE026_28.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_SE_10HCE026_28.xls
L'OREAL	TEST SUBSTANCE L17:	EIVS_LOREAL_SE_10HCE026_28.xls
L'OREAL	The vial overturned: There is no more than 8 mL left in the vial	EIVS_LOREAL_SE_10HCE026_28.xls

laboratory	remark	filename
L'OREAL	TEST SUBSTANCE L30:	EIVS_LOREAL_SE_10HCE027_29.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface.	EIVS_LOREAL_SE_10HCE027_29.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal.	EIVS_LOREAL_SE_10HCE027_29.xls
L'OREAL	TEST SUBSTANCE L66:	EIVS_LOREAL_SE_10HCE027_29.xls
L'OREAL	The membrane was melted.	EIVS_LOREAL_SE_10HCE027_29.xls
L'OREAL	TEST SUBSTANCE L43:	EIVS_LOREAL_SE_10HCE027_29.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE027_29.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues	EIVS_LOREAL_SE_10HCE027_29.xls
L'OREAL	TEST SUBSTANCE L55:	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	TEST SUBSTANCE L30:	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	MTT interaction was observed during the run (and not during the checking step of potential direct MTT reduction of test chemical).	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	So adapted killed tissues controls were added afterwards	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	TEST SUBSTANCE L11: (SOLID)	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	In the SOP, 30 ?L PBS are applied onto the tissue in order to improve the contact between the powder and the epithelium.	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	To improve such contact, the PBS was not aspirate before applying the powder L11.	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	The tissue should be well pre-wetting	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	This technical aspect might explain that the 2 first runs were invalids.	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	A SD > 18% and contradictorily classification were observed for the 3 tissues (high intra-run variability).	EIVS_LOREAL_SE_10HCE028_30.xls
L'OREAL	TEST SUBSTANCE L81:	EIVS_LOREAL_SE_10HCE029_35.xls

laboratory	remark	filename
L'OREAL	The test substance L81 dissolved the membrane of tissue constructs,	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	but the integrity of the HCE tissue was not affected	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	TEST SUBSTANCE L94:	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	TEST SUBSTANCE L74:	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	L74 is a strong MTT-reducer given a NSMTT > 50% in the controls	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	L74 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	We still acquired three qualified tests for this chemical following the rules set out in the Performance	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	Criteria document, independently of the control tissues (NSMTT>50%)	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	The values are imported in the design import spreadsheet	EIVS_LOREAL_SE_10HCE029_35.xls
L'OREAL	ADAPTED CONTROLS:	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	The direct MTT reduction of test substances was evaluated using killed HCE tissues controls (one single run, 3 tissues / substance).	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	The killed tissues used for the evaluation were provided from HCE tissues batch Nø10HCE029 (produced on March3 2010: less than a year)	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	TEST SUBSTANCE L94:	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	TEST SUBSTANCE L74:	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	L74 is a strong MTT-reducer given a NSMTT > 50% in the controls	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	L74 was not retest since the SD was < 18% (qualified	EIVS_LOREAL_SE_10HCE031_37.xls

laboratory	remark	filename
	test).	
L'OREAL	We still acquired three qualified tests for this chemical following the rules set out in the Performance	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	Criteria document, independently of the control tissues (NSMTT>50%)	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	The values are imported in the design import spreadsheet	EIVS_LOREAL_SE_10HCE031_37.xls
L'OREAL	TEST SUBSTANCE L81:	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	The test substance L81 dissolved the membrane of tissue constructs,	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	but the integrity of the HCE tissue was not affected	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	The tissue is intact, but the membrane below is melted	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	TEST SUBSTANCE L94:	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	TEST SUBSTANCE L74:	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	L74 is a strong MTT-reducer given a NSMTT > 50% in the controls	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	L7 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	We still acquired three qualified tests for this chemical following the rules set out in the Performance	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	Criteria document, independently of the control tissues (NSMTT>50%)	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	The values are imported in the design import spreadsheet	EIVS_LOREAL_SE_10HCE032_38.xls
L'OREAL	TEST SUBSTANCE L81:	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	The test substance L81 dissolved the membrane of tissue constructs,	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	but the integrity of the HCE tissue was not affected	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	The tissue is intact, but the membrane below is melted	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	TEST SUBSTANCE L11:	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	In the SOP, 30 ?L PBS are applied onto the tissue in order to improve the contact between the powder and	EIVS_LOREAL_SE_10HCE033_39.xls

laboratory	remark	filename
	the epithelium.	
L'OREAL	To improve such contact, the PBS was not aspirate before applying the powder L11.	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	The tissue should be well pre-wetting	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	This technical aspect might explain that the 2 first runs were invalids	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	A SD>18% and contradictorily classification were observed for the 3 tissues (high intra-run variability).	EIVS_LOREAL_SE_10HCE033_39.xls
L'OREAL	ADAPTED CONTROLS:	EIVS_LOREAL_SE_10HCE034_40.xls
L'OREAL	The direct MTT reduction of test substances was evaluated using killed HCE tissues controls (one single run, 3 tissues / substance).	EIVS_LOREAL_SE_10HCE034_40.xls
L'OREAL	The killed tissues used for the evaluation were provided from HCE tissues batch Nø10HCE033	EIVS_LOREAL_SE_10HCE034_40.xls
L'OREAL	(produced on September,27 2010: less than a year)	EIVS_LOREAL_SE_10HCE034_40.xls
L'OREAL	TEST SUBSTANCE L7:	EIVS_LOREAL_SE_10HCE034_40.xls
L'OREAL	L7 is a strong MTT-reducer given a NSMTT > 97% in the controls	EIVS_LOREAL_SE_10HCE034_40.xls
L'OREAL	L7 was not retest since the SD was < 18% (qualified test)	EIVS_LOREAL_SE_10HCE034_40.xls
L'OREAL	The values are imported in the design import spreadsheet	EIVS_LOREAL_SE_10HCE034_40.xls
L'OREAL	TEST SUBSTANCE L7:	EIVS_LOREAL_SE_10HCE035_41.xls
L'OREAL	L7 is a strong MTT-reducer given a NSMTT > 50% in the controls	EIVS_LOREAL_SE_10HCE035_41.xls
L'OREAL	L7 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_SE_10HCE035_41.xls
L'OREAL	We still acquired three qualified tests for this chemical following the rules set out in the Performance Criteria document, independently of the control tissues (NSMTT>50%)	EIVS_LOREAL_SE_10HCE035_41.xls
L'OREAL	The values are imported in the design import spreadsheet	EIVS_LOREAL_SE_10HCE035_41.xls
L'OREAL	TEST SUBSTANCE L63:	EIVS_LOREAL_SE_10HCE035_41.xls
L'OREAL	L63 should be withdrawn from the chemicals selection because of inconsistent chemical states	EIVS_LOREAL_SE_10HCE035_41.xls
L'OREAL	The test substance evaluated in the run was a liquid	EIVS_LOREAL_SE_10HCE035_41.xls

laboratory	remark	filename
L'OREAL	TEST SUBSTANCE L7:	EIVS_LOREAL_SE_10HCE036_42.xls
L'OREAL	L7 is a strong MTT-reducer given a NSMTT > 50% in the controls	EIVS_LOREAL_SE_10HCE036_42.xls
L'OREAL	L7 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_SE_10HCE036_42.xls
L'OREAL	We still acquired three qualified tests for this chemical following the rules set out in the Performance Criteria document	EIVS_LOREAL_SE_10HCE036_42.xls
L'OREAL	independently of the control tissues (NSMTT>50%)	EIVS_LOREAL_SE_10HCE036_42.xls
L'OREAL	The values are imported in the design import spreadsheet	EIVS_LOREAL_SE_10HCE036_42.xls
L'OREAL	TEST SUBSTANCE L63:	EIVS_LOREAL_SE_10HCE037_43.xls
L'OREAL	L63 should be withdrawn from the chemicals selection because of inconsistent chemical states	EIVS_LOREAL_SE_10HCE037_43.xls
L'OREAL	The test substance evaluated within the run was a liquid	EIVS_LOREAL_SE_10HCE037_43.xls
L'OREAL	TEST SUBSTANCE L63:	EIVS_LOREAL_SE_10HCE040_46.xls
L'OREAL	L63 should be withdrawn from the chemicals selection because of inconsistent chemical states	EIVS_LOREAL_SE_10HCE040_46.xls
L'OREAL	The test substance evaluated was a liquid	EIVS_LOREAL_SE_10HCE040_46.xls
L'OREAL	TEST SUBSTANCE L30:	EIVS_LOREAL_SE_10HCE040_46.xls
L'OREAL	MTT interaction was observed during the run (and not during the checking step of potential direct MTT reduction of test chemical).	EIVS_LOREAL_SE_10HCE040_46.xls
L'OREAL	So adapted killed tissues controls were added afterwards	EIVS_LOREAL_SE_10HCE040_46.xls
L'OREAL	NONE	EIVS_LOREAL_SE_10HCE041_47.xls
L'OREAL	TEST SUBSTANCE L119:	EIVS_LOREAL_SE_10HCE042_48.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_SE_10HCE042_48.xls
L'OREAL	TEST SUBSTANCE L104:	EIVS_LOREAL_SE_10HCE043_49.xls
L'OREAL	Post treatment, it has been noticed that the test substance applied onto the three epithelial tissues was not the chemical L104.	EIVS_LOREAL_SE_10HCE043_49.xls
L'OREAL	The raw data could not therefore be taken into account	EIVS_LOREAL_SE_10HCE043_49.xls
L'OREAL	NONE	EIVS_LOREAL_SE_10HCE044_50.xls
L'OREAL	Substances L133 and L140: The membrane of the insert	EIVS_LOREAL_SE_11HCE002_2.xls

laboratory	remark	filename
	was damaged during the rinsing step procedure	
L'OREAL	Test substance L137	EIVS_LOREAL_SE_11HCE002_2.xls
L'OREAL	This solid hardens and retracts in the presence of atmosphere.	EIVS_LOREAL_SE_11HCE002_2.xls
L'OREAL	It is important to apply it onto the tissues as soon as it was weighed.	EIVS_LOREAL_SE_11HCE002_2.xls
L'OREAL	It was notice that its volume was considerably reduced if the weighing occurred 1 hour before topical application.	EIVS_LOREAL_SE_11HCE002_2.xls
L'OREAL	Very difficult application: contact with the surface was not homogeneous even by using a mesh - > partial contact which can explain inter-tissues variability.	EIVS_LOREAL_SE_11HCE002_2.xls
L'OREAL	TEST SUBSTANCE L119:	EIVS_LOREAL_SE_11HCE007_7.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_SE_11HCE007_7.xls
L'OREAL	TEST SUBSTANCE L119:	EIVS_LOREAL_SE_11HCE008_8.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_SE_11HCE008_8.xls
L'OREAL	TEST SUBSTANCE L131:	EIVS_LOREAL_SE_11HCE009_9.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_SE_11HCE009_9.xls
L'OREAL	TEST SUBSTANCE L137:	EIVS_LOREAL_SE_11HCE009_9.xls
L'OREAL	This solid hardens and retracts in the presence of atmosphere.	EIVS_LOREAL_SE_11HCE009_9.xls
L'OREAL	It is important to apply it onto the tissues as soon as it was weighed.	EIVS_LOREAL_SE_11HCE009_9.xls
L'OREAL	It was notice that its volume was considerably reduced if the weighing occurred 1 hour before topical application.	EIVS_LOREAL_SE_11HCE009_9.xls
L'OREAL	Very difficult application: contact with the surface was not homogeneous even by using a mesh - > partial contact which can explain inter-tissues variability.	EIVS_LOREAL_SE_11HCE009_9.xls
L'OREAL	TEST SUBSTANCE L137:	EIVS_LOREAL_SE_11HCE014_14.xls
L'OREAL	This solid hardens and retracts in the presence of atmosphere.	EIVS_LOREAL_SE_11HCE014_14.xls
L'OREAL	It is important to apply it onto the tissues as soon as it was weighed.	EIVS_LOREAL_SE_11HCE014_14.xls

laboratory	remark	filename
L'OREAL	It was notice that its volume was considerably reduced if the weighing occurred 1 hour before topical application.	EIVS_LOREAL_SE_11HCE014_14.xls
L'OREAL	Very difficult application: contact with the surface was not homogeneous even by using a mesh - > partial contact which can explain inter-tissues variability.	EIVS_LOREAL_SE_11HCE014_14.xls
L'OREAL	Substance L6:	EIVS_LOREAL_SE_11HCE020_18.xls
L'OREAL	very strong coloring chemical (red)	EIVS_LOREAL_SE_11HCE020_18.xls
L'OREAL	High variability due to the staining coloring properties of the chemical (critical washing step)	EIVS_LOREAL_SE_11HCE020_18.xls
L'OREAL	TEST SUBSTANCES L15	EIVS_LOREAL_SE_11HCE020_18.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface.	EIVS_LOREAL_SE_11HCE020_18.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal	EIVS_LOREAL_SE_11HCE020_18.xls
L'OREAL	Initial remarks: 06/10/2011	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	TEST SUBSTANCE L58:	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	strong MTT reducer - no issue during the washing step	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	TEST SUBSTANCE L100:	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	MTT and coloring test substance	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	Visual observation: the tissues are not dead but only stained due to the color (red)	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	--> not cytotoxicity observed	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	12/10/2012:	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	Evaluation of L58 using killed tissues, as requested by the EIVS core group	EIVS_LOREAL_SE_11HCE022_19.xls
L'OREAL	TEST SUBSTANCES L15	EIVS_LOREAL_SE_11HCE024_20.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface.	EIVS_LOREAL_SE_11HCE024_20.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal	EIVS_LOREAL_SE_11HCE024_20.xls
L'OREAL	TEST SUBSTANCE L6:	EIVS_LOREAL_SE_11HCE024_20.xls
L'OREAL	strong coloring chemical (powder): critical washing step	EIVS_LOREAL_SE_11HCE024_20.xls
L'OREAL	high variability due to the chemical which was very difficult to remove completely from the tissues (critical washing)	EIVS_LOREAL_SE_11HCE024_20.xls

laboratory	remark	filename
L'OREAL	TEST SUBSTANCE L185:	EIVS_LOREAL_SE_11HCE024_20.xls
L'OREAL	Sticky chemical : mesh was used to uniformly spread the chemical on the tissues	EIVS_LOREAL_SE_11HCE024_20.xls
L'OREAL	INITIAL REMARKS ON 06/10/2011	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	TEST SUBSTANCES L174	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	The vial overturned: There is no more than 7 mL left in the vial	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	TEST SUBSTANCE L6:	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	The experiment was performed ONLY with KILLED tissues to determine the individual NSMTT values	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	Cell viability determination: The data obtained with the living tissues are defined on files Nø 11HCE020_18;	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	11HCE024_20, 11HCE032_25, 11HCE034_26 and 11HCE036_27	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	MTT REDUCERS: TEST SUBSTANCES L6, L33, L58, L100, L161, L169 and L174	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	To determine the NSMTT% of the MTT reducers, the experiment was performed using killed HCE tissues (batch Nø 11HCE028).	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	The individual Ku and Kt-Cx values (6) obtained in this run was then reported to the respective Excel spreadsheets of each test substance	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	12/10/2012:	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	Evaluation of L58 using killed tissues, as requested by the EIVS core group	EIVS_LOREAL_SE_11HCE029_23.xls
L'OREAL	Initial remarks: 24/06/2011	EIVS_LOREAL_SE_11HCE032_25(1).xls
L'OREAL	TEST SUBSTANCE L185:	EIVS_LOREAL_SE_11HCE032_25(1).xls
L'OREAL	Sticky chemical: A mesh was used to uniformly spread the chemical on the three tissues	EIVS_LOREAL_SE_11HCE032_25(1).xls
L'OREAL	TEST SUBSTANCE L6:	EIVS_LOREAL_SE_11HCE032_25(1).xls
L'OREAL	Difficult to rinse this MTT and coloring test substance : high variation observed	EIVS_LOREAL_SE_11HCE032_25(1).xls
L'OREAL	TEST SUBSTANCE L158:	EIVS_LOREAL_SE_11HCE032_25(1).xls
L'OREAL	Difficult to rinse this MTT reducer	EIVS_LOREAL_SE_11HCE032_25(1).xls
L'OREAL	12/10/2012:	EIVS_LOREAL_SE_11HCE032_25(1).xls

laboratory	remark	filename
L'OREAL	Evaluation of L58 using killed tissues, as requested by the EIVS core group	EIVS_LOREAL_SE_11HCE032_25(1).xls
L'OREAL	INITIAL REMARKS ON 07/01/2011	EIVS_LOREAL_SE_11HCE034_26(1).xls
L'OREAL	TEST SUBSTANCE L58:	EIVS_LOREAL_SE_11HCE034_26(1).xls
L'OREAL	MTT reducer diffucilt to rinse: high variability observed	EIVS_LOREAL_SE_11HCE034_26(1).xls
L'OREAL	TEST SUBSTANCE L15:	EIVS_LOREAL_SE_11HCE034_26(1).xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface	EIVS_LOREAL_SE_11HCE034_26(1).xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal	EIVS_LOREAL_SE_11HCE034_26(1).xls
L'OREAL	12/10/2012:	EIVS_LOREAL_SE_11HCE034_26(1).xls
L'OREAL	Evaluation of L58 using killed tissues, as requested by the EIVS core group	EIVS_LOREAL_SE_11HCE034_26(1).xls
L'OREAL	INITIAL REMARKS ON 07/08/2011	EIVS_LOREAL_SE_11HCE036_27.xls
L'OREAL	TEST SUBSTANCE L6:	EIVS_LOREAL_SE_11HCE036_27.xls
L'OREAL	difficult to rinse: more intense staining observed in one tissue	EIVS_LOREAL_SE_11HCE036_27.xls
L'OREAL	12/10/2012:	EIVS_LOREAL_SE_11HCE036_27.xls
L'OREAL	Evaluation of L58 using killed tissues, as requested by the EIVS core group	EIVS_LOREAL_SE_11HCE036_27.xls

LE

laboratory	remark	filename
CARDAM	C66 tissues are damaged by the test item	EIVS_CARDAM_LE1_10HCE035_41.xls
CARDAM	C66 tissues are damaged by the test item	EIVS_CARDAM_LE1_10HCE036_42.xls
CARDAM	C90 tissues eaten away	EIVS_CARDAM_LE1_10HCE037_43.xls
CARDAM	C82, hole in tissues caused by test item	EIVS_CARDAM_LE1_10HCE037_43.xls
CARDAM	C11 and C13 tissue came loose during washing step	EIVS_CARDAM_LE1_10HCE040_46.xls
CARDAM	C11 and C13 tissue came loose during washing step	EIVS_CARDAM_LE1_10HCE041_47.xls
CARDAM	C45 tissues are still colored after washing step	EIVS_CARDAM_LE1_10HCE041_47.xls
CARDAM	C50: Half the tissue was gone in cup 1, in cup 3 was the tissue completely gone	EIVS_CARDAM_LE1_10HCE042_48.xls
CARDAM	C45 tissues are still colored after washing step	EIVS_CARDAM_LE1_10HCE042_48.xls
CARDAM	C53: %NSMTT is unqualified because >50%; condition 2!	EIVS_CARDAM_LE1_10HCE042_48.xls

laboratory	remark	filename
	(see e-mail from Nathalie 5th Nov 2010!)	
CARDAM	SD >18% for killed tissue C53 but this is not the case in run LE from week 47. Not repeat killed tissue because test	EIVS_CARDAM_LE1_10HCE042_48.xls
CARDAM	item is not compatible for HCE test	EIVS_CARDAM_LE1_10HCE042_48.xls
CARDAM	C96 washing was preformed using a cotton bud	EIVS_CARDAM_LE2_10HCE035_41.xls
CARDAM	C82 tissues are damaged by the test item	EIVS_CARDAM_LE2_10HCE035_41.xls
CARDAM	New data killed tissue C87 (from week 45). SD>18% in runs 10HCE036 and 10HCE037 with data killed	EIVS_CARDAM_LE2_10HCE035_41.xls
CARDAM	tissue from week 40.	EIVS_CARDAM_LE2_10HCE035_41.xls
CARDAM	With this new data from killed tissue, C87 changes from a non-irritant call to a irritant call	EIVS_CARDAM_LE2_10HCE035_41.xls
CARDAM	Test item C82 has created a hole in the tissues	EIVS_CARDAM_LE2_10HCE036_42.xls
CARDAM	Test item C94 has created a hole in tissue 2	EIVS_CARDAM_LE2_10HCE036_42.xls
CARDAM	C11, C12, tissue eaten away partially to complete	EIVS_CARDAM_LE2_10HCE037_43.xls
CARDAM	C45 tissues are still colored after washing step	EIVS_CARDAM_LE2_10HCE040_46.xls
CARDAM	C53: %NSMTT is unqualified because >50%; condition 2! (see e-mail from Nathalie 5th Nov 2010!)	EIVS_CARDAM_LE2_10HCE040_46.xls
CARDAM	SD >18% for killed tissue C53 but this is not the case in run LE from week 47. Not repeat killed tissue because test	EIVS_CARDAM_LE2_10HCE040_46.xls
CARDAM	item is not compatible for HCE test	EIVS_CARDAM_LE2_10HCE040_46.xls
CARDAM	C6, no pictures, test item can not leave L0210, terrible smell	EIVS_CARDAM_LE2_10HCE041_47.xls
CARDAM	C53: %NSMTT is unqualified because >50%; condition 2! (see e-mail from Nathalie 5th Nov 2010!)	EIVS_CARDAM_LE2_10HCE041_47.xls
CARDAM	SD >18% for killed tissue C53 but this is not the case in run LE from week 47. Not repeat killed tissue because test	EIVS_CARDAM_LE2_10HCE041_47.xls
CARDAM	item is not compatible for HCE test	EIVS_CARDAM_LE2_10HCE041_47.xls
CARDAM	C134 test item reacts with the plastic cup, leaves a white precipitate on tissue;	EIVS_CARDAM_LE2_10HCE042_48.xls
CARDAM	C6, no pictures, test item can not leave L0210, terrible smell	EIVS_CARDAM_LE2_10HCE042_48.xls
CARDAM	No pictures from C30 en C33, short exposure.	EIVS_CARDAM_LE_10HCE029_35.xls

laboratory	remark	filename
	Observation done without pictures	
CARDAM	Test item C17 sticks to tissue, wash off with cotton bud.	EIVS_CARDAM_LE_10HCE029_35.xls
CARDAM	Test item C17and testitem C30, MTT solution beneath tissue is purple after 3H incubation and not just tissue	EIVS_CARDAM_LE_10HCE029_35.xls
CARDAM	PBS without Ca and Mg is used from set 4 short exposure untill positive controle long exposure	EIVS_CARDAM_LE_10HCE029_35.xls
CARDAM	c17 was hard to spread across the surface of the tissue	EIVS_CARDAM_LE_10HCE031_37.xls
CARDAM	The first tissue of c19 was damaged in the middle	EIVS_CARDAM_LE_10HCE031_37.xls
CARDAM	Test item C17 sticks to tissue, wash off with cotton bud.	EIVS_CARDAM_LE_10HCE031_37.xls
CARDAM	Test item C17and testitem C30, MTT solution beneath tissue is purple after 3H incubation and not just tissue	EIVS_CARDAM_LE_10HCE031_37.xls
CARDAM	Tissue 2 and 3 of C26 came loose during washing step	EIVS_CARDAM_LE_10HCE032_38.xls
CARDAM	C34, C34-MTT and C77 applied with normal pipette (AVR)	EIVS_CARDAM_LE_10HCE032_38.xls
CARDAM	C77 tissues are eaten away by the test item	EIVS_CARDAM_LE_10HCE033_39(C77).xls
CARDAM	C66 tissues are eaten away by the test item	EIVS_CARDAM_LE_10HCE033_39.xls
CARDAM	NC tissue 1 air bubble present	EIVS_CARDAM_LE_10HCE033_39.xls
CARDAM	C51-C54-C65: After 3 h MTT-incubation: living tissues on edge (purple) while white in the middle (AVR)	EIVS_CARDAM_LE_10HCE033_39.xls
CARDAM	C35 by mistake 4 valid runs (AVR 04/01/2011)	EIVS_CARDAM_LE_10HCE033_39.xls
CARDAM	C45 and C101 tissues are still colored after washing step	EIVS_CARDAM_LE_10HCE044_50.xls
CARDAM	C127 andC132, hole in all tissues due to the test item	EIVS_CARDAM_LE_10HCE044_50.xls
CARDAM	C6 no picture taken after 3h MTT because needs to stay in Biohazard because of smell	EIVS_CARDAM_LE_10HCE044_50.xls
CARDAM	C6: %NSMTT is unqualified because >50%; condition 2! (see e-mail from Nathalie 5th Nov 2010!)	EIVS_CARDAM_LE_10HCE044_50.xls
CARDAM	C134: It looks like a white precipitate is formed on the tissues. Reaction of test item with the tissue???	EIVS_CARDAM_LE_11HCE003_3.xls
CARDAM	C127, C132, hole in tissue caused by test item	EIVS_CARDAM_LE_11HCE003_3.xls
CARDAM	C106 forms a mucus on tissue, remove with cotton tip	EIVS_CARDAM_LE_11HCE003_3.xls
CARDAM	Tissues might have had extra stress, Since the delivery by courier went first wrongly to UK and then to CARDAM	EIVS_CARDAM_LE_11HCE003_3.xls
CARDAM	C134, C138: It looks like a white precipitate is formed on the tissues. Reaction of test item with the tissue???	EIVS_CARDAM_LE_11HCE005_5.xls
CARDAM	C106 forms a mucus on tissue, remove with cotton tip	EIVS_CARDAM_LE_11HCE005_5.xls

laboratory	remark	filename
CARDAM	C138: It looks like a white precipitate is formed on the tissues. Reaction of test item with the tissue???	EIVS_CARDAM_LE_11HCE006_6.xls
CARDAM	C106 forms a mucus on tissue, remove with cotton tip	EIVS_CARDAM_LE_11HCE006_6.xls
CARDAM	C109, sticky but with positive displacement pipette is OK.	EIVS_CARDAM_LE_11HCE007_7.xls
CARDAM	wash with cotton tip	EIVS_CARDAM_LE_11HCE007_7.xls
CARDAM	C109, sticky but with positive displacement pipette is OK.	EIVS_CARDAM_LE_11HCE008_8.xls
CARDAM	wash with cotton tip	EIVS_CARDAM_LE_11HCE008_8.xls
CARDAM	C124, resin, difficult to cover whole tissue	EIVS_CARDAM_LE_11HCE008_8.xls
CARDAM	C109, sticky but with positive displacement pipette is OK.	EIVS_CARDAM_LE_11HCE009_9.xls
CARDAM	wash with cotton tip	EIVS_CARDAM_LE_11HCE009_9.xls
CARDAM	C124, resin, difficult to cover whole tissue	EIVS_CARDAM_LE_11HCE009_9.xls
CARDAM	C28 washed once more after MTT incubation, before isopropanol incubation	EIVS_CARDAM_LE_11HCE020_18.xls
CARDAM	C124, resin, difficult to spread	EIVS_CARDAM_LE_11HCE020_18.xls
CARDAM	C28 and C52, washed once more after 16 h incubation, before MTT incubation	EIVS_CARDAM_LE_11HCE022_19.xls
CARDAM	C28 and C52, washed once more after post incubation, before MTT incubation	EIVS_CARDAM_LE_11HCE024_20.xls
CARDAM	C52, washed once more after post incubation, before MTT incubation	EIVS_CARDAM_LE_11HCE026_21.xls
CARDAM	C52, washed once more after post incubation, before MTT incubation	EIVS_CARDAM_LE_11HCE029_23.xls
CARDAM	C55, wash with cotton tip, forms mucus layer	EIVS_CARDAM_LE_11HCE029_23.xls
CARDAM	C55, wash with cotton tip, forms mucus layer	EIVS_CARDAM_LE_11HCE032_25.xls
CARDAM	C163, viscous, difficult to spread	EIVS_CARDAM_LE_11HCE032_25.xls
CARDAM	C55, wash with cotton tip, mucus layer	EIVS_CARDAM_LE_11HCE034_26.xls
CARDAM	C163, viscous, difficult to spread	EIVS_CARDAM_LE_11HCE034_26.xls
CARDAM	C163, difficult to spread, viscous	EIVS_CARDAM_LE_11HCE038_28.xls
CEETOX	PC -- some compound on sides of each insert	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C1 -- some clumps, mostly spread	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C2b -- dosed 10 seconds late	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C3 -- difficult to spread, pulled to sides of insert	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls

laboratory	remark	filename
CEETOX	C4 -- difficult to spread, but mostly staying spread	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C5 -- very difficult to spread, pulled to sides, not covering the tissue	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C6 -- a little clumpy, some sticking to glass weigh boat	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C7 -- will not spread, pulls to the sides	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C9c -- a lot on the side of the insert, not as uniform spreading	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	PC -- transferred late	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C3 -- plastic degrading, tissue pulled away	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C4 -- tissue is see through in places, very rippled; c -- tore the tissue	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C6 -- compound looks melted on to the tissue some	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	a -- looks rippled and torn	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C7 -- plastic degrading	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	a -- tissue may be cracked	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C8 -- tissue washed off (c slightly less than a and b)	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	C9 -- compound came off in a clump from a; but b and c had liquid	EIVS_CEETOX_LE_10HCE023_25_v1.0 UPDATED.xls
CEETOX	PCb - clumped to the side, tried to tap and spread	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C3 - difficulty spreading, pulled to sides	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C4 - same as C3, very thin	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C5 - difficult to spread, may have been evaporating	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C6 - a -- looks clumped, but good coverage	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	b -- some compound fell out of insert	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C7b - better coverage than a; some difficulty spreading compound	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C9a - a little clumped on side, but good coverage	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C3 - tissue wrinkled, plastic degraded	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C4 - wrinkled tissues	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	a -- tissue ripped and fell off	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	b -- tissue rolled up	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	c -- tissue fell off	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C5 - plastic degraded; not full coverage	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C6 - melted compound, a and b have bubbles under the	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls

laboratory	remark	filename
	tissue	
CEETOX	C7 - not covered, plastic degraded a little around the edge	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C8 - tissue looks broken	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	C9 - compound turned to liquid on the tissue	EIVS_CEETOX_LE_10HCE024_26_v1.0.xls
CEETOX	PC1a -- compound was very wet on top of tissue	EIVS_CEETOX_LE_10HCE042_48_v1.0 UPDATED.xls
CEETOX	C3 or C13 -- compound difficult to spread	EIVS_CEETOX_LE_10HCE042_48_v1.0 UPDATED.xls
CEETOX	C5 or C15 -- compound difficult to spread	EIVS_CEETOX_LE_10HCE042_48_v1.0 UPDATED.xls
CEETOX	C7 or C17 -- compound difficult to spread	EIVS_CEETOX_LE_10HCE042_48_v1.0 UPDATED.xls
CEETOX	C9 or C19 -- compound difficult to spread	EIVS_CEETOX_LE_10HCE042_48_v1.0 UPDATED.xls
CEETOX	C8 or C18 -- tissue lost during rinsing or dissolved	EIVS_CEETOX_LE_10HCE042_48_v1.0 UPDATED.xls
CEETOX	C1 b or C11 b -- clumps, not great coverage over the tissue	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C3 or C13 -- some difficulty spreading the compound	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C4 b or C14 b -- dosed 10 seconds late	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C5 or C15 -- very hard to spread; had better coverage not spreading	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C6 a or C16 a -- lost some compound in weigh boat	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C6 b or C16 b -- some compound left in glass weigh boat	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C7 or C17 -- very difficult to spread the compound	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C9 or C19 b and c -- clumps/rocks; had ok coverage over tissue	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C8 or C18 -- tissue dissolved	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C9 or C19 -- compound dissolved into a liquid	EIVS_CEETOX_LE_10HCE043_49_v1.0 UPDATED.xls
CEETOX	C4/C14 -- hard to spread	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C5/C15 -- very difficult to spread	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C6/C16 b -- some clumps, but good coverage	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C6/C16 c -- tissue spilled; 1/4 of compound left in weigh boat (estimate)	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C7/C17 -- thin, somewhat hard to spread	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C9/C19 -- clumpy, but ok coverage	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C9/C19 a -- clumps, dosed 20 seconds late	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C3/C13 -- plastic degraded	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C4/C14 -- tissue degraded, holes in it	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls

laboratory	remark	filename
CEETOX	C5/C15 -- plastic degraded	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C8/C18 -- no tissue	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	C10/C20 -- did not cover tissue	EIVS_CEETOX_LE_10HCE044_50_v1.0 UPDATED.xls
CEETOX	PC b -- some compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C1 -- difficult to spread the compound	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C2 -- clumpy compound, but managed to get good coverage	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	b -- lots of compound stuck in glass weigh boat	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	c -- lots of compound in glass weigh boat and secondary weigh boat	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C3 -- clumps or rocks, but spread over tissue	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	b -- some in weigh boat	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	c -- used tip to spread, some compound in weigh boat	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C5 -- compound left in glass weigh boats	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C5 c -- tissue dropped, compound still covered the insert	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C6 -- compound thin, and difficult to spread	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C9 -- some compound left in glass weigh boats, and used tip to spread for all three tissues	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C6 -- tissues wrinkled	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C3 -- tissue dropped, but recovered	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	C7 -- tissues rippled and wrinkled	EIVS_CEETOX_LE_11HCE003_3_v1.0.xls
CEETOX	PC -- used tip to spread	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY UPDATED.xls
CEETOX	C2 -- some compound in glass weigh boat; used tip	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY UPDATED.xls
CEETOX	C3 a -- used tip to spread	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY UPDATED.xls
CEETOX	C6 -- thin; difficult to spread	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY UPDATED.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY UPDATED.xls
CEETOX	C1 -- tissue looks smooth	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY UPDATED.xls
CEETOX	C4 -- looks like the tissue was lost (applies to all three tissues)	EIVS_CEETOX_LE_11HCE004_4_v1.0 JOEY UPDATED.xls
CeeTox	PCb- 15 seconds late on dosing	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls
CeeTox	C1b- bubbles in compound on tissue	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls
CeeTox	C4- not all compound removed from tissue with extra rinse	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls
CeeTox	C4a- some compund left in weigh boat	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls

laboratory	remark	filename
CeeTox	C6a- 1 min late on dosing	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls
CeeTox	C7- soapy, extra rinse	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls
CeeTox	C8c- dropped in flask	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls
CeeTox	C4 - After incubation the compound stained the media and tissue a dark color see pictures in 11HCE007 Lisa	EIVS_CEETOX_LE_11HCE004_4_v1.0.xls
CEETOX	PC b -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	PC -- used tip on all tissues	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	C12 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	C13 -- compound is staticky; some compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	C15 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	C11 -- plastic degraded	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	C16 -- tissues rippled	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	C17 -- tissues rippled	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 1 JOEY.xls
CEETOX	PC -- compound in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	C2 -- used tip to spread	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	C3 -- used tip to spread; difficult to spread	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	C6 FK -- harder to spread on FK tissues	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	C1 -- bumps on tissues	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	C4 -- lost tissues in bucket; no chance in saving	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	C4 FK a and c -- tissue cracked	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	C6 -- not spread well on the tissues	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	C7 -- tissues cracked	EIVS_CEETOX_LE_11HCE006_6_v1.0 SET 2 JOEY.xls
CEETOX	PC - Spread with tip	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls
CEETOX	C2b - 30 seconds early rinse	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls
CEETOX	C4 - not all compound removed with extra rinse	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls
CEETOX	C4a - clumps of compound	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls
CEETOX	C5 - extra rinse, 30 seconds late on rinsing	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls
CEETOX	C6a - nicked tissue	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls
CEETOX	C7c - nicked tissue	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls
CEETOX	C4 - After incubation the compound stained the media and tissue a dark color see pictures in 11HCE007 Lisa	EIVS_CEETOX_LE_11HCE006_6_v1.0.xls
CEETOX	PC a -- compound spilled; however, recovered	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 JOEY.xls

laboratory	remark	filename
CEETOX	PC -- used tip	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 JOEY.xls
CEETOX	C2 -- used tip to spread	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 JOEY.xls
CEETOX	C3 -- used tip to spread	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 JOEY.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 JOEY.xls
CEETOX	C4 -- tissue looks like it washed off the insert	EIVS_CEETOX_LE_11HCE007_7_v1.0 SET 2 JOEY.xls
CEETOX	PC -- used tip to spread	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	C11 -- hard to spread compound, tended to pull to the sides of the insert	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	C12 -- used tip to spread	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	C13 -- used tip to spread	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	C19 -- used tip to spread	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	Compound left in all glass weigh boats	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	Rinisng	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	C13 -- compound seemed to dissolve on the tissue	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	C14 -- tissue appears to be gone	EIVS_CEETOX_LE_11HCE007_7_v1.0 set 1.xls
CEETOX	PC - spread with tip	EIVS_CEETOX_LE_11HCE007_7_v1.0.xls
CEETOX	C1 - extra rinse	EIVS_CEETOX_LE_11HCE007_7_v1.0.xls
CEETOX	C1 - all tissue appears detatched from membrane	EIVS_CEETOX_LE_11HCE007_7_v1.0.xls
CEETOX	C4b - compound remaining in weigh boat	EIVS_CEETOX_LE_11HCE007_7_v1.0.xls
CEETOX	C4 - not all compound removed after extra rinse	EIVS_CEETOX_LE_11HCE007_7_v1.0.xls
CEETOX	C4 - After incubation the compound stained the media and tissue a dark color see pictures in 11HCE007 Lisa	EIVS_CEETOX_LE_11HCE007_7_v1.0.xls
CEETOX	PC -- used tip to spread, some compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls
CEETOX	PCb -- dosed 30 seconds late	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls
CEETOX	x13 C1 -- used tip to spread	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls
CEETOX	x39 C2 -- some compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls
CEETOX	x8 C2 -- used tip to spread; compound in glass weigh boat and outer weigh boat	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls
CEETOX	X49 C7 -- used tip to spread	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls
CEETOX	x128 C4 -- tissues cracked after rinsing	EIVS_CEETOX_LE_11HCE008_8_v1.0 JOEY.xls
CEETOX	PC - spread with tip	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls
CEETOX	C1 - spread with tip	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls
CEETOX	C2 - spread with tip	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls
CEETOX	C2 - two extra rinses	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls

laboratory	remark	filename
CEETOX	C3 - extra rinse	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls
CEETOX	C4 - spread with tip	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls
CEETOX	C8a - spread with tip	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls
CEETOX	C8 - minute late rinsing, compound cemented to tissue used a swab to remove	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls
CEETOX	C8c - after recovery compound remained on tissue, re-rinsed with swab	EIVS_CEETOX_LE_11HCE008_8_v1.0 LISA.xls
CEETOX	PC -- used tip	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	C1 x13 -- used tip; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	C3 x8 -- used tip	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	C3-MTT x8-MTT -- used tip	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	C7 x43 -- used tip	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	C3 x8 and C3-MTT x8-MTT -- behind on rinsing; color would not come off	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	C8 x44 -- very difficult to rinse off; cemented to the tissue; had to use swab to break away	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	C3 x8 -- rinsed after post incubation to remove residual color 4 Mar 11	EIVS_CEETOX_LE_11HCE009_9_v1.0 JOEY FAILED RUN UPDATED.xls
CEETOX	PC invalid, no comments	EIVS_CEETOX_LE_11HCE009_9_v1.0 LISA FAILED RUN UPDATED.xls
CEETOX	PC -- used tip to spread	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 1.xls
CEETOX	C1 X13 -- used tip to spread	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 1.xls
CEETOX	C3 X8 -- staticy, all over glass weigh boat, used tip to spread	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 1.xls
CEETOX	C3-MTT X8-MTT -- same as above	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 1.xls
CEETOX	C4 X128 -- 1 minute late rinsing, extra rinse, ripped tissues	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 1.xls
CEETOX	C15 X103 -- hard to spread compound	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 2.xls

laboratory	remark	filename
CEETOX	C16 X63 -- compound would not stay spread	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 2.xls
CEETOX	C17 X47 -- stuck to glass weigh boat, used tip to apply and spread	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 2.xls
CEETOX	C18 X17 -- hard to spread compound	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 2.xls
CEETOX	C13 X126 -- compound dissolved on the tissues	EIVS_CEETOX_LE_11HCE013_13_v1.0 set 2.xls
CEETOX	PC -- used tip to spread	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 1.xls
CEETOX	C1 X13 -- used tip to spread compound	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 1.xls
CEETOX	C4 X126 -- did not spread well over the tissues	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 1.xls
CEETOX	C6 X47 -- used tip to spread	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 1.xls
CEETOX	C8 X8 -- used tip to spread; all tissues received extra swab; one minute behind	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 1.xls
CEETOX	C8-MTT X8-MTT -- used tip to spread; all tissues received extra swab	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 1.xls
CEETOX	C5 X43 -- tissues a and c slightly ripped during rinsing	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 1.xls
CEETOX	After Post-Incubation swabbed X13, X8 and X8-MTT with PBS and cotton tip to remove excess color before placing in MTT	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 1.xls
CEETOX	C17 X128 -- thin, difficult to spread	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 2.xls
CEETOX	C18 X39 -- used tip to spread	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 2.xls
CEETOX	PC2 -- used tip to spread	EIVS_CEETOX_LE_11HCE020_18_v1.0 set 2.xls
CEETOX	PC LE -- used tip to spread; compound left in weigh boat	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C1 X21 -- used tip to spread	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C3 X126 -- compound did not cover the tissue well; compound left in weigh boat	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C4 X14 -- compound did not cover well; used tip to spread; compound left in weigh boat	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C5 X46 -- compound left in weigh boat; c dropped in funnel; all tissues had compound left after rinsing	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C6 X27 -- compound left in weigh boat; all tissues received extra rinses	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C7 X50 -- compound left in weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C8 X53 -- tissues received extra rinse	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C10 X84 -- compound left in weigh boat; b dropped in funnel	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls

laboratory	remark	filename
CEETOX	C11 X87 -- compound left in weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C12 X102 -- compound left in weigh boat	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C13 X107 -- used tip to spread; compound left in weigh boat	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 1.xls
CEETOX	C14 X108 -- compound left in weigh boat; used tip; did not get good coverage with the compound	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C15 X109 -- compound left in weight boat; used tip to spread; compound solidified as a clump in weigh boat	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C16 X110 -- dosed as a liquid; a dosed 20 seconds late; extra rinse for all tissues	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C17 X118 b -- dosed 30 seconds late; tissue torn at rinsing	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C18 X138 -- compound left on tissue at rinsing	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C19 X139 -- tissues tearing at rinsing	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C21 X13 -- used tip to spread; compound left in weigh boats	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C22 X43 -- compound left in weigh boats; tissues ripped in the middle	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C23 X47 -- used tip to spread; compound left in weigh boats	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	PC2 -- compound left in weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C25 X68 -- precipitate in liquid	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C26 X8 -- compound left in weigh boat; extra rinse and swab; extra rinse and swab before transfer to MTT	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C26-MTT X8-MTT -- compound left in weigh boat; extra rinse and swab; extra rinse and swab before transfer to MTT	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	CdJ	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	X47 is recorded as run 5 but is infact run 6. This is changed in the import program.	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 2.xls
CEETOX	C30 X81 -- extra swab; globs left on the tissue	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 3.xls
CEETOX	C31 X82 -- 10 seconds late rinsing tissue a	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 3.xls
CEETOX	C34 X39 -- compound left in weigh boat	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 3.xls
CEETOX	PC3 -- used tip to spread; compound left in weigh boat	EIVS_CEETOX_LE_11HCE022_19_v1.0 set 3.xls

laboratory	remark	filename
CEETOX	PC -- used tip to spread; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	C1 X14 -- used tip; rocks on the tissues, did not cover well; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	C2 X46 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	C8 X87 -- compound left in glass weigh boat; used tip to spread; not good coverage	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	C1 X14 -- compound dissolved on tissue	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	C3 X27 and C3-MTT X27-MTT -- hole in the color; color coming off only a little; extra rinse and swab	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	C6 X70 -- extra swab	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	C1 X14 and C1-MTT X14-MTT -- received two extra swabs before MTT	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 1.xls
CEETOX	PC -- used tip; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C11 X108 -- not good coverage; used tip to spread; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C12 X109 -- compound left in glass weigh boat; used tip to spread; compound gummed up on the tissue	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C14 X118 -- compound thin and difficult to spread	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C16 X138 -- compound thin and difficult to spread	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C17 X139 -- compound thin	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C19 X21 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C20 X112 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C21 X126 -- compound left in glass weigh boat; used tip to spread; would not come off of glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C11 X108 -- dissolved on tissue	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C12 X109 -- stuck on tissue, had to be wiped off with wet swab	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C12 a X109 a -- gel on top of tissue	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C14 X118 -- tissue degraded	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C15 X136 -- may have washed off the tissue	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	C16 X138 -- tissue cracked	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	CdJ	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls

laboratory	remark	filename
CEETOX	X39 is recorded as run 5 but is infact run 6. This is changed in the import program	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 2.xls
CEETOX	PC -- used tip to spread	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	C22 X111 -- used tip to spread; compound left in glass weight boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	C22c X111c -- compound spilled into plastic weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	C23 X114 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	C25 X116 -- used tip to spread	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	C28 X125 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	C30 X131 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	C31 X133 -- compound thin	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	C32 X134 -- compound would not spread; sat in the middle of the tissues	EIVS_CEETOX_LE_11HCE034_26_v1.0 set 3.xls
CEETOX	PC -- used tip to spread; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C1 X14 -- used tip to spread; compound left in glass weigh boat; in a and b some compound came out of the glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C1-MTT X14-MTT --used tip to spread; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C2 X46 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C3 X27 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C3-MTT c X27-MTT c -- tissue flipped; used tip to better spread remaining compound	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C4 X50 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C4 a X50 a -- some compound came out of glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C6 X70 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C6 a X70 a -- compound hardened and could not spread; had better coverage with b and c	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C8 X87 -- compound left in glass weigh boat; used tip to spread; dissolved on tissues	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C9 X102 -- compound left in glass weigh boat; used tip to	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls

laboratory	remark	filename
	spread	
CEETOX	C10 X07 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C2 X46 -- extra swab	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C3 X27 and C3-MTT and X27-MTT -- extra rinse and swab	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C3b and X27b -- ripped tissue	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C5 X53 -- extra swab	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	C6 X70 -- extra swab, had to push the compound off	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 1.xls
CEETOX	PC -- used tip to spread; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C11 X108 -- poor coverage; used tip to spread; melted on the tissue	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C12 X109 -- had to scrape out of the weigh boat; used tip to spread; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C18 X111 -- used tip to spread; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C19 X114 a -- lost some compound in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	compound left in all glass weigh boats	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C20 X115 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C21 X116 -- used tip to spread; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C11 X108 -- completely dissolved	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C13 X110 -- rinsed 30 seconds late; had to do extra swab	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C14 X118 -- tissues cracked	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C16 X138 -- tissues cracked	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	C17 X139 -- tissues ripped	EIVS_CEETOX_LE_11HCE040_29_v1.0 set 2.xls
CEETOX	PC -- used tip to spread compound, compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C13 X111 -- used tip to spread compound, compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C14 X114 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C15 X115 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C16 X116 -- compound left in glass weigh boat; can't tell	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls

laboratory	remark	filename
	if the compound completely covered the tissue visually	
CEETOX	C17 X50 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C18 X119 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C19 X123 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C20 X125 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C21 X129 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	C22 X131 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE047_37_v1.0.xls
CEETOX	PC -- used tip to spread compound; compound left in glass weigh boat; tissue a looked very wet	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C1 X111 -- used tip to spread compound; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C2 X114 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C3 X115 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C4 X116 -- compound left in glass weigh boat; could not see compound well on tissue; used tip to spread compound	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C5 X50 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C6 X119 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C7 X123 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C8 X125 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C9 X129 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	C10 X131 -- compound left in glass weigh boat; used tip to spread; tissue a looked wet	EIVS_CEETOX_LE_11HCE049_38_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE051_39_v1.0.xls
CEETOX	C14 X134 -- compound sat in the middle of the tissue; one rock, but not spread well; lost tissue a during rinsing	EIVS_CEETOX_LE_11HCE051_39_v1.0.xls
CEETOX	C15 X119 -- compound left in glass weigh boat; used tip to spread compound; staticy; compound dissolved	EIVS_CEETOX_LE_11HCE051_39_v1.0.xls
CEETOX	C16 X123 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE051_39_v1.0.xls
CEETOX	C17 X125 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE051_39_v1.0.xls
CEETOX	C18 X129 -- compound left in glass weigh boat;	EIVS_CEETOX_LE_11HCE051_39_v1.0.xls

laboratory	remark	filename
	compound dissolved	
CEETOX	C19 X131 -- compound left in glass weigh boat; used tip to spread; compound dissolved	EIVS_CEETOX_LE_11HCE051_39_v1.0.xls
CEETOX	C22 X29 -- no tissue after rinsing	EIVS_CEETOX_LE_11HCE051_39_v1.0.xls
CEETOX	Dosing	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C16 X134 -- compound left in glass weigh boat; compound did not cover the tissue	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C17 X11 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C20 X24 -- compound left in glass weigh boat; tissue turned blue	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C20-MTT X24-MTT -- compound left in glass weigh boat; tissue turned blue	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C21 X32 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C21-MTT X32-MTT -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C15 X133 -- tissues pulled away	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C19 X29 -- lost tissues a and b and half of c	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C20 X24 and C20-MTT X24-MTT -- very difficult to rinse off; approximately 30 seconds behind on later tissues	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	C21 X32 and C21-MTT X32-MTT -- very difficult to rinse off; approximately 30 seconds behind on later tissues	EIVS_CEETOX_LE_11HCE053_40_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE055_41_v1.0.xls
CEETOX	PC FK -- compound left in glass weigh boat; used tip to spread; tissues b and c had better coverage	EIVS_CEETOX_LE_11HCE055_41_v1.0.xls
CEETOX	C18 X131 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE055_41_v1.0.xls
CEETOX	C19 X119 -- compound left in glass weigh boat; compound dissolved on the tissues	EIVS_CEETOX_LE_11HCE055_41_v1.0.xls
CEETOX	C20 X173 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE055_41_v1.0.xls
CEETOX	C21 X169 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE055_41_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to	EIVS_CEETOX_LE_11HCE057_42_v1.0.xls

laboratory	remark	filename
	spread compound	
CEETOX	C18 X131 -- compound left in glass weigh boat; compound staticy and dissolved on the tissue	EIVS_CEETOX_LE_11HCE057_42_v1.0.xls
CEETOX	C19 X119 -- compound left in glass weigh boat; compound dissolved on the tissue	EIVS_CEETOX_LE_11HCE057_42_v1.0.xls
CEETOX	C20 X173 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE057_42_v1.0.xls
CEETOX	C24 X40 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE057_42_v1.0.xls
CEETOX	C25 X111 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE057_42_v1.0.xls
CEETOX	PC -- compound left in weigh boat; used tip to spread compound; tissues a and b were a little wet	EIVS_CEETOX_LE_11HCE059_43_v1.0.xls
CEETOX	C18 X173 -- compound left in weigh boat	EIVS_CEETOX_LE_11HCE059_43_v1.0.xls
CEETOX	C19 X169 -- compound left in weigh boat	EIVS_CEETOX_LE_11HCE059_43_v1.0.xls
CEETOX	C21 X40 -- compound left in weigh boat; staticy, good coverage, needed extra swab	EIVS_CEETOX_LE_11HCE059_43_v1.0.xls
CEETOX	C22 X134 -- compound left in weigh boat; sticky; less than when I weighed it out, used tip to spread	EIVS_CEETOX_LE_11HCE059_43_v1.0.xls
CEETOX	C23 X196 -- compound left in weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE059_43_v1.0.xls
CEETOX	C24 X11 -- compound left in weigh boat	EIVS_CEETOX_LE_11HCE059_43_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	C16 X173 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	C17 X40 -- compound left in glass weigh boat; staticy	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	C18 X196 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	C19 X11 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	C20 X24 -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	C20-MTT X24-MTT -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	C21 X32 -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	C21-MTT X32-MTT -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls

laboratory	remark	filename
CEETOX	C21 FK X32 FK -- compound left in glass weigh boat; extra swab; tissue is more colored, stained tissue and the media	EIVS_CEETOX_LE_11HCE061_44_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip	EIVS_CEETOX_LE_11HCE063_45_v1.0.xls
CEETOX	C11 X173 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE063_45_v1.0.xls
CEETOX	C12 X24 -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_LE_11HCE063_45_v1.0.xls
CEETOX	C12-MTT X24-MTT -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_LE_11HCE063_45_v1.0.xls
CEETOX	C13 X196 -- compound left in glass weigh boat; extra swab	EIVS_CEETOX_LE_11HCE063_45_v1.0.xls
CEETOX	C16 X55 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE063_45_v1.0.xls
CEETOX	C18 X61 -- not good coverage; clumped on tissue; extra swab	EIVS_CEETOX_LE_11HCE063_45_v1.0.xls
CEETOX	C20 X75 -- very staticy; compound left in glass and plastic weigh boats; used extra swab	EIVS_CEETOX_LE_11HCE063_45_v1.0.xls
CEETOX	Dosing	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C13 X32 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C13-MTT X32-MTT -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C15 X55 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C19 X75 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C21 X80 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C22 X94 -- compound would not stay spread over the tissues	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	Rinsing	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C16 X56 -- lost some of the tissues	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C17 X61 -- extra rinse and swab required	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C18 X66 -- lost tissues	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	C20 X77 -- extra swab	EIVS_CEETOX_LE_11HCE065_46_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C14 X29 -- tissues started to come off	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls

laboratory	remark	filename
CEETOX	C15 X77 -- extra swab used	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C16 X80 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C17 X94 -- poor coverage on tissue	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C18 X95 -- compound left in glass weigh boat; extra swab used	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C18-MTT X95-MTT -- compound left in glass weigh boat; extra swab used	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C20 X120 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C21 X157 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C22 X158 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	C23 X160 -- compound left in glass weigh boat; used tip to spread compound	EIVS_CEETOX_LE_11HCE068_48_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C13 X24 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C13-MTT X24-MTT -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C15 X55 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C16 X95 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C16-MTT X95-MTT -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C18 X120 -- tissue b dropped in funnel; compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C19 X157 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C20 X158 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	C21 X160 -- compound left in glass weigh boat	EIVS_CEETOX_LE_11HCE070_49_v1.0.xls
CEETOX	PC -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C5 X24 -- compound left in glass weigh boat; tissue b damaged during rinsing	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C5-MTT X24-MTT -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C6 X32 -- compound left in glass weigh boat; tissue c nicked	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C6-MTT X32-MTT -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C6 FK X32 FK -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C7 X42 -- extra rinse and swab required; tissue a nicked	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls

laboratory	remark	filename
CEETOX	C8 X55 -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C9 X56 -- lost all tissues during rinsing	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C10 X165 -- extra rinse required	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C11 X66 -- extra rinse; lost half of tissues a and b; lost tissue c	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 1.xls
CEETOX	C12 X75 -- compound left in glass weigh boat; staticy	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C13 X77 -- extra swab	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C14 X80 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C16 X95 -- compound left in glass weigh boat; extra swab used	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C16-MTT X95-MTT -- compound left in glass weigh boat; extra swab used; 30 seconds late on all tissues	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C18 X120 -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C19 X157 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C20 X158 -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C21 X160 -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	C22 X61 -- compound changed; could not pipette as easily as previous runs; all tissues dosed late	EIVS_CEETOX_LE_12HCE002_2_v1.0 set 2.xls
CEETOX	PC LE -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_12HCE004_3_v1.0.xls
CEETOX	C14 X95 -- compound left in glass weigh boat; rinsed 20-30 seconds late; used extra swab	EIVS_CEETOX_LE_12HCE004_3_v1.0.xls
CEETOX	C14-MTT X95-MTT -- compound left in glass weigh boat; rinsed 20-30 seconds late; used extra swab	EIVS_CEETOX_LE_12HCE004_3_v1.0.xls
CEETOX	C16 X120 -- compound left in glass weigh weigh boat	EIVS_CEETOX_LE_12HCE004_3_v1.0.xls
CEETOX	C17 X157 -- compound left in glass weigh boat; used tip to spread	EIVS_CEETOX_LE_12HCE004_3_v1.0.xls
CEETOX	C18 X158 -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE004_3_v1.0.xls
CEETOX	C19 X160 -- compound left in glass weigh boat	EIVS_CEETOX_LE_12HCE004_3_v1.0.xls
CEETOX	C21 X61 -- very sticky; could not get a consistent dose; used extra swab during rinsing	EIVS_CEETOX_LE_12HCE004_3_v1.0.xls
CEETOX	PC - used tip to spread	EIVS_CEETOX_LE_12HCE009_7_v1.0.xls
CEETOX	X95 - used tip to sread	EIVS_CEETOX_LE_12HCE009_7_v1.0.xls

laboratory	remark	filename
CEETOX	X95-MTT - used tip to spread	EIVS_CEETOX_LE_12HCE009_7_v1.0.xls
CEETOX	PC2- used tip to spread	EIVS_CEETOX_LE_12HCE009_7_v1.0.xls
CEETOX	PC- nicks on tissues	EIVS_CEETOX_LE_12HCE009_7_v1.0.xls
CEETOX	X95- extra rinse and swab	EIVS_CEETOX_LE_12HCE009_7_v1.0.xls
CEETOX	X95a- nick on tissue	EIVS_CEETOX_LE_12HCE009_7_v1.0.xls
CEETOX	X95-MTT - extra rinse and swab	EIVS_CEETOX_LE_12HCE009_7_v1.0.xls
L'OREAL	TEST SUBSTANCES L9 and L20:	EIVS_LOREAL_LE_10HCE023_25.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_LE_10HCE023_25.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_LE_10HCE023_25.xls
L'OREAL	TEST SUBSTANCE L12:	EIVS_LOREAL_LE_10HCE023_25.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_10HCE023_25.xls
L'OREAL	TEST SUBSTANCES L9 AND L20	EIVS_LOREAL_LE_10HCE024_26.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_LE_10HCE024_26.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_LE_10HCE024_26.xls
L'OREAL	TEST SUBSTANCE L12	EIVS_LOREAL_LE_10HCE024_26.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_10HCE024_26.xls
L'OREAL	TEST SUBSTANCE L11:	EIVS_LOREAL_LE_10HCE024_26.xls
L'OREAL	Discrepancy observed between the three tissues : UNQUALIFIED run	EIVS_LOREAL_LE_10HCE024_26.xls
L'OREAL	TEST SUBSTANCE L30	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	The test substance stuck onto the HCE tissues. The rinsing step was very difficult	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface.	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal.	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	Visually, the tissues are dead at both exposure times.	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	The cell viability measured (above 50% suggesting non irritancy potential of the test substance) should not be	EIVS_LOREAL_LE_10HCE025_27.xls

laboratory	remark	filename
	considered as relevant.	
L'OREAL	The L30 should be classified as irritant.	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCE L66:	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	The membrane was melted.	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCE L51:	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCE L11:	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	In the SOP, 30 ?L PBS are applied onto the tissue in order to improve the contact between the powder and the epithelium	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	To improve such contact, the PBS was not aspirate before applying the powder L11.	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	The tissue should be well pre-wetting	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	This technical aspect might explain that the 2 first runs were invalids.	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	A SD > 18% and contradictorily classification were observed for the 3 tissues (high intra-run variability).	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCE L43:	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure	EIVS_LOREAL_LE_10HCE025_27.xls
L'OREAL	TEST SUBSTANCES L12, L43:	EIVS_LOREAL_LE_10HCE026_28.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_10HCE026_28.xls
L'OREAL	TEST SUBSTANCES L9 L20 and L43:	EIVS_LOREAL_LE_10HCE026_28.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_LE_10HCE026_28.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_LE_10HCE026_28.xls
L'OREAL	TEST SUBSTANCE L30:	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface.	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal.	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	Visually, the tissues are dead at both exposure times.	EIVS_LOREAL_LE_10HCE027_29.xls

laboratory	remark	filename
L'OREAL	The cell viability measured (above 50% suggesting non irritancy potential of the test substance) should not be considered as relevant.	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	The test substance L30 should be classified as an irritant.	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	TEST SUBSTANCE L66:	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	The membrane was melted.	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	TEST SUBSTANCE L51:	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	TEST SUBSTANCE L39:	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	During the rinsing step procedure, the cell seeding on a tissue removed from the membrane	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	(issue observed only with 1 out of 3 tissues)	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	TEST SUBSTANCE L43:	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure	EIVS_LOREAL_LE_10HCE027_29.xls
L'OREAL	TEST SUBSTANCE L51	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	TEST SUBSTANCE L55:	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	TEST SUBSTANCE L30:	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface.	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal.	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	Visually, the tissues are dead at both exposure times.	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	The cell viability measured (above 50% suggesting non irritancy potential of the test substance) should not be considered as relevant	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	The test substance L30 should be classified as an irritant.	EIVS_LOREAL_LE_10HCE028_30.xls
L'OREAL	INVALID RUN / POSITIVE CONTROL (PC) DID NOT MEET	EIVS_LOREAL_LE_10HCE029_35.xls

laboratory	remark	filename
	THE ACCEPTANCE CRITERIA / MEAN VIABILITY VALUE ABOVE 50%	
L'OREAL	TEST SUBSTANCE L80	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	The test substance L81 dissolved the membrane of tissue constructs,	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	The membrane is melted	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	TEST SUBSTANCES L94 and L98:	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	TEST SUBSTANCE L85:	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	L85 is a MTT-reducer given a NSMTT < 50% in the controls	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	L85 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	Visually, the tissues are dead at both exposure times.	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	At the long exposure time, on the living tissues the crystals are permanent and could not be removed.	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	The cell viability measured (above 50% suggesting non irritancy potential of the test substance) should not be considered as relevant.	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	Visually, the cells are dead and we will classified L85 is an irritant.	EIVS_LOREAL_LE_10HCE029_35.xls
L'OREAL	TEST SUBSTANCE L66:	EIVS_LOREAL_LE_10HCE031_37.xls
L'OREAL	The membrane Is melted.	EIVS_LOREAL_LE_10HCE031_37.xls
L'OREAL	TEST SUBSTANCE L94:	EIVS_LOREAL_LE_10HCE031_37.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_LE_10HCE031_37.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues	EIVS_LOREAL_LE_10HCE031_37.xls
L'OREAL	ADAPTED CONTROLS:	EIVS_LOREAL_LE_10HCE031_37.xls
L'OREAL	The direct MTT reduction of test substances was evaluated using killed HCE tissues controls (one single run, 3 tissues/substance).	EIVS_LOREAL_LE_10HCE031_37.xls

laboratory	remark	filename
L'OREAL	The killed tissues used for the evaluation were provided from HCE tissues batch Nø10HCE029 (produced on March3 2010: less than a year)	EIVS_LOREAL_LE_10HCE031_37.xls
L'OREAL	TEST SUBSTANCE L81:	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	The test substance L81 dissolved the membrane of tissue constructs,	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	The membrane is melted	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	TEST SUBSTANCES L94 and L98:	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	TEST SUBSTANCE L85:	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	L85 is a MTT-reducer given a NSMTT < 50% in the controls	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	L85 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	Visually, the tissues are dead at both exposure times.	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	At the long exposure time, on the living tissues the crystals are permanent and could not be removed.	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	The cell viability measured (above 50% suggesting non irritancy potential of the test substance) should not be considered as relevant.	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	Visually, the cells are dead and we will classify L85 is an irritant.	EIVS_LOREAL_LE_10HCE032_38.xls
L'OREAL	TEST SUBSTANCE L81:	EIVS_LOREAL_LE_10HCE033_39.xls
L'OREAL	The membrane is melted	EIVS_LOREAL_LE_10HCE033_39.xls
L'OREAL	TEST SUBSTANCE L85:	EIVS_LOREAL_LE_10HCE033_39.xls
L'OREAL	L85 is a MTT-reducer given a NSMTT < 50% in the controls	EIVS_LOREAL_LE_10HCE033_39.xls
L'OREAL	L85 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_LE_10HCE033_39.xls
L'OREAL	Visually, the tissues are dead at both exposure times.	EIVS_LOREAL_LE_10HCE033_39.xls
L'OREAL	At the long exposure time, on the living tissues the crystals are permanent and could not be removed.	EIVS_LOREAL_LE_10HCE033_39.xls

laboratory	remark	filename
L'OREAL	The cell viability measured (above 50% suggesting non irritancy potential of the test substance) should not be considered as relevant.	EIVS_LOREAL_LE_10HCE033_39.xls
L'OREAL	Visually, the cells are dead and we will classified L85 is an irritant.	EIVS_LOREAL_LE_10HCE033_39.xls
L'OREAL	TEST SUBSTANCE L81:	EIVS_LOREAL_LE_10HCE034_40(1).xls
L'OREAL	The test substance L81 dissolved the membrane of tissue constructs,	EIVS_LOREAL_LE_10HCE034_40(1).xls
L'OREAL	The membrane is melted	EIVS_LOREAL_LE_10HCE034_40(1).xls
L'OREAL	TEST SUBSTANCES L94 andL98:	EIVS_LOREAL_LE_10HCE034_40(1).xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_LE_10HCE034_40(1).xls
L'OREAL	The rinsing procedure was very difficult. Substances might be not completely removed from the tissues.	EIVS_LOREAL_LE_10HCE034_40(1).xls
L'OREAL	ADAPTED CONTROLS:	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	The direct MTT reduction of test substances was evaluated using killed HCE tissues controls	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	(one single run, 3 tissues / substance)	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	The killed tissues used for the evaluation were provided from HCE tissues batch Nø10HCE033	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	(produced on September 27, 2010: less than a year)	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	TEST SUBSTANCE L7:	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	L7 is a strong MTT-reducer given a NSMTT > 50% in the controls	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	L7 was not retest since the SD was < 18% (qualified test)	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	We still acquired three qualified tests for this chemical following the rules set out in the Performance Criteria document,	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	, independently of the control tissues (NSMTT>50%)	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	The values are imported in the design import spreadsheet	EIVS_LOREAL_LE_10HCE034_40(2).xls
L'OREAL	TEST SUBSTANCE L98:	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	The substances stuck on the plastic which is not anymore transparent.	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	The rinsing procedure was very difficult. Substances	EIVS_LOREAL_LE_10HCE035_41.xls

laboratory	remark	filename
	might be not completely removed from the tissues.	
L'OREAL	TEST SUBSTANCE L7:	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	Nota bene: L7 is a strong MTT-reducer given a NSMTT > 28% in the controls	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	L7 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	The values are imported in the design import spreadsheet	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	TEST SUBSTANCE L85:	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	L85 is a MTT-reducer given a NSMTT < 50% in the controls	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	L85 was not retest since the SD was < 18% (qualified test).	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	Visually, the tissues are dead at both exposure times.	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	At the long exposure time, on the living tissues the crystals are permanent and could not be removed.	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	The cell viability measured (above 50% suggesting non irritancy potential of the test substance) should not be considered as relevant	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	Visually, the cells are dead and the test substance L85 should be classified as an irritant.	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	TEST SUBSTANCE L63:	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	L63 should be withdrawn from the chemicals selection because of inconsistent chemical states	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	The test substance evaluated in the run was a liquid	EIVS_LOREAL_LE_10HCE035_41.xls
L'OREAL	TEST SUBSTANCE L7:	EIVS_LOREAL_LE_10HCE036_42.xls
L'OREAL	L7 is a strong MTT-reducer given a NSMTT >26 % in the controls	EIVS_LOREAL_LE_10HCE036_42.xls
L'OREAL	TEST SUBSTANCE L63:	EIVS_LOREAL_LE_10HCE037_43.xls
L'OREAL	L63 should be withdrawn from the chemicals selection because of inconsistent chemical states	EIVS_LOREAL_LE_10HCE037_43.xls
L'OREAL	The test substance evaluated was a liquid	EIVS_LOREAL_LE_10HCE037_43.xls
L'OREAL	TEST SUBSTANCE L63:	EIVS_LOREAL_LE_10HCE040_46.xls
L'OREAL	L63 should be withdrawn from the chemicals selection because of inconsistent chemical states	EIVS_LOREAL_LE_10HCE040_46.xls
L'OREAL	The test substance evaluated was a liquid	EIVS_LOREAL_LE_10HCE040_46.xls

laboratory	remark	filename
L'OREAL	NONE	EIVS_LOREAL_LE_10HCE041_47.xls
L'OREAL	TEST SUBSTANCES L119 and L131:	EIVS_LOREAL_LE_10HCE042_48.xls
L'OREAL	The membrane of the inserts was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_10HCE042_48.xls
L'OREAL	TEST SUBSTANCE L113	EIVS_LOREAL_LE_10HCE043_49.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_10HCE043_49.xls
L'OREAL	TEST SUBSTANCE L113:	EIVS_LOREAL_LE_10HCE044_50.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_10HCE044_50.xls
L'OREAL	Substances L133 and L140: The membrane of the insert was damaged during the rinsing step procedure	EIVS_LOREAL_LE_11HCE002_2.xls
L'OREAL	Test substance L137	EIVS_LOREAL_LE_11HCE002_2.xls
L'OREAL	This solid hardens and retracts in the presence of atmosphere.	EIVS_LOREAL_LE_11HCE002_2.xls
L'OREAL	It is important to apply it onto the tissues as soon as it was weighed.	EIVS_LOREAL_LE_11HCE002_2.xls
L'OREAL	It was notice that its volume was considerably reduced if the weighing occurred 1 hour before topical application.	EIVS_LOREAL_LE_11HCE002_2.xls
L'OREAL	Very difficult application: contact with the surface was not homogeneous even by using a mesh - > partial contact which can explain inter-tissues variability.	EIVS_LOREAL_LE_11HCE002_2.xls
L'OREAL	At the long exposure time (1 hour+16hrs), the substance is irritating but the results very are dependent	EIVS_LOREAL_LE_11HCE002_2.xls
L'OREAL	of the topical application (contact of the substance with the surface of the tissues)	EIVS_LOREAL_LE_11HCE002_2.xls
L'OREAL	TEST SUBSTANCE L119:	EIVS_LOREAL_LE_11HCE007_7.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_11HCE007_7.xls
L'OREAL	TEST SUBSTANCES L119 and L131:	EIVS_LOREAL_LE_11HCE008_8.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_11HCE008_8.xls
L'OREAL	TEST SUBSTANCES L131 and L133:	EIVS_LOREAL_LE_11HCE009_9.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_11HCE009_9.xls

laboratory	remark	filename
L'OREAL	TEST SUBSTANCE L137:	EIVS_LOREAL_LE_11HCE009_9.xls
L'OREAL	This solid hardens and retracts in the presence of atmosphere.	EIVS_LOREAL_LE_11HCE009_9.xls
L'OREAL	It is important to apply it onto the tissues as soon as it was weighed.	EIVS_LOREAL_LE_11HCE009_9.xls
L'OREAL	It was notice that its volume was considerably reduced if the weighing occurred 1 hour before topical application.	EIVS_LOREAL_LE_11HCE009_9.xls
L'OREAL	Very difficult application: contact with the surface was not homogeneous even by using a mesh - > partial contact which can explain inter-tissues variability.	EIVS_LOREAL_LE_11HCE009_9.xls
L'OREAL	At the long exposure time (1 hour+16hrs), the substance is irritating but the results very are dependent	EIVS_LOREAL_LE_11HCE009_9.xls
L'OREAL	of the topical application (contact of the substance with the surface of the tissues)	EIVS_LOREAL_LE_11HCE009_9.xls
L'OREAL	TEST SUBSTANCE L137:	EIVS_LOREAL_LE_11HCE014_14.xls
L'OREAL	This solid hardens and retracts in the presence of atmosphere.	EIVS_LOREAL_LE_11HCE014_14.xls
L'OREAL	It is important to apply it onto the tissues as soon as it was weighed.	EIVS_LOREAL_LE_11HCE014_14.xls
L'OREAL	It was notice that its volume was considerably reduced if the weighing occurred 1 hour before topical application.	EIVS_LOREAL_LE_11HCE014_14.xls
L'OREAL	Very difficult application: contact with the surface was not homogeneous even by using a mesh - > partial contact which can explain inter-tissues variability.	EIVS_LOREAL_LE_11HCE014_14.xls
L'OREAL	At the long exposure time (1 hour+16hrs), the substance is irritating but the results very are dependent	EIVS_LOREAL_LE_11HCE014_14.xls
L'OREAL	of the topical application (contact of the substance with the surface of the tissues)	EIVS_LOREAL_LE_11HCE014_14.xls
L'OREAL	Substance L6:	EIVS_LOREAL_LE_11HCE020_18.xls
L'OREAL	Very strong coloring chemical (red)	EIVS_LOREAL_LE_11HCE020_18.xls
L'OREAL	High variability due to its coloring properties	EIVS_LOREAL_LE_11HCE020_18.xls
L'OREAL	TEST SUBSTANCE L125	EIVS_LOREAL_LE_11HCE022_19.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_11HCE022_19.xls
L'OREAL	TEST SUBSTANCE L58	EIVS_LOREAL_LE_11HCE022_19.xls

laboratory	remark	filename
L'OREAL	Strong MTT reducer	EIVS_LOREAL_LE_11HCE022_19.xls
L'OREAL	Not issue during the rinsing procedure	EIVS_LOREAL_LE_11HCE022_19.xls
L'OREAL	TEST SUBSTANCE L6:	EIVS_LOREAL_LE_11HCE024_20.xls
L'OREAL	very strong coloring chemical	EIVS_LOREAL_LE_11HCE024_20.xls
L'OREAL	Visual observation: the tissues are not dead but only stained due to the color (red)	EIVS_LOREAL_LE_11HCE024_20.xls
L'OREAL	TEST SUBSTANCE L148:	EIVS_LOREAL_LE_11HCE024_20.xls
L'OREAL	Technical issue: the plate dropped during the MTT incubation step : no data acquisition	EIVS_LOREAL_LE_11HCE024_20.xls
L'OREAL	TEST SUBSTANCE L185:	EIVS_LOREAL_LE_11HCE024_20.xls
L'OREAL	Sticky chemical: A mesh was used to uniformly spread the chemical on the 3 tissues	EIVS_LOREAL_LE_11HCE024_20.xls
L'OREAL	TEST SUBSTANCE L15:	EIVS_LOREAL_LE_11HCE026_21.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface	EIVS_LOREAL_LE_11HCE026_21.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal	EIVS_LOREAL_LE_11HCE026_21.xls
L'OREAL	TEST SUBSTANCE L174:	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	The vial overturned: There is no more than 6 mL left in the vial	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	TEST SUBSTANCE L58:	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	strong MTT reducer	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	visual observation: cytotoxicity observed for the three treated tissues	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	TEST SUBSTANCE L6:	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	The experiment was performed ONLY with KILLED tissues to determine the individual NSMTT values	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	Cell viability determination: The data obtained with the living tissues are defined on files Nø 11HCE020_18;	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	11HCE024_20, 11HCE032_25, 11HCE034_26 and 11HCE036_27	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	MTT REDUCERS / killed tissues: TEST SUBSTANCES L6, L33, L58, L100, L161, L169 and L174	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	To determine the NSMTT% of the MTT reducers, the experiment was performed using killed HCE tissues	EIVS_LOREAL_LE_11HCE029_23.xls

laboratory	remark	filename
	(batch Nø 11HCE028).	
L'OREAL	The individual Ku and Kt-Cx values (6) obtained in this run was then reported to the respective Excel spreadsheets of each test substance	EIVS_LOREAL_LE_11HCE029_23.xls
L'OREAL	TEST SUBSTANCE L125:	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	TEST SUBSTANCE L185	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	Sticky chemical: A mesh was used to uniformly spread the chemical on the three tissues	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	TEST SUBSTANCE L6:	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	very strong coloring chemical	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	very difficult to remove the staining chemical during the rinsing step procedure	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	TEST SUBSTANCE L58:	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	visual observation: cytotoxicity observed in the 3 treated tissues (Irritant)	EIVS_LOREAL_LE_11HCE032_25(1).xls
L'OREAL	TEST SUBSTANCE L125	EIVS_LOREAL_LE_11HCE034_26.xls
L'OREAL	The membrane of the insert was damaged during the rinsing step procedure.	EIVS_LOREAL_LE_11HCE034_26.xls
L'OREAL	TEST SUBSTANCE L6:	EIVS_LOREAL_LE_11HCE034_26.xls
L'OREAL	MTT and coloring substance difficult to rinse: high variability observed	EIVS_LOREAL_LE_11HCE034_26.xls
L'OREAL	TEST SUBSTANCE L15:	EIVS_LOREAL_LE_11HCE034_26.xls
L'OREAL	In contact with the pre-wetted HCE tissue, the powder pebbled and stuck to the surface.	EIVS_LOREAL_LE_11HCE034_26.xls
L'OREAL	During the rinsing step procedure, the substance (dense solid) was scratched to facilitate its removal	EIVS_LOREAL_LE_11HCE034_26.xls

Appendix V Reasoning for non-qualified test results

NCqual = Negative control did not pass the criteria
PCqual = Positive control did not pass the criteria
qQual_sd = Replicates did not pass the criteria

SE

conclusion	laboratory	Chemical	run	NCqual	PCqual	qual_sd
Non-Qualified	CARDAM	4	1	Qualified	Qualified	Non-qualified
		34	1	Qualified	Qualified	Non-qualified
		17	1	Qualified	Qualified	Non-qualified
		75	2	Qualified	Qualified	Non-qualified
	CEETOX	18	2	Qualified	Qualified	Non-qualified
	L'OREAL	75	1	Qualified	Qualified	Non-qualified
		75	2	Qualified	Qualified	Non-qualified

LE

conclusion	laboratory	Chemical	run	NCqual	PCqual	qual_sd
Non-Qualified	CARDAM	52	1	Qualified	Qualified	Non-qualified
		34	3	Qualified	Qualified	Non-qualified
	CEETOX	28	1	Qualified	Non-qualified	Qualified
		28	2	Qualified	Non-qualified	Qualified
		16	3	Qualified	Non-qualified	Qualified
		38	1	Qualified	Non-qualified	Qualified
		44	5	Qualified	Non-qualified	Qualified
		19	2	Qualified	Non-qualified	Qualified

		55	4	Qualified	Non-qualified	Qualified
		55	5	Qualified	Non-qualified	Qualified
		29	2	Qualified	Non-qualified	Qualified
		79	5	Qualified	Non-qualified	Qualified
		24	3	Qualified	Non-qualified	Qualified
		24	5	Qualified	Non-qualified	Qualified
		35	3	Qualified	Non-qualified	Qualified
		35	5	Qualified	Non-qualified	Qualified
		58	1	Qualified	Non-qualified	Qualified
		65	1	Qualified	Non-qualified	Qualified
		53	2	Qualified	Non-qualified	Qualified
		50	2	Qualified	Non-qualified	Qualified
		93	1	Qualified	Non-qualified	Qualified
		93	2	Qualified	Non-qualified	Qualified
		52	2	Qualified	Non-qualified	Qualified
		92	2	Qualified	Non-qualified	Qualified
		49	4	Qualified	Qualified	Non-qualified
		18	1	Qualified	Non-qualified	Qualified
		9	1	Qualified	Non-qualified	Qualified
		9	2	Qualified	Non-qualified	Qualified
		99	5	Qualified	Non-qualified	Qualified
		2	1	Qualified	Non-qualified	Qualified
		2	2	Qualified	Non-qualified	Qualified
		98	1	Qualified	Non-qualified	Qualified
		98	2	Qualified	Non-qualified	Qualified
		85	1	Qualified	Non-qualified	Qualified
		85	2	Qualified	Non-qualified	Qualified
		84	1	Qualified	Non-qualified	Qualified

		75	2	Qualified	Non-qualified	Qualified
		20	1	Qualified	Non-qualified	Qualified
		11	1	Qualified	Non-qualified	Qualified
		11	2	Qualified	Non-qualified	Qualified
		74	3	Qualified	Non-qualified	Qualified
		74	5	Qualified	Non-qualified	Qualified
		88	2	Qualified	Non-qualified	Qualified
		94	3	Qualified	Non-qualified	Qualified
		94	5	Qualified	Non-qualified	Qualified
		73	1	Qualified	Qualified	Non-qualified
		73	2	Qualified	Qualified	Non-qualified
		73	5	Qualified	Non-qualified	Qualified
		1	1	Qualified	Non-qualified	Qualified
		1	2	Qualified	Non-qualified	Qualified
		64	2	Qualified	Qualified	Non-qualified
		39	2	Qualified	Non-qualified	Qualified
		14	5	Qualified	Non-qualified	Qualified
		54	1	Qualified	Non-qualified	Qualified
		54	2	Qualified	Non-qualified	Qualified
		4	4	Qualified	Non-qualified	Qualified
		4	5	Qualified	Non-qualified	Qualified
		8	3	Qualified	Non-qualified	Qualified
		90	3	Qualified	Non-qualified	Qualified
		90	5	Qualified	Non-qualified	Qualified
		71	4	Qualified	Non-qualified	Qualified
		71	5	Qualified	Non-qualified	Qualified
		5	5	Qualified	Non-qualified	Qualified
		6	1	Qualified	Non-qualified	Qualified

		6	2	Qualified	Non-qualified	Qualified
		33	3	Qualified	Non-qualified	Qualified
		33	5	Qualified	Non-qualified	Qualified
		91	4	Qualified	Non-qualified	Qualified
		91	5	Qualified	Non-qualified	Qualified
		21	4	Qualified	Non-qualified	Qualified
		21	5	Qualified	Non-qualified	Qualified
	L'OREAL	74	1	Qualified	Non-qualified	Qualified
		75	2	Qualified	Qualified	Non-qualified
		65	3	Qualified	Qualified	Non-qualified
		14	1	Qualified	Non-qualified	Qualified
		81	1	Qualified	Non-qualified	Qualified
		54	1	Qualified	Non-qualified	Qualified
		83	1	Qualified	Non-qualified	Qualified
		35	1	Qualified	Non-qualified	Qualified
		93	1	Qualified	Non-qualified	Qualified
		1	1	Qualified	Non-qualified	Qualified
		94	1	Qualified	Non-qualified	Qualified
		8	1	Qualified	Non-qualified	Qualified

Appendix VI Summary of all test results

Mean = mean of viability (corrected for %NSC or %NSMTT)
Std = standard deviation
NQ = Non-qualified

Note to chemical 4 (Cardam, CeeTox and L'Oréal), chemical 20 (Cardam only), chemical 23 (CeeTox only) and chemical 91 (CeeTox only) for the SE protocol, and to chemical 4 (Cardam and CeeTox) and chemical 80 (CeeTox only) for the LE protocol:

On May 10th 2012, after an evaluation of the first draft of the statistics report, the core VMG overrode the rule identifying 50% NSMTT as a cut-off to consider a chemical compatible with the test system as described in Chapter 2.5.1. of this report. In all these cases, rule 3 in Chapter 2.5.1. is fulfilled since the mean %NSC of all qualified tests is greater than (>) 50% and the classification of these qualified tests changes upon correction (from non-irritant to irritant). However, the viability values obtained in the qualified tests are definitely within the linear range of the OD measurements (within the 100% scale) and therefore, even though there is a strong MTT reduction occurring this is not interfering with the analytical capacity to measure formazan production. Moreover, the variability obtained between the different tests and controls is low. As such, these chemicals were considered compatible with the test method and their data were therefore included in all of the statistical analyses.

SE

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
1	CARDAM	no cat			1	0.9726	6.2232		14.6177	1.7458		92.275	5.4172		.	.		.	0		92.275		NI
1	CARDAM	no cat			2	0.9459	5.8678		10.1547	0.3097		83.357	1.7607		.	.		.	0		83.357		NI
1	CARDAM	no cat			3	1.0342	6.596		17.2116	4.0284		84.324	3.4535		.	.		.	0		84.324		NI
2	CARDAM	no cat			1	0.9244	7.503		8.8632	1.6731		103.757	3.5331		.	.		.	0		103.757		NI
2	CARDAM	no cat			2	1.017	4.957		7.2385	0.8518		76.972	5.3119		.	.		.	0		76.972		NI
2	CARDAM	no cat			3	0.718	0.5669		11.8486	1.8037		76.029	0.3932		.	.		.	0		76.029		NI
3	CARDAM	no cat			1	0.9726	6.2232		14.6177	1.7458		76.452	5.92		.	.		.	0		76.452		NI
3	CARDAM	no cat			2	0.9459	5.8678		10.1547	0.3097		136.02	4.8978		.	.		.	0		136.02		NI
3	CARDAM	no cat			3	1.0342	6.596		17.2116	4.0284		67.773	0.2797		.	.		.	0		67.773		NI
4	CARDAM	no cat	Yes		1	0.718	0.5669		11.8486	1.8037		89.215	20.054	NQ	.	.		103.231	28.525	NQ	0.669	NQ	I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
4	CARDAM	no cat	Yes		2	1.0409	3.7109		11.1134	0.688		105.338	10.585		.	.		71.201	19.674	NQ	34.138		I
4	CARDAM	no cat	Yes		3	1.3506	1.4834		15.3147	2.0773		91.774	8.5707		.	.		54.878	15.164		36.896		I
4	CARDAM	no cat	Yes		4	0.7983	6.6925		8.8647	1.3042		114.767	13.627		.	.		92.841	25.654	NQ	21.926		I
5	CARDAM	no cat	Yes		1	0.9244	7.503		8.8632	1.6731		101.5	6.2602		.	.		0	0		101.5		NI
5	CARDAM	no cat	Yes		2	1.017	4.957		7.2385	0.8518		86	7.1475		.	.		0	0		86		NI
5	CARDAM	no cat	Yes		3	0.718	0.5669		11.8486	1.8037		76.034	3.6143		.	.		0	0		76.034		NI
6	CARDAM	no cat			1	0.9459	5.8678		10.1547	0.3097		117.848	4.721		.	.		.	0		117.848		NI
6	CARDAM	no cat			2	1.0342	6.596		17.2116	4.0284		105.91	6.3091		.	.		.	0		105.91		NI
6	CARDAM	no cat			3	0.9244	7.503		8.8632	1.6731		108.019	5.5762		.	.		.	0		108.019		NI
7	CARDAM	no cat			1	1.0351	6.5903		17.2836	4.0249		88.226	8.0545		.	.		.	0		88.226		NI
7	CARDAM	no cat			2	0.9244	7.503		8.8632	1.6731		82.557	3.3443		.	.		.	0		82.557		NI
7	CARDAM	no cat			3	1.017	4.957		7.2385	0.8518		65.282	4.8168		.	.		.	0		65.282		NI
8	CARDAM	no cat			1	0.9726	6.2232		14.6177	1.7458		101.086	0.5218		.	.		.	0		101.086		NI
8	CARDAM	no cat			2	0.9459	5.8678		10.1547	0.3097		124.276	7.8789		.	.		.	0		124.276		NI
8	CARDAM	no cat			3	1.0342	6.596		17.2116	4.0284		102.184	4.4809		.	.		.	0		102.184		NI
9	CARDAM	no cat	Yes		1	0.9726	6.2232		14.6177	1.7458		98.987	5.4953		.	.		0	0		98.987		NI
9	CARDAM	no cat	Yes		2	0.9459	5.8678		10.1547	0.3097		112.225	10.558		.	.		0	0		112.225		NI
9	CARDAM	no cat	Yes		3	1.0342	6.596		17.2116	4.0284		96.55	7.2268		.	.		0	0		96.55		NI
10	CARDAM	no cat			1	0.9247	7.5008		8.8895	1.6726		48.516	6.9841		.	.		.	0		48.516		I
10	CARDAM	no cat			2	1.017	4.957		7.2385	0.8518		29.652	6.0345		.	.		.	0		29.652		I
10	CARDAM	no cat			3	0.718	0.5669		11.8486	1.8037		33.651	2.4865		.	.		.	0		33.651		I
11	CARDAM	no cat			1	0.9726	6.2232		14.6177	1.7458		68.347	8.2132		.	.		.	0		68.347		NI
11	CARDAM	no cat			2	0.9459	5.8678		10.1547	0.3097		81.335	4.1797		.	.		.	0		81.335		NI
11	CARDAM	no cat			3	1.0342	6.596		17.2116	4.0284		70.212	13.507		.	.		.	0		70.212		NI
12	CARDAM	no cat			1	0.9764	3.0137		9.7414	1.6474		102.612	8.3303		.	.		.	0		102.612		NI
12	CARDAM	no cat			2	1.068	12.107		9.0451	0.5407		107.319	7.4457		.	.		.	0		107.319		NI
12	CARDAM	no cat			3	1.1217	5.8363		9.2331	2.1018		104.484	1.3521		.	.		.	0		104.484		NI
13	CARDAM	no cat			1	0.9764	3.0137		9.7414	1.6474		100.415	4.6175		.	.		.	0		100.415		NI
13	CARDAM	no cat			2	1.068	12.107		9.0451	0.5407		103.24	3.3193		.	.		.	0		103.24		NI
13	CARDAM	no cat			3	1.169	5.4702		13.7342	2.2905		95.885	5.131		.	.		.	0		95.885		NI
14	CARDAM	no cat			1	0.9455	5.8699		10.123	0.3098		109.45	6.6504		.	.		.	0		109.45		NI
14	CARDAM	no cat			2	1.0342	6.596		17.2116	4.0284		94.292	6.708		.	.		.	0		94.292		NI
14	CARDAM	no cat			3	0.9244	7.503		8.8632	1.6731		101.365	2.16		.	.		.	0		101.365		NI
15	CARDAM	no cat			1	1.169	5.4702		13.7342	2.2905		92.258	4.1258		.	.		.	0		92.258		NI
15	CARDAM	no cat			2	1.0074	8.5376		11.5659	1.2203		94.484	2.675		.	.		.	0		94.484		NI
15	CARDAM	no cat			3	1.0398	3.5464		8.5117	0.9677		101.431	6.3823		.	.		.	0		101.431		NI
16	CARDAM	no cat			1	0.9726	6.2232		14.6177	1.7458		95.889	6.7644		.	.		.	0		95.889		NI
16	CARDAM	no cat			2	0.9459	5.8678		10.1547	0.3097		104.824	13.922		.	.		.	0		104.824		NI
16	CARDAM	no cat			3	1.0342	6.596		17.2116	4.0284		94.298	3.1332		.	.		.	0		94.298		NI
17	CARDAM	no cat			1	0.718	0.5669		11.8486	1.8037		82.311	19.427	NQ	.	.		.	0		82.311	NQ	NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
17	CARDAM	no cat			2	1.0409	3.7109		11.1134	0.688		108.099	4.7171		.	.		.	0		108.099		NI
17	CARDAM	no cat			3	1.3506	1.4834		15.3147	2.0773		80.918	6.8003		.	.		.	0		80.918		NI
17	CARDAM	no cat			4	0.7983	6.6925		8.8647	1.3042		102.702	7.1078		.	.		.	0		102.702		NI
18	CARDAM	no cat			1	1.169	5.4702		13.7342	2.2905		94.048	10.641		.	.		.	0		94.048		NI
18	CARDAM	no cat			2	1.0074	8.5376		11.5659	1.2203		84.439	7.7825		.	.		.	0		84.439		NI
18	CARDAM	no cat			3	1.0398	3.5464		8.5117	0.9677		98.956	4.841		.	.		.	0		98.956		NI
19	CARDAM	no cat			1	1.169	5.4702		13.7342	2.2905		95.161	6.7015		.	.		.	0		95.161		NI
19	CARDAM	no cat			2	1.1543	3.3335		11.3124	1.9334		101.948	7.2522		.	.		.	0		101.948		NI
19	CARDAM	no cat			3	1.0398	3.5464		8.5117	0.9677		104.822	8.5237		.	.		.	0		104.822		NI
20	CARDAM	no cat	Yes		1	0.9764	3.0137		9.7414	1.6474		98.102	2.9969		.	.		51.803	8.5228		46.299		I
20	CARDAM	no cat	Yes		2	1.1217	5.8363		9.2331	2.1018		90.395	8.6378		.	.		45.457	7.419		44.938		I
20	CARDAM	no cat	Yes		3	0.9438	9.67		16.1907	2.7495		119.378	12.966		.	.		53.837	8.8178		65.542		NI
21	CARDAM	no cat			1	0.718	0.5669		11.8486	1.8037		64.928	9.9996		.	.		.	0		64.928		NI
21	CARDAM	no cat			2	1.0409	3.7109		11.1134	0.688		99.492	5.9378		.	.		.	0		99.492		NI
21	CARDAM	no cat			3	1.3506	1.4834		15.3147	2.0773		76.674	3.6515		.	.		.	0		76.674		NI
22	CARDAM	no cat			1	0.718	0.5669		11.8486	1.8037		60.51	2.9225		.	.		.	0		60.51		NI
22	CARDAM	no cat			2	1.0409	3.7109		11.1134	0.688		93.528	5.3215		.	.		.	0		93.528		NI
22	CARDAM	no cat			3	1.3506	1.4834		15.3147	2.0773		94.325	5.8117		.	.		.	0		94.325		NI
23	CARDAM	no cat	Yes		1	1.0797	7.8357		6.7566	1.011		27.601	1.5061		.	.		29.509	1.3447		0		I
23	CARDAM	no cat	Yes		2	0.9533	3.5881		8.6662	1.4874		31.198	0.9651		.	.		33.569	1.5229		0		I
23	CARDAM	no cat	Yes		3	1.1437	1.1112		17.6846	0.1487		25.784	2.2355		.	.		27.95	1.2694		0		I
24	CARDAM	no cat			1	1.0797	7.8357		6.7566	1.011		77.392	8.0488		.	.		.	0		77.392		NI
24	CARDAM	no cat			2	0.9533	3.5881		8.6662	1.4874		72.514	0.297		.	.		.	0		72.514		NI
24	CARDAM	no cat			3	1.1437	1.1112		17.6846	0.1487		61.339	0.7428		.	.		.	0		61.339		NI
25	CARDAM	no cat	Yes		1	0.9438	9.67		16.1907	2.7495		123.325	1.3277		.	.		0.215	0.1312		123.11		NI
25	CARDAM	no cat	Yes		2	1.1543	3.3335		11.3124	1.9334		103.496	1.2803		.	.		0.205	0.1072		103.29		NI
25	CARDAM	no cat	Yes		3	1.0398	3.5464		8.5117	0.9677		92.303	9.367		.	.		0.168	0.1191		92.134		NI
26	CARDAM	no cat			1	1.0074	8.5376		11.5659	1.2203		99.628	5.8942		.	.		.	0		99.628		NI
26	CARDAM	no cat			2	1.1543	3.3335		11.3124	1.9334		107.131	8.9299		.	.		.	0		107.131		NI
26	CARDAM	no cat			3	1.0398	3.5464		8.5117	0.9677		102.528	8.7221		.	.		.	0		102.528		NI
28	CARDAM	no cat			1	1.0351	6.5903		17.2836	4.0249		88.407	6.3071		.	.		.	0		88.407		NI
28	CARDAM	no cat			2	0.9244	7.503		8.8632	1.6731		107.255	2.0699		.	.		.	0		107.255		NI
28	CARDAM	no cat			3	1.017	4.957		7.2385	0.8518		76.859	4.3915		.	.		.	0		76.859		NI
29	CARDAM	no cat			1	0.9438	9.67		16.1907	2.7495		109.72	13.364		.	.		.	0		109.72		NI
29	CARDAM	no cat			2	1.1543	3.3335		11.3124	1.9334		100.941	13.87		.	.		.	0		100.941		NI
29	CARDAM	no cat			3	1.0398	3.5464		8.5117	0.9677		104.08	6.6817		.	.		.	0		104.08		NI
30	CARDAM	no cat			1	1.1585	5.6912		5.4455	2.2462		87.801	3.9968		.	.		.	0		87.801		NI
30	CARDAM	no cat			2	1.0661	4.9967		19.5735	6.345		105.709	10.484		.	.		.	0		105.709		NI
30	CARDAM	no cat			3	1.0748	9.2837		11.954	3.093		86.309	3.5904		.	.		.	0		86.309		NI
31	CARDAM	no cat			1	1.1585	5.6912		5.4455	2.2462		93.012	6.0722		.	.		.	0		93.012		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
31	CARDAM	no cat			2	1.0661	4.9967		19.5735	6.345		112.06	9.2893		.	.		.	0		112.06		NI
31	CARDAM	no cat			3	1.0748	9.2837		11.954	3.093		97.516	5.0105		.	.		.	0		97.516		NI
32	CARDAM	no cat		Yes	1	1.0166	4.9593		7.1959	0.8522		53.483	6.9763		1.3001	0.465		.	0		52.183		NI
32	CARDAM	no cat		Yes	2	0.718	0.5669		11.8486	1.8037		64.624	4.9133		0.6895	0.661		.	0		63.934		NI
32	CARDAM	no cat		Yes	3	1.0409	3.7109		11.1134	0.688		68.847	1.116		1.2905	0.475		.	0		67.556		NI
33	CARDAM	no cat	Yes	Yes	1	1.0409	3.7109		11.1134	0.688		98.713	3.3601		1.3978	1.639		1.084	1.3688		96.231		NI
33	CARDAM	no cat	Yes	Yes	2	1.3506	1.4834		15.3147	2.0773		79.4	6.3094		1.8523	1.316		0.755	1.055		76.792		NI
33	CARDAM	no cat	Yes	Yes	3	0.7983	6.6925		8.8647	1.3042		96.478	4.4473		1.7663	0.848		1.315	1.7848		93.396		NI
34	CARDAM	no cat	Yes	Yes	1	0.718	0.5669		11.8486	1.8037		136.405	21.505	NQ	5.5041	2.417		8.062	1.4602		122.838	NQ	NI
34	CARDAM	no cat	Yes	Yes	2	1.0409	3.7109		11.1134	0.688		124.653	16.352		3.3768	0.129		4.85	1.0072		116.426		NI
34	CARDAM	no cat	Yes	Yes	3	1.3506	1.4834		15.3147	2.0773		97.199	7.5249		1.8721	0.131		3.738	0.7763		91.589		NI
34	CARDAM	no cat	Yes	Yes	4	0.7983	6.6925		8.8647	1.3042		123.162	0.5154		4.0753	0.295		6.324	1.3133		112.763		NI
35	CARDAM	no cat	Yes		1	0.9699	2.5093		30.0959	3.9456		47.675	3.7452		.	.		25.855	3.2968		21.82		I
35	CARDAM	no cat	Yes		2	0.9148	3.1781		12.341	1.4603		95.617	10.612		.	.		27.411	3.4952		68.206		NI
35	CARDAM	no cat	Yes		3	0.7795	7.0435		21.6844	6.85		46.146	15.984		.	.		32.17	4.1019		13.977		I
36	CARDAM	no cat			1	0.9699	2.5093		30.0959	3.9456		99.852	4.947		.	.		.	0		99.852		NI
36	CARDAM	no cat			2	0.9148	3.1781		12.341	1.4603		113.055	13.812		.	.		.	0		113.055		NI
36	CARDAM	no cat			3	0.7795	7.0435		21.6844	6.85		102.598	2.3385		.	.		.	0		102.598		NI
37	CARDAM	no cat			1	1.1585	5.6912		5.4455	2.2462		93.422	0.8073		.	.		.	0		93.422		NI
37	CARDAM	no cat			2	1.0661	4.9967		19.5735	6.345		107.126	10.007		.	.		.	0		107.126		NI
37	CARDAM	no cat			3	1.0748	9.2837		11.954	3.093		79.587	12.585		.	.		.	0		79.587		NI
38	CARDAM	no cat			1	0.9764	3.0137		9.7414	1.6474		106.52	1.8409		.	.		.	0		106.52		NI
38	CARDAM	no cat			2	1.068	12.107		9.0451	0.5407		105.829	12.991		.	.		.	0		105.829		NI
38	CARDAM	no cat			3	0.9438	9.67		16.1907	2.7495		87.475	12.289		.	.		.	0		87.475		NI
39	CARDAM	no cat			1	1.068	12.107		9.0451	0.5407		105.125	5.171		.	.		.	0		105.125		NI
39	CARDAM	no cat			2	1.1217	5.8363		9.2331	2.1018		95.771	2.4882		.	.		.	0		95.771		NI
39	CARDAM	no cat			3	1.169	5.4702		13.7342	2.2905		98.159	3.9652		.	.		.	0		98.159		NI
40	CARDAM	no cat			1	0.9764	3.0137		9.7414	1.6474		96.509	8.0542		.	.		.	0		96.509		NI
40	CARDAM	no cat			2	0.9438	9.67		16.1907	2.7495		99.936	3.1692		.	.		.	0		99.936		NI
40	CARDAM	no cat			3	1.0074	8.5376		11.5659	1.2203		93.281	9.598		.	.		.	0		93.281		NI
41	CARDAM	no cat			1	1.0797	7.8357		6.7566	1.011		107.241	3.6838		.	.		.	0		107.241		NI
41	CARDAM	no cat			2	0.9533	3.5881		8.6662	1.4874		95.187	1.132		.	.		.	0		95.187		NI
41	CARDAM	no cat			3	1.1437	1.1112		17.6846	0.1487		98.544	3.0184		.	.		.	0		98.544		NI
42	CARDAM	no cat	Yes		1	0.9533	3.5881		8.6662	1.4874		90.657	2.3402		.	.		1.482	1.9881		89.225		NI
42	CARDAM	no cat	Yes		2	1.1437	1.1112		17.6846	0.1487		89.963	7.4368		.	.		1.232	1.6556		88.774		NI
42	CARDAM	no cat	Yes		3	1.1585	5.6912		5.4455	2.2462		93.766	8.0832		.	.		1.22	1.6361		92.588		NI
43	CARDAM	no cat			1	1.0797	7.8357		6.7566	1.011		99.518	4.5152		.	.		.	0		99.518		NI
43	CARDAM	no cat			2	0.9533	3.5881		8.6662	1.4874		94.493	7.4649		.	.		.	0		94.493		NI
43	CARDAM	no cat			3	1.1437	1.1112		17.6846	0.1487		92.957	1.4856		.	.		.	0		92.957		NI
44	CARDAM	no cat			1	1.0797	7.8357		6.7566	1.011		104.572	5.5815		.	.		.	0		104.572		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
44	CARDAM	no cat			2	0.9533	3.5881		8.6662	1.4874		96.147	7.2442		.	.		.	0		96.147		NI
44	CARDAM	no cat			3	1.1437	1.1112		17.6846	0.1487		93.732	7.2587		.	.		.	0		93.732		NI
45	CARDAM	no cat			1	1.0797	7.8357		6.7566	1.011		104.348	2.6337		.	.		.	0		104.348		NI
45	CARDAM	no cat			2	0.9533	3.5881		8.6662	1.4874		98.565	4.7463		.	.		.	0		98.565		NI
45	CARDAM	no cat			3	1.1437	1.1112		17.6846	0.1487		91.599	5.3653		.	.		.	0		91.599		NI
46	CARDAM	no cat			1	1.0797	7.8357		6.7566	1.011		92.703	8.392		.	.		.	0		92.703		NI
46	CARDAM	no cat			2	0.9533	3.5881		8.6662	1.4874		85.911	2.7426		.	.		.	0		85.911		NI
46	CARDAM	no cat			3	1.1437	1.1112		17.6846	0.1487		89.977	2.8635		.	.		.	0		89.977		NI
47	CARDAM	no cat			1	1.0797	7.8357		6.7566	1.011		95.673	9.7519		.	.		.	0		95.673		NI
47	CARDAM	no cat			2	0.9533	3.5881		8.6662	1.4874		101.694	7.7071		.	.		.	0		101.694		NI
47	CARDAM	no cat			3	1.1437	1.1112		17.6846	0.1487		89.557	6.3812		.	.		.	0		89.557		NI
48	CARDAM	no cat	Yes		1	1.3506	1.4834		15.3147	2.0773		39.332	7.2528		.	.		0	0		39.332		I
48	CARDAM	no cat	Yes		2	1.0797	7.8357		6.7566	1.011		44.016	2.9106		.	.		0.391	0.0722		43.625		I
48	CARDAM	no cat	Yes		3	0.9533	3.5881		8.6662	1.4874		54.218	8.0634		.	.		0.558	0.0818		53.66		NI
49	CARDAM	no cat	Yes		1	1.0074	8.5376		11.5659	1.2203		105.731	5.4549		.	.		0.083	0.0732		105.731		NI
49	CARDAM	no cat	Yes		2	1.0398	3.5464		8.5117	0.9677		101.019	5.2457		.	.		0	0		101.019		NI
49	CARDAM	no cat	Yes		3	1.0153	3.8417		9.8825	1.2486		109.157	2.0682		.	.		0.009	0.0147		109.157		NI
50	CARDAM	no cat			1	1.0074	8.5376		11.5659	1.2203		96.92	7.9794		.	.		.	0		96.92		NI
50	CARDAM	no cat			2	1.1543	3.3335		11.3124	1.9334		83.084	9.7338		.	.		.	0		83.084		NI
50	CARDAM	no cat			3	1.0153	3.8417		9.8825	1.2486		98.199	1.4852		.	.		.	0		98.199		NI
51	CARDAM	no cat			1	1.0074	8.5376		11.5659	1.2203		93.144	6.7264		.	.		.	0		93.144		NI
51	CARDAM	no cat			2	1.1543	3.3335		11.3124	1.9334		91.194	7.9805		.	.		.	0		91.194		NI
51	CARDAM	no cat			3	1.0153	3.8417		9.8825	1.2486		98.247	6.306		.	.		.	0		98.247		NI
52	CARDAM	no cat			1	1.0074	8.5376		11.5659	1.2203		101.924	4.1812		.	.		.	0		101.924		NI
52	CARDAM	no cat			2	1.1543	3.3335		11.3124	1.9334		99.435	1.805		.	.		.	0		99.435		NI
52	CARDAM	no cat			3	1.0153	3.8417		9.8825	1.2486		95.505	14.394		.	.		.	0		95.505		NI
53	CARDAM	no cat			1	1.0074	8.5376		11.5659	1.2203		81.845	8.6247		.	.		.	0		81.845		NI
53	CARDAM	no cat			2	1.0398	3.5464		8.5117	0.9677		94.292	8.3623		.	.		.	0		94.292		NI
53	CARDAM	no cat			3	1.0153	3.8417		9.8825	1.2486		96.457	4.8582		.	.		.	0		96.457		NI
54	CARDAM	cat 2B			1	0.9699	2.5093		30.0959	3.9456		81.737	4.9264		.	.		.	0		81.737		NI
54	CARDAM	cat 2B			2	0.9148	3.1781		12.341	1.4603		68.543	8.6383		.	.		.	0		68.543		NI
54	CARDAM	cat 2B			3	0.7795	7.0435		21.6844	6.85		65.893	10.711		.	.		.	0		65.893		NI
55	CARDAM	cat 2B			1	1.0417	3.7082		11.1788	0.6875		2.71	0.385		.	.		.	0		2.71		I
55	CARDAM	cat 2B			2	1.3506	1.4834		15.3147	2.0773		1.958	0.3357		.	.		.	0		1.958		I
55	CARDAM	cat 2B			3	1.0797	7.8357		6.7566	1.011		3.691	1.7996		.	.		.	0		3.691		I
56	CARDAM	cat 2B			1	1.0417	3.7082		11.1788	0.6875		89.207	15.167		.	.		.	0		89.207		NI
56	CARDAM	cat 2B			2	1.3506	1.4834		15.3147	2.0773		66.585	8.282		.	.		.	0		66.585		NI
56	CARDAM	cat 2B			3	0.7983	6.6925		8.8647	1.3042		88.728	5.683		.	.		.	0		88.728		NI
57	CARDAM	cat 2B			1	0.718	0.5669		11.8486	1.8037		25.995	4.4113		.	.		.	0		25.995		I
57	CARDAM	cat 2B			2	1.0409	3.7109		11.1134	0.688		41.469	1.898		.	.		.	0		41.469		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
57	CARDAM	cat 2B			3	1.3506	1.4834		15.3147	2.0773		34.219	5.507		.	.		.	0		34.219		I
58	CARDAM	cat 2B			1	1.0409	3.7109		11.1134	0.688		42.893	2.9612		.	.		.	0		42.893		I
58	CARDAM	cat 2B			2	1.3506	1.4834		15.3147	2.0773		26.087	3.8693		.	.		.	0		26.087		I
58	CARDAM	cat 2B			3	0.7983	6.6925		8.8647	1.3042		34.145	11.685		.	.		.	0		34.145		I
59	CARDAM	cat 2B			1	1.0417	3.7082		11.1788	0.6875		87.943	4.9369		.	.		.	0		87.943		NI
59	CARDAM	cat 2B			2	1.3506	1.4834		15.3147	2.0773		70.27	10.403		.	.		.	0		70.27		NI
59	CARDAM	cat 2B			3	0.7983	6.6925		8.8647	1.3042		84.807	4.2651		.	.		.	0		84.807		NI
60	CARDAM	cat 2B			1	0.9438	9.67		16.1907	2.7495		36.569	1.3007		.	.		.	0		36.569		I
60	CARDAM	cat 2B			2	1.1543	3.3335		11.3124	1.9334		29.781	4.6129		.	.		.	0		29.781		I
60	CARDAM	cat 2B			3	1.0398	3.5464		8.5117	0.9677		33.864	8.0422		.	.		.	0		33.864		I
61	CARDAM	cat 2B		Yes	1	1.0351	6.5903		17.2836	4.0249		74.108	2.5023		0.0923	0.16		.	0		74.016		NI
61	CARDAM	cat 2B		Yes	2	0.9244	7.503		8.8632	1.6731		96.675	12.875		0.0343	0.003		.	0		96.641		NI
61	CARDAM	cat 2B		Yes	3	1.017	4.957		7.2385	0.8518		91.988	2.6932		0.0503	0.053		.	0		91.938		NI
62	CARDAM	cat 2B			1	1.1437	1.1112		17.6846	0.1487		95.694	7.5369		.	.		.	0		95.694		NI
62	CARDAM	cat 2B			2	1.1585	5.6912		5.4455	2.2462		97.927	6.0566		.	.		.	0		97.927		NI
62	CARDAM	cat 2B			3	1.0748	9.2837		11.954	3.093		92.158	9.3776		.	.		.	0		92.158		NI
63	CARDAM	cat 2B			1	1.1437	1.1112		17.6846	0.1487		92.492	8.9927		.	.		.	0		92.492		NI
63	CARDAM	cat 2B			2	1.1585	5.6912		5.4455	2.2462		92.809	6.5504		.	.		.	0		92.809		NI
63	CARDAM	cat 2B			3	1.0748	9.2837		11.954	3.093		97.079	8.074		.	.		.	0		97.079		NI
64	CARDAM	cat 2B			1	0.718	0.5669		11.8486	1.8037		99.666	9.123		.	.		.	0		99.666		NI
64	CARDAM	cat 2B			2	1.0409	3.7109		11.1134	0.688		96.663	9.0489		.	.		.	0		96.663		NI
64	CARDAM	cat 2B			3	1.3506	1.4834		15.3147	2.0773		84.183	6.9135		.	.		.	0		84.183		NI
65	CARDAM	cat 2B			1	1.1437	1.1112		17.6846	0.1487		88.923	6.3514		.	.		.	0		88.923		NI
65	CARDAM	cat 2B			2	1.0661	4.9967		19.5735	6.345		117.382	5.6354		.	.		.	0		117.382		NI
65	CARDAM	cat 2B			3	1.0748	9.2837		11.954	3.093		100.513	2.3703		.	.		.	0		100.513		NI
66	CARDAM	cat 2B			1	1.1585	5.6912		5.4455	2.2462		65.224	5.4812		.	.		.	0		65.224		NI
66	CARDAM	cat 2B			2	1.0661	4.9967		19.5735	6.345		105.119	2.4342		.	.		.	0		105.119		NI
66	CARDAM	cat 2B			3	1.0748	9.2837		11.954	3.093		88.662	9.2228		.	.		.	0		88.662		NI
67	CARDAM	cat 2A			1	1.0351	6.5903		17.2836	4.0249		3.426	1.1561		.	.		.	0		3.426		I
67	CARDAM	cat 2A			2	0.9244	7.503		8.8632	1.6731		6.783	6.1918		.	.		.	0		6.783		I
67	CARDAM	cat 2A			3	1.017	4.957		7.2385	0.8518		3.228	2.5722		.	.		.	0		3.228		I
68	CARDAM	cat 2A*			1	0.9699	2.5093		30.0959	3.9456		2.959	2.1141		.	.		.	0		2.959		I
68	CARDAM	cat 2A*			2	0.9148	3.1781		12.341	1.4603		4.509	0.7577		.	.		.	0		4.509		I
68	CARDAM	cat 2A*			3	0.7795	7.0435		21.6844	6.85		0.306	0.057		.	.		.	0		0.306		I
69	CARDAM	cat 2A*			1	0.9699	2.5093		30.0959	3.9456		81.825	6.1383		.	.		.	0		81.825		NI
69	CARDAM	cat 2A*			2	0.9148	3.1781		12.341	1.4603		34.715	0.496		.	.		.	0		34.715		I
69	CARDAM	cat 2A*			3	0.7795	7.0435		21.6844	6.85		68.611	13.418		.	.		.	0		68.611		NI
70	CARDAM	cat 2A			1	1.0417	3.7082		11.1788	0.6875		10.22	2.1655		.	.		.	0		10.22		I
70	CARDAM	cat 2A			2	1.3506	1.4834		15.3147	2.0773		12.23	1.5189		.	.		.	0		12.23		I
70	CARDAM	cat 2A			3	0.7983	6.6925		8.8647	1.3042		7.829	1.1619		.	.		.	0		7.829		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
71	CARDAM	cat 2A*			1	0.9247	7.5008		8.8895	1.6726		4.544	1.0999		.	.		.	0		4.544		I
71	CARDAM	cat 2A*			2	1.017	4.957		7.2385	0.8518		2.789	4.5093		.	.		.	0		2.789		I
71	CARDAM	cat 2A*			3	0.718	0.5669		11.8486	1.8037		12.603	5.6128		.	.		.	0		12.603		I
72	CARDAM	cat 2A*			1	1.3506	1.4834		15.3147	2.0773		4.665	0.2324		.	.		.	0		4.665		I
72	CARDAM	cat 2A*			2	1.0797	7.8357		6.7566	1.011		3.425	0.1528		.	.		.	0		3.425		I
72	CARDAM	cat 2A*			3	0.9533	3.5881		8.6662	1.4874		3.582	0.1649		.	.		.	0		3.582		I
73	CARDAM	cat 2A*			1	0.9726	6.2232		14.6177	1.7458		94.405	6.0759		.	.		.	0		94.405		NI
73	CARDAM	cat 2A*			2	0.9459	5.8678		10.1547	0.3097		99.419	15.949		.	.		.	0		99.419		NI
73	CARDAM	cat 2A*			3	1.0342	6.596		17.2116	4.0284		87.589	7.7248		.	.		.	0		87.589		NI
74	CARDAM	cat 2A	Yes	Yes	1	0.9699	2.5093		30.0959	3.9456		93.632	10.828		0.2801	0.142		0.794	0.999		92.723		NI
74	CARDAM	cat 2A	Yes	Yes	2	0.9148	3.1781		12.341	1.4603		104.835	4.8754		0.4992	0.247		0.952	1.1264		103.505		NI
74	CARDAM	cat 2A	Yes	Yes	3	0.7795	7.0435		21.6844	6.85		85.884	8.0964		0	0		0.812	1.143		85.367		NI
75	CARDAM	cat 2A			1	0.9699	2.5093		30.0959	3.9456		61.585	12.217		.	.		.	0		61.585		NI
75	CARDAM	cat 2A			2	0.9148	3.1781		12.341	1.4603		30.63	21.58	NQ	.	.		.	0		30.63	NQ	I
75	CARDAM	cat 2A			3	0.7795	7.0435		21.6844	6.85		19.942	5.2349		.	.		.	0		19.942		I
75	CARDAM	cat 2A			4	0.9726	6.2232		14.6177	1.7458		10.124	3.3472		.	.		.	0		10.124		I
76	CARDAM	cat 2A			1	0.718	0.5669		11.8486	1.8037		87.481	2.4592		.	.		.	0		87.481		NI
76	CARDAM	cat 2A			2	1.0409	3.7109		11.1134	0.688		83.878	6.7189		.	.		.	0		83.878		NI
76	CARDAM	cat 2A			3	1.3506	1.4834		15.3147	2.0773		70.896	1.938		.	.		.	0		70.896		NI
77	CARDAM	cat 2A			1	0.9247	7.5008		8.8895	1.6726		113.567	7.5771		.	.		.	0		113.567		NI
77	CARDAM	cat 2A			2	1.0166	4.9593		7.1959	0.8522		84.767	0.4835		.	.		.	0		84.767		NI
77	CARDAM	cat 2A			3	0.718	0.5669		11.8486	1.8037		90.478	8.5524		.	.		.	0		90.478		NI
78	CARDAM	cat 2A			1	0.9247	7.5008		8.8895	1.6726		103.042	12.363		.	.		.	0		103.042		NI
78	CARDAM	cat 2A			2	1.0166	4.9593		7.1959	0.8522		82.037	3.984		.	.		.	0		82.037		NI
78	CARDAM	cat 2A			3	0.718	0.5669		11.8486	1.8037		88.226	10.393		.	.		.	0		88.226		NI
79	CARDAM	cat 2A*			1	1.3506	1.4834		15.3147	2.0773		71.794	9.6879		.	.		.	0		71.794		NI
79	CARDAM	cat 2A*			2	1.0797	7.8357		6.7566	1.011		73.894	4.8026		.	.		.	0		73.894		NI
79	CARDAM	cat 2A*			3	0.9533	3.5881		8.6662	1.4874		74.685	7.1851		.	.		.	0		74.685		NI
80	CARDAM	cat 1	Yes		1	1.0417	3.7082		11.1788	0.6875		30.074	7.897		.	.		24.041	1.8953		6.352		I
80	CARDAM	cat 1	Yes		2	1.3506	1.4834		15.3147	2.0773		21.219	1.9561		.	.		18.51	1.4619		2.709		I
80	CARDAM	cat 1	Yes		3	0.7983	6.6925		8.8647	1.3042		23.304	1.9433		.	.		34.022	2.4732		0		I
81	CARDAM	cat 1	Yes		1	1.0351	6.5903		17.2836	4.0249		0.383	0.1334		.	.		0	0		0.383		I
81	CARDAM	cat 1	Yes		2	0.9244	7.503		8.8632	1.6731		0.447	0.1912		.	.		0	0		0.447		I
81	CARDAM	cat 1	Yes		3	1.017	4.957		7.2385	0.8518		0.518	0.0252		.	.		0	0		0.518		I
82	CARDAM	cat 1			1	1.169	5.4702		13.7342	2.2905		2.743	0.9543		.	.		.	0		2.743		I
82	CARDAM	cat 1			2	1.0074	8.5376		11.5659	1.2203		4.698	0.2423		.	.		.	0		4.698		I
82	CARDAM	cat 1			3	1.0398	3.5464		8.5117	0.9677		2.714	1.067		.	.		.	0		2.714		I
83	CARDAM	cat 1			1	0.9699	2.5093		30.0959	3.9456		6.43	1.376		.	.		.	0		6.43		I
83	CARDAM	cat 1			2	0.9148	3.1781		12.341	1.4603		1.794	0.574		.	.		.	0		1.794		I
83	CARDAM	cat 1			3	0.9726	6.2232		14.6177	1.7458		2.644	0.0564		.	.		.	0		2.644		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
84	CARDAM	cat 1			1	1.169	5.4702		13.7342	2.2905		35.127	1.6084		.	.		.	0		35.127		I
84	CARDAM	cat 1			2	1.1543	3.3335		11.3124	1.9334		16.848	1.7839		.	.		.	0		16.848		I
84	CARDAM	cat 1			3	1.0398	3.5464		8.5117	0.9677		16.9	3.0001		.	.		.	0		16.9		I
85	CARDAM	cat 1			1	0.9726	6.2232		14.6177	1.7458		66.681	1.0694		.	.		.	0		66.681		NI
85	CARDAM	cat 1			2	0.9459	5.8678		10.1547	0.3097		74.581	16.28		.	.		.	0		74.581		NI
85	CARDAM	cat 1			3	1.0342	6.596		17.2116	4.0284		73.485	8.5837		.	.		.	0		73.485		NI
86	CARDAM	cat 1			1	1.068	12.107		9.0451	0.5407		107.101	6.1067		.	.		.	0		107.101		NI
86	CARDAM	cat 1			2	1.1217	5.8363		9.2331	2.1018		99.868	5.2194		.	.		.	0		99.868		NI
86	CARDAM	cat 1			3	1.169	5.4702		13.7342	2.2905		79.511	7.8438		.	.		.	0		79.511		NI
87	CARDAM	cat 1			1	0.7795	7.0435		21.6844	6.85		101.8	9.226		.	.		.	0		101.8		NI
87	CARDAM	cat 1			2	0.9727	6.2224		14.6279	1.7456		86.969	4.9984		.	.		.	0		86.969		NI
87	CARDAM	cat 1			3	0.9459	5.8678		10.1547	0.3097		91.447	7.6121		.	.		.	0		91.447		NI
88	CARDAM	cat 1	Yes		1	0.9764	3.0137		9.7414	1.6474		3.924	0.6689		.	.		0.647	0.3668		3.277		I
88	CARDAM	cat 1	Yes		2	1.068	12.107		9.0451	0.5407		10.827	5.0381		.	.		0.63	0.3354		10.197		I
88	CARDAM	cat 1	Yes		3	0.9438	9.67		16.1907	2.7495		7.654	1.3621		.	.		0.669	0.3795		6.985		I
89	CARDAM	cat 1			1	0.9247	7.5008		8.8895	1.6726		71.785	7.0267		.	.		.	0		71.785		NI
89	CARDAM	cat 1			2	1.0166	4.9593		7.1959	0.8522		72.118	12.97		.	.		.	0		72.118		NI
89	CARDAM	cat 1			3	0.718	0.5669		11.8486	1.8037		83.982	11.36		.	.		.	0		83.982		NI
90	CARDAM	cat 1			1	0.9247	7.5008		8.8895	1.6726		92.832	3.3154		.	.		.	0		92.832		NI
90	CARDAM	cat 1			2	1.0166	4.9593		7.1959	0.8522		50.848	9.8944		.	.		.	0		50.848		NI
90	CARDAM	cat 1			3	0.718	0.5669		11.8486	1.8037		88.836	12.08		.	.		.	0		88.836		NI
91	CARDAM	cat 1	Yes		1	0.9244	7.503		8.8632	1.6731		59.041	1.1191		.	.		1.716	2.9718		58.08		NI
91	CARDAM	cat 1	Yes		2	1.017	4.957		7.2385	0.8518		42.331	4.3717		.	.		1.536	2.6596		41.53		I
91	CARDAM	cat 1	Yes		3	0.718	0.5669		11.8486	1.8037		60.914	2.0661		.	.		5.184	4.7038		55.73		NI
92	CARDAM	cat 1	Yes		1	1.0074	8.5376		11.5659	1.2203		85.314	8.8093		.	.		0.039	0.0669		85.314		NI
92	CARDAM	cat 1	Yes		2	1.1543	3.3335		11.3124	1.9334		78.705	8.8592		.	.		0.054	0.0934		78.705		NI
92	CARDAM	cat 1	Yes		3	1.0153	3.8417		9.8825	1.2486		82.758	4.6571		.	.		0.038	0.0663		82.758		NI
93	CARDAM	cat 1			1	0.9726	6.2232		14.6177	1.7458		71.054	0.5019		.	.		.	0		71.054		NI
93	CARDAM	cat 1			2	0.9459	5.8678		10.1547	0.3097		87.403	0.6975		.	.		.	0		87.403		NI
93	CARDAM	cat 1			3	1.0342	6.596		17.2116	4.0284		82.998	1.1613		.	.		.	0		82.998		NI
94	CARDAM	cat 1			1	1.0351	6.5903		17.2836	4.0249		75.506	2.8963		.	.		.	0		75.506		NI
94	CARDAM	cat 1			2	0.9244	7.503		8.8632	1.6731		78.067	2.9615		.	.		.	0		78.067		NI
94	CARDAM	cat 1			3	1.017	4.957		7.2385	0.8518		81.782	7.3965		.	.		.	0		81.782		NI
95	CARDAM	cat 1	Yes		1	0.9726	6.2232		14.6177	1.7458		1.292	0.4721		.	.		0	0		1.292		I
95	CARDAM	cat 1	Yes		2	0.9459	5.8678		10.1547	0.3097		1.574	0.9569		.	.		0	0		1.574		I
95	CARDAM	cat 1	Yes		3	1.0342	6.596		17.2116	4.0284		2.546	0.7959		.	.		0	0		2.546		I
96	CARDAM	cat 1			1	1.0351	6.5903		17.2836	4.0249		82.077	10.057		.	.		.	0		82.077		NI
96	CARDAM	cat 1			2	0.9244	7.503		8.8632	1.6731		91.422	4.1949		.	.		.	0		91.422		NI
96	CARDAM	cat 1			3	1.017	4.957		7.2385	0.8518		98.738	13.049		.	.		.	0		98.738		NI
97	CARDAM	cat 1			1	0.9726	6.2232		14.6177	1.7458		94.352	1.5769		.	.		.	0		94.352		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
97	CARDAM	cat 1			2	0.9459	5.8678		10.1547	0.3097		98.659	4.954		.	.		.	0		98.659		NI
97	CARDAM	cat 1			3	1.0342	6.596		17.2116	4.0284		94.351	1.795		.	.		.	0		94.351		NI
98	CARDAM	cat 1		Yes	1	0.9764	3.0137		9.7414	1.6474		105.916	6.4749		5.9503	2.468		.	0		99.966		NI
98	CARDAM	cat 1		Yes	2	1.068	12.107		9.0451	0.5407		106.829	5.294		5.5291	3.555		.	0		101.3		NI
98	CARDAM	cat 1		Yes	3	1.1217	5.8363		9.2331	2.1018		105.514	10.694		28.4231	8.107		.	0		77.091		NI
99	CARDAM	cat 1			1	0.9247	7.5008		8.8895	1.6726		25.616	6.4178		.	.		.	0		25.616		I
99	CARDAM	cat 1			2	1.0166	4.9593		7.1959	0.8522		16.795	1.7866		.	.		.	0		16.795		I
99	CARDAM	cat 1			3	0.718	0.5669		11.8486	1.8037		23.581	1.9576		.	.		.	0		23.581		I
100	CARDAM	cat 1			1	1.0074	8.5376		11.5659	1.2203		28.052	9.7589		.	.		.	0		28.052		I
100	CARDAM	cat 1			2	1.1543	3.3335		11.3124	1.9334		55.149	0.8796		.	.		.	0		55.149		NI
100	CARDAM	cat 1			3	1.0153	3.8417		9.8825	1.2486		27.078	1.1857		.	.		.	0		27.078		I
101	CARDAM	cat 1		Yes	1	0.9764	3.0137		9.7414	1.6474		87.149	2.305		0.1092	0.088		.	0		87.039		NI
101	CARDAM	cat 1		Yes	2	1.068	12.107		9.0451	0.5407		101.361	5.1278		0	0		.	0		101.361		NI
101	CARDAM	cat 1		Yes	3	1.1217	5.8363		9.2331	2.1018		86.822	7.3901		0	0		.	0		86.822		NI
102	CARDAM	cat 1			1	0.9438	9.67		16.1907	2.7495		115.424	5.6026		.	.		.	0		115.424		NI
102	CARDAM	cat 1			2	1.1543	3.3335		11.3124	1.9334		107.739	8.9385		.	.		.	0		107.739		NI
102	CARDAM	cat 1			3	1.0398	3.5464		8.5117	0.9677		111.7	2.8527		.	.		.	0		111.7		NI
103	CARDAM	cat 1			1	0.718	0.5669		11.8486	1.8037		9.095	1.8573		.	.		.	0		9.095		I
103	CARDAM	cat 1			2	1.0409	3.7109		11.1134	0.688		4.994	0.1312		.	.		.	0		4.994		I
103	CARDAM	cat 1			3	1.3506	1.4834		15.3147	2.0773		8.596	2.6823		.	.		.	0		8.596		I
104	CARDAM	cat 1			1	0.9247	7.5008		8.8895	1.6726		111.647	6.9033		.	.		.	0		111.647		NI
104	CARDAM	cat 1			2	1.0166	4.9593		7.1959	0.8522		87.276	1.4991		.	.		.	0		87.276		NI
104	CARDAM	cat 1			3	0.718	0.5669		11.8486	1.8037		90.327	7.4102		.	.		.	0		90.327		NI
105	CARDAM	cat 1			1	1.0409	3.7109		11.1134	0.688		9.048	2.5785		.	.		.	0		9.048		I
105	CARDAM	cat 1			2	1.3506	1.4834		15.3147	2.0773		10.814	1.5779		.	.		.	0		10.814		I
105	CARDAM	cat 1			3	0.7983	6.6925		8.8647	1.3042		7.685	0.3038		.	.		.	0		7.685		I
1	CEETOX	no cat			1	0.962	4.611		22.9903	4.4348		88.999	8.1062		.	.		.	0		88.999		NI
1	CEETOX	no cat			2	0.929	3.9191		29.0097	6.2734		83.872	1.4925		.	.		.	0		83.872		NI
1	CEETOX	no cat			3	0.9467	4.8488		29.1021	9.2982		83.275	8.2948		.	.		.	0		83.275		NI
2	CEETOX	no cat			1	0.962	4.611		22.9903	4.4348		104.262	7.3549		.	.		.	0		104.262		NI
2	CEETOX	no cat			2	0.929	3.9191		29.0097	6.2734		86.796	2.5441		.	.		.	0		86.796		NI
2	CEETOX	no cat			3	0.9467	4.8488		29.1021	9.2982		84.965	6.5128		.	.		.	0		84.965		NI
3	CEETOX	no cat			1	0.987	5.3233		31.5772	5.9588		81.476	4.9045		.	.		.	0		81.476		NI
3	CEETOX	no cat			2	0.8937	5.0139		18.0716	3.251		70.533	1.1873		.	.		.	0		70.533		NI
3	CEETOX	no cat			3	1.0388	7.2757		17.1346	4.4428		87.309	3.1201		.	.		.	0		87.309		NI
4	CEETOX	no cat	Yes		1	1.0737	1.4905		13.7069	3.6941		95.359	6.5897		.	.		91.4	4.176		0		I
4	CEETOX	no cat	Yes		2	1.1075	6.7453		13.9804	2.5428		101.084	4.9123		.	.		88.608	4.0485		0		I
4	CEETOX	no cat	Yes		3	1.0803	4.2089		5.7853	1.2081		105.137	16.336		.	.		90.836	4.1503		0		I
5	CEETOX	no cat	Yes		1	1.0298	1.4609		13.5297	3.9804		108.189	5.0904		.	.		0.599	0.3032		107.59		NI
5	CEETOX	no cat	Yes		2	1.0467	1.2874		6.1306	0.4308		96.146	9.3872		.	.		0.621	0.2983		95.525		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
5	CEETOX	no cat	Yes		3	1.0643	12.666		3.2884	0.6509		102.834	2.2476		.	.		0.579	0.2934		102.255		NI
6	CEETOX	no cat			1	0.962	4.611		22.9903	4.4348		123.164	10.087		.	.		.	0		123.164		NI
6	CEETOX	no cat			2	0.929	3.9191		29.0097	6.2734		102.96	11.851		.	.		.	0		102.96		NI
6	CEETOX	no cat			3	0.9467	4.8488		29.1021	9.2982		105.704	7.8612		.	.		.	0		105.704		NI
7	CEETOX	no cat			1	0.987	5.3233		31.5772	5.9588		84.228	3.9401		.	.		.	0		84.228		NI
7	CEETOX	no cat			2	0.8937	5.0139		18.0716	3.251		89.183	6.434		.	.		.	0		89.183		NI
7	CEETOX	no cat			3	1.0388	7.2757		17.1346	4.4428		87.085	3.0809		.	.		.	0		87.085		NI
8	CEETOX	no cat			1	0.987	5.3233		31.5772	5.9588		97.45	10.719		.	.		.	0		97.45		NI
8	CEETOX	no cat			2	0.8937	5.0139		18.0716	3.251		106.621	15.611		.	.		.	0		106.621		NI
8	CEETOX	no cat			3	1.0388	7.2757		17.1346	4.4428		114.519	5.4271		.	.		.	0		114.519		NI
9	CEETOX	no cat			1	0.962	4.611		22.9903	4.4348		95.911	6.2223		.	.		.	0		95.911		NI
9	CEETOX	no cat			2	0.929	3.9191		29.0097	6.2734		98.762	2.3585		.	.		.	0		98.762		NI
9	CEETOX	no cat			3	0.9467	4.8488		29.1021	9.2982		89.736	2.0729		.	.		.	0		89.736		NI
10	CEETOX	no cat			1	1.0373	6.1774		21.4332	3.0371		45.067	6.4625		.	.		.	0		45.067		I
10	CEETOX	no cat			2	1.1943	4.4215		6.2238	1.3201		41.027	2.2565		.	.		.	0		41.027		I
10	CEETOX	no cat			3	1.0052	11.181		4.6427	0.4745		36.229	2.5968		.	.		.	0		36.229		I
11	CEETOX	no cat			1	0.962	4.611		22.9903	4.4348		81.41	4.9396		.	.		.	0		81.41		NI
11	CEETOX	no cat			2	0.929	3.9191		29.0097	6.2734		84.284	2.9333		.	.		.	0		84.284		NI
11	CEETOX	no cat			3	0.9467	4.8488		29.1021	9.2982		79.261	2.1657		.	.		.	0		79.261		NI
12	CEETOX	no cat			1	0.961	2.7115		6.0527	0.4834		91.103	7.1983		.	.		.	0		91.103		NI
12	CEETOX	no cat			2	0.933	6.0005		9.6642	0.8844		101.268	5.7898		.	.		.	0		101.268		NI
12	CEETOX	no cat			3	0.9652	5.0074		4.4552	0.9126		95.959	2.8294		.	.		.	0		95.959		NI
13	CEETOX	no cat			1	0.961	2.7115		6.0527	0.4834		100.919	11.279		.	.		.	0		100.919		NI
13	CEETOX	no cat			2	0.933	6.0005		9.6642	0.8844		96.927	3.3228		.	.		.	0		96.927		NI
13	CEETOX	no cat			3	0.9652	5.0074		4.4552	0.9126		97.289	5.0307		.	.		.	0		97.289		NI
14	CEETOX	no cat	Yes		1	1.0298	1.4609		13.5297	3.9804		101.376	3.3641		.	.		0.022	0.0374		101.376		NI
14	CEETOX	no cat	Yes		2	1.0467	1.2874		6.1306	0.4308		103.471	14.014		.	.		0.032	0.0552		103.471		NI
14	CEETOX	no cat	Yes		3	1.0643	12.666		3.2884	0.6509		93	9.1391		.	.		0.021	0.0362		93		NI
15	CEETOX	no cat			1	0.933	6.0005		9.6642	0.8844		102.608	5.76		.	.		.	0		102.608		NI
15	CEETOX	no cat			2	0.9425	4.0652		4.916	0.9039		92.927	4.1179		.	.		.	0		92.927		NI
15	CEETOX	no cat			3	0.9652	5.0074		4.4552	0.9126		101.105	2.6427		.	.		.	0		101.105		NI
16	CEETOX	no cat			1	0.987	5.3233		31.5772	5.9588		89.97	5.7747		.	.		.	0		89.97		NI
16	CEETOX	no cat			2	0.8937	5.0139		18.0716	3.251		92.335	6.2466		.	.		.	0		92.335		NI
16	CEETOX	no cat			3	1.0388	7.2757		17.1346	4.4428		99.358	5.0657		.	.		.	0		99.358		NI
17	CEETOX	no cat			1	1.062	4.7143		10.1224	1.3169		95.182	4.5071		.	.		.	0		95.182		NI
17	CEETOX	no cat			2	1.022	4.0686		4.2727	1.2027		100.277	4.1103		.	.		.	0		100.277		NI
17	CEETOX	no cat			3	1.01	6.3364		15.7591	5.7839		104.736	5.2909		.	.		.	0		104.736		NI
18	CEETOX	no cat			1	0.962	2.955		9.806	1.8214		103.222	2.7839		.	.		.	0		103.222		NI
18	CEETOX	no cat			2	0.9745	7.154		6.4135	1.4749		64.666	36.156	NQ	.	.		.	0		0	NQ	I
18	CEETOX	no cat			3	0.961	2.7115		6.0527	0.4834		95.421	2.716		.	.		.	0		95.421		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
18	CEETOX	no cat			4	0.9425	4.0652		4.916	0.9039		78.373	2.4463		.	.		.	0		78.373		NI
19	CEETOX	no cat			1	0.933	6.0005		9.6642	0.8844		103.573	2.7243		.	.		.	0		103.573		NI
19	CEETOX	no cat			2	0.9425	4.0652		4.916	0.9039		91.972	4.7335		.	.		.	0		91.972		NI
19	CEETOX	no cat			3	0.9652	5.0074		4.4552	0.9126		105.837	0.8326		.	.		.	0		105.837		NI
20	CEETOX	no cat			1	1.0203	4.686		14.8808	2.8659		103.316	9.4194		.	.		.	0		103.316		NI
20	CEETOX	no cat			2	0.9472	2.2448		15.344	2.6984		122.787	7.1064		.	.		.	0		122.787		NI
20	CEETOX	no cat			3	0.9055	5.6584		4.1598	0.7497		107.362	10.663		.	.		.	0		107.362		NI
21	CEETOX	no cat			1	1.0737	1.4905		13.7069	3.6941		85.998	5.7337		.	.		.	0		85.998		NI
21	CEETOX	no cat			2	1.1075	6.7453		13.9804	2.5428		86.697	2.7047		.	.		.	0		86.697		NI
21	CEETOX	no cat			3	1.0803	4.2089		5.7853	1.2081		86.1	5.3932		.	.		.	0		86.1		NI
22	CEETOX	no cat			1	1.0373	6.1774		21.4332	3.0371		82.712	6.3753		.	.		.	0		82.712		NI
22	CEETOX	no cat			2	1.1943	4.4215		6.2238	1.3201		48.284	10.198		.	.		.	0		48.284		I
22	CEETOX	no cat			3	1.0052	11.181		4.6427	0.4745		40.507	17.077		.	.		.	0		40.507		I
23	CEETOX	no cat	Yes		1	1.0203	4.686		14.8808	2.8659		30.154	2.3838		.	.		52.123	5.6635		0		I
23	CEETOX	no cat	Yes		2	0.9472	2.2448		15.344	2.6984		30.565	1.1886		.	.		56.308	6.101		0		I
23	CEETOX	no cat	Yes		3	0.9055	5.6584		4.1598	0.7497		38.671	5.5412		.	.		64.2	6.3817		0		I
24	CEETOX	no cat			1	1.0945	5.8222		5.7865	0.6135		72.651	1.9894		.	.		.	0		72.651		NI
24	CEETOX	no cat			2	1.0692	5.1104		13.2502	3.2509		70.709	4.005		.	.		.	0		70.709		NI
24	CEETOX	no cat			3	1.0803	4.2089		5.7853	1.2081		60.969	2.0847		.	.		.	0		60.969		NI
25	CEETOX	no cat	Yes		1	1.0203	4.686		14.8808	2.8659		94.169	5.1214		.	.		0.011	0.0189		94.169		NI
25	CEETOX	no cat	Yes		2	0.9472	2.2448		15.344	2.6984		98.803	2.8861		.	.		0.012	0.0203		98.803		NI
25	CEETOX	no cat	Yes		3	0.9055	5.6584		4.1598	0.7497		95.03	3.2494		.	.		0.012	0.0213		95.03		NI
26	CEETOX	no cat			1	1.0203	4.686		14.8808	2.8659		98.269	1.6697		.	.		.	0		98.269		NI
26	CEETOX	no cat			2	0.9472	2.2448		15.344	2.6984		99.367	7.4379		.	.		.	0		99.367		NI
26	CEETOX	no cat			3	0.9055	5.6584		4.1598	0.7497		96.024	2.2025		.	.		.	0		96.024		NI
28	CEETOX	no cat			1	0.962	4.611		22.9903	4.4348		95.495	8.4962		.	.		.	0		95.495		NI
28	CEETOX	no cat			2	0.929	3.9191		29.0097	6.2734		92.483	4.4081		.	.		.	0		92.483		NI
28	CEETOX	no cat			3	0.9467	4.8488		29.1021	9.2982		87.148	6.2354		.	.		.	0		87.148		NI
29	CEETOX	no cat			1	0.933	6.0005		9.6642	0.8844		102.805	1.4568		.	.		.	0		102.805		NI
29	CEETOX	no cat			2	0.9425	4.0652		4.916	0.9039		94.783	0.6675		.	.		.	0		94.783		NI
29	CEETOX	no cat			3	0.9652	5.0074		4.4552	0.9126		99.948	2.4933		.	.		.	0		99.948		NI
30	CEETOX	no cat			1	0.9935	6.2229		13.0683	3.082		82.922	3.1007		.	.		.	0		82.922		NI
30	CEETOX	no cat			2	1.0203	4.686		14.8808	2.8659		76.609	5.1048		.	.		.	0		76.609		NI
30	CEETOX	no cat			3	0.9472	2.2448		15.344	2.6984		80.943	2.4604		.	.		.	0		80.943		NI
31	CEETOX	no cat			1	1.01	6.3364		15.7591	5.7839		99.257	5.0622		.	.		.	0		99.257		NI
31	CEETOX	no cat			2	0.9935	6.2229		13.0683	3.082		98.49	5.1602		.	.		.	0		98.49		NI
31	CEETOX	no cat			3	0.962	2.955		9.806	1.8214		99.082	1.6972		.	.		.	0		99.082		NI
32	CEETOX	no cat			1	1.0373	6.1774		21.4332	3.0371		47.976	8.3111		.	.		.	0		47.976		I
32	CEETOX	no cat			2	1.1943	4.4215		6.2238	1.3201		38.752	2.7597		.	.		.	0		38.752		I
32	CEETOX	no cat			3	1.0052	11.181		4.6427	0.4745		47.322	5.1095		.	.		.	0		47.322		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
33	CEETOX	no cat	Yes	Yes	1	1.0945	5.8222		5.7865	0.6135		89.95	12.639		0.8223	0.121		0.005	0.0088		89.127		NI
33	CEETOX	no cat	Yes	Yes	2	1.0692	5.1104		13.2502	3.2509		99.002	2.5367		1.0133	0.619		0.005	0.009		97.989		NI
33	CEETOX	no cat	Yes	Yes	3	1.0803	4.2089		5.7853	1.2081		89.972	7.1893		0.5091	0.255		2.083	1.6982		87.38		NI
34	CEETOX	no cat	Yes	Yes	1	0.9827	1.3599		9.7015	1.7119		134.447	7.6462		5.6479	0.404		3.223	1.7525		125.577		NI
34	CEETOX	no cat	Yes	Yes	2	1.062	4.7143		10.1224	1.3169		99.733	10.574		3.4369	0.483		7.957	1.6216		88.34		NI
34	CEETOX	no cat	Yes	Yes	3	1.022	4.0686		4.2727	1.2027		117.123	6.1789		3.7997	1.045		3.033	1.6851		110.29		NI
35	CEETOX	no cat	Yes		1	1.0945	5.8222		5.7865	0.6135		25.187	1.263		.	.		15.304	2.0211		9.883		I
35	CEETOX	no cat	Yes		2	1.0803	4.2089		5.7853	1.2081		85.653	4.865		.	.		19.161	2.0476		66.492		NI
35	CEETOX	no cat	Yes		3	0.9783	10.415		7.4957	0.5606		25.792	1.3428		.	.		21.363	2.2611		4.429		I
36	CEETOX	no cat			1	0.987	5.3233		31.5772	5.9588		93.026	3.3828		.	.		.	0		93.026		NI
36	CEETOX	no cat			2	0.8937	5.0139		18.0716	3.251		93.659	3.8639		.	.		.	0		93.659		NI
36	CEETOX	no cat			3	1.0388	7.2757		17.1346	4.4428		102.743	6.5144		.	.		.	0		102.743		NI
37	CEETOX	no cat	Yes		1	1.01	6.3364		15.7591	5.7839		85.198	2.3148		.	.		0	0		85.198		NI
37	CEETOX	no cat	Yes		2	0.9935	6.2229		13.0683	3.082		83.426	5.9951		.	.		0	0		83.426		NI
37	CEETOX	no cat	Yes		3	0.962	2.955		9.806	1.8214		91.216	1.2903		.	.		0.04	0.07		91.216		NI
38	CEETOX	no cat			1	0.962	2.955		9.806	1.8214		104.66	2.4912		.	.		.	0		104.66		NI
38	CEETOX	no cat			2	0.9745	7.154		6.4135	1.4749		91.397	1.1346		.	.		.	0		91.397		NI
38	CEETOX	no cat			3	0.9425	4.0652		4.916	0.9039		86.844	2.49		.	.		.	0		86.844		NI
39	CEETOX	no cat			1	0.9745	7.154		6.4135	1.4749		103.506	5.492		.	.		.	0		103.506		NI
39	CEETOX	no cat			2	0.961	2.7115		6.0527	0.4834		94.78	3.038		.	.		.	0		94.78		NI
39	CEETOX	no cat			3	0.9597	3.8851		5.1059	1.2355		96.058	3.5692		.	.		.	0		96.058		NI
40	CEETOX	no cat			1	1.0203	4.686		14.8808	2.8659		84.874	3.8958		.	.		.	0		84.874		NI
40	CEETOX	no cat			2	0.9472	2.2448		15.344	2.6984		83.706	6.9922		.	.		.	0		83.706		NI
40	CEETOX	no cat			3	0.9055	5.6584		4.1598	0.7497		86.159	5.8756		.	.		.	0		86.159		NI
41	CEETOX	no cat			1	1.01	6.3364		15.7591	5.7839		105.578	2.9381		.	.		.	0		105.578		NI
41	CEETOX	no cat			2	0.9935	6.2229		13.0683	3.082		95.269	2.3406		.	.		.	0		95.269		NI
41	CEETOX	no cat			3	0.962	2.955		9.806	1.8214		96.362	2.484		.	.		.	0		96.362		NI
42	CEETOX	no cat	Yes		1	1.062	4.7143		10.1224	1.3169		92.075	5.0713		.	.		12.963	9.1546		79.112		NI
42	CEETOX	no cat	Yes		2	1.022	4.0686		4.2727	1.2027		103.164	9.6486		.	.		9.301	8.8012		94.309		NI
42	CEETOX	no cat	Yes		3	1.01	6.3364		15.7591	5.7839		87.921	2.0692		.	.		9.268	8.7926		79.175		NI
43	CEETOX	no cat			1	1.062	4.7143		10.1224	1.3169		97.473	1.9746		.	.		.	0		97.473		NI
43	CEETOX	no cat			2	1.022	4.0686		4.2727	1.2027		102.984	4.8927		.	.		.	0		102.984		NI
43	CEETOX	no cat			3	1.01	6.3364		15.7591	5.7839		102.822	3.8741		.	.		.	0		102.822		NI
44	CEETOX	no cat			1	1.0803	4.2089		5.7853	1.2081		101.728	14.237		.	.		.	0		101.728		NI
44	CEETOX	no cat			2	0.9783	10.415		7.4957	0.5606		101.329	2.7661		.	.		.	0		101.329		NI
44	CEETOX	no cat			3	0.9827	1.3599		9.7015	1.7119		98.287	4.9426		.	.		.	0		98.287		NI
45	CEETOX	no cat			1	1.01	6.3364		15.7591	5.7839		96.881	4.1138		.	.		.	0		96.881		NI
45	CEETOX	no cat			2	0.9935	6.2229		13.0683	3.082		90.102	3.0365		.	.		.	0		90.102		NI
45	CEETOX	no cat			3	0.962	2.955		9.806	1.8214		98.233	5.6561		.	.		.	0		98.233		NI
46	CEETOX	no cat	Yes		1	1.062	4.7143		10.1224	1.3169		82.69	2.2867		.	.		0.549	0.1438		82.141		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
46	CEETOX	no cat	Yes		2	1.022	4.0686		4.2727	1.2027		102.038	4.1933		.	.		0	0		102.038		NI
46	CEETOX	no cat	Yes		3	1.01	6.3364		15.7591	5.7839		92.31	3.3846		.	.		0	0		92.31		NI
47	CEETOX	no cat			1	1.01	6.3364		15.7591	5.7839		100.066	1.3861		.	.		.	0		100.066		NI
47	CEETOX	no cat			2	0.9935	6.2229		13.0683	3.082		88.794	4.0964		.	.		.	0		88.794		NI
47	CEETOX	no cat			3	1.0203	4.686		14.8808	2.8659		101.323	4.2981		.	.		.	0		101.323		NI
48	CEETOX	no cat	Yes		1	0.9935	6.2229		13.0683	3.082		37.292	8.707		.	.		0	0		37.292		I
48	CEETOX	no cat	Yes		2	1.0203	4.686		14.8808	2.8659		18.817	1.4573		.	.		2.336	0.637		16.482		I
48	CEETOX	no cat	Yes		3	0.9472	2.2448		15.344	2.6984		33.943	9.1642		.	.		2.516	0.6863		31.427		I
49	CEETOX	no cat	Yes		1	1.0203	4.686		14.8808	2.8659		102.172	6.4932		.	.		0.011	0.0189		102.172		NI
49	CEETOX	no cat	Yes		2	0.9472	2.2448		15.344	2.6984		114.288	6.8928		.	.		0.012	0.0203		114.288		NI
49	CEETOX	no cat	Yes		3	0.9055	5.6584		4.1598	0.7497		100.626	5.9619		.	.		0.012	0.0213		100.626		NI
50	CEETOX	no cat			1	0.933	6.0005		9.6642	0.8844		95.105	3.5322		.	.		.	0		95.105		NI
50	CEETOX	no cat			2	0.9425	4.0652		4.916	0.9039		88.912	3.4201		.	.		.	0		88.912		NI
50	CEETOX	no cat			3	0.9652	5.0074		4.4552	0.9126		86.22	1.9205		.	.		.	0		86.22		NI
51	CEETOX	no cat			1	1.0203	4.686		14.8808	2.8659		93.548	2.7237		.	.		.	0		93.548		NI
51	CEETOX	no cat			2	0.9472	2.2448		15.344	2.6984		101.936	4.844		.	.		.	0		101.936		NI
51	CEETOX	no cat			3	0.9055	5.6584		4.1598	0.7497		101.896	1.5621		.	.		.	0		101.896		NI
52	CEETOX	no cat			1	0.933	6.0005		9.6642	0.8844		113.362	3.2346		.	.		.	0		113.362		NI
52	CEETOX	no cat			2	0.9425	4.0652		4.916	0.9039		103.148	7.7354		.	.		.	0		103.148		NI
52	CEETOX	no cat			3	0.9652	5.0074		4.4552	0.9126		105.06	4.0535		.	.		.	0		105.06		NI
53	CEETOX	no cat			1	0.933	6.0005		9.6642	0.8844		102.036	7.9822		.	.		.	0		102.036		NI
53	CEETOX	no cat			2	0.9425	4.0652		4.916	0.9039		94.147	5.5948		.	.		.	0		94.147		NI
53	CEETOX	no cat			3	0.9652	5.0074		4.4552	0.9126		98.895	3.6268		.	.		.	0		98.895		NI
54	CEETOX	cat 2B			1	0.962	4.611		22.9903	4.4348		86.902	6.9151		.	.		.	0		86.902		NI
54	CEETOX	cat 2B			2	0.929	3.9191		29.0097	6.2734		82.921	4.1573		.	.		.	0		82.921		NI
54	CEETOX	cat 2B			3	0.9467	4.8488		29.1021	9.2982		72.993	3.1714		.	.		.	0		72.993		NI
55	CEETOX	cat 2B	Yes		1	1.0737	1.4905		13.7069	3.6941		4.579	0.7068		.	.		0	0		4.579		I
55	CEETOX	cat 2B	Yes		2	1.1075	6.7453		13.9804	2.5428		4.424	0.2486		.	.		0	0		4.424		I
55	CEETOX	cat 2B	Yes		3	1.0803	4.2089		5.7853	1.2081		3.163	0.9564		.	.		0	0		3.163		I
56	CEETOX	cat 2B	Yes		1	1.0203	4.686		14.8808	2.8659		91.751	6.4633		.	.		0.86	1.4901		91.751		NI
56	CEETOX	cat 2B	Yes		2	0.9472	2.2448		15.344	2.6984		92.786	8.3754		.	.		0.98	1.6966		92.786		NI
56	CEETOX	cat 2B	Yes		3	0.9055	5.6584		4.1598	0.7497		85.514	8.5609		.	.		0.81	1.4027		85.514		NI
57	CEETOX	cat 2B			1	1.0373	6.1774		21.4332	3.0371		39.589	4.1517		.	.		.	0		39.589		I
57	CEETOX	cat 2B			2	1.1943	4.4215		6.2238	1.3201		33.352	1.7953		.	.		.	0		33.352		I
57	CEETOX	cat 2B			3	1.0052	11.181		4.6427	0.4745		29.1	5.8378		.	.		.	0		29.1		I
58	CEETOX	cat 2B	Yes		1	0.9935	6.2229		13.0683	3.082		30.817	4.868		.	.		0	0		30.817		I
58	CEETOX	cat 2B	Yes		2	1.0203	4.686		14.8808	2.8659		31.999	1.3619		.	.		0	0		31.999		I
58	CEETOX	cat 2B	Yes		3	0.9472	2.2448		15.344	2.6984		34.594	5.6601		.	.		0	0		34.594		I
59	CEETOX	cat 2B	Yes		1	0.9935	6.2229		13.0683	3.082		89.096	3.7206		.	.		0	0		89.096		NI
59	CEETOX	cat 2B	Yes		2	0.9055	5.6584		4.1598	0.7497		86.49	2.6507		.	.		0	0		86.49		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
59	CEETOX	cat 2B	Yes		3	0.962	2.955		9.806	1.8214		91.632	4.3861		.	.		0.133	0.2152		91.545		NI
60	CEETOX	cat 2B			1	1.0203	4.686		14.8808	2.8659		25.041	4.7602		.	.		.	0		25.041		I
60	CEETOX	cat 2B			2	0.9472	2.2448		15.344	2.6984		36.6	3.7269		.	.		.	0		36.6		I
60	CEETOX	cat 2B			3	0.9055	5.6584		4.1598	0.7497		39.849	6.216		.	.		.	0		39.849		I
61	CEETOX	cat 2B			1	0.987	5.3233		31.5772	5.9588		90.003	6.2584		.	.		.	0		90.003		NI
61	CEETOX	cat 2B			2	0.8937	5.0139		18.0716	3.251		84.502	0.5337		.	.		.	0		84.502		NI
61	CEETOX	cat 2B			3	1.0388	7.2757		17.1346	4.4428		96.358	10.1		.	.		.	0		96.358		NI
62	CEETOX	cat 2B			1	0.9935	6.2229		13.0683	3.082		91.662	7.0008		.	.		.	0		91.662		NI
62	CEETOX	cat 2B			2	0.9055	5.6584		4.1598	0.7497		100.626	8.194		.	.		.	0		100.626		NI
62	CEETOX	cat 2B			3	0.962	2.955		9.806	1.8214		98.77	3.1117		.	.		.	0		98.77		NI
63	CEETOX	cat 2B			1	0.9935	6.2229		13.0683	3.082		89.23	2.4298		.	.		.	0		89.23		NI
63	CEETOX	cat 2B			2	0.9055	5.6584		4.1598	0.7497		84.392	17.053		.	.		.	0		84.392		NI
63	CEETOX	cat 2B			3	0.962	2.955		9.806	1.8214		100.641	9.0449		.	.		.	0		100.641		NI
64	CEETOX	cat 2B			1	1.062	4.7143		10.1224	1.3169		84.338	0.7299		.	.		.	0		84.338		NI
64	CEETOX	cat 2B			2	1.022	4.0686		4.2727	1.2027		94.08	4.6801		.	.		.	0		94.08		NI
64	CEETOX	cat 2B			3	1.01	6.3364		15.7591	5.7839		94.043	6.417		.	.		.	0		94.043		NI
65	CEETOX	cat 2B			1	0.9935	6.2229		13.0683	3.082		99.262	9.8788		.	.		.	0		99.262		NI
65	CEETOX	cat 2B			2	0.9055	5.6584		4.1598	0.7497		106.35	5.4272		.	.		.	0		106.35		NI
65	CEETOX	cat 2B			3	0.962	2.955		9.806	1.8214		103.361	2.2887		.	.		.	0		103.361		NI
66	CEETOX	cat 2B			1	0.9935	6.2229		13.0683	3.082		80.674	2.4253		.	.		.	0		80.674		NI
66	CEETOX	cat 2B			2	0.9055	5.6584		4.1598	0.7497		82.938	13.165		.	.		.	0		82.938		NI
66	CEETOX	cat 2B			3	0.962	2.955		9.806	1.8214		84.685	2.6914		.	.		.	0		84.685		NI
67	CEETOX	cat 2A			1	1.0298	1.4609		13.5297	3.9804		16.459	4.0131		.	.		.	0		16.459		I
67	CEETOX	cat 2A			2	1.0467	1.2874		6.1306	0.4308		20.844	2.6813		.	.		.	0		20.844		I
67	CEETOX	cat 2A			3	1.0643	12.666		3.2884	0.6509		33.683	5.035		.	.		.	0		33.683		I
68	CEETOX	cat 2A*			1	1.0298	1.4609		13.5297	3.9804		4.58	0.4511		.	.		.	0		4.58		I
68	CEETOX	cat 2A*			2	1.0467	1.2874		6.1306	0.4308		5.43	1.9229		.	.		.	0		5.43		I
68	CEETOX	cat 2A*			3	1.0643	12.666		3.2884	0.6509		4.557	0.8801		.	.		.	0		4.557		I
69	CEETOX	cat 2A*			1	0.987	5.3233		31.5772	5.9588		72.915	2.3595		.	.		.	0		72.915		NI
69	CEETOX	cat 2A*			2	0.8937	5.0139		18.0716	3.251		58.187	7.3608		.	.		.	0		58.187		NI
69	CEETOX	cat 2A*			3	1.0388	7.2757		17.1346	4.4428		63.838	7.6709		.	.		.	0		63.838		NI
70	CEETOX	cat 2A			1	1.0373	6.1774		21.4332	3.0371		12.404	1.1211		.	.		.	0		12.404		I
70	CEETOX	cat 2A			2	1.1943	4.4215		6.2238	1.3201		8.554	0.6298		.	.		.	0		8.554		I
70	CEETOX	cat 2A			3	1.0052	11.181		4.6427	0.4745		5.72	0.8209		.	.		.	0		5.72		I
71	CEETOX	cat 2A*	Yes		1	1.0737	1.4905		13.7069	3.6941		4.735	1.1717		.	.		0	0		4.735		I
71	CEETOX	cat 2A*	Yes		2	1.1075	6.7453		13.9804	2.5428		5.388	1.3095		.	.		0	0		5.388		I
71	CEETOX	cat 2A*	Yes		3	1.0803	4.2089		5.7853	1.2081		4.243	0.9306		.	.		0	0		4.243		I
72	CEETOX	cat 2A*	Yes		1	0.9935	6.2229		13.0683	3.082		4.026	0.5544		.	.		0	0		4.026		I
72	CEETOX	cat 2A*	Yes		2	0.962	2.955		9.806	1.8214		3.915	0.2101		.	.		0	0		3.915		I
72	CEETOX	cat 2A*	Yes		3	0.9745	7.154		6.4135	1.4749		3.079	0.2236		.	.		5.883	0.2136		0		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
73	CEETOX	cat 2A*			1	1.0298	1.4609		13.5297	3.9804		65.464	4.6913		.	.		.	0		65.464		NI
73	CEETOX	cat 2A*			2	1.0467	1.2874		6.1306	0.4308		47.596	4.9355		.	.		.	0		47.596		I
73	CEETOX	cat 2A*			3	1.0643	12.666		3.2884	0.6509		35.656	5.5386		.	.		.	0		35.656		I
74	CEETOX	cat 2A	Yes		1	1.0945	5.8222		5.7865	0.6135		88.001	4.071		.	.		0.117	0.1525		88.001		NI
74	CEETOX	cat 2A	Yes		2	1.0692	5.1104		13.2502	3.2509		86.08	8.0847		.	.		0.12	0.1561		86.08		NI
74	CEETOX	cat 2A	Yes		3	1.0803	4.2089		5.7853	1.2081		25.208	4.4499		.	.		3.548	0.5077		21.66		I
75	CEETOX	cat 2A			1	0.962	4.611		22.9903	4.4348		60.412	5.258		.	.		.	0		60.412		NI
75	CEETOX	cat 2A			2	0.929	3.9191		29.0097	6.2734		64.442	9.0425		.	.		.	0		64.442		NI
75	CEETOX	cat 2A			3	0.9467	4.8488		29.1021	9.2982		59.296	2.0017		.	.		.	0		59.296		NI
76	CEETOX	cat 2A			1	1.062	4.7143		10.1224	1.3169		44.397	15.556		.	.		.	0		44.397		I
76	CEETOX	cat 2A			2	1.022	4.0686		4.2727	1.2027		58.806	10.25		.	.		.	0		58.806		NI
76	CEETOX	cat 2A			3	1.01	6.3364		15.7591	5.7839		75.627	5.2326		.	.		.	0		75.627		NI
77	CEETOX	cat 2A			1	1.062	4.7143		10.1224	1.3169		49.749	4.6346		.	.		.	0		49.749		I
77	CEETOX	cat 2A			2	1.022	4.0686		4.2727	1.2027		102.332	5.4269		.	.		.	0		102.332		NI
77	CEETOX	cat 2A			3	1.01	6.3364		15.7591	5.7839		101.634	4.4001		.	.		.	0		101.634		NI
78	CEETOX	cat 2A			1	1.062	4.7143		10.1224	1.3169		93.158	6.9012		.	.		.	0		93.158		NI
78	CEETOX	cat 2A			2	1.022	4.0686		4.2727	1.2027		97.603	2.7109		.	.		.	0		97.603		NI
78	CEETOX	cat 2A			3	1.01	6.3364		15.7591	5.7839		106.205	7.4845		.	.		.	0		106.205		NI
79	CEETOX	cat 2A*			1	1.0803	4.2089		5.7853	1.2081		75.332	2.7213		.	.		.	0		75.332		NI
79	CEETOX	cat 2A*			2	0.9783	10.415		7.4957	0.5606		81.38	3.0819		.	.		.	0		81.38		NI
79	CEETOX	cat 2A*			3	0.9827	1.3599		9.7015	1.7119		88.382	7.4347		.	.		.	0		88.382		NI
80	CEETOX	cat 1	Yes		1	1.0373	6.1774		21.4332	3.0371		29.9	1.5058		.	.		34.769	2.4445		0		I
80	CEETOX	cat 1	Yes		2	1.1943	4.4215		6.2238	1.3201		26.263	3.3251		.	.		30.198	2.1231		0.05		I
80	CEETOX	cat 1	Yes		3	1.0052	11.181		4.6427	0.4745		33.228	4.0675		.	.		35.881	2.5227		0.68		I
81	CEETOX	cat 1	Yes		1	1.0298	1.4609		13.5297	3.9804		3.771	2.5014		.	.		0.534	0.4665		3.237		I
81	CEETOX	cat 1	Yes		2	1.0467	1.2874		6.1306	0.4308		1.704	0.3344		.	.		0.525	0.459		1.178		I
81	CEETOX	cat 1	Yes		3	1.0643	12.666		3.2884	0.6509		1.832	0.047		.	.		0.517	0.4514		1.315		I
82	CEETOX	cat 1			1	0.9745	7.154		6.4135	1.4749		1.642	0.543		.	.		.	0		1.642		I
82	CEETOX	cat 1			2	0.961	2.7115		6.0527	0.4834		0.902	0.2103		.	.		.	0		0.902		I
82	CEETOX	cat 1			3	0.9597	3.8851		5.1059	1.2355		1.494	0.2388		.	.		.	0		1.494		I
83	CEETOX	cat 1			1	0.987	5.3233		31.5772	5.9588		10.233	1.8753		.	.		.	0		10.233		I
83	CEETOX	cat 1			2	0.8937	5.0139		18.0716	3.251		3.786	1.203		.	.		.	0		3.786		I
83	CEETOX	cat 1			3	1.0388	7.2757		17.1346	4.4428		2.005	0.2206		.	.		.	0		2.005		I
84	CEETOX	cat 1			1	0.962	2.955		9.806	1.8214		13.704	2.471		.	.		.	0		13.704		I
84	CEETOX	cat 1			2	0.9745	7.154		6.4135	1.4749		10.091	0.6013		.	.		.	0		10.091		I
84	CEETOX	cat 1			3	0.9425	4.0652		4.916	0.9039		2.034	0.3611		.	.		.	0		2.034		I
85	CEETOX	cat 1			1	0.962	4.611		22.9903	4.4348		77.685	6.0936		.	.		.	0		77.685		NI
85	CEETOX	cat 1			2	0.929	3.9191		29.0097	6.2734		90.133	1.7764		.	.		.	0		90.133		NI
85	CEETOX	cat 1			3	0.9467	4.8488		29.1021	9.2982		79.736	2.6975		.	.		.	0		79.736		NI
86	CEETOX	cat 1			1	0.961	2.7115		6.0527	0.4834		79.032	8.1917		.	.		.	0		79.032		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
86	CEETOX	cat 1			2	0.933	6.0005		9.6642	0.8844		86.031	2.9163		.	.		.	0		86.031		NI
86	CEETOX	cat 1			3	0.9652	5.0074		4.4552	0.9126		75.496	2.8619		.	.		.	0		75.496		NI
87	CEETOX	cat 1			1	1.0373	6.1774		21.4332	3.0371		81.973	5.1766		.	.		.	0		81.973		NI
87	CEETOX	cat 1			2	1.1943	4.4215		6.2238	1.3201		87.036	6.4852		.	.		.	0		87.036		NI
87	CEETOX	cat 1			3	1.0052	11.181		4.6427	0.4745		31.902	2.8872		.	.		.	0		31.902		I
88	CEETOX	cat 1	Yes		1	0.9745	7.154		6.4135	1.4749		5.952	2.774		.	.		2.446	0.1649		3.506		I
88	CEETOX	cat 1	Yes		2	0.961	2.7115		6.0527	0.4834		8.29	2.7714		.	.		0.486	0.1673		7.804		I
88	CEETOX	cat 1	Yes		3	0.9597	3.8851		5.1059	1.2355		4.672	0.8385		.	.		1.667	0.1675		3.005		I
89	CEETOX	cat 1			1	1.0373	6.1774		21.4332	3.0371		66.308	1.467		.	.		.	0		66.308		NI
89	CEETOX	cat 1			2	1.1943	4.4215		6.2238	1.3201		56.433	4.5137		.	.		.	0		56.433		NI
89	CEETOX	cat 1			3	1.0052	11.181		4.6427	0.4745		16.697	1.693		.	.		.	0		16.697		I
90	CEETOX	cat 1			1	1.0737	1.4905		13.7069	3.6941		79.292	7.9398		.	.		.	0		79.292		NI
90	CEETOX	cat 1			2	1.0692	5.1104		13.2502	3.2509		82.541	6.4582		.	.		.	0		82.541		NI
90	CEETOX	cat 1			3	1.0803	4.2089		5.7853	1.2081		64.579	5.417		.	.		.	0		64.579		NI
91	CEETOX	cat 1	Yes		1	1.0737	1.4905		13.7069	3.6941		73.549	5.8708		.	.		87.644	9.3139		0		I
91	CEETOX	cat 1	Yes		2	1.1075	6.7453		13.9804	2.5428		72.009	4.1564		.	.		84.966	9.0294		0		I
91	CEETOX	cat 1	Yes		3	1.0803	4.2089		5.7853	1.2081		64.039	1.82		.	.		87.103	9.2564		0		I
92	CEETOX	cat 1	Yes		1	0.933	6.0005		9.6642	0.8844		87.049	6.4445		.	.		0.857	0.1072		86.191		NI
92	CEETOX	cat 1	Yes		2	0.9425	4.0652		4.916	0.9039		82.935	5.8363		.	.		0.849	0.1061		82.087		NI
92	CEETOX	cat 1	Yes		3	0.9652	5.0074		4.4552	0.9126		77.327	5.6474		.	.		0.622	0.1036		76.705		NI
93	CEETOX	cat 1			1	0.962	4.611		22.9903	4.4348		99.099	12.165		.	.		.	0		99.099		NI
93	CEETOX	cat 1			2	0.929	3.9191		29.0097	6.2734		86.311	3.36		.	.		.	0		86.311		NI
93	CEETOX	cat 1			3	0.9467	4.8488		29.1021	9.2982		90.282	5.4575		.	.		.	0		90.282		NI
94	CEETOX	cat 1			1	1.0737	1.4905		13.7069	3.6941		52.546	1.2057		.	.		.	0		52.546		NI
94	CEETOX	cat 1			2	1.0692	5.1104		13.2502	3.2509		74.606	6.6967		.	.		.	0		74.606		NI
94	CEETOX	cat 1			3	1.0803	4.2089		5.7853	1.2081		54.613	8.2217		.	.		.	0		54.613		NI
95	CEETOX	cat 1			1	0.987	5.3233		31.5772	5.9588		9.591	0.5066		.	.		.	0		9.591		I
95	CEETOX	cat 1			2	0.8937	5.0139		18.0716	3.251		4.42	0.6996		.	.		.	0		4.42		I
95	CEETOX	cat 1			3	1.0388	7.2757		17.1346	4.4428		16.958	4.3729		.	.		.	0		16.958		I
96	CEETOX	cat 1			1	0.987	5.3233		31.5772	5.9588		101.013	13.472		.	.		.	0		101.013		NI
96	CEETOX	cat 1			2	0.8937	5.0139		18.0716	3.251		98.844	8.903		.	.		.	0		98.844		NI
96	CEETOX	cat 1			3	1.0388	7.2757		17.1346	4.4428		97.176	8.3087		.	.		.	0		97.176		NI
97	CEETOX	cat 1			1	1.0298	1.4609		13.5297	3.9804		100.858	8.3212		.	.		.	0		100.858		NI
97	CEETOX	cat 1			2	1.0467	1.2874		6.1306	0.4308		85.287	4.845		.	.		.	0		85.287		NI
97	CEETOX	cat 1			3	1.0643	12.666		3.2884	0.6509		73.567	5.563		.	.		.	0		73.567		NI
98	CEETOX	cat 1	Yes	Yes	1	0.9745	7.154		6.4135	1.4749		99.555	4.1917		2.2405	0.427		20.079	14.127		77.236		NI
98	CEETOX	cat 1	Yes	Yes	2	0.961	2.7115		6.0527	0.4834		100.364	5.8154		1.8557	0.433		18.262	14.326		80.246		NI
98	CEETOX	cat 1	Yes	Yes	3	0.9425	4.0652		4.916	0.9039		88.665	2.8786		2.0159	0.652		18.621	14.607		68.028		NI
99	CEETOX	cat 1			1	1.0803	4.2089		5.7853	1.2081		7.93	3.7807		.	.		.	0		7.93		I
99	CEETOX	cat 1			2	0.9783	10.415		7.4957	0.5606		2.606	0.3992		.	.		.	0		2.606		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
99	CEETOX	cat 1			3	0.9827	1.3599		9.7015	1.7119		13.67	2.5729		.	.		.	0		13.67		I
100	CEETOX	cat 1			1	0.962	2.955		9.806	1.8214		44.404	11.157		.	.		.	0		44.404		I
100	CEETOX	cat 1			2	0.9745	7.154		6.4135	1.4749		23.978	7.9548		.	.		.	0		23.978		I
100	CEETOX	cat 1			3	0.961	2.7115		6.0527	0.4834		23.344	0.534		.	.		.	0		23.344		I
101	CEETOX	cat 1			1	0.961	2.7115		6.0527	0.4834		84.929	7.9872		.	.		.	0		84.929		NI
101	CEETOX	cat 1			2	0.933	6.0005		9.6642	0.8844		97.535	8.6294		.	.		.	0		97.535		NI
101	CEETOX	cat 1			3	0.9652	5.0074		4.4552	0.9126		90.641	4.8994		.	.		.	0		90.641		NI
102	CEETOX	cat 1			1	0.961	2.7115		6.0527	0.4834		98.144	11.429		.	.		.	0		98.144		NI
102	CEETOX	cat 1			2	0.933	6.0005		9.6642	0.8844		102.733	5.0127		.	.		.	0		102.733		NI
102	CEETOX	cat 1			3	0.9652	5.0074		4.4552	0.9126		97.772	4.8564		.	.		.	0		97.772		NI
103	CEETOX	cat 1	Yes		1	1.062	4.7143		10.1224	1.3169		2.401	0.3063		.	.		0.659	0.0815		1.742		I
103	CEETOX	cat 1	Yes		2	1.022	4.0686		4.2727	1.2027		5.235	0.3954		.	.		0	0		5.235		I
103	CEETOX	cat 1	Yes		3	1.01	6.3364		15.7591	5.7839		5.594	0.2756		.	.		0	0		5.594		I
104	CEETOX	cat 1	Yes		1	0.9827	1.3599		9.7015	1.7119		94.607	6.9748		.	.		0	0		94.607		NI
104	CEETOX	cat 1	Yes		2	1.062	4.7143		10.1224	1.3169		82.847	3.1681		.	.		0.989	0.5165		81.858		NI
104	CEETOX	cat 1	Yes		3	1.022	4.0686		4.2727	1.2027		90.46	7.2585		.	.		0	0		90.46		NI
105	CEETOX	cat 1		Yes	1	0.9827	1.3599		9.7015	1.7119		6.954	0.4347		0.5597	0.206		.	0		6.394		I
105	CEETOX	cat 1		Yes	2	1.062	4.7143		10.1224	1.3169		6.026	1.1234		0.4551	0.082		.	0		5.571		I
105	CEETOX	cat 1		Yes	3	1.022	4.0686		4.2727	1.2027		5.887	0.3954		0.2283	0.185		.	0		5.659		I
1	L'OREAL	no cat	Yes		1	1.0984	6.2426		10.0373	3.1479		83.884	3.9556		.	.		0	0		83.884		NI
1	L'OREAL	no cat	Yes		2	0.9895	8.2623		12.4962	0.7382		78.733	4.1519		.	.		0	0		78.733		NI
1	L'OREAL	no cat	Yes		3	1.1226	6.9506		7.1143	0.5129		82.899	2.5844		.	.		0	0		82.899		NI
2	L'OREAL	no cat	Yes		1	1.0714	5.8627		13.4695	6.1612		89.309	0.3494		.	.		0	0		89.309		NI
2	L'OREAL	no cat	Yes		2	1.0381	6.4191		29.1556	3.9327		94.087	5.4835		.	.		0	0		94.087		NI
2	L'OREAL	no cat	Yes		3	1.0069	11.957		16.5246	1.7463		96.363	3.3758		.	.		0	0		96.363		NI
3	L'OREAL	no cat			1	1.0714	5.8627		13.4695	6.1612		80.867	4.995		.	.		.	0		80.867		NI
3	L'OREAL	no cat			2	1.0069	11.957		16.5246	1.7463		87.188	8.0931		.	.		.	0		87.188		NI
3	L'OREAL	no cat			3	1.062	3.9289		23.3122	2.3466		80.733	2.9814		.	.		.	0		80.733		NI
4	L'OREAL	no cat	Yes		1	0.9378	6.6852		10.5136	1.0684		109.936	6.1005		.	.		97.771	4.6386		12.165		I
4	L'OREAL	no cat	Yes		2	1.0796	2.8004		22.9833	3.7713		95.131	6.7051		.	.		84.937	4.0297		10.194		I
4	L'OREAL	no cat	Yes		3	0.9759	7.716		5.137	2.0706		91.36	15.53		.	.		94.257	4.4575		4.046		I
5	L'OREAL	no cat	Yes		1	1.0312	7.8231		19.1107	2.864		89.536	6.2483		.	.		0.664	0.8588		88.958		NI
5	L'OREAL	no cat	Yes		2	1.0434	3.8172		15.872	3.6247		89.713	10.446		.	.		0.641	0.8396		89.165		NI
5	L'OREAL	no cat	Yes		3	1.0381	6.4191		29.1556	3.9327		86.99	4.0985		.	.		0.575	0.8059		86.542		NI
6	L'OREAL	no cat			1	1.0714	5.8627		13.4695	6.1612		107.535	6.6454		.	.		.	0		107.535		NI
6	L'OREAL	no cat			2	1.0069	11.957		16.5246	1.7463		118.996	6.8327		.	.		.	0		118.996		NI
6	L'OREAL	no cat			3	1.062	3.9289		23.3122	2.3466		111.776	3.2603		.	.		.	0		111.776		NI
7	L'OREAL	no cat	Yes		1	1.0714	5.8627		13.4695	6.1612		94.35	6.4871		.	.		0	0		94.35		NI
7	L'OREAL	no cat	Yes		2	1.0069	11.957		16.5246	1.7463		93.728	7.9472		.	.		0	0		93.728		NI
7	L'OREAL	no cat	Yes		3	0.9895	8.2623		12.4962	0.7382		87.014	10.102		.	.		0	0		87.014		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
8	L'OREAL	no cat			1	1.0984	6.2426		10.0373	3.1479		102.575	6.0462		.	.		.	0		102.575		NI
8	L'OREAL	no cat			2	1.1226	6.9506		7.1143	0.5129		104.311	5.1186		.	.		.	0		104.311		NI
8	L'OREAL	no cat			3	0.9378	6.6852		10.5136	1.0684		105.555	6.1904		.	.		.	0		105.555		NI
9	L'OREAL	no cat	Yes		1	1.0312	7.8231		19.1107	2.864		95.442	6.0667		.	.		0.2	0.1116		95.242		NI
9	L'OREAL	no cat	Yes		2	1.0434	3.8172		15.872	3.6247		88.272	5.5605		.	.		0.174	0.1103		88.098		NI
9	L'OREAL	no cat	Yes		3	1.0381	6.4191		29.1556	3.9327		99.225	3.0594		.	.		0.086	0.0911		99.152		NI
10	L'OREAL	no cat			1	1.054	3.814		16.0283	1.7483		33.831	8.0064		.	.		.	0		33.831		I
10	L'OREAL	no cat			2	1.0116	6.9056		18.2308	1.401		26.668	10.422		.	.		.	0		26.668		I
10	L'OREAL	no cat			3	1.1381	4.2836		22.3701	1.5167		31.592	10.389		.	.		.	0		31.592		I
11	L'OREAL	no cat	Yes		1	1.0312	7.8231		19.1107	2.864		76.499	2.4345		.	.		0	0		76.499		NI
11	L'OREAL	no cat	Yes		2	1.0434	3.8172		15.872	3.6247		76.687	4.4172		.	.		0	0		76.687		NI
11	L'OREAL	no cat	Yes		3	1.0381	6.4191		29.1556	3.9327		86.69	1.59		.	.		0	0		86.69		NI
12	L'OREAL	no cat			1	1.1657	2.2252		14.1003	4.5157		84.012	2.2886		.	.		.	0		84.012		NI
12	L'OREAL	no cat			2	1.0699	1.3117		7.9993	2.1576		91.829	5.6058		.	.		.	0		91.829		NI
12	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		93.686	7.3358		.	.		.	0		93.686		NI
13	L'OREAL	no cat			1	1.1507	5.8417		10.5126	2.2159		97.985	7.3522		.	.		.	0		97.985		NI
13	L'OREAL	no cat			2	1.0839	3.4473		11.3807	1.6156		93.98	4.1011		.	.		.	0		93.98		NI
13	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		94.041	4.6537		.	.		.	0		94.041		NI
14	L'OREAL	no cat			1	1.0984	6.2426		10.0373	3.1479		88.863	2.9379		.	.		.	0		88.863		NI
14	L'OREAL	no cat			2	1.1226	6.9506		7.1143	0.5129		89.318	4.9467		.	.		.	0		89.318		NI
14	L'OREAL	no cat			3	1.1342	6.6464		7.7929	0.3475		84.668	5.8571		.	.		.	0		84.668		NI
15	L'OREAL	no cat			1	1.1657	2.2252		14.1003	4.5157		83.947	3.681		.	.		.	0		83.947		NI
15	L'OREAL	no cat			2	1.0839	3.4473		11.3807	1.6156		99.986	7.1608		.	.		.	0		99.986		NI
15	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		96.984	2.237		.	.		.	0		96.984		NI
16	L'OREAL	no cat	Yes		1	1.0312	7.8231		19.1107	2.864		99.053	4.6327		.	.		0	0		99.053		NI
16	L'OREAL	no cat	Yes		2	1.0434	3.8172		15.872	3.6247		107.495	10.205		.	.		0	0		107.495		NI
16	L'OREAL	no cat	Yes		3	1.0381	6.4191		29.1556	3.9327		109.614	2.3275		.	.		0	0		109.614		NI
17	L'OREAL	no cat			1	1.0796	2.8004		22.9833	3.7713		101.477	3.4135		.	.		.	0		101.477		NI
17	L'OREAL	no cat			2	1.0711	4.8318		18.988	2.0633		99.788	3.2822		.	.		.	0		99.788		NI
17	L'OREAL	no cat			3	1.054	3.814		16.0283	1.7483		91.719	5.7436		.	.		.	0		91.719		NI
18	L'OREAL	no cat			1	1.1657	2.2252		14.1003	4.5157		94.779	4.4616		.	.		.	0		94.779		NI
18	L'OREAL	no cat			2	1.0839	3.4473		11.3807	1.6156		103.584	3.278		.	.		.	0		103.584		NI
18	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		102.575	2.4754		.	.		.	0		102.575		NI
19	L'OREAL	no cat			1	1.1657	2.2252		14.1003	4.5157		94.942	2.9532		.	.		.	0		94.942		NI
19	L'OREAL	no cat			2	1.0699	1.3117		7.9993	2.1576		102.123	4.2152		.	.		.	0		102.123		NI
19	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		101.162	7.4486		.	.		.	0		101.162		NI
20	L'OREAL	no cat	Yes		1	1.1657	2.2252		14.1003	4.5157		90.072	13.35		.	.		33.864	5.9876		56.208		NI
20	L'OREAL	no cat	Yes		2	1.0699	1.3117		7.9993	2.1576		91.691	23.903	NQ	.	.		37.021	6.5239		54.67	NQ	NI
20	L'OREAL	no cat	Yes		3	1.0151	10.577		10.1356	2.2709		84.5	16.983		.	.		38.896	6.8762		45.605		I
20	L'OREAL	no cat	Yes		4	1.0886	2.3885		13.0998	3.6209		67.246	22.275	NQ	.	.		36.187	6.4119		31.059	NQ	I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
20	L'OREAL	no cat	Yes		5	1.0775	4.8828		7.542	1.545		77.926	14.643		.	.		36.635	6.4777		41.291		I
21	L'OREAL	no cat	Yes		1	1.054	3.814		16.0283	1.7483		83.815	13.003		.	.		0.191	0.0457		83.624		NI
21	L'OREAL	no cat	Yes		2	1.0116	6.9056		18.2308	1.401		86.836	2.9332		.	.		0.209	0.0477		86.626		NI
21	L'OREAL	no cat	Yes		3	1.0525	12.287		12.4424	1.9531		87.333	2.877		.	.		0.217	0.0458		87.116		NI
22	L'OREAL	no cat			1	1.0116	6.9056		18.2308	1.401		87.63	6.1188		.	.		.	0		87.63		NI
22	L'OREAL	no cat			2	1.0572	3.0636		22.3841	2.3749		56.048	1.7457		.	.		.	0		56.048		NI
22	L'OREAL	no cat			3	1.1011	8.6438		10.2576	1.8071		62.478	11.7		.	.		.	0		62.478		NI
23	L'OREAL	no cat	Yes		1	0.9104	3.4928		11.7281	1.7263		35.025	2.669		.	.		35.926	2.2777		0.651		I
23	L'OREAL	no cat	Yes		2	1.2025	4.9661		15.5048	2.8848		26.146	4.5367		.	.		27.165	1.7243		1.259		I
23	L'OREAL	no cat	Yes		3	1.1119	11.947		12.3524	3.4802		29.988	1.4163		.	.		28.338	1.8648		1.65		I
24	L'OREAL	no cat	Yes		1	1.1381	4.2836		22.3701	1.5167		71.888	6.9645		.	.		0.07	0.1218		71.888		NI
24	L'OREAL	no cat	Yes		2	1.1842	4.5251		10.6102	2.3635		66.601	3.7353		.	.		0.092	0.1601		66.549		NI
24	L'OREAL	no cat	Yes		3	1.1528	5.5368		18.3909	5.9045		66.558	3.2551		.	.		0.085	0.1469		66.535		NI
25	L'OREAL	no cat	Yes		1	1.13	3.7783		3.5811	2.501		86.555	2.8489		.	.		0	0		86.555		NI
25	L'OREAL	no cat	Yes		2	1.0699	1.3117		7.9993	2.1576		98.977	5.2493		.	.		0	0		98.977		NI
25	L'OREAL	no cat	Yes		3	1.0886	2.3885		13.0998	3.6209		95.404	4.3855		.	.		0	0		95.404		NI
26	L'OREAL	no cat			1	1.13	3.7783		3.5811	2.501		87.513	3.861		.	.		.	0		87.513		NI
26	L'OREAL	no cat			2	1.0151	10.577		10.1356	2.2709		93.94	11.702		.	.		.	0		93.94		NI
26	L'OREAL	no cat			3	1.0775	4.8828		7.542	1.545		101.579	4.5672		.	.		.	0		101.579		NI
28	L'OREAL	no cat			1	1.0714	5.8627		13.4695	6.1612		97.961	6.7204		.	.		.	0		97.961		NI
28	L'OREAL	no cat			2	1.0069	11.957		16.5246	1.7463		100.909	6.1952		.	.		.	0		100.909		NI
28	L'OREAL	no cat			3	1.062	3.9289		23.3122	2.3466		95.516	0.4666		.	.		.	0		95.516		NI
29	L'OREAL	no cat			1	1.1657	2.2252		14.1003	4.5157		90.795	5.7409		.	.		.	0		90.795		NI
29	L'OREAL	no cat			2	1.0151	10.577		10.1356	2.2709		90.487	4.5973		.	.		.	0		90.487		NI
29	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		91.097	3.5566		.	.		.	0		91.097		NI
30	L'OREAL	no cat			1	0.9104	3.4928		11.7281	1.7263		96.305	5.4845		.	.		.	0		96.305		NI
30	L'OREAL	no cat			2	1.1528	5.5368		18.3909	5.9045		85.122	7.1817		.	.		.	0		85.122		NI
30	L'OREAL	no cat			3	1.2025	4.9661		15.5048	2.8848		85.949	3.617		.	.		.	0		85.949		NI
31	L'OREAL	no cat			1	0.9104	3.4928		11.7281	1.7263		95.873	6.0786		.	.		.	0		95.873		NI
31	L'OREAL	no cat			2	1.1842	4.5251		10.6102	2.3635		96.608	5.2356		.	.		.	0		96.608		NI
31	L'OREAL	no cat			3	1.1528	5.5368		18.3909	5.9045		88.655	2.7941		.	.		.	0		88.655		NI
32	L'OREAL	no cat	Yes	Yes	1	1.0796	2.8004		22.9833	3.7713		64.791	0.609		0.704	0.195		32.407	9.0174		31.68		I
32	L'OREAL	no cat	Yes	Yes	2	0.9759	7.716		5.137	2.0706		58.163	10.819		1.9247	0.612		36.21	9.9748		20.029		I
32	L'OREAL	no cat	Yes	Yes	3	1.0711	4.8318		18.988	2.0633		53.682	3.7176		1.4595	0.077		32.647	9.0767		19.576		I
33	L'OREAL	no cat	Yes	Yes	1	1.0116	6.9056		18.2308	1.401		92.757	6.609		1.1121	0.315		0.503	0.0897		91.142		NI
33	L'OREAL	no cat	Yes	Yes	2	1.1381	4.2836		22.3701	1.5167		85.68	2.6537		0.8875	0.169		0.523	0.0797		84.27		NI
33	L'OREAL	no cat	Yes	Yes	3	1.0525	12.287		12.4424	1.9531		100.169	5.7993		1.0452	0.237		0.565	0.0862		98.559		NI
34	L'OREAL	no cat	Yes	Yes	1	1.0116	6.9056		18.2308	1.401		128.461	7.4773		3.5901	0.405		4.697	0.1338		120.173		NI
34	L'OREAL	no cat	Yes	Yes	2	1.1381	4.2836		22.3701	1.5167		110.206	7.0392		2.7855	0.075		4.186	0.1189		103.235		NI
34	L'OREAL	no cat	Yes	Yes	3	1.0525	12.287		12.4424	1.9531		109.902	2.1476		2.7301	0.463		4.526	0.1286		102.646		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
35	L'OREAL	no cat	Yes		1	1.0984	6.2426		10.0373	3.1479		40.476	14.543		.	.		11.699	7.7253		28.777		I
35	L'OREAL	no cat	Yes		2	1.1226	6.9506		7.1143	0.5129		27.801	1.0372		.	.		11.69	7.5586		16.111		I
35	L'OREAL	no cat	Yes		3	1.1342	6.6464		7.7929	0.3475		44.22	12.207		.	.		11.514	7.4818		32.706		I
36	L'OREAL	no cat			1	1.0312	7.8231		19.1107	2.864		96.533	0.934		.	.		.	0		96.533		NI
36	L'OREAL	no cat			2	1.0434	3.8172		15.872	3.6247		92.502	5.1353		.	.		.	0		92.502		NI
36	L'OREAL	no cat			3	1.1342	6.6464		7.7929	0.3475		92.566	2.983		.	.		.	0		92.566		NI
37	L'OREAL	no cat			1	1.0572	3.0636		22.3841	2.3749		86	5.4976		.	.		.	0		86		NI
37	L'OREAL	no cat			2	1.1011	8.6438		10.2576	1.8071		85.012	9.1275		.	.		.	0		85.012		NI
37	L'OREAL	no cat			3	1.1842	4.5251		10.6102	2.3635		86.419	4.4792		.	.		.	0		86.419		NI
38	L'OREAL	no cat			1	1.1657	2.2252		14.1003	4.5157		89.168	7.214		.	.		.	0		89.168		NI
38	L'OREAL	no cat			2	1.0699	1.3117		7.9993	2.1576		99.752	4.5226		.	.		.	0		99.752		NI
38	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		93.919	7.3003		.	.		.	0		93.919		NI
39	L'OREAL	no cat			1	1.1657	2.2252		14.1003	4.5157		94.404	3.6505		.	.		.	0		94.404		NI
39	L'OREAL	no cat			2	1.0699	1.3117		7.9993	2.1576		93.241	6.2094		.	.		.	0		93.241		NI
39	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		104.481	4.4225		.	.		.	0		104.481		NI
40	L'OREAL	no cat			1	1.1507	5.8417		10.5126	2.2159		78.801	12.385		.	.		.	0		78.801		NI
40	L'OREAL	no cat			2	1.13	3.7783		3.5811	2.501		77.304	8.3865		.	.		.	0		77.304		NI
40	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		99.969	6.4781		.	.		.	0		99.969		NI
41	L'OREAL	no cat			1	1.0572	3.0636		22.3841	2.3749		91.124	9.1357		.	.		.	0		91.124		NI
41	L'OREAL	no cat			2	1.1011	8.6438		10.2576	1.8071		101.028	5.2708		.	.		.	0		101.028		NI
41	L'OREAL	no cat			3	1.0525	12.287		12.4424	1.9531		96.139	11.391		.	.		.	0		96.139		NI
42	L'OREAL	no cat	Yes		1	1.0572	3.0636		22.3841	2.3749		78.587	1.9679		.	.		0.018	0.0162		78.587		NI
42	L'OREAL	no cat	Yes		2	1.1011	8.6438		10.2576	1.8071		100.18	3.066		.	.		0.091	0.0788		100.101		NI
42	L'OREAL	no cat	Yes		3	1.0525	12.287		12.4424	1.9531		96.491	9.788		.	.		0.059	0.0514		96.462		NI
43	L'OREAL	no cat			1	1.1011	8.6438		10.2576	1.8071		98.897	5.2429		.	.		.	0		98.897		NI
43	L'OREAL	no cat			2	0.9104	3.4928		11.7281	1.7263		102.353	1.4535		.	.		.	0		102.353		NI
43	L'OREAL	no cat			3	1.1842	4.5251		10.6102	2.3635		94.002	4.4696		.	.		.	0		94.002		NI
44	L'OREAL	no cat			1	1.0572	3.0636		22.3841	2.3749		97.421	9.8347		.	.		.	0		97.421		NI
44	L'OREAL	no cat			2	1.1011	8.6438		10.2576	1.8071		100.224	4.8996		.	.		.	0		100.224		NI
44	L'OREAL	no cat			3	1.1842	4.5251		10.6102	2.3635		93.435	6.972		.	.		.	0		93.435		NI
45	L'OREAL	no cat			1	1.0572	3.0636		22.3841	2.3749		83.055	17.169		.	.		.	0		83.055		NI
45	L'OREAL	no cat			2	1.1011	8.6438		10.2576	1.8071		93.065	5.3908		.	.		.	0		93.065		NI
45	L'OREAL	no cat			3	1.0525	12.287		12.4424	1.9531		96.481	4.2385		.	.		.	0		96.481		NI
46	L'OREAL	no cat			1	1.1011	8.6438		10.2576	1.8071		84.188	4.1097		.	.		.	0		84.188		NI
46	L'OREAL	no cat			2	0.9104	3.4928		11.7281	1.7263		93.178	11.114		.	.		.	0		93.178		NI
46	L'OREAL	no cat			3	1.1842	4.5251		10.6102	2.3635		82.178	10.68		.	.		.	0		82.178		NI
47	L'OREAL	no cat			1	1.0572	3.0636		22.3841	2.3749		92.994	8.2059		.	.		.	0		92.994		NI
47	L'OREAL	no cat			2	1.1011	8.6438		10.2576	1.8071		85.395	7.5384		.	.		.	0		85.395		NI
47	L'OREAL	no cat			3	1.1842	4.5251		10.6102	2.3635		95.92	2.1998		.	.		.	0		95.92		NI
48	L'OREAL	no cat			1	0.9104	3.4928		11.7281	1.7263		37.672	1.3768		.	.		.	0		37.672		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
48	L'OREAL	no cat			2	1.1528	5.5368		18.3909	5.9045		34.986	9.8848		.	.		.	0		34.986		I
48	L'OREAL	no cat			3	1.2025	4.9661		15.5048	2.8848		45.487	6.6064		.	.		.	0		45.487		I
49	L'OREAL	no cat	Yes		1	1.13	3.7783		3.5811	2.501		95.54	4.7689		.	.		0	0		95.54		NI
49	L'OREAL	no cat	Yes		2	1.0699	1.3117		7.9993	2.1576		99.966	2.8576		.	.		0	0		99.966		NI
49	L'OREAL	no cat	Yes		3	1.0775	4.8828		7.542	1.545		104.942	6.7551		.	.		0	0		104.942		NI
50	L'OREAL	no cat			1	1.13	3.7783		3.5811	2.501		85.763	1.7401		.	.		.	0		85.763		NI
50	L'OREAL	no cat			2	1.0151	10.577		10.1356	2.2709		91.006	7.1958		.	.		.	0		91.006		NI
50	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		96.659	4.2045		.	.		.	0		96.659		NI
51	L'OREAL	no cat			1	1.13	3.7783		3.5811	2.501		85.82	2.1741		.	.		.	0		85.82		NI
51	L'OREAL	no cat			2	1.0151	10.577		10.1356	2.2709		94.291	4.8561		.	.		.	0		94.291		NI
51	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		103.479	4.2837		.	.		.	0		103.479		NI
52	L'OREAL	no cat			1	1.13	3.7783		3.5811	2.501		97.931	8.0403		.	.		.	0		97.931		NI
52	L'OREAL	no cat			2	1.0151	10.577		10.1356	2.2709		104.011	5.393		.	.		.	0		104.011		NI
52	L'OREAL	no cat			3	1.0886	2.3885		13.0998	3.6209		87.771	7.7624		.	.		.	0		87.771		NI
53	L'OREAL	no cat			1	1.13	3.7783		3.5811	2.501		97.499	3.3428		.	.		.	0		97.499		NI
53	L'OREAL	no cat			2	1.0151	10.577		10.1356	2.2709		92.009	1.055		.	.		.	0		92.009		NI
53	L'OREAL	no cat			3	1.0775	4.8828		7.542	1.545		96.546	4.645		.	.		.	0		96.546		NI
54	L'OREAL	cat 2B			1	1.0984	6.2426		10.0373	3.1479		76.698	2.154		.	.		.	0		76.698		NI
54	L'OREAL	cat 2B			2	1.1226	6.9506		7.1143	0.5129		71.114	10.373		.	.		.	0		71.114		NI
54	L'OREAL	cat 2B			3	1.1342	6.6464		7.7929	0.3475		43.178	9.6577		.	.		.	0		43.178		I
55	L'OREAL	cat 2B	Yes		1	1.1381	4.2836		22.3701	1.5167		2.242	0.2234		.	.		0.017	0.0287		2.242		I
55	L'OREAL	cat 2B	Yes		2	1.1528	5.5368		18.3909	5.9045		1.258	0.2918		.	.		0	0		1.258		I
55	L'OREAL	cat 2B	Yes		3	1.2025	4.9661		15.5048	2.8848		1.408	0.353		.	.		0.025	0.0432		1.408		I
56	L'OREAL	cat 2B			1	1.1381	4.2836		22.3701	1.5167		71.561	13.63		.	.		.	0		71.561		NI
56	L'OREAL	cat 2B			2	1.1528	5.5368		18.3909	5.9045		73.694	7.1339		.	.		.	0		73.694		NI
56	L'OREAL	cat 2B			3	1.2025	4.9661		15.5048	2.8848		68.033	6.7306		.	.		.	0		68.033		NI
57	L'OREAL	cat 2B			1	1.0116	6.9056		18.2308	1.401		32.761	2.0249		.	.		.	0		32.761		I
57	L'OREAL	cat 2B			2	1.1381	4.2836		22.3701	1.5167		36.866	9.0975		.	.		.	0		36.866		I
57	L'OREAL	cat 2B			3	1.2025	4.9661		15.5048	2.8848		10.841	0.4724		.	.		.	0		10.841		I
58	L'OREAL	cat 2B	Yes		1	1.1381	4.2836		22.3701	1.5167		12.283	10.054		.	.		0	0		12.283		I
58	L'OREAL	cat 2B	Yes		2	1.1842	4.5251		10.6102	2.3635		22.044	9.3965		.	.		0	0		22.044		I
58	L'OREAL	cat 2B	Yes		3	1.1528	5.5368		18.3909	5.9045		13.577	3.3783		.	.		0	0		13.577		I
59	L'OREAL	cat 2B	Yes		1	0.9104	3.4928		11.7281	1.7263		66.956	10.188		.	.		0	0		66.956		NI
59	L'OREAL	cat 2B	Yes		2	1.1528	5.5368		18.3909	5.9045		77.813	4.1308		.	.		0	0		77.813		NI
59	L'OREAL	cat 2B	Yes		3	1.2025	4.9661		15.5048	2.8848		66.406	5.1893		.	.		0	0		66.406		NI
60	L'OREAL	cat 2B			1	1.1657	2.2252		14.1003	4.5157		17.698	5.1189		.	.		.	0		17.698		I
60	L'OREAL	cat 2B			2	1.0151	10.577		10.1356	2.2709		25.514	2.9665		.	.		.	0		25.514		I
60	L'OREAL	cat 2B			3	1.0886	2.3885		13.0998	3.6209		20.356	5.2293		.	.		.	0		20.356		I
61	L'OREAL	cat 2B		Yes	1	1.0312	7.8231		19.1107	2.864		83.223	4.7391		0.2974	0.151		.	0		82.926		NI
61	L'OREAL	cat 2B		Yes	2	1.0434	3.8172		15.872	3.6247		90.197	7.1552		0.0527	0.091		.	0		90.144		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
61	L'OREAL	cat 2B		Yes	3	1.062	3.9289		23.3122	2.3466		87.526	1.1488		0.3719	0.122		.	0		87.154		NI
62	L'OREAL	cat 2B			1	1.1011	8.6438		10.2576	1.8071		94.846	6.6608		.	.		.	0		94.846		NI
62	L'OREAL	cat 2B			2	1.1842	4.5251		10.6102	2.3635		84.686	1.2626		.	.		.	0		84.686		NI
62	L'OREAL	cat 2B			3	1.1528	5.5368		18.3909	5.9045		95.739	3.5673		.	.		.	0		95.739		NI
63	L'OREAL	cat 2B			1	0.9104	3.4928		11.7281	1.7263		98.704	2.393		.	.		.	0		98.704		NI
63	L'OREAL	cat 2B			2	1.1528	5.5368		18.3909	5.9045		84.754	1.2674		.	.		.	0		84.754		NI
63	L'OREAL	cat 2B			3	1.2025	4.9661		15.5048	2.8848		106.136	5.0759		.	.		.	0		106.136		NI
64	L'OREAL	cat 2B			1	1.054	3.814		16.0283	1.7483		86.556	2.774		.	.		.	0		86.556		NI
64	L'OREAL	cat 2B			2	1.0116	6.9056		18.2308	1.401		97.435	1.2197		.	.		.	0		97.435		NI
64	L'OREAL	cat 2B			3	1.1011	8.6438		10.2576	1.8071		101.645	8.2815		.	.		.	0		101.645		NI
65	L'OREAL	cat 2B			1	0.9104	3.4928		11.7281	1.7263		95.293	4.1005		.	.		.	0		95.293		NI
65	L'OREAL	cat 2B			2	1.2025	4.9661		15.5048	2.8848		93.189	3.339		.	.		.	0		93.189		NI
65	L'OREAL	cat 2B			3	1.1119	11.947		12.3524	3.4802		95.267	4.1656		.	.		.	0		95.267		NI
66	L'OREAL	cat 2B			1	0.9104	3.4928		11.7281	1.7263		80.894	0.8714		.	.		.	0		80.894		NI
66	L'OREAL	cat 2B			2	1.1842	4.5251		10.6102	2.3635		84.41	5.8328		.	.		.	0		84.41		NI
66	L'OREAL	cat 2B			3	1.1528	5.5368		18.3909	5.9045		79.478	2.8162		.	.		.	0		79.478		NI
67	L'OREAL	cat 2A	Yes		1	1.0714	5.8627		13.4695	6.1612		15.711	2.6862		.	.		0	0		15.711		I
67	L'OREAL	cat 2A	Yes		2	1.0069	11.957		16.5246	1.7463		2.509	0.8883		.	.		0	0		2.509		I
67	L'OREAL	cat 2A	Yes		3	0.9895	8.2623		12.4962	0.7382		8.098	1.0784		.	.		0.018	0.0311		8.098		I
68	L'OREAL	cat 2A*			1	1.0714	5.8627		13.4695	6.1612		5.241	0.1331		.	.		.	0		5.241		I
68	L'OREAL	cat 2A*			2	1.0069	11.957		16.5246	1.7463		0.7	0.1294		.	.		.	0		0.7		I
68	L'OREAL	cat 2A*			3	1.062	3.9289		23.3122	2.3466		6.166	0.3488		.	.		.	0		6.166		I
69	L'OREAL	cat 2A*			1	1.0312	7.8231		19.1107	2.864		64.953	6.0409		.	.		.	0		64.953		NI
69	L'OREAL	cat 2A*			2	1.0434	3.8172		15.872	3.6247		76.012	2.818		.	.		.	0		76.012		NI
69	L'OREAL	cat 2A*			3	1.062	3.9289		23.3122	2.3466		58.066	5.4003		.	.		.	0		58.066		NI
70	L'OREAL	cat 2A			1	1.1381	4.2836		22.3701	1.5167		17.852	3.4889		.	.		.	0		17.852		I
70	L'OREAL	cat 2A			2	1.1528	5.5368		18.3909	5.9045		15.784	1.0041		.	.		.	0		15.784		I
70	L'OREAL	cat 2A			3	1.2025	4.9661		15.5048	2.8848		9.919	1.3042		.	.		.	0		9.919		I
71	L'OREAL	cat 2A*	Yes		1	1.0711	4.8318		18.988	2.0633		4.984	3.7342		.	.		0	0		4.984		I
71	L'OREAL	cat 2A*	Yes		2	1.054	3.814		16.0283	1.7483		7.434	2.2329		.	.		0.102	0.1136		7.375		I
71	L'OREAL	cat 2A*	Yes		3	1.0525	12.287		12.4424	1.9531		5.258	1.5095		.	.		0.119	0.1255		5.174		I
72	L'OREAL	cat 2A*	Yes		1	0.9104	3.4928		11.7281	1.7263		5.22	0.7859		.	.		3.07	2.9811		2.149		I
72	L'OREAL	cat 2A*	Yes		2	1.2025	4.9661		15.5048	2.8848		4.791	0.3088		.	.		2.294	2.2568		2.498		I
72	L'OREAL	cat 2A*	Yes		3	1.1119	11.947		12.3524	3.4802		6.579	2.4369		.	.		1.498	2.3831		5.14		I
73	L'OREAL	cat 2A*			1	1.0069	11.957		16.5246	1.7463		105.519	7.1159		.	.		.	0		105.519		NI
73	L'OREAL	cat 2A*			2	1.1342	6.6464		7.7929	0.3475		78.839	2.5109		.	.		.	0		78.839		NI
73	L'OREAL	cat 2A*			3	0.9378	6.6852		10.5136	1.0684		88.916	8.3904		.	.		.	0		88.916		NI
74	L'OREAL	cat 2A	Yes	Yes	1	1.0984	6.2426		10.0373	3.1479		88.938	4.0111		1.1668	1.355		1.22	0.1917		86.552		NI
74	L'OREAL	cat 2A	Yes	Yes	2	1.1226	6.9506		7.1143	0.5129		89.817	4.4035		0.533	0.125		1.461	0.1876		87.823		NI
74	L'OREAL	cat 2A	Yes	Yes	3	0.9759	7.716		5.137	2.0706		92.404	3.1866		0.2271	0.111		1.988	0.2158		90.189		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
75	L'OREAL	cat 2A			1	1.0312	7.8231		19.1107	2.864		32.679	27.365	NQ	.	.		.	0		32.679	NQ	I
75	L'OREAL	cat 2A			2	1.0434	3.8172		15.872	3.6247		24.707	39.171	NQ	.	.		.	0		24.707	NQ	I
75	L'OREAL	cat 2A			3	1.0714	5.8627		13.4695	6.1612		13.477	9.6748		.	.		.	0		13.477		I
75	L'OREAL	cat 2A			4	1.062	3.9289		23.3122	2.3466		14.162	3.9196		.	.		.	0		14.162		I
75	L'OREAL	cat 2A			5	1.1342	6.6464		7.7929	0.3475		12.354	2.7362		.	.		.	0		12.354		I
76	L'OREAL	cat 2A			1	0.9378	6.6852		10.5136	1.0684		65.68	11.069		.	.		.	0		65.68		NI
76	L'OREAL	cat 2A			2	1.0796	2.8004		22.9833	3.7713		53.811	3.444		.	.		.	0		53.811		NI
76	L'OREAL	cat 2A			3	1.0711	4.8318		18.988	2.0633		60.588	7.5801		.	.		.	0		60.588		NI
77	L'OREAL	cat 2A			1	1.0711	4.8318		18.988	2.0633		98.805	4.4425		.	.		.	0		98.805		NI
77	L'OREAL	cat 2A			2	1.054	3.814		16.0283	1.7483		95.696	4.0743		.	.		.	0		95.696		NI
77	L'OREAL	cat 2A			3	1.0116	6.9056		18.2308	1.401		97.929	3.7123		.	.		.	0		97.929		NI
78	L'OREAL	cat 2A			1	1.0796	2.8004		22.9833	3.7713		93.38	3.5729		.	.		.	0		93.38		NI
78	L'OREAL	cat 2A			2	1.0711	4.8318		18.988	2.0633		91.097	3.7193		.	.		.	0		91.097		NI
78	L'OREAL	cat 2A			3	1.054	3.814		16.0283	1.7483		89.321	1.3172		.	.		.	0		89.321		NI
79	L'OREAL	cat 2A*			1	0.9104	3.4928		11.7281	1.7263		87.21	7.9302		.	.		.	0		87.21		NI
79	L'OREAL	cat 2A*			2	1.2025	4.9661		15.5048	2.8848		75.65	5.3726		.	.		.	0		75.65		NI
79	L'OREAL	cat 2A*			3	1.1119	11.947		12.3524	3.4802		88.361	4.7695		.	.		.	0		88.361		NI
80	L'OREAL	cat 1	Yes		1	1.0312	7.8231		19.1107	2.864		25.876	4.7809		.	.		35.681	4.024		0		I
80	L'OREAL	cat 1	Yes		2	1.0434	3.8172		15.872	3.6247		30.442	3.9044		.	.		35.265	3.977		0		I
80	L'OREAL	cat 1	Yes		3	1.0381	6.4191		29.1556	3.9327		29.323	0.591		.	.		35.445	3.9973		0		I
81	L'OREAL	cat 1			1	1.0984	6.2426		10.0373	3.1479		0.587	0.1202		.	.		.	0		0.587		I
81	L'OREAL	cat 1			2	1.1226	6.9506		7.1143	0.5129		0.966	0.2649		.	.		.	0		0.966		I
81	L'OREAL	cat 1			3	1.1342	6.6464		7.7929	0.3475		0.654	0.0511		.	.		.	0		0.654		I
82	L'OREAL	cat 1			1	1.1657	2.2252		14.1003	4.5157		6.318	1.1729		.	.		.	0		6.318		I
82	L'OREAL	cat 1			2	1.0699	1.3117		7.9993	2.1576		4.412	0.5134		.	.		.	0		4.412		I
82	L'OREAL	cat 1			3	1.0886	2.3885		13.0998	3.6209		3.724	1.2376		.	.		.	0		3.724		I
83	L'OREAL	cat 1	Yes		1	1.0984	6.2426		10.0373	3.1479		2.968	1.4839		.	.		0	0		2.968		I
83	L'OREAL	cat 1	Yes		2	0.9895	8.2623		12.4962	0.7382		2.946	0.091		.	.		0	0		2.946		I
83	L'OREAL	cat 1	Yes		3	1.1226	6.9506		7.1143	0.5129		1.777	0.0379		.	.		0.019	0.0326		1.777		I
84	L'OREAL	cat 1			1	1.1507	5.8417		10.5126	2.2159		17.469	5.7766		.	.		.	0		17.469		I
84	L'OREAL	cat 1			2	1.0839	3.4473		11.3807	1.6156		26.008	6.0469		.	.		.	0		26.008		I
84	L'OREAL	cat 1			3	1.0886	2.3885		13.0998	3.6209		17.443	3.4609		.	.		.	0		17.443		I
85	L'OREAL	cat 1			1	1.0312	7.8231		19.1107	2.864		65.553	17.15		.	.		.	0		65.553		NI
85	L'OREAL	cat 1			2	1.0434	3.8172		15.872	3.6247		64.576	7.4549		.	.		.	0		64.576		NI
85	L'OREAL	cat 1			3	1.062	3.9289		23.3122	2.3466		80.66	5.9342		.	.		.	0		80.66		NI
86	L'OREAL	cat 1			1	1.1507	5.8417		10.5126	2.2159		89.358	8.1023		.	.		.	0		89.358		NI
86	L'OREAL	cat 1			2	1.0839	3.4473		11.3807	1.6156		84.85	7.839		.	.		.	0		84.85		NI
86	L'OREAL	cat 1			3	1.0151	10.577		10.1356	2.2709		87.973	5.6462		.	.		.	0		87.973		NI
87	L'OREAL	cat 1	Yes		1	1.0714	5.8627		13.4695	6.1612		83.601	6.97		.	.		0.273	0.4724		83.601		NI
87	L'OREAL	cat 1	Yes		2	1.0069	11.957		16.5246	1.7463		98.135	7.1749		.	.		0.188	0.3259		98.135		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
87	L'OREAL	cat 1	Yes		3	0.9895	8.2623		12.4962	0.7382		88.024	4.4284		.	.		0.405	0.6338		87.849		NI
88	L'OREAL	cat 1	Yes		1	1.1507	5.8417		10.5126	2.2159		3.313	0.4661		.	.		0	0		3.313		I
88	L'OREAL	cat 1	Yes		2	1.0839	3.4473		11.3807	1.6156		3.952	1.2749		.	.		0	0		3.952		I
88	L'OREAL	cat 1	Yes		3	1.0699	1.3117		7.9993	2.1576		4.34	0.3353		.	.		0	0		4.34		I
89	L'OREAL	cat 1			1	1.0796	2.8004		22.9833	3.7713		73.923	5.6655		.	.		.	0		73.923		NI
89	L'OREAL	cat 1			2	1.0711	4.8318		18.988	2.0633		58.025	5.3204		.	.		.	0		58.025		NI
89	L'OREAL	cat 1			3	1.054	3.814		16.0283	1.7483		72.412	4.1878		.	.		.	0		72.412		NI
90	L'OREAL	cat 1	Yes		1	1.1381	4.2836		22.3701	1.5167		51.581	12.975		.	.		0.089	0.0811		51.516		NI
90	L'OREAL	cat 1	Yes		2	1.0525	12.287		12.4424	1.9531		23.331	9.1629		.	.		0.158	0.1329		23.173		I
90	L'OREAL	cat 1	Yes		3	1.2025	4.9661		15.5048	2.8848		32.779	5.2349		.	.		0.089	0.0805		32.711		I
91	L'OREAL	cat 1	Yes		1	1.0796	2.8004		22.9833	3.7713		52.168	9.4291		.	.		3.466	0.8625		48.702		I
91	L'OREAL	cat 1	Yes		2	0.9759	7.716		5.137	2.0706		36.705	12.081		.	.		4.136	0.9541		32.569		I
91	L'OREAL	cat 1	Yes		3	1.0711	4.8318		18.988	2.0633		22.349	4.2611		.	.		3.464	0.8886		18.885		I
92	L'OREAL	cat 1	Yes		1	1.13	3.7783		3.5811	2.501		77.68	2.3545		.	.		0	0		77.68		NI
92	L'OREAL	cat 1	Yes		2	1.0699	1.3117		7.9993	2.1576		82.503	3.6032		.	.		0	0		82.503		NI
92	L'OREAL	cat 1	Yes		3	1.0775	4.8828		7.542	1.545		79.261	1.4825		.	.		0	0		79.261		NI
93	L'OREAL	cat 1			1	1.0984	6.2426		10.0373	3.1479		86.307	10.015		.	.		.	0		86.307		NI
93	L'OREAL	cat 1			2	1.1226	6.9506		7.1143	0.5129		66.461	10.029		.	.		.	0		66.461		NI
93	L'OREAL	cat 1			3	1.1342	6.6464		7.7929	0.3475		68.626	10.599		.	.		.	0		68.626		NI
94	L'OREAL	cat 1			1	1.0984	6.2426		10.0373	3.1479		77.957	4.6101		.	.		.	0		77.957		NI
94	L'OREAL	cat 1			2	1.1226	6.9506		7.1143	0.5129		75.07	5.4602		.	.		.	0		75.07		NI
94	L'OREAL	cat 1			3	1.1342	6.6464		7.7929	0.3475		77.647	2.5004		.	.		.	0		77.647		NI
95	L'OREAL	cat 1			1	1.0714	5.8627		13.4695	6.1612		1.422	0.2358		.	.		.	0		1.422		I
95	L'OREAL	cat 1			2	1.0069	11.957		16.5246	1.7463		1.324	0.1125		.	.		.	0		1.324		I
95	L'OREAL	cat 1			3	1.062	3.9289		23.3122	2.3466		1.35	0.1964		.	.		.	0		1.35		I
96	L'OREAL	cat 1			1	1.0312	7.8231		19.1107	2.864		92.161	2.6444		.	.		.	0		92.161		NI
96	L'OREAL	cat 1			2	1.0434	3.8172		15.872	3.6247		108.885	2.7002		.	.		.	0		108.885		NI
96	L'OREAL	cat 1			3	1.1342	6.6464		7.7929	0.3475		74.15	8.8212		.	.		.	0		74.15		NI
97	L'OREAL	cat 1			1	1.0714	5.8627		13.4695	6.1612		94.949	0.1641		.	.		.	0		94.949		NI
97	L'OREAL	cat 1			2	1.0069	11.957		16.5246	1.7463		88.122	2.0609		.	.		.	0		88.122		NI
97	L'OREAL	cat 1			3	1.062	3.9289		23.3122	2.3466		89.454	5.6991		.	.		.	0		89.454		NI
98	L'OREAL	cat 1		Yes	1	1.1507	5.8417		10.5126	2.2159		89.315	6.7229		1.4238	0.205		.	0		87.891		NI
98	L'OREAL	cat 1		Yes	2	1.0839	3.4473		11.3807	1.6156		80.588	3.2231		2.4096	0.46		.	0		78.178		NI
98	L'OREAL	cat 1		Yes	3	1.0151	10.577		10.1356	2.2709		86.595	0.3864		4.2247	1.544		.	0		82.371		NI
99	L'OREAL	cat 1			1	1.054	3.814		16.0283	1.7483		17.403	2.6717		.	.		.	0		17.403		I
99	L'OREAL	cat 1			2	1.0116	6.9056		18.2308	1.401		26.113	1.7162		.	.		.	0		26.113		I
99	L'OREAL	cat 1			3	1.0572	3.0636		22.3841	2.3749		26.262	2.4977		.	.		.	0		26.262		I
100	L'OREAL	cat 1			1	1.13	3.7783		3.5811	2.501		27.798	11.068		.	.		.	0		27.798		I
100	L'OREAL	cat 1			2	1.0151	10.577		10.1356	2.2709		69.408	1.7058		.	.		.	0		69.408		NI
100	L'OREAL	cat 1			3	1.0775	4.8828		7.542	1.545		56.67	3.7312		.	.		.	0		56.67		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
101	L'OREAL	cat 1		Yes	1	1.1507	5.8417		10.5126	2.2159		80.51	5.1756		0.4374	0.136		.	0		80.073		NI
101	L'OREAL	cat 1		Yes	2	1.0839	3.4473		11.3807	1.6156		77.429	4.4023		0.0846	0.063		.	0		77.345		NI
101	L'OREAL	cat 1		Yes	3	1.0151	10.577		10.1356	2.2709		80.292	6.6746		0.1806	0.055		.	0		80.111		NI
102	L'OREAL	cat 1			1	1.1507	5.8417		10.5126	2.2159		94.247	14.794		.	.		.	0		94.247		NI
102	L'OREAL	cat 1			2	1.0839	3.4473		11.3807	1.6156		86.167	3.0025		.	.		.	0		86.167		NI
102	L'OREAL	cat 1			3	1.0886	2.3885		13.0998	3.6209		95.534	0.9852		.	.		.	0		95.534		NI
103	L'OREAL	cat 1			1	1.0796	2.8004		22.9833	3.7713		5.033	0.8176		.	.		.	0		5.033		I
103	L'OREAL	cat 1			2	1.0711	4.8318		18.988	2.0633		5.528	0.2059		.	.		.	0		5.528		I
103	L'OREAL	cat 1			3	1.054	3.814		16.0283	1.7483		4.75	0.1362		.	.		.	0		4.75		I
104	L'OREAL	cat 1			1	1.0116	6.9056		18.2308	1.401		94.181	4.9305		.	.		.	0		94.181		NI
104	L'OREAL	cat 1			2	1.0572	3.0636		22.3841	2.3749		83.325	3.8567		.	.		.	0		83.325		NI
104	L'OREAL	cat 1			3	1.1011	8.6438		10.2576	1.8071		94.951	1.8167		.	.		.	0		94.951		NI
105	L'OREAL	cat 1			1	0.9378	6.6852		10.5136	1.0684		8.783	0.7349		.	.		.	0		8.783		I
105	L'OREAL	cat 1			2	1.0796	2.8004		22.9833	3.7713		7.39	0.0809		.	.		.	0		7.39		I
105	L'OREAL	cat 1			3	1.0711	4.8318		18.988	2.0633		7.408	0.5224		.	.		.	0		7.408		I

Chemical 106 and 107 are considered incompatible with the test method because of strong colour interference and so SkinEthic^{TM} HCE shows a limitation for colours that strongly interfere with MTT using the current system of photometry. These two chemicals are excluded for the statistical analysis.

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability
106	CARDAM	cat 1	No	Yes	1	0.976	3.0137		9.7414	1.6474		302.354	143.08	NQ	113.225	68.9216	NQ	.			189.129
106	CARDAM	cat 1	No	Yes	2	1.068	12.107		9.0451	0.5407		127.641	6.526		38.008	6.1534		.			89.633
106	CARDAM	cat 1	No	Yes	3	1.122	5.8363		9.2331	2.1018		157.851	11.792		53.201	13.7369		.			104.649
106	CARDAM	cat 1	No	Yes	4	1.169	5.4702		13.7342	2.2905		141.654	42.681	NQ	40.789	7.4833		.			100.865
106	CARDAM	cat 1	No	Yes	5	0.944	9.67		16.1907	2.7495		181.669	9.382		46.755	11.4809		.			134.914
107	CARDAM	cat 1	No	Yes	1	1.122	5.8363		9.2331	2.1018		94.926	7.962		9.594	1.4075		.			85.332
107	CARDAM	cat 1	No	Yes	2	1.169	5.4702		13.7342	2.2905		115.09	10.187		14.118	3.1246		.			100.972
107	CARDAM	cat 1	No	Yes	3	0.944	9.67		16.1907	2.7495		120.772	14.917		26.57	7.7849		.			94.202
106	CEETOX	cat 1	Yes	Yes	1	0.933	6.0005		9.6642	0.8844		116.827	11.997		21.15	10.1158		369.453	9.1978		0
106	CEETOX	cat 1	Yes	Yes	2	0.943	4.0652		4.916	0.9039		95.367	15.265		17.224	3.6529		365.853	9.1051		0
106	CEETOX	cat 1	Yes	Yes	3	0.965	5.0074		4.4552	0.9126		102.383	10.761		10.309	6.8809		357.14	8.8913		0
107	CEETOX	cat 1	Yes	Yes	1	0.975	7.154		6.4135	1.4749		95.69	10.332		10.501	12.2832		45.972	20.3287	NQ	0
107	CEETOX	cat 1	Yes	Yes	2	0.961	2.7115		6.0527	0.4834		100.85	1.033		8.012	2.692		87.496	76.6765	NQ	0
107	CEETOX	cat 1	Yes	Yes	3	0.96	3.8851		5.1059	1.2355		90.57	1.928		8.927	2.7099		171.778	45.0243	NQ	0
106	L'OREAL	cat 1	Yes	Yes	1	1.151	5.8417		10.5126	2.2158		129.626	29.204	NQ	44.458	32.2886	NQ	38.515	26.5231	NQ	46.653
106	L'OREAL	cat 1	Yes	Yes	2	1.13	3.7783		3.5811	2.501		151.154	23.624	NQ	40.603	17.0624		39.185	27.0057	NQ	71.366

106	L'OREAL	cat 1	Yes	Yes	3	1.015	10.577		10.1356	2.2709		122.012	8.34		17.142	2.3774		43.309	30.0667	NQ	61.561
106	L'OREAL	cat 1	Yes	Yes	4	1.089	2.3885		13.0998	3.6209		100.194	12.88		28.386	11.1773		40.382	28.0366	NQ	31.427
106	L'OREAL	cat 1	Yes	Yes	5	1.078	4.8828		7.542	1.545		108.042	28.288	NQ	25.794	8.8653		40.796	28.3241	NQ	41.452
107	L'OREAL	cat 1	Yes	Yes	1	1.166	2.2252		14.1003	4.5157		97.605	6.456		18.475	20.4689	NQ	35.767	19.5041	NQ	43.363
107	L'OREAL	cat 1	Yes	Yes	2	1.07	1.3117		7.9993	2.1576		100.28	12.892		11.632	7.3035		39.077	21.2509	NQ	49.571
107	L'OREAL	cat 1	Yes	Yes	3	1.015	10.577		10.1356	2.2709		104.737	5.261		17.687	3.3834		42.073	22.3985	NQ	44.977
107	L'OREAL	cat 1	Yes	Yes	4	1.089	2.3885		13.0998	3.6209		91.598	3.139		6.042	1.3004		38.344	20.8711	NQ	47.212
107	L'OREAL	cat 1	Yes	Yes	5	1.078	4.8828		7.542	1.545		103.845	16.615		15.534	6.8141		38.7	21.0852	NQ	49.611

LE

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
1	CARDAM	no cat	No	No	1	0.995	8.509		37.816	5.18		22.312	4.817		.	.		.			22.312		I
1	CARDAM	no cat	No	No	2	1.239	7.199		48.279	4.314		5.335	3.399		.	.		.			5.335		I
1	CARDAM	no cat	No	No	3	0.868	2.37		16.136	6.351		9.402	4.759		.	.		.			9.402		I
2	CARDAM	no cat	No	No	1	0.973	6.201		17.996	5.229		9.655	2.66		.	.		.			9.655		I
2	CARDAM	no cat	No	No	2	0.81	1.341		32.239	2.548		2.647	0.564		.	.		.			2.647		I
2	CARDAM	no cat	No	No	3	1.206	7.734		17.834	6.314		2.076	0.206		.	.		.			2.076		I
3	CARDAM	no cat	No	No	1	0.995	8.509		37.816	5.18		1.278	0.654		.	.		.			1.278		I
3	CARDAM	no cat	No	No	2	1.239	7.199		48.279	4.314		3.518	2.872		.	.		.			3.518		I
3	CARDAM	no cat	No	No	3	0.868	2.37		16.136	6.351		2.403	1.461		.	.		.			2.403		I
4	CARDAM	no cat	Yes	No	1	0.811	1.341		32.262	2.547		59.204	12.23		.	.		84.184	27.4	NQ	0		I
4	CARDAM	no cat	Yes	No	2	1.206	7.734		17.834	6.314		51.154	9.87		.	.		56.781	18.423	NQ	0.706		I
4	CARDAM	no cat	Yes	No	3	1.18	12.54		25.225	3.808		62.867	8.699		.	.		57.757	18.822	NQ	6.576		I
5	CARDAM	no cat	Yes	No	1	0.973	6.201		17.996	5.229		5.834	3.187		.	.		0.93	0		4.9		I
5	CARDAM	no cat	Yes	No	2	0.81	1.341		32.239	2.548		13.931	2.76		.	.		1.1229	0.8371		12.808		I
5	CARDAM	no cat	Yes	No	3	1.206	7.734		17.834	6.314		3.879	1.722		.	.		0.7547	0.5626		3.124		I
6	CARDAM	no cat	No	No	1	1.239	7.199		48.279	4.314		12.402	8.108		.	.		.			12.402		I
6	CARDAM	no cat	No	No	2	0.868	2.37		16.136	6.351		20.19	0.807		.	.		.			20.19		I
6	CARDAM	no cat	No	No	3	0.973	6.201		17.996	5.229		19.609	8.038		.	.		.			19.609		I
7	CARDAM	no cat	No	No	1	1.239	7.199		48.281	4.314		5.541	5.757		.	.		.			5.541		I
7	CARDAM	no cat	No	No	2	0.869	2.369		16.153	6.349		5.285	1.145		.	.		.			5.285		I
7	CARDAM	no cat	No	No	3	0.973	6.201		17.996	5.229		6.501	2.141		.	.		.			6.501		I
8	CARDAM	no cat	No	No	1	0.995	8.509		37.816	5.18		43.931	6.75		.	.		.			43.931		I
8	CARDAM	no cat	No	No	2	1.239	7.199		48.279	4.314		21.448	2.351		.	.		.			21.448		I
8	CARDAM	no cat	No	No	3	0.868	2.37		16.136	6.351		37.506	2.856		.	.		.			37.506		I
9	CARDAM	no cat	Yes	No	1	0.995	8.509		37.816	5.18		56.286	3.471		.	.		0.2178	0.2944		56.085		NI
9	CARDAM	no cat	Yes	No	2	1.239	7.199		48.279	4.314		31.341	12.95		.	.		0.1748	0.2364		31.179		I
9	CARDAM	no cat	Yes	No	3	0.868	2.37		16.136	6.351		58.77	9.122		.	.		0.2636	0.3454		58.519		NI
10	CARDAM	no cat	No	No	1	0.973	6.201		17.996	5.229		0.406	0.301		.	.		.			0.406		I
10	CARDAM	no cat	No	No	2	0.81	1.341		32.239	2.548		1.954	0.524		.	.		.			1.954		I
10	CARDAM	no cat	No	No	3	1.206	7.734		17.834	6.314		1.085	0.315		.	.		.			1.085		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
11	CARDAM	no cat	No	No	1	0.995	8.509		37.816	5.18		32.285	15.84		.	.		.			32.285		I
11	CARDAM	no cat	No	No	2	1.239	7.199		48.279	4.314		26.327	0.646		.	.		.			26.327		I
11	CARDAM	no cat	No	No	3	0.868	2.37		16.136	6.351		24.933	6.934		.	.		.			24.933		I
12	CARDAM	no cat	No	No	1	1.22	3.711		36.294	7.468		99.068	8.198		.	.		.			99.068		NI
12	CARDAM	no cat	No	No	2	1.051	9.065		10.033	2.886		98.767	13.27		.	.		.			98.767		NI
12	CARDAM	no cat	No	No	3	1.083	4.893		10.142	3.1		92.19	3.924		.	.		.			92.19		NI
13	CARDAM	no cat	No	No	1	1.22	3.711		36.294	7.468		103.01	7.253		.	.		.			103.012		NI
13	CARDAM	no cat	No	No	2	1.051	9.065		10.033	2.886		114.66	11.3		.	.		.			114.661		NI
13	CARDAM	no cat	No	No	3	0.887	9.248		23.751	10		100.53	8.418		.	.		.			100.532		NI
14	CARDAM	no cat	No	No	1	1.239	7.199		48.281	4.314		70.273	7.2		.	.		.			70.273		NI
14	CARDAM	no cat	No	No	2	0.868	2.37		16.136	6.351		110.11	3.526		.	.		.			110.11		NI
14	CARDAM	no cat	No	No	3	0.973	6.201		17.996	5.229		105.45	4.39		.	.		.			105.447		NI
15	CARDAM	no cat	No	No	1	0.887	9.248		23.751	10		100.83	9.644		.	.		.			100.83		NI
15	CARDAM	no cat	No	No	2	0.9	3.814		14.278	3.816		100.48	15.56		.	.		.			100.476		NI
15	CARDAM	no cat	No	No	3	0.99	8.386		37.684	6.95		93.329	6.11		.	.		.			93.329		NI
16	CARDAM	no cat	No	No	1	0.995	8.509		37.816	5.18		99.586	9.613		.	.		.			99.586		NI
16	CARDAM	no cat	No	No	2	1.239	7.199		48.279	4.314		73.629	9.717		.	.		.			73.629		NI
16	CARDAM	no cat	No	No	3	0.868	2.37		16.136	6.351		109.86	8.408		.	.		.			109.855		NI
17	CARDAM	no cat	No	No	1	0.811	1.341		32.262	2.547		88.816	6.554		.	.		.			88.816		NI
17	CARDAM	no cat	No	No	2	1.206	7.734		17.834	6.314		74.963	7.226		.	.		.			74.963		NI
17	CARDAM	no cat	No	No	3	1.18	12.54		25.225	3.808		95.166	3.711		.	.		.			95.166		NI
18	CARDAM	no cat	No	No	1	0.887	9.248		23.751	10		94.652	7.192		.	.		.			94.652		NI
18	CARDAM	no cat	No	No	2	0.943	4.444		25.036	15.37		104.76	2.061		.	.		.			104.758		NI
18	CARDAM	no cat	No	No	3	0.99	8.386		37.684	6.95		104.92	5.04		.	.		.			104.919		NI
19	CARDAM	no cat	No	No	1	0.887	9.248		23.751	10		97.537	9.182		.	.		.			97.537		NI
19	CARDAM	no cat	No	No	2	0.943	4.444		25.036	15.37		108.46	10.64		.	.		.			108.459		NI
19	CARDAM	no cat	No	No	3	0.99	8.386		37.684	6.95		97.17	15		.	.		.			97.17		NI
20	CARDAM	no cat	Yes	No	1	1.22	3.711		36.294	7.468		62.958	17.64		.	.		40.874	10.611		22.084		I
20	CARDAM	no cat	Yes	No	2	1.083	4.893		10.142	3.1		63.854	12.15		.	.		46.089	11.958		17.765		I
20	CARDAM	no cat	Yes	No	3	0.992	2.274		10.261	2.629		57.127	6.099		.	.		50.26	13.046		6.867		I
21	CARDAM	no cat	No	No	1	0.811	1.341		32.262	2.547		63.786	2.671		.	.		.			63.786		NI
21	CARDAM	no cat	No	No	2	1.206	7.734		17.834	6.314		55.806	2.202		.	.		.			55.806		NI
21	CARDAM	no cat	No	No	3	1.18	12.54		25.225	3.808		60.57	2.536		.	.		.			60.57		NI
22	CARDAM	no cat	No	No	1	0.811	1.341		32.262	2.547		1.231	0.205		.	.		.			1.231		I
22	CARDAM	no cat	No	No	2	1.206	7.734		17.834	6.314		0.918	0.167		.	.		.			0.918		I
22	CARDAM	no cat	No	No	3	1.18	12.54		25.225	3.808		1.076	0.167		.	.		.			1.076		I
23	CARDAM	no cat	Yes	No	1	1.169	3.808		3.2487	0.788		53.793	0.812		.	.		38.178	4.2769		15.614		I
23	CARDAM	no cat	Yes	No	2	1.005	2.625		25.131	3.811		61.723	3.259		.	.		44.612	4.9753		17.111		I
23	CARDAM	no cat	Yes	No	3	1.062	9.186		13.713	4.398		60.934	7.034		.	.		42.043	4.7065		18.89		I
24	CARDAM	no cat	No	No	1	1.005	2.625		25.131	3.811		1.04	0.162		.	.		.			1.04		I
24	CARDAM	no cat	No	No	2	1.062	9.186		13.713	4.398		1.486	1.313		.	.		.			1.486		I
24	CARDAM	no cat	No	No	3	1.253	4.783		49.521	4.149		1.254	0.062		.	.		.			1.254		I
25	CARDAM	no cat	Yes	No	1	0.992	2.274		10.261	2.629		100.13	4.771		.	.		0.2877	0.25		99.887		NI
25	CARDAM	no cat	Yes	No	2	0.943	4.444		25.036	15.37		100.02	13.44		.	.		0.3523	0.3059		99.696		NI
25	CARDAM	no cat	Yes	No	3	0.982	7.089		28.69	3.421		95.643	8.221		.	.		0.2908	0.2527		95.4		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
26	CARDAM	no cat	No	No	1	0.9	3.814		14.278	3.816		3.457	0.523		.	.		.			3.457		I
26	CARDAM	no cat	No	No	2	0.943	4.444		25.036	15.37		4.055	0.531		.	.		.			4.055		I
26	CARDAM	no cat	No	No	3	0.982	7.089		28.69	3.421		3.327	0.515		.	.		.			3.327		I
28	CARDAM	no cat	No	No	1	1.239	7.199		48.281	4.314		76.263	6.953		.	.		.			76.263		NI
28	CARDAM	no cat	No	No	2	0.869	2.369		16.153	6.349		108.8	6.285		.	.		.			108.801		NI
28	CARDAM	no cat	No	No	3	0.973	6.201		17.996	5.229		107.48	1.542		.	.		.			107.476		NI
29	CARDAM	no cat	No	No	1	0.992	2.274		10.261	2.629		107.06	2.243		.	.		.			107.059		NI
29	CARDAM	no cat	No	No	2	0.943	4.444		25.036	15.37		93.867	4.295		.	.		.			93.867		NI
29	CARDAM	no cat	No	No	3	0.982	7.089		28.69	3.421		101.11	9.111		.	.		.			101.114		NI
30	CARDAM	no cat	No	No	1	1.12	9.591		48.297	3.425		74.85	6.843		.	.		.			74.85		NI
30	CARDAM	no cat	No	No	2	1.018	9.297		44.999	2.039		93.499	0.616		.	.		.			93.499		NI
30	CARDAM	no cat	No	No	3	1.22	3.711		36.294	7.468		75.832	4.094		.	.		.			75.832		NI
31	CARDAM	no cat	No	No	1	1.12	9.591		48.297	3.425		99.9	4.298		.	.		.			99.9		NI
31	CARDAM	no cat	No	No	2	1.018	9.297		44.999	2.039		114.34	7.73		.	.		.			114.336		NI
31	CARDAM	no cat	No	No	3	1.22	3.711		36.294	7.468		99.743	9.781		.	.		.			99.743		NI
32	CARDAM	no cat	No	Yes	1	0.81	1.341		32.239	2.548		8.911	1.715		0.327	0.08		.			8.584		I
32	CARDAM	no cat	No	Yes	2	1.206	7.734		17.834	6.314		6.721	0.156		0.4727	0.11		.			6.248		I
32	CARDAM	no cat	No	Yes	3	1.18	12.54		25.225	3.808		10.274	0.563		0.5988	0.31		.			9.675		I
33	CARDAM	no cat	Yes	Yes	1	1.18	12.54		25.225	3.808		110.8	4.261		1.4814	1.63		0.9109	0.68		108.405		NI
33	CARDAM	no cat	Yes	Yes	2	0.72	9.549		13.318	7.805		112.61	2.66		4.7196	3.28		1.6118	1.1151		106.283		NI
33	CARDAM	no cat	Yes	Yes	3	1.169	3.808		3.2487	0.788		108.8	5.514		2.1121	1.35		0.9926	0.6867		105.697		NI
34	CARDAM	no cat	Yes	Yes	1	0.811	1.341		32.262	2.547		70.721	11.82		8.0733	2.47		12.781	1.379		49.866		I
34	CARDAM	no cat	Yes	Yes	2	1.206	7.734		17.834	6.314		57.885	8.321		5.5083	0.97		8.823	0.9272		43.554		I
34	CARDAM	no cat	Yes	Yes	3	1.18	12.54		25.225	3.808		57.861	42.38	NQ	5.7717	0.78		8.7797	0.9473		45.181	NQ	I
34	CARDAM	no cat	Yes	Yes	4	0.72	9.549		13.318	7.805		80.325	9.077		9.4299	1.53		14.397	1.5534		56.498		NI
35	CARDAM	no cat	Yes	No	1	1.11	3.386		33.855	6.392		82.25	6.144		.	.		4.9572	6.6349		77.293		NI
35	CARDAM	no cat	Yes	No	2	0.896	13.12		16.769	5.392		104.56	8.027		.	.		6.1417	8.2203		98.42		NI
35	CARDAM	no cat	Yes	No	3	0.907	10.72		44.643	5.2		106.21	13.05		.	.		6.0624	8.1141		100.151		NI
36	CARDAM	no cat	No	No	1	1.11	3.386		33.855	6.392		99.449	7.484		.	.		.			99.449		NI
36	CARDAM	no cat	No	No	2	0.896	13.12		16.769	5.392		103.7	5.461		.	.		.			103.698		NI
36	CARDAM	no cat	No	No	3	0.907	10.72		44.643	5.2		110.54	3.823		.	.		.			110.541		NI
37	CARDAM	no cat	No	No	1	1.12	9.591		48.297	3.425		106.93	17.32		.	.		.			106.933		NI
37	CARDAM	no cat	No	No	2	1.018	9.297		44.999	2.039		100.01	5.358		.	.		.			100.005		NI
37	CARDAM	no cat	No	No	3	1.253	4.783		49.521	4.149		90.2	16.12		.	.		.			90.2		NI
38	CARDAM	no cat	No	No	1	1.051	9.065		10.033	2.886		108.1	7.177		.	.		.			108.104		NI
38	CARDAM	no cat	No	No	2	0.992	2.274		10.261	2.629		91.689	1.357		.	.		.			91.689		NI
38	CARDAM	no cat	No	No	3	0.9	3.814		14.278	3.816		115.41	10.83		.	.		.			115.413		NI
39	CARDAM	no cat	No	No	1	1.051	9.065		10.033	2.886		114.96	3.986		.	.		.			114.959		NI
39	CARDAM	no cat	No	No	2	1.083	4.893		10.142	3.1		96.432	4.691		.	.		.			96.432		NI
39	CARDAM	no cat	No	No	3	0.887	9.248		23.751	10		92.495	3.849		.	.		.			92.495		NI
40	CARDAM	no cat	No	No	1	0.992	2.274		10.261	2.629		77.558	1.751		.	.		.			77.558		NI
40	CARDAM	no cat	No	No	2	0.9	3.814		14.278	3.816		87.26	2.807		.	.		.			87.26		NI
40	CARDAM	no cat	No	No	3	0.943	4.444		25.036	15.37		98.529	5.082		.	.		.			98.529		NI
41	CARDAM	no cat	No	No	1	1.005	2.625		25.131	3.811		96.488	5.97		.	.		.			96.488		NI
41	CARDAM	no cat	No	No	2	1.062	9.186		13.713	4.398		98.938	5.177		.	.		.			98.938		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
41	CARDAM	no cat	No	No	3	1.12	9.591		48.297	3.425		99.025	5.407		.	.		.			99.025		NI
42	CARDAM	no cat	Yes	No	1	1.062	9.186		13.713	4.398		83.843	3.249		.	.		0.1507	0.1155		83.693		NI
42	CARDAM	no cat	Yes	No	2	1.12	9.591		48.297	3.425		94.847	11.69		.	.		0.1429	0.1096		94.704		NI
42	CARDAM	no cat	Yes	No	3	1.253	4.783		49.521	4.149		75.451	3.937		.	.		0.1277	0.0979		75.324		NI
43	CARDAM	no cat	No	No	1	1.005	2.625		25.131	3.811		107.74	2.867		.	.		.			107.736		NI
43	CARDAM	no cat	No	No	2	1.062	9.186		13.713	4.398		104.11	6.317		.	.		.			104.107		NI
43	CARDAM	no cat	No	No	3	1.12	9.591		48.297	3.425		107.14	8.894		.	.		.			107.143		NI
44	CARDAM	no cat	No	No	1	1.169	3.808		3.2487	0.788		95.817	7.899		.	.		.			95.817		NI
44	CARDAM	no cat	No	No	2	1.005	2.625		25.131	3.811		100.72	9.625		.	.		.			100.715		NI
44	CARDAM	no cat	No	No	3	1.062	9.186		13.713	4.398		94.253	9.322		.	.		.			94.253		NI
45	CARDAM	no cat	No	No	1	1.005	2.625		25.131	3.811		101.25	9.078		.	.		.			101.253		NI
45	CARDAM	no cat	No	No	2	1.062	9.186		13.713	4.398		99.964	2.401		.	.		.			99.964		NI
45	CARDAM	no cat	No	No	3	1.018	9.297		44.999	2.039		114.67	6.06		.	.		.			114.667		NI
46	CARDAM	no cat	No	No	1	1.169	3.808		3.2487	0.788		74.948	16.6		.	.		.			74.948		NI
46	CARDAM	no cat	No	No	2	1.005	2.625		25.131	3.811		95.383	6.715		.	.		.			95.383		NI
46	CARDAM	no cat	No	No	3	1.062	9.186		13.713	4.398		92.867	5.376		.	.		.			92.867		NI
47	CARDAM	no cat	No	No	1	1.005	2.625		25.131	3.811		85.746	11.25		.	.		.			85.746		NI
47	CARDAM	no cat	No	No	2	1.062	9.186		13.713	4.398		74.644	4.353		.	.		.			74.644		NI
47	CARDAM	no cat	No	No	3	1.253	4.783		49.521	4.149		82.926	8.546		.	.		.			82.926		NI
48	CARDAM	no cat	Yes	No	1	1.18	12.54		25.225	3.808		3.684	0.115		.	.		2.1889	0.6913		1.496		I
48	CARDAM	no cat	Yes	No	2	0.72	9.549		13.318	7.805		5.217	0.344		.	.		3.476	1.1336		1.741		I
48	CARDAM	no cat	Yes	No	3	1.169	3.808		3.2487	0.788		3.514	2.422		.	.		2.1135	0.6981		1.815		I
48	CARDAM	no cat	Yes	No	4	1.005	2.625		25.131	3.811		3.15	0.318		.	.		2.6577	0.8121		0.51		I
49	CARDAM	no cat	Yes	No	1	0.9	3.814		14.278	3.816		77.871	7.246		.	.		0.5113	0.8192		77.395		NI
49	CARDAM	no cat	Yes	No	2	0.99	8.386		37.684	6.95		69.814	8.698		.	.		0.3401	0.589		69.685		NI
49	CARDAM	no cat	Yes	No	3	0.982	7.089		28.69	3.421		51.767	13.35		.	.		0.4708	0.7517		51.327		NI
50	CARDAM	no cat	No	No	1	0.9	3.814		14.278	3.816		106.07	1.877		.	.		.			106.067		NI
50	CARDAM	no cat	No	No	2	0.99	8.386		37.684	6.95		97.354	8.425		.	.		.			97.354		NI
50	CARDAM	no cat	No	No	3	0.982	7.089		28.69	3.421		101.44	3.22		.	.		.			101.441		NI
51	CARDAM	no cat	No	No	1	0.9	3.814		14.278	3.816		108.97	9.861		.	.		.			108.968		NI
51	CARDAM	no cat	No	No	2	0.943	4.444		25.036	15.37		100.66	5.001		.	.		.			100.656		NI
51	CARDAM	no cat	No	No	3	0.982	7.089		28.69	3.421		103.91	13.66		.	.		.			103.911		NI
52	CARDAM	no cat	No	No	1	0.9	3.814		14.278	3.816		74.507	55.16	NQ	.	.		.			74.507	NQ	NI
52	CARDAM	no cat	No	No	2	0.943	4.444		25.036	15.37		105.92	3.977		.	.		.			105.921		NI
52	CARDAM	no cat	No	No	3	0.99	8.386		37.684	6.95		85.6	12.75		.	.		.			85.6		NI
52	CARDAM	no cat	No	No	4	0.982	7.089		28.69	3.421		96.77	7.122		.	.		.			96.77		NI
53	CARDAM	no cat	No	No	1	0.9	3.814		14.278	3.816		125.65	3.404		.	.		.			125.653		NI
53	CARDAM	no cat	No	No	2	0.99	8.386		37.684	6.95		110.36	7.849		.	.		.			110.355		NI
53	CARDAM	no cat	No	No	3	0.982	7.089		28.69	3.421		106.08	5.216		.	.		.			106.084		NI
54	CARDAM	cat 2B	No	No	1	1.11	3.386		33.855	6.392		2.512	0.539		.	.		.			2.512		I
54	CARDAM	cat 2B	No	No	2	0.896	13.12		16.769	5.392		1.937	1.223		.	.		.			1.937		I
54	CARDAM	cat 2B	No	No	3	0.907	10.72		44.643	5.2		0.68	0.225		.	.		.			0.68		I
55	CARDAM	cat 2B	No	No	1	1.18	12.54		25.225	3.808		0.712	0.062		.	.		.			0.712		I
55	CARDAM	cat 2B	No	No	2	1.169	3.808		3.2487	0.788		0.955	0.092		.	.		.			0.955		I
55	CARDAM	cat 2B	No	No	3	1.005	2.625		25.131	3.811		0.737	0.08		.	.		.			0.737		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
56	CARDAM	cat 2B	No	No	1	1.18	12.54		25.225	3.808		10.087	2.767		.	.		.			10.087		I
56	CARDAM	cat 2B	No	No	2	0.72	9.549		13.318	7.805		9.733	3.148		.	.		.			9.733		I
56	CARDAM	cat 2B	No	No	3	1.169	3.808		3.2487	0.788		4.86	2.646		.	.		.			4.86		I
57	CARDAM	cat 2B	No	No	1	0.811	1.341		32.262	2.547		0.454	0.272		.	.		.			0.454		I
57	CARDAM	cat 2B	No	No	2	1.206	7.734		17.834	6.314		0.957	0.512		.	.		.			0.957		I
57	CARDAM	cat 2B	No	No	3	1.18	12.54		25.225	3.808		0.965	0.591		.	.		.			0.965		I
58	CARDAM	cat 2B	No	No	1	1.206	7.734		17.834	6.314		1.284	0.964		.	.		.			1.284		I
58	CARDAM	cat 2B	No	No	2	1.18	12.54		25.225	3.808		0.726	0.363		.	.		.			0.726		I
58	CARDAM	cat 2B	No	No	3	0.72	9.549		13.318	7.805		0.44	0.121		.	.		.			0.44		I
59	CARDAM	cat 2B	No	No	1	1.18	12.54		25.225	3.808		33.087	1.029		.	.		.			33.087		I
59	CARDAM	cat 2B	No	No	2	0.72	9.549		13.318	7.805		39.88	8.414		.	.		.			39.88		I
59	CARDAM	cat 2B	No	No	3	1.169	3.808		3.2487	0.788		21.355	5.464		.	.		.			21.355		I
60	CARDAM	cat 2B	No	No	1	0.992	2.274		10.261	2.629		0.991	0.467		.	.		.			0.991		I
60	CARDAM	cat 2B	No	No	2	0.943	4.444		25.036	15.37		0.785	0.352		.	.		.			0.785		I
60	CARDAM	cat 2B	No	No	3	0.99	8.386		37.684	6.95		0.643	0.146		.	.		.			0.643		I
61	CARDAM	cat 2B	No	Yes	1	1.239	7.199		48.281	4.314		59.817	3.134		0.0865	0.08		.			59.731		NI
61	CARDAM	cat 2B	No	Yes	2	0.869	2.369		16.153	6.349		90.072	3.802		0	0		.			90.072		NI
61	CARDAM	cat 2B	No	Yes	3	0.973	6.201		17.996	5.229		89.007	3.647		0.4263	0.16		.			88.581		NI
62	CARDAM	cat 2B	No	No	1	1.062	9.186		13.713	4.398		98.47	7.422		.	.		.			98.47		NI
62	CARDAM	cat 2B	No	No	2	1.12	9.591		48.297	3.425		101.6	7.958		.	.		.			101.597		NI
62	CARDAM	cat 2B	No	No	3	1.253	4.783		49.521	4.149		78.449	9.032		.	.		.			78.449		NI
63	CARDAM	cat 2B	No	No	1	1.12	9.591		48.297	3.425		83.959	6.982		.	.		.			83.959		NI
63	CARDAM	cat 2B	No	No	2	1.018	9.297		44.999	2.039		95.894	2.384		.	.		.			95.894		NI
63	CARDAM	cat 2B	No	No	3	1.253	4.783		49.521	4.149		73.414	4.24		.	.		.			73.414		NI
64	CARDAM	cat 2B	No	No	1	0.811	1.341		32.262	2.547		74.312	6.765		.	.		.			74.312		NI
64	CARDAM	cat 2B	No	No	2	1.206	7.734		17.834	6.314		61.939	7.556		.	.		.			61.939		NI
64	CARDAM	cat 2B	No	No	3	1.18	12.54		25.225	3.808		75.775	4.704		.	.		.			75.775		NI
65	CARDAM	cat 2B	No	No	1	1.018	9.297		44.999	2.039		74.621	10.12		.	.		.			74.621		NI
65	CARDAM	cat 2B	No	No	2	1.253	4.783		49.521	4.149		40.455	1.5		.	.		.			40.455		I
65	CARDAM	cat 2B	No	No	3	1.22	3.711		36.294	7.468		41.957	8.924		.	.		.			41.957		I
66	CARDAM	cat 2B	No	No	1	1.12	9.591		48.297	3.425		1.203	0.386		.	.		.			1.203		I
66	CARDAM	cat 2B	No	No	2	1.018	9.297		44.999	2.039		1.39	0.264		.	.		.			1.39		I
66	CARDAM	cat 2B	No	No	3	1.22	3.711		36.294	7.468		8.415	2.637		.	.		.			8.415		I
67	CARDAM	cat 2A	No	No	1	1.239	7.199		48.281	4.314		0.795	0.305		.	.		.			0.795		I
67	CARDAM	cat 2A	No	No	2	0.869	2.369		16.153	6.349		0.85	0.423		.	.		.			0.85		I
67	CARDAM	cat 2A	No	No	3	0.973	6.201		17.996	5.229		1.082	0.475		.	.		.			1.082		I
68	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	1	1.11	3.386		33.855	6.392		0.668	0.383		.	.		.			0.668		I
68	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	2	0.896	13.12		16.769	5.392		0.733	0.067		.	.		.			0.733		I
68	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	3	0.907	10.72		44.643	5.2		1.264	0.8		.	.		.			1.264		I
69	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	1	1.11	3.386		33.855	6.392		0.847	0.893		.	.		.			0.847		I
69	CARDAM	cat 2A	No	No	2	0.896	13.12		16.769	5.392		0.283	0.034		.	.		.			0.283		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
		(ICCVAM:cat2B)																					
69	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	3	0.907	10.72		44.643	5.2		0.119	0.102		.	.		.			0.119		I
70	CARDAM	cat 2A	No	No	1	1.18	12.54		25.225	3.808		1.302	0.433		.	.		.			1.302		I
70	CARDAM	cat 2A	No	No	2	0.72	9.549		13.318	7.805		1.292	0.739		.	.		.			1.292		I
70	CARDAM	cat 2A	No	No	3	1.169	3.808		3.2487	0.788		0.667	0.074		.	.		.			0.667		I
71	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	1	0.973	6.201		17.996	5.229		0.519	0.302		.	.		.			0.519		I
71	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	2	0.81	1.341		32.239	2.548		0.792	0.057		.	.		.			0.792		I
71	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	3	1.206	7.734		17.834	6.314		0.916	0.177		.	.		.			0.916		I
72	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	1	1.005	2.625		25.131	3.811		0.957	0.234		.	.		.			0.957		I
72	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	2	1.062	9.186		13.713	4.398		0.712	0.021		.	.		.			0.712		I
72	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	3	1.253	4.783		49.521	4.149		0.818	0.21		.	.		.			0.818		I
73	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	1	0.995	8.509		37.816	5.18		98.245	7.368		.	.		.			98.245		NI
73	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	2	1.239	7.199		48.279	4.314		66.704	8.227		.	.		.			66.704		NI
73	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	3	0.868	2.37		16.136	6.351		97.236	2.04		.	.		.			97.236		NI
74	CARDAM	cat 2A	Yes	Yes	1	1.11	3.386		33.855	6.392		91.954	3.991		0.2118	0.04		1.7455	0.385		89.997		NI
74	CARDAM	cat 2A	Yes	Yes	2	0.896	13.12		16.769	5.392		211.33	6.195		0.1092	0.12		2.2464	0.477		208.979		NI
74	CARDAM	cat 2A	Yes	Yes	3	0.907	10.72		44.643	5.2		105.13	4.029		0	0		2.0667	0.4709		103.061		NI
75	CARDAM	cat 2A	No	No	1	1.11	3.386		33.855	6.392		0.994	0.084		.	.		.			0.994		I
75	CARDAM	cat 2A	No	No	2	0.896	13.12		16.769	5.392		0.765	0.048		.	.		.			0.765		I
75	CARDAM	cat 2A	No	No	3	0.907	10.72		44.643	5.2		0.867	0.108		.	.		.			0.867		I
75	CARDAM	cat 2A	No	No	4	0.995	8.509		37.816	5.18		0.69	0.138		.	.		.			0.69		I
76	CARDAM	cat 2A	No	No	1	1.18	12.54		25.225	3.808		85.477	3.58		.	.		.			85.477		NI
76	CARDAM	cat 2A	No	No	2	0.72	9.549		13.318	7.805		98.356	1.491		.	.		.			98.356		NI
76	CARDAM	cat 2A	No	No	3	1.169	3.808		3.2487	0.788		74.255	9.515		.	.		.			74.255		NI
77	CARDAM	cat 2A	No	No	1	0.973	6.201		17.996	5.229		101.18	6.643		.	.		.			101.178		NI
77	CARDAM	cat 2A	No	No	2	0.81	1.341		32.239	2.548		80.837	4.582		.	.		.			80.837		NI
77	CARDAM	cat 2A	No	No	3	1.206	7.734		17.834	6.314		100.18	4.666		.	.		.			100.177		NI
78	CARDAM	cat 2A	No	No	1	0.973	6.201		17.996	5.229		101.1	1.148		.	.		.			101.101		NI
78	CARDAM	cat 2A	No	No	2	0.81	1.341		32.239	2.548		75.821	10.23		.	.		.			75.821		NI
78	CARDAM	cat 2A	No	No	3	1.206	7.734		17.834	6.314		86.389	3.516		.	.		.			86.389		NI
79	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	1	1.005	2.625		25.131	3.811		59.792	4.648		.	.		.			59.792		NI
79	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	2	1.062	9.186		13.713	4.398		67.72	4.899		.	.		.			67.72		NI
79	CARDAM	cat 2A (ICCVAM:cat2B)	No	No	3	1.253	4.783		49.521	4.149		64.159	7.333		.	.		.			64.159		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
80	CARDAM	cat 1	Yes	No	1	1.206	7.734		17.834	6.314		33.506	5.1		.	.		35.62	7.7812		1.028		I
80	CARDAM	cat 1	Yes	No	2	1.18	12.54		25.225	3.808		38.559	5.519		.	.		36.28	7.9498		3.18		I
80	CARDAM	cat 1	Yes	No	3	0.72	9.549		13.318	7.805		39.748	1.637		.	.		59.379	13.036		0		I
81	CARDAM	cat 1	Yes	No	1	1.239	7.199		48.281	4.314		0.418	0.399		.	.		0.0238	0.0412		0.418		I
81	CARDAM	cat 1	Yes	No	2	0.869	2.369		16.153	6.349		0.397	0.061		.	.		0.0371	0.0643		0.397		I
81	CARDAM	cat 1	Yes	No	3	0.973	6.201		17.996	5.229		0.514	0.229		.	.		0.036	0.0623		0.514		I
82	CARDAM	cat 1	No	No	1	0.887	9.248		23.751	10		1.091	0.899		.	.		.			1.091		I
82	CARDAM	cat 1	No	No	2	0.9	3.814		14.278	3.816		0.676	0.064		.	.		.			0.676		I
82	CARDAM	cat 1	No	No	3	0.99	8.386		37.684	6.95		0.401	0.184		.	.		.			0.401		I
83	CARDAM	cat 1	No	No	1	1.11	3.386		33.855	6.392		0.245	0.062		.	.		.			0.245		I
83	CARDAM	cat 1	No	No	2	0.896	13.12		16.769	5.392		0.374	0.048		.	.		.			0.374		I
83	CARDAM	cat 1	No	No	3	0.995	8.509		37.816	5.18		0.134	0.003		.	.		.			0.134		I
84	CARDAM	cat 1	No	No	1	0.887	9.248		23.751	10		0.68	0.497		.	.		.			0.68		I
84	CARDAM	cat 1	No	No	2	0.943	4.444		25.036	15.37		0.362	0.072		.	.		.			0.362		I
84	CARDAM	cat 1	No	No	3	0.99	8.386		37.684	6.95		0.535	0.142		.	.		.			0.535		I
85	CARDAM	cat 1	No	No	1	0.995	8.509		37.816	5.18		0.824	0.305		.	.		.			0.824		I
85	CARDAM	cat 1	No	No	2	1.239	7.199		48.279	4.314		0.256	0.026		.	.		.			0.256		I
85	CARDAM	cat 1	No	No	3	0.868	2.37		16.136	6.351		0.622	0.084		.	.		.			0.622		I
86	CARDAM	cat 1	No	No	1	1.051	9.065		10.033	2.886		5.675	3.8		.	.		.			5.675		I
86	CARDAM	cat 1	No	No	2	1.083	4.893		10.142	3.1		15.114	4.678		.	.		.			15.114		I
86	CARDAM	cat 1	No	No	3	0.887	9.248		23.751	10		3.823	0.775		.	.		.			3.823		I
87	CARDAM	cat 1	No	No	1	0.907	10.72		44.643	5.2		0.522	0.067		.	.		.			0.522		I
87	CARDAM	cat 1	No	No	2	0.997	8.495		37.918	5.171		0.311	0.08		.	.		.			0.311		I
87	CARDAM	cat 1	No	No	3	1.239	7.199		48.279	4.314		0.451	0.157		.	.		.			0.451		I
88	CARDAM	cat 1	Yes	No	1	1.22	3.711		36.294	7.468		0.47	0.027		.	.		0.056	0.0537		0.414		I
88	CARDAM	cat 1	Yes	No	2	1.051	9.065		10.033	2.886		0.976	0.299		.	.		0.1126	0.0624		0.863		I
88	CARDAM	cat 1	Yes	No	3	0.992	2.274		10.261	2.629		0.972	0.395		.	.		0.0739	0.0661		0.898		I
89	CARDAM	cat 1	No	No	1	0.973	6.201		17.996	5.229		1.419	0.121		.	.		.			1.419		I
89	CARDAM	cat 1	No	No	2	0.81	1.341		32.239	2.548		1.211	0.18		.	.		.			1.211		I
89	CARDAM	cat 1	No	No	3	1.206	7.734		17.834	6.314		1.208	0.18		.	.		.			1.208		I
90	CARDAM	cat 1	No	No	1	0.973	6.201		17.996	5.229		5.918	3.882		.	.		.			5.918		I
90	CARDAM	cat 1	No	No	2	0.81	1.341		32.239	2.548		13.625	16.84		.	.		.			13.625		I
90	CARDAM	cat 1	No	No	3	1.206	7.734		17.834	6.314		9.211	7.196		.	.		.			9.211		I
91	CARDAM	cat 1	Yes	No	1	0.973	6.201		17.996	5.229		9.285	7.417		.	.		0.0936	0.0825		9.203		I
91	CARDAM	cat 1	Yes	No	2	0.81	1.341		32.239	2.548		1.516	0.326		.	.		0.1138	0.1003		1.415		I
91	CARDAM	cat 1	Yes	No	3	1.206	7.734		17.834	6.314		1.661	0.631		.	.		0.0765	0.0674		1.594		I
92	CARDAM	cat 1	Yes	No	1	0.9	3.814		14.278	3.816		7.529	1.753		.	.		0.4687	0.3505		7.06		I
92	CARDAM	cat 1	Yes	No	2	0.943	4.444		25.036	15.37		7.031	0.531		.	.		0.5037	0.3344		6.527		I
92	CARDAM	cat 1	Yes	No	3	0.982	7.089		28.69	3.421		5.427	0.391		.	.		0.4125	0.3212		5.014		I
93	CARDAM	cat 1	No	No	1	0.995	8.509		37.816	5.18		34.64	2.09		.	.		.			34.64		I
93	CARDAM	cat 1	No	No	2	1.239	7.199		48.279	4.314		25.605	4.628		.	.		.			25.605		I
93	CARDAM	cat 1	No	No	3	0.868	2.37		16.136	6.351		25.069	7.207		.	.		.			25.069		I
94	CARDAM	cat 1	No	No	1	0.869	2.369		16.153	6.349		17.47	2.054		.	.		.			17.47		I
94	CARDAM	cat 1	No	No	2	0.973	6.201		17.996	5.229		14.357	6.445		.	.		.			14.357		I
94	CARDAM	cat 1	No	No	3	0.81	1.341		32.239	2.548		23.821	14.95		.	.		.			23.821		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
95	CARDAM	cat 1	Yes	No	1	0.995	8.509		37.816	5.18		0.33	0.051		.	.		0.0045	0.0077		0.33		I
95	CARDAM	cat 1	Yes	No	2	1.239	7.199		48.279	4.314		0.212	0.061		.	.		0	0		0.212		I
95	CARDAM	cat 1	Yes	No	3	0.868	2.37		16.136	6.351		0.756	0.106		.	.		0	0		0.756		I
96	CARDAM	cat 1	No	No	1	1.239	7.199		48.281	4.314		42.678	7.727		.	.		.			42.678		I
96	CARDAM	cat 1	No	No	2	0.869	2.369		16.153	6.349		68.453	4.497		.	.		.			68.453		NI
96	CARDAM	cat 1	No	No	3	0.973	6.201		17.996	5.229		77.196	5.952		.	.		.			77.196		NI
97	CARDAM	cat 1	No	No	1	0.995	8.509		37.816	5.18		65.492	2.707		.	.		.			65.492		NI
97	CARDAM	cat 1	No	No	2	1.239	7.199		48.279	4.314		49.507	3.455		.	.		.			49.507		I
97	CARDAM	cat 1	No	No	3	0.868	2.37		16.136	6.351		73.543	4.676		.	.		.			73.543		NI
98	CARDAM	cat 1	No	Yes	1	1.22	3.711		36.294	7.468		79.215	10.79		10.202	5.95		.			69.013		NI
98	CARDAM	cat 1	No	Yes	2	1.051	9.065		10.033	2.886		79.587	9.083		10.856	9.77		.			68.731		NI
98	CARDAM	cat 1	No	Yes	3	1.083	4.893		10.142	3.1		88.405	12.45		3.9575	0.51		.			84.447		NI
99	CARDAM	cat 1	No	No	1	0.973	6.201		17.996	5.229		1.601	0.31		.	.		.			1.601		I
99	CARDAM	cat 1	No	No	2	0.81	1.341		32.239	2.548		2.312	0.58		.	.		.			2.312		I
99	CARDAM	cat 1	No	No	3	1.206	7.734		17.834	6.314		1.88	0.143		.	.		.			1.88		I
100	CARDAM	cat 1	No	No	1	0.9	3.814		14.278	3.816		1.891	0.258		.	.		.			1.891		I
100	CARDAM	cat 1	No	No	2	0.99	8.386		37.684	6.95		1.473	0.682		.	.		.			1.473		I
100	CARDAM	cat 1	No	No	3	0.982	7.089		28.69	3.421		1.585	0.499		.	.		.			1.585		I
101	CARDAM	cat 1	No	Yes	1	1.22	3.711		36.294	7.468		64.654	3.649		0.5532	0.46		.			64.101		NI
101	CARDAM	cat 1	No	Yes	2	1.051	9.065		10.033	2.886		77.647	8.13		0.119	0.1		.			77.528		NI
101	CARDAM	cat 1	No	Yes	3	1.083	4.893		10.142	3.1		59.991	3.287		0.5511	0.34		.			59.44		NI
102	CARDAM	cat 1	No	No	1	0.992	2.274		10.261	2.629		90.011	9.478		.	.		.			90.011		NI
102	CARDAM	cat 1	No	No	2	0.943	4.444		25.036	15.37		95.049	5.04		.	.		.			95.049		NI
102	CARDAM	cat 1	No	No	3	0.99	8.386		37.684	6.95		100.03	5.422		.	.		.			100.027		NI
103	CARDAM	cat 1	No	No	1	0.811	1.341		32.262	2.547		1.174	0.072		.	.		.			1.174		I
103	CARDAM	cat 1	No	No	2	1.206	7.734		17.834	6.314		1.508	0.141		.	.		.			1.508		I
103	CARDAM	cat 1	No	No	3	1.18	12.54		25.225	3.808		1.157	0.381		.	.		.			1.157		I
104	CARDAM	cat 1	No	No	1	0.973	6.201		17.996	5.229		96.175	7.28		.	.		.			96.175		NI
104	CARDAM	cat 1	No	No	2	0.81	1.341		32.239	2.548		70.493	4.594		.	.		.			70.493		NI
104	CARDAM	cat 1	No	No	3	1.206	7.734		17.834	6.314		85.336	1.747		.	.		.			85.336		NI
105	CARDAM	cat 1	No	No	1	1.18	12.54		25.225	3.808		2.347	1.984		.	.		.			2.347		I
105	CARDAM	cat 1	No	No	2	0.72	9.549		13.318	7.805		1.695	1.029		.	.		.			1.695		I
105	CARDAM	cat 1	No	No	3	1.169	3.808		3.2487	0.788		1.01	0.194		.	.		.			1.01		I
1	CEETOX	no cat	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.			0	NQ	I
1	CEETOX	no cat	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.			0	NQ	I
1	CEETOX	no cat	No	No	3	1.061	3.431		18.843	5.17		8.125	2.448		.	.		.			8.125		I
1	CEETOX	no cat	No	No	4	1.099	1.557		26.79	5.02		2.442	0.835		.	.		.			2.442		I
1	CEETOX	no cat	No	No	5	1.097	2.786		36.449	2.106		7.539	1.634		.	.		.			7.539		I
2	CEETOX	no cat	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.			0	NQ	I
2	CEETOX	no cat	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.			0	NQ	I
2	CEETOX	no cat	No	No	3	1.061	3.431		18.843	5.17		2.687	0.288		.	.		.			2.687		I
2	CEETOX	no cat	No	No	4	1.099	1.557		26.79	5.02		1.942	0.115		.	.		.			1.942		I
2	CEETOX	no cat	No	No	5	1.097	2.786		36.449	2.106		2.645	0.184		.	.		.			2.645		I
3	CEETOX	no cat	No	No	1	1.109	7.989		44.805	3.75		1.879	0.104		.	.		.			1.879		I
3	CEETOX	no cat	No	No	2	1.219	9.931		24.606	3.854		1.34	0.024		.	.		.			1.34		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
3	CEETOX	no cat	No	No	3	0.814	4.296		4.0131	1.662		2.928	0.303		.	.		.			2.928		I
4	CEETOX	no cat	Yes	No	1	0.984	11.67		4.1935	4.007		66.272	3.026		.	.		64.629	17.96		0		I
4	CEETOX	no cat	Yes	No	2	1.074	3.69		13.347	3.511		60.627	5.247		.	.		59.183	16.468		0		I
4	CEETOX	no cat	No	No	3	1.117	7.674		70.816	2.256	NQ	.	.		.	.		.	.		0	NQ	I
4	CEETOX	no cat	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.	17.225		0	NQ	I
4	CEETOX	no cat	Yes	No	5	1.11	5.842		53.747	6.399		67.343	6.169		.	.		62.975	17.225		0		I
5	CEETOX	no cat	Yes	No	1	1.126	12.55		38.801	3.402		0	0		.	.		2.3242	0.2003		0		I
5	CEETOX	no cat	Yes	No	2	1.168	7.79		34.309	1.912		5.666	3.084		.	.		2.1122	0.1931		3.554		I
5	CEETOX	no cat	Yes	No	3	1.026	4.323		2.3871	0.22		6.772	5.383		.	.		2.5171	0.2197		4.255		I
5	CEETOX	no cat	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.	.		0	NQ	I
6	CEETOX	no cat	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.	.		0	NQ	I
6	CEETOX	no cat	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.	.		0	NQ	I
6	CEETOX	no cat	No	No	3	1.061	3.431		18.843	5.17		8.974	6.199		.	.		.			8.974		I
6	CEETOX	no cat	No	No	4	1.099	1.557		26.79	5.02		2.685	0.315		.	.		.			2.685		I
6	CEETOX	no cat	No	No	5	1.097	2.786		36.449	2.106		6.384	1.492		.	.		.			6.384		I
7	CEETOX	no cat	No	No	1	1.109	7.989		44.805	3.75		4.315	0.702		.	.		.			4.315		I
7	CEETOX	no cat	No	No	2	1.219	9.931		24.606	3.854		6.016	2.157		.	.		.			6.016		I
7	CEETOX	no cat	No	No	3	0.814	4.296		4.0131	1.662		9.869	1.304		.	.		.			9.869		I
8	CEETOX	no cat	No	No	1	1.109	7.989		44.805	3.75		36.19	11.37		.	.		.			36.19		I
8	CEETOX	no cat	No	No	2	0.814	4.296		4.0131	1.662		28.01	3.747		.	.		.			28.01		I
8	CEETOX	no cat	No	No	3	1.038	3.122		66.148	3.566	NQ	.	.		.	.		.			0	NQ	I
8	CEETOX	no cat	No	No	4	1.074	3.69		13.347	3.511		22.015	5.525		.	.		.			22.015		I
9	CEETOX	no cat	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.			0	NQ	I
9	CEETOX	no cat	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.			0	NQ	I
9	CEETOX	no cat	No	No	3	1.061	3.431		18.843	5.17		42.496	4.526		.	.		.			42.496		I
9	CEETOX	no cat	No	No	4	1.099	1.557		26.79	5.02		34.451	3.367		.	.		.			34.451		I
9	CEETOX	no cat	No	No	5	1.097	2.786		36.449	2.106		48.67	3.803		.	.		.			48.67		I
10	CEETOX	no cat	No	No	1	1.022	1.825		49.764	7.681		2.104	1.152		.	.		.			2.104		I
10	CEETOX	no cat	No	No	2	1.011	6.903		31.312	5.994		3.708	0.804		.	.		.			3.708		I
10	CEETOX	no cat	No	No	3	0.808	6.022		3.1753	0.179		1.897	0.588		.	.		.			1.897		I
11	CEETOX	no cat	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.			0	NQ	I
11	CEETOX	no cat	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.			0	NQ	I
11	CEETOX	no cat	No	No	3	1.061	3.431		18.843	5.17		82.257	8.263		.	.		.			82.257		NI
11	CEETOX	no cat	No	No	4	1.099	1.557		26.79	5.02		57.646	6.937		.	.		.			57.646		NI
11	CEETOX	no cat	No	No	5	1.097	2.786		36.449	2.106		60.283	2.673		.	.		.			60.283		NI
12	CEETOX	no cat	No	No	1	0.955	1.687		23.277	7.239		114.17	4.642		.	.		.			114.169		NI
12	CEETOX	no cat	No	No	2	1.117	6.85		19.866	5.959		94.463	3.444		.	.		.			94.463		NI
12	CEETOX	no cat	No	No	3	0.997	8.889		9.1441	3.404		95.67	7.566		.	.		.			95.67		NI
13	CEETOX	no cat	No	No	1	1.117	6.85		19.866	5.959		97.119	2.853		.	.		.			97.119		NI
13	CEETOX	no cat	No	No	2	0.986	9.055		41.765	3.931		104.28	2.336		.	.		.			104.278		NI
13	CEETOX	no cat	No	No	3	1.108	15.91		36.132	3.321		120.51	11.64		.	.		.			120.512		NI
14	CEETOX	no cat	Yes	No	1	1.126	12.55		38.801	3.402		94.33	6.774		.	.		0.0395	0.0684		94.33		NI
14	CEETOX	no cat	Yes	No	2	1.168	7.79		34.309	1.912		92.793	7.007		.	.		0	0		92.793		NI
14	CEETOX	no cat	Yes	No	3	1.026	4.323		2.3871	0.22		111.4	5.398		.	.		0.0325	0.0563		111.4		NI
14	CEETOX	no cat	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.	.		0	NQ	I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
15	CEETOX	no cat	No	No	1	1.117	6.85		19.866	5.959		97.642	5.08		.	.		.			97.642		NI
15	CEETOX	no cat	No	No	2	0.986	9.055		41.765	3.931		102.4	6.79		.	.		.			102.401		NI
15	CEETOX	no cat	No	No	3	1.108	15.91		36.132	3.321		88.247	3.977		.	.		.			88.247		NI
16	CEETOX	no cat	No	No	1	1.109	7.989		44.805	3.75		100.12	1.569		.	.		.			100.12		NI
16	CEETOX	no cat	No	No	2	1.066	7.842		3.9856	2.185		99.078	2.767		.	.		.			99.078		NI
16	CEETOX	no cat	No	No	3	1.038	3.122		66.148	3.566	NQ	.	.		.	.		.			0	NQ	I
16	CEETOX	no cat	No	No	4	1.074	3.69		13.347	3.511		95.979	2.94		.	.		.			95.979		NI
17	CEETOX	no cat	No	No	1	1.026	4.323		2.3871	0.22		99.659	5.782		.	.		.			99.659		NI
17	CEETOX	no cat	No	No	2	1.354	3.187		31.068	12.67		93.88	4.209		.	.		.			93.88		NI
17	CEETOX	no cat	No	No	3	1.017	7.024		26.217	4.983		98.935	5.031		.	.		.			98.935		NI
18	CEETOX	no cat	No	No	1	1.114	3.349		38.602	7.556		93.429	2.181		.	.		.			93.429		NI
18	CEETOX	no cat	No	No	2	1.114	3.349		38.602	7.556	NQ	.	.		.	.		.			0	NQ	I
18	CEETOX	no cat	No	No	3	0.936	3.064		30.876	8.046		104.02	8.227		.	.		.			104.024		NI
18	CEETOX	no cat	No	No	4	0.99	7.261		33.12	5.324		103.92	2.648		.	.		.			103.921		NI
19	CEETOX	no cat	No	No	1	0.986	9.055		41.765	3.931		115.81	3.313		.	.		.			115.81		NI
19	CEETOX	no cat	No	No	2	0.872	8.034		61.365	6.357	NQ	.	.		.	.		.			0	NQ	I
19	CEETOX	no cat	No	No	3	1.108	15.91		36.132	3.321		90.91	7.137		.	.		.			90.91		NI
19	CEETOX	no cat	No	No	4	0.997	8.889		9.1441	3.404		97.125	3.651		.	.		.			97.125		NI
20	CEETOX	no cat	No	No	1	1.102	4.826		52.117	3.403	NQ	.	.		.	.		.			0	NQ	I
20	CEETOX	no cat	No	No	2	1.066	10.35		39.425	8.798		37.111	11.04		.	.		.			37.111		I
20	CEETOX	no cat	No	No	3	0.99	7.261		33.12	5.324		24.217	14.44		.	.		.			24.217		I
21	CEETOX	no cat	No	No	1	0.984	11.67		4.1935	4.007		86.116	1.363		.	.		.			86.116		NI
21	CEETOX	no cat	No	No	2	1.074	3.69		13.347	3.511		57.134	3.677		.	.		.			57.134		NI
21	CEETOX	no cat	No	No	3	1.117	7.674		70.816	2.256	NQ	.	.		.	.		.			0	NQ	I
21	CEETOX	no cat	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.			0	NQ	I
21	CEETOX	no cat	No	No	5	1.11	5.842		53.747	6.399		76.259	2.579		.	.		.			76.259		NI
22	CEETOX	no cat	No	No	1	1.022	1.825		49.764	7.681		1.925	0.396		.	.		.			1.925		I
22	CEETOX	no cat	No	No	2	1.011	6.903		31.312	5.994		3.214	0.329		.	.		.			3.214		I
22	CEETOX	no cat	No	No	3	0.808	6.022		3.1753	0.179		3.897	0.373		.	.		.			3.897		I
23	CEETOX	no cat	Yes	No	1	1.026	4.323		2.3871	0.22		54.791	1.961		.	.		49.091	0.659		5.7		I
23	CEETOX	no cat	Yes	No	2	1.281	2.862		35.038	5.007		59.927	1.721		.	.		39.24	0.528		20.687		I
23	CEETOX	no cat	Yes	No	3	1.006	1.79		41.106	8.615		55.83	4.349		.	.		49.95	0.6721		5.879		I
24	CEETOX	no cat	No	No	1	1.066	7.842		3.9856	2.185		1.876	0.355		.	.		.			1.876		I
24	CEETOX	no cat	No	No	2	1.038	3.122		66.148	3.566	NQ	.	.		.	.		.			0	NQ	I
24	CEETOX	no cat	No	No	3	1.038	3.122		66.148	3.566		1.382	0.142		.	.		.			1.382		I
24	CEETOX	no cat	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.			0	NQ	I
24	CEETOX	no cat	No	No	5	1.11	5.842		53.747	6.399		1.738	0.123		.	.		.			1.738		I
25	CEETOX	no cat	Yes	No	1	1.066	10.35		39.425	8.798		80.319	3.111		.	.		0	0		80.319		NI
25	CEETOX	no cat	Yes	No	2	0.953	8.886		46.459	4.808		102.31	8.918		.	.		0	0		102.308		NI
25	CEETOX	no cat	Yes	No	3	0.936	3.064		30.876	8.046		84.437	7.975		.	.		0	0		84.437		NI
26	CEETOX	no cat	No	No	1	1.066	10.35		39.425	8.798		3.658	0.891		.	.		.			3.658		I
26	CEETOX	no cat	No	No	2	0.953	8.886		46.459	4.808		2.535	0.517		.	.		.			2.535		I
26	CEETOX	no cat	No	No	3	0.936	3.064		30.876	8.046		2.991	0.608		.	.		.			2.991		I
28	CEETOX	no cat	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.			0	NQ	I
28	CEETOX	no cat	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.			0	NQ	I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
28	CEETOX	no cat	No	No	3	1.061	3.431		18.843	5.17		99.717	2.292		.	.		.			99.717		NI
28	CEETOX	no cat	No	No	4	1.099	1.557		26.79	5.02		97.633	3.167		.	.		.			97.633		NI
28	CEETOX	no cat	No	No	5	1.097	2.786		36.449	2.106		97.644	4.025		.	.		.			97.644		NI
29	CEETOX	no cat	No	No	1	0.986	9.055		41.765	3.931		106.66	3.482		.	.		.			106.662		NI
29	CEETOX	no cat	No	No	2	0.872	8.034		61.365	6.357	NQ	.	.		.	.		.			0	NQ	I
29	CEETOX	no cat	No	No	3	1.108	15.91		36.132	3.321		89.857	6.604		.	.		.			89.857		NI
29	CEETOX	no cat	No	No	4	0.997	8.889		9.1441	3.404		101.92	6.066		.	.		.			101.922		NI
30	CEETOX	no cat	No	No	2	1.336	6.791		37.862	2.415		75.25	1.397		.	.		.			75.25		NI
30	CEETOX	no cat	No	No	3	0.971	8.015		29.607	1.188		79.495	12.62		.	.		.			79.495		NI
30	CEETOX	no cat	No	No	4	1.114	3.349		38.602	7.556		81.185	1.448		.	.		.			81.185		NI
31	CEETOX	no cat	No	No	2	1.336	6.791		37.862	2.415		97.904	4.043		.	.		.			97.904		NI
31	CEETOX	no cat	No	No	3	1.006	1.79		41.106	8.615		103.25	0.459		.	.		.			103.246		NI
31	CEETOX	no cat	No	No	4	0.971	8.015		29.607	1.188		99.966	3.789		.	.		.			99.966		NI
32	CEETOX	no cat	No	No	1	1.022	1.825		49.764	7.681		12.2	1.314		.	.		.			12.2		I
32	CEETOX	no cat	No	No	2	1.011	6.903		31.312	5.994		31.625	9.075		.	.		.			31.625		I
32	CEETOX	no cat	No	No	3	0.808	6.022		3.1753	0.179		21.052	0.842		.	.		.			21.052		I
33	CEETOX	no cat	Yes	Yes	1	1.066	7.842		3.9856	2.185		104.22	1.498		1.4067	0.38		0.7346	0.3392		102.079		NI
33	CEETOX	no cat	No	No	2	1.038	3.122		66.148	3.566	NQ	.	.		.	0.75		.	0.3101		0	NQ	I
33	CEETOX	no cat	Yes	Yes	3	1.038	3.122		66.148	3.566		90.126	3.363		2.2823	0.75		0.3571	0.3101		87.502		NI
33	CEETOX	no cat	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	0.28		.	0.3524		0	NQ	I
33	CEETOX	no cat	Yes	Yes	5	1.11	5.842		53.747	6.399		115.05	5.045		1.0231	0.28		0.6983	0.3524		113.332		NI
34	CEETOX	no cat	Yes	Yes	1	1.026	4.323		2.3871	0.22		108.54	3.289		10.052	1.62		7.2426	0.3042		91.247		NI
34	CEETOX	no cat	Yes	Yes	2	1.354	3.187		31.068	12.67		68.575	5.127		5.7013	0.47		5.4057	0.2307		57.468		NI
34	CEETOX	no cat	Yes	Yes	3	1.017	7.024		26.217	4.983		80.206	13.57		1.005	1.74		12.633	0		66.568		NI
35	CEETOX	no cat	Yes	No	1	1.066	7.842		3.9856	2.185		86.199	16.47		.	.		0.9378	0.1952		85.261		NI
35	CEETOX	no cat	No	No	2	1.038	3.122		66.148	3.566	NQ	.	.		.	.		.	0.1939		0	NQ	I
35	CEETOX	no cat	Yes	No	3	1.038	3.122		66.148	3.566		79.77	3.964		.	.		0.5434	0.1939		79.227		NI
35	CEETOX	no cat	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.	0.2028		0	NQ	I
35	CEETOX	no cat	Yes	No	5	1.11	5.842		53.747	6.399		107.36	3.143		.	.		0.9094	0.2028		106.447		NI
36	CEETOX	no cat	No	No	1	1.109	7.989		44.805	3.75		99.504	4.259		.	.		.			99.504		NI
36	CEETOX	no cat	No	No	2	1.219	9.931		24.606	3.854		100.97	2.893		.	.		.			100.971		NI
36	CEETOX	no cat	No	No	3	0.814	4.296		4.0131	1.662		108.48	1.339		.	.		.			108.477		NI
37	CEETOX	no cat	Yes	No	1	1.026	4.323		2.3871	0.22		96.119	4.265		.	.		0.5684	0.0487		95.551		NI
37	CEETOX	no cat	Yes	No	2	1.281	2.862		35.038	5.007		90.749	6.111		.	.		0.3643	0.039		90.385		NI
37	CEETOX	no cat	Yes	No	3	1.006	1.79		41.106	8.615		103.78	4.473		.	.		0.4637	0.0497		103.312		NI
38	CEETOX	no cat	No	No	1	1.114	3.349		38.602	7.556		89.732	6.101		.	.		.			89.732		NI
38	CEETOX	no cat	No	No	2	1.114	3.349		38.602	7.556	NQ	.	.		.	.		.			0	NQ	I
38	CEETOX	no cat	No	No	3	0.936	3.064		30.876	8.046		103.47	5.83		.	.		.			103.472		NI
38	CEETOX	no cat	No	No	4	0.99	7.261		33.12	5.324		109.29	5.938		.	.		.			109.29		NI
39	CEETOX	no cat	No	No	1	0.955	1.687		23.277	7.239		112.88	7.391		.	.		.			112.877		NI
39	CEETOX	no cat	No	No	2	1.117	6.85		19.866	5.959		97.045	7.459		.	.		.			97.045		NI
39	CEETOX	no cat	No	No	3	1.117	6.85		19.866	5.959	NQ	.	.		.	.		.			0	NQ	I
39	CEETOX	no cat	No	No	4	1.108	15.91		36.132	3.321		88.322	4.675		.	.		.			88.322		NI
40	CEETOX	no cat	No	No	1	0.953	8.886		46.459	4.808		82.637	2.689		.	.		.			82.637		NI
40	CEETOX	no cat	No	No	2	0.936	3.064		30.876	8.046		84.972	11		.	.		.			84.972		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
40	CEETOX	no cat	No	No	3	0.99	7.261		33.12	5.324		80.007	10.1		.	.		.			80.007		NI
41	CEETOX	no cat	No	No	2	1.336	6.791		37.862	2.415		95.609	6.104		.	.		.			95.609		NI
41	CEETOX	no cat	No	No	3	1.006	1.79		41.106	8.615		106.26	4.339		.	.		.			106.26		NI
41	CEETOX	no cat	No	No	4	0.971	8.015		29.607	1.188		91.31	2.873		.	.		.			91.31		NI
42	CEETOX	no cat	Yes	No	1	1.026	4.323		2.3871	0.22		81.195	5.517		.	.		0.341	0.1226		80.854		NI
42	CEETOX	no cat	Yes	No	2	1.281	2.862		35.038	5.007		73.588	4.495		.	.		0.2732	0.0982		73.315		NI
42	CEETOX	no cat	Yes	No	3	1.006	1.79		41.106	8.615		80.242	8.3		.	.		0.3478	0.125		79.894		NI
43	CEETOX	no cat	No	No	1	1.026	4.323		2.3871	0.22		107.18	4.826		.	.		.			107.178		NI
43	CEETOX	no cat	No	No	2	1.354	3.187		31.068	12.67		91.996	0.544		.	.		.			91.996		NI
43	CEETOX	no cat	No	No	3	1.017	7.024		26.217	4.983		97.722	5.728		.	.		.			97.722		NI
44	CEETOX	no cat	No	No	1	1.074	3.69		13.347	3.511		96.848	6.924		.	.		.			96.848		NI
44	CEETOX	no cat	No	No	2	1.026	4.323		2.3871	0.22		96.119	1.05		.	.		.			96.119		NI
44	CEETOX	no cat	No	No	3	1.281	2.862		35.038	5.007		104.32	4.311		.	.		.			104.32		NI
44	CEETOX	no cat	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.			0	NQ	I
45	CEETOX	no cat	No	No	2	1.336	6.791		37.862	2.415		88.772	9.699		.	.		.			88.772		NI
45	CEETOX	no cat	No	No	3	1.006	1.79		41.106	8.615		104.03	7.731		.	.		.			104.025		NI
45	CEETOX	no cat	No	No	4	0.971	8.015		29.607	1.188		87.223	3.854		.	.		.			87.223		NI
46	CEETOX	no cat	Yes	No	1	1.026	4.323		2.3871	0.22		73.595	6.09		.	.		8.1195	1.1813		65.476		NI
46	CEETOX	no cat	Yes	No	2	1.281	2.862		35.038	5.007		83.984	7.081		.	.		6.4143	0.9465		77.57		NI
46	CEETOX	no cat	Yes	No	3	1.006	1.79		41.106	8.615		92.647	6.073		.	.		8.165	1.2048		84.482		NI
47	CEETOX	no cat	No	No	2	1.336	6.791		37.862	2.415		40.706	2.147		.	.		.			40.706		I
47	CEETOX	no cat	No	No	3	1.006	1.79		41.106	8.615		48.741	9.853		.	.		.			48.741		I
47	CEETOX	no cat	No	No	4	0.971	8.015		29.607	1.188		57.17	6.438		.	.		.			57.17		NI
48	CEETOX	no cat	Yes	No	2	1.336	6.791		37.862	2.415		3.456	0.369		.	.		1.9461	0.2547		1.509		I
48	CEETOX	no cat	Yes	No	3	0.971	8.015		29.607	1.188		5.41	0.568		.	.		2.679	0.3507		2.731		I
48	CEETOX	no cat	Yes	No	4	1.114	3.349		38.602	7.556		3.682	0.36		.	.		2.335	0.3057		1.347		I
49	CEETOX	no cat	Yes	No	1	1.066	10.35		39.425	8.798		82.648	3.517		.	.		0.3074	0.4794		82.429		NI
49	CEETOX	no cat	Yes	No	2	0.953	8.886		46.459	4.808		85.487	7.43		.	.		0.3789	0.5536		85.19		NI
49	CEETOX	no cat	Yes	No	3	0.99	7.261		33.12	5.324		77.095	29.23	NQ	.	.		0.791	0.6231		0	NQ	I
49	CEETOX	no cat	Yes	No	4	0.955	1.687		23.277	7.239		95.865	0.366		.	.		0.9073	0.6461		94.957		NI
50	CEETOX	no cat	No	No	1	0.986	9.055		41.765	3.931		103.59	4.937		.	.		.			103.585		NI
50	CEETOX	no cat	No	No	2	0.872	8.034		61.365	6.357	NQ	.	.		.	.		.			0	NQ	I
50	CEETOX	no cat	No	No	3	1.108	15.91		36.132	3.321		80.557	5.827		.	.		.			80.557		NI
50	CEETOX	no cat	No	No	4	0.997	8.889		9.1441	3.404		95.921	4.929		.	.		.			95.921		NI
51	CEETOX	no cat	No	No	1	1.066	10.35		39.425	8.798		90.105	6.198		.	.		.			90.105		NI
51	CEETOX	no cat	No	No	2	0.953	8.886		46.459	4.808		94.999	12.22		.	.		.			94.999		NI
51	CEETOX	no cat	No	No	3	0.936	3.064		30.876	8.046		113.43	2.593		.	.		.			113.426		NI
52	CEETOX	no cat	No	No	1	0.986	9.055		41.765	3.931		111.19	3.216		.	.		.			111.194		NI
52	CEETOX	no cat	No	No	2	0.872	8.034		61.365	6.357	NQ	.	.		.	.		.			0	NQ	I
52	CEETOX	no cat	No	No	3	1.108	15.91		36.132	3.321		93.619	13.69		.	.		.			93.619		NI
52	CEETOX	no cat	No	No	4	0.997	8.889		9.1441	3.404		97.192	8.061		.	.		.			97.192		NI
53	CEETOX	no cat	No	No	1	0.986	9.055		41.765	3.931		104.48	4.017		.	.		.			104.481		NI
53	CEETOX	no cat	No	No	2	0.872	8.034		61.365	6.357	NQ	.	.		.	.		.			0	NQ	I
53	CEETOX	no cat	No	No	3	1.108	15.91		36.132	3.321		81.58	8.688		.	.		.			81.58		NI
53	CEETOX	no cat	No	No	4	0.997	8.889		9.1441	3.404		91.909	2.692		.	.		.			91.909		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
54	CEETOX	cat 2B	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.			0	NQ	I
54	CEETOX	cat 2B	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.			0	NQ	I
54	CEETOX	cat 2B	No	No	3	1.061	3.431		18.843	5.17		2.766	1.19		.	.		.			2.766		I
54	CEETOX	cat 2B	No	No	4	1.099	1.557		26.79	5.02		1.547	0.298		.	.		.			1.547		I
54	CEETOX	cat 2B	No	No	5	1.097	2.786		36.449	2.106		4.606	1.914		.	.		.			4.606		I
55	CEETOX	cat 2B	Yes	No	1	0.984	11.67		4.1935	4.007		2.845	0.31		.	.		0	0		2.845		I
55	CEETOX	cat 2B	Yes	No	2	1.074	3.69		13.347	3.511		1.227	0.257		.	.		0	0		1.227		I
55	CEETOX	cat 2B	No	No	3	1.117	7.674		70.816	2.256	NQ	.	.		.	.		.	.		0	NQ	I
55	CEETOX	cat 2B	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.			0	NQ	I
55	CEETOX	cat 2B	Yes	No	5	1.11	5.842		53.747	6.399		1.77	0.649		.	.		0.3789	0.4087		1.462		I
56	CEETOX	cat 2B	Yes	No	1	1.026	4.323		2.3871	0.22		8.818	5.993		.	.		0.341	0.1711		8.477		I
56	CEETOX	cat 2B	Yes	No	2	1.281	2.862		35.038	5.007		8.639	6.421		.	.		0.1821	0.1371		8.457		I
56	CEETOX	cat 2B	Yes	No	3	1.006	1.79		41.106	8.615		7.751	4.657		.	.		0.2319	0.1745		7.519		I
57	CEETOX	cat 2B	No	No	1	1.022	1.825		49.764	7.681		0.913	0.361		.	.		.			0.913		I
57	CEETOX	cat 2B	No	No	2	1.011	6.903		31.312	5.994		1.45	0.151		.	.		.			1.45		I
57	CEETOX	cat 2B	No	No	3	0.808	6.022		3.1753	0.179		2.536	0.446		.	.		.			2.536		I
58	CEETOX	cat 2B	Yes	No	1	1.336	6.791		37.862	2.415		1.085	0.404		.	.		0.3368	0.3198		0.761		I
58	CEETOX	cat 2B	No	No	2	1.336	6.791		37.862	2.415	NQ	.	.		.	.		.	0.3198		0	NQ	I
58	CEETOX	cat 2B	Yes	No	3	1.114	3.349		38.602	7.556		2.994	0.604		.	.		0.3243	0.3218		2.724		I
58	CEETOX	cat 2B	Yes	No	4	1.066	10.35		39.425	8.798		1.938	0.098		.	.		0.0677	0.1173		1.938		I
59	CEETOX	cat 2B	Yes	No	1	1.026	4.323		2.3871	0.22		26.437	3.041		.	.		0.0379	0.0409		26.437		I
59	CEETOX	cat 2B	Yes	No	2	1.281	2.862		35.038	5.007		22.17	5.285		.	.		0	0		22.17		I
59	CEETOX	cat 2B	Yes	No	3	1.006	1.79		41.106	8.615		26.681	6.426		.	.		0	0		26.681		I
60	CEETOX	cat 2B	No	No	1	1.066	10.35		39.425	8.798		2.22	0.151		.	.		.			2.22		I
60	CEETOX	cat 2B	No	No	2	0.953	8.886		46.459	4.808		1.853	0.429		.	.		.			1.853		I
60	CEETOX	cat 2B	No	No	3	0.936	3.064		30.876	8.046		1.959	0.269		.	.		.			1.959		I
61	CEETOX	cat 2B	No	No	1	1.109	7.989		44.805	3.75		10.149	0.636		.	.		.			10.149		I
61	CEETOX	cat 2B	No	No	2	1.219	9.931		24.606	3.854		7.752	3.093		.	.		.			7.752		I
61	CEETOX	cat 2B	No	No	3	0.814	4.296		4.0131	1.662		8.661	0.307		.	.		.			8.661		I
62	CEETOX	cat 2B	No	No	2	1.336	6.791		37.862	2.415		93.875	3.449		.	.		.			93.875		NI
62	CEETOX	cat 2B	No	No	3	0.971	8.015		29.607	1.188		98.472	10.74		.	.		.			98.472		NI
62	CEETOX	cat 2B	No	No	4	1.114	3.349		38.602	7.556		97.86	11.12		.	.		.			97.86		NI
63	CEETOX	cat 2B	No	No	2	1.336	6.791		37.862	2.415		77.682	8.06		.	.		.			77.682		NI
63	CEETOX	cat 2B	No	No	3	0.971	8.015		29.607	1.188		78.276	5.153		.	.		.			78.276		NI
63	CEETOX	cat 2B	No	No	4	1.114	3.349		38.602	7.556		94.477	3.552		.	.		.			94.477		NI
64	CEETOX	cat 2B	No	No	2	1.026	4.323		2.3871	0.22		69.763	17.98		.	.		.			69.763		NI
64	CEETOX	cat 2B	No	No	3	1.354	3.187		31.068	12.67		48.898	33.97	NQ	.	.		.			0	NQ	I
64	CEETOX	cat 2B	No	No	4	1.017	7.024		26.217	4.983		76.307	5.501		.	.		.			76.307		NI
64	CEETOX	cat 2B	No	No	5	0.971	8.015		29.607	1.188		86.656	4.464		.	.		.			86.656		NI
65	CEETOX	cat 2B	No	No	1	1.336	6.791		37.862	2.415		62.113	16.81		.	.		.			62.113		NI
65	CEETOX	cat 2B	No	No	2	1.336	6.791		37.862	2.415	NQ	.	.		.	.		.			0	NQ	I
65	CEETOX	cat 2B	No	No	3	1.114	3.349		38.602	7.556		86.499	12.22		.	.		.			86.499		NI
65	CEETOX	cat 2B	No	No	4	0.936	3.064		30.876	8.046		79.558	11.58		.	.		.			79.558		NI
66	CEETOX	cat 2B	No	No	2	1.336	6.791		37.862	2.415		4.516	2.293		.	.		.			4.516		I
66	CEETOX	cat 2B	No	No	3	0.971	8.015		29.607	1.188		2.851	0.665		.	.		.			2.851		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
66	CEETOX	cat 2B	No	No	4	1.114	3.349		38.602	7.556		46.535	10.61		.	.		.			46.535		I
67	CEETOX	cat 2A	No	No	1	1.126	12.55		38.801	3.402		9.164	0.683		.	.		.			9.164		I
67	CEETOX	cat 2A	No	No	2	1.168	7.79		34.309	1.912		22.092	6.167		.	.		.			22.092		I
67	CEETOX	cat 2A	No	No	3	1.033	4.978		17.027	15.53		6.02	0.561		.	.		.			6.02		I
68	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	1	1.126	12.55		38.801	3.402		1.554	0.118		.	.		.			1.554		I
68	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	2	1.168	7.79		34.309	1.912		1.028	0.065		.	.		.			1.028		I
68	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	3	1.033	4.978		17.027	15.53		1.323	0.267		.	.		.			1.323		I
69	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	1	1.109	7.989		44.805	3.75		0.601	0.282		.	.		.			0.601		I
69	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	2	1.219	9.931		24.606	3.854		0.834	0.109		.	.		.			0.834		I
69	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	3	0.814	4.296		4.0131	1.662		1.188	0.094		.	.		.			1.188		I
70	CEETOX	cat 2A	No	No	1	1.022	1.825		49.764	7.681		1.354	0.246		.	.		.			1.354		I
70	CEETOX	cat 2A	No	No	2	1.011	6.903		31.312	5.994		1.796	0.318		.	.		.			1.796		I
70	CEETOX	cat 2A	No	No	3	0.808	6.022		3.1753	0.179		2.103	0.554		.	.		.			2.103		I
71	CEETOX	cat 2A (ICCVAM:cat2B)	Yes	No	1	0.984	11.67		4.1935	4.007		1.405	0.485		.	.		0	0		1.405		I
71	CEETOX	cat 2A (ICCVAM:cat2B)	Yes	No	2	1.074	3.69		13.347	3.511		1.04	0.047		.	.		0	0		1.04		I
71	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	3	1.117	7.674		70.816	2.256	NQ	.	.		.	.		.	.		0	NQ	I
71	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.	0.4334		0	NQ	I
71	CEETOX	cat 2A (ICCVAM:cat2B)	Yes	No	5	1.11	5.842		53.747	6.399		1.526	0.197		.	.		0.4601	0.4334		1.088		I
72	CEETOX	cat 2A (ICCVAM:cat2B)	Yes	No	1	1.026	4.323		2.3871	0.22		1.315	0.439		.	.		0.4114	0.528		0.926		I
72	CEETOX	cat 2A (ICCVAM:cat2B)	Yes	No	2	1.281	2.862		35.038	5.007		1.158	0.185		.	.		0.2689	0.3895		0.937		I
72	CEETOX	cat 2A (ICCVAM:cat2B)	Yes	No	3	1.006	1.79		41.106	8.615		1.093	0.057		.	.		0.3423	0.4958		0.812		I
73	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	1	1.126	12.55		38.801	3.402		34.611	20.98	NQ	.	.		.			0	NQ	I
73	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	2	1.168	7.79		34.309	1.912		71.2	27.38	NQ	.	.		.			0	NQ	I
73	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	3	1.033	4.978		17.027	15.53		88.315	6.26		.	.		.			88.315		NI
73	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	4	1.074	3.69		13.347	3.511		86.555	5.787		.	.		.			86.555		NI
73	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	5	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.			0	NQ	I
73	CEETOX	cat 2A	No	No	6	1.11	5.842		53.747	6.399		100.67	5.11		.	.		.			100.666		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
		(ICCVAM:cat2B)																					
74	CEETOX	cat 2A	Yes	No	1	1.066	7.842		3.9856	2.185		85.777	4.406		.	.		2.4539	0.3722		83.323		NI
74	CEETOX	cat 2A	No	No	2	1.038	3.122		66.148	3.566	NQ	.	.		.	.		.	.		0	NQ	I
74	CEETOX	cat 2A	No	No	3	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.	0.3867		0	NQ	I
74	CEETOX	cat 2A	Yes	No	4	1.11	5.842		53.747	6.399		95.372	6.375		.	.		3.1504	0.3867		92.222		NI
74	CEETOX	cat 2A	Yes	No	5	1.11	5.842		53.747	6.399		78.506	6.095		.	.		2.0947	0.3867		76.412		NI
75	CEETOX	cat 2A	No	No	1	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.			0	NQ	I
75	CEETOX	cat 2A	No	No	2	0.931	4.593		85.407	7.847		1.273	0.125		.	.		.			1.273		I
75	CEETOX	cat 2A	No	No	3	1.099	1.557		26.79	5.02		1.305	0.026		.	.		.			1.305		I
75	CEETOX	cat 2A	No	No	4	1.097	2.786		36.449	2.106		1.201	0.173		.	.		.			1.201		I
76	CEETOX	cat 2A	No	No	1	1.026	4.323		2.3871	0.22		53.394	5.53		.	.		.			53.394		NI
76	CEETOX	cat 2A	No	No	2	1.354	3.187		31.068	12.67		77.86	4.815		.	.		.			77.86		NI
76	CEETOX	cat 2A	No	No	3	1.017	7.024		26.217	4.983		66.262	7.789		.	.		.			66.262		NI
77	CEETOX	cat 2A	No	No	1	1.026	4.323		2.3871	0.22		85.596	9.926		.	.		.			85.596		NI
77	CEETOX	cat 2A	No	No	2	1.354	3.187		31.068	12.67		79.313	15.68		.	.		.			79.313		NI
77	CEETOX	cat 2A	No	No	3	1.017	7.024		26.217	4.983		95.838	0.768		.	.		.			95.838		NI
78	CEETOX	cat 2A	No	No	1	1.026	4.323		2.3871	0.22		86.457	6.712		.	.		.			86.457		NI
78	CEETOX	cat 2A	No	No	2	1.354	3.187		31.068	12.67		85.31	6.583		.	.		.			85.31		NI
78	CEETOX	cat 2A	No	No	3	1.017	7.024		26.217	4.983		75.881	7.205		.	.		.			75.881		NI
79	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	1	1.074	3.69		13.347	3.511		35.973	3.711		.	.		.			35.973		I
79	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	2	1.026	4.323		2.3871	0.22		32.754	4.192		.	.		.			32.754		I
79	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	3	1.281	2.862		35.038	5.007		48.686	10.77		.	.		.			48.686		I
79	CEETOX	cat 2A (ICCVAM:cat2B)	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.	.		0	NQ	I
80	CEETOX	cat 1	Yes	No	1	1.022	1.825		49.764	7.681		44.055	2.365		.	.		55.701	1.1774		0		I
80	CEETOX	cat 1	Yes	No	2	1.011	6.903		31.312	5.994		57.663	6.246		.	.		56.279	1.1896		0		I
80	CEETOX	cat 1	Yes	No	3	0.808	6.022		3.1753	0.179		50.825	2.677		.	.		70.412	1.4884		0		I
81	CEETOX	cat 1	Yes	No	1	1.126	12.55		38.801	3.402		0.947	0.093		.	.		0.4885	0.2279		0.459		I
81	CEETOX	cat 1	Yes	No	2	1.168	7.79		34.309	1.912		0.97	0.108		.	.		0.3282	0.2197		0.642		I
81	CEETOX	cat 1	Yes	No	3	1.033	4.978		17.027	15.53		0.823	0.256		.	.		0.3712	0.2485		0.457		I
82	CEETOX	cat 1	No	No	1	0.955	1.687		23.277	7.239		1.169	0.151		.	.		.			1.169		I
82	CEETOX	cat 1	No	No	2	1.117	6.85		19.866	5.959		1.015	0.362		.	.		.			1.015		I
82	CEETOX	cat 1	No	No	3	1.108	15.91		36.132	3.321		0.482	0.209		.	.		.			0.482		I
83	CEETOX	cat 1	No	No	1	1.109	7.989		44.805	3.75		0.857	0.119		.	.		.			0.857		I
83	CEETOX	cat 1	No	No	2	1.219	9.931		24.606	3.854		0.725	0.247		.	.		.			0.725		I
83	CEETOX	cat 1	No	No	3	0.814	4.296		4.0131	1.662		1.126	0.256		.	.		.			1.126		I
84	CEETOX	cat 1	No	No	1	1.114	3.349		38.602	7.556		1.272	0.144		.	.		.			1.272		I
84	CEETOX	cat 1	No	No	2	1.114	3.349		38.602	7.556	NQ	.	.		.	.		.			0	NQ	I
84	CEETOX	cat 1	No	No	3	0.955	1.687		23.277	7.239		2.129	0.673		.	.		.			2.129		I
84	CEETOX	cat 1	No	No	4	0.986	9.055		41.765	3.931		1.167	0.128		.	.		.			1.167		I
85	CEETOX	cat 1	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.			0	NQ	I
85	CEETOX	cat 1	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.			0	NQ	I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
85	CEETOX	cat 1	No	No	3	1.061	3.431		18.843	5.17		0.597	0.314		.	.		.			0.597		I
85	CEETOX	cat 1	No	No	4	1.099	1.557		26.79	5.02		0.85	0.205		.	.		.			0.85		I
85	CEETOX	cat 1	No	No	5	1.097	2.786		36.449	2.106		0.623	0.121		.	.		.			0.623		I
86	CEETOX	cat 1	No	No	1	0.955	1.687		23.277	7.239		2.862	3.128		.	.		.			2.862		I
86	CEETOX	cat 1	No	No	2	1.117	6.85		19.866	5.959		1.403	0.416		.	.		.			1.403		I
86	CEETOX	cat 1	No	No	3	1.108	15.91		36.132	3.321		3.928	3.049		.	.		.			3.928		I
87	CEETOX	cat 1	No	No	1	1.022	1.825		49.764	7.681		1.272	0.482		.	.		.			1.272		I
87	CEETOX	cat 1	No	No	2	1.011	6.903		31.312	5.994		1.154	0.446		.	.		.			1.154		I
87	CEETOX	cat 1	No	No	3	0.808	6.022		3.1753	0.179		2.124	1.553		.	.		.			2.124		I
88	CEETOX	cat 1	Yes	No	1	0.955	1.687		23.277	7.239		2.111	0.332		.	.		0.157	0.1982		1.954		I
88	CEETOX	cat 1	Yes	No	2	1.117	6.85		19.866	5.959		1.866	0.052		.	.		0.3134	0.1695		1.552		I
88	CEETOX	cat 1	No	No	3	1.117	6.85		19.866	5.959	NQ	.	.		.	.		.	0.1695		0	NQ	I
88	CEETOX	cat 1	Yes	No	4	1.108	15.91		36.132	3.321		1.67	0.326		.	.		2.0767	0.1709		0		I
89	CEETOX	cat 1	No	No	1	1.022	1.825		49.764	7.681		1.99	0.057		.	.		.			1.99		I
89	CEETOX	cat 1	No	No	2	1.011	6.903		31.312	5.994		1.813	0.198		.	.		.			1.813		I
89	CEETOX	cat 1	No	No	3	0.808	6.022		3.1753	0.179		2.474	0.373		.	.		.			2.474		I
90	CEETOX	cat 1	No	No	1	0.984	11.67		4.1935	4.007		2.387	0.414		.	.		.			2.387		I
90	CEETOX	cat 1	No	No	2	1.038	3.122		66.148	3.566	NQ	.	.		.	.		.			0	NQ	I
90	CEETOX	cat 1	No	No	3	1.038	3.122		66.148	3.566		2.111	0.44		.	.		.			2.111		I
90	CEETOX	cat 1	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.			0	NQ	I
90	CEETOX	cat 1	No	No	5	1.11	5.842		53.747	6.399		3.914	1.001		.	.		.			3.914		I
91	CEETOX	cat 1	Yes	No	1	0.984	11.67		4.1935	4.007		14.477	2.874		.	.		0	0		14.477		I
91	CEETOX	cat 1	Yes	No	2	1.074	3.69		13.347	3.511		4.642	4.533		.	.		0	0		4.642		I
91	CEETOX	cat 1	No	No	3	1.117	7.674		70.816	2.256	NQ	.	.		.	.		.	.		0	NQ	I
91	CEETOX	cat 1	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.	0.3431		0	NQ	I
91	CEETOX	cat 1	Yes	No	5	1.11	5.842		53.747	6.399		16.06	6.581		.	.		0.3951	0.3431		15.719		I
92	CEETOX	cat 1	Yes	No	1	0.986	9.055		41.765	3.931		11.684	2.476		.	.		0.6087	0.4314		11.075		I
92	CEETOX	cat 1	No	No	2	0.872	8.034		61.365	6.357	NQ	.	.		.	.		.	.		0	NQ	I
92	CEETOX	cat 1	Yes	No	3	1.108	15.91		36.132	3.321		9.27	0.847		.	.		2.468	0.384		6.802		I
92	CEETOX	cat 1	Yes	No	4	0.997	8.889		9.1441	3.404		5.567	2.101		.	.		0.5015	0.4265		5.065		I
93	CEETOX	cat 1	No	No	1	1.061	5.816		83.276	0.966	NQ	.	.		.	.		.	.		0	NQ	I
93	CEETOX	cat 1	No	No	2	0.931	4.593		85.407	7.847	NQ	.	.		.	.		.	.		0	NQ	I
93	CEETOX	cat 1	No	No	3	1.061	3.431		18.843	5.17		38.111	13.42		.	.		.			38.111		I
93	CEETOX	cat 1	No	No	4	1.099	1.557		26.79	5.02		65.473	5.144		.	.		.			65.473		NI
93	CEETOX	cat 1	No	No	5	1.097	2.786		36.449	2.106		55.221	13.45		.	.		.			55.221		NI
94	CEETOX	cat 1	No	No	1	0.984	11.67		4.1935	4.007		2.337	0.346		.	.		.			2.337		I
94	CEETOX	cat 1	No	No	2	1.038	3.122		66.148	3.566	NQ	.	.		.	.		.			0	NQ	I
94	CEETOX	cat 1	No	No	3	1.038	3.122		66.148	3.566		8.865	2.352		.	.		.			8.865		I
94	CEETOX	cat 1	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.			0	NQ	I
94	CEETOX	cat 1	No	No	5	1.11	5.842		53.747	6.399		26.811	6.292		.	.		.			26.811		I
95	CEETOX	cat 1	No	No	1	1.109	7.989		44.805	3.75		1.068	0.452		.	.		.			1.068		I
95	CEETOX	cat 1	No	No	2	1.219	9.931		24.606	3.854		1.189	0.226		.	.		.			1.189		I
95	CEETOX	cat 1	No	No	3	0.814	4.296		4.0131	1.662		1.454	0.912		.	.		.			1.454		I
96	CEETOX	cat 1	No	No	1	1.109	7.989		44.805	3.75		41.708	7.646		.	.		.			41.708		I
96	CEETOX	cat 1	No	No	2	1.219	9.931		24.606	3.854		45.584	9.022		.	.		.			45.584		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
96	CEETOX	cat 1	No	No	3	0.814	4.296		4.0131	1.662		50.491	6.507		.	.		.			50.491		NI
97	CEETOX	cat 1	No	No	1	1.168	7.79		34.309	1.912		61.781	1.522		.	.		.			61.781		NI
97	CEETOX	cat 1	No	No	2	1.033	4.978		17.027	15.53		59.555	4.387		.	.		.			59.555		NI
97	CEETOX	cat 1	No	No	3	1.066	7.842		3.9856	2.185		65.192	1.71		.	.		.			65.192		NI
98	CEETOX	cat 1	No	No	1	1.102	4.826		52.117	3.403	NQ	.	.		.	.		.	.		0	NQ	I
98	CEETOX	cat 1	Yes	Yes	2	0.99	7.261		33.12	5.324		92.124	3.229		6.2773	1.49		10.821	2.2536		75.025		NI
98	CEETOX	cat 1	No	No	3	0.99	7.261		33.12	5.324	NQ	.	.		.	1.49		.	2.2536		0	NQ	I
98	CEETOX	cat 1	Yes	Yes	4	0.955	1.687		23.277	7.239		91.729	8.983		5.6535	1.3		11.639	2.3365		74.437		NI
98	CEETOX	cat 1	Yes	Yes	5	1.108	15.91		36.132	3.321		74.432	7.182		21.866	7.28		11.603	2.0151		40.963		I
99	CEETOX	cat 1	No	No	1	1.074	3.69		13.347	3.511		1.133	0.117		.	.		.			1.133		I
99	CEETOX	cat 1	No	No	2	1.026	4.323		2.3871	0.22		1.543	0.296		.	.		.			1.543		I
99	CEETOX	cat 1	No	No	3	1.281	2.862		35.038	5.007		1.665	0.158		.	.		.			1.665		I
99	CEETOX	cat 1	No	No	4	1.11	5.842		53.747	6.399	NQ	.	.		.	.		.			0	NQ	I
100	CEETOX	cat 1	No	No	1	0.936	3.064		30.876	8.046		2.422	0.51		.	.		.			2.422		I
100	CEETOX	cat 1	No	No	2	0.99	7.261		33.12	5.324		1.75	0.127		.	.		.			1.75		I
100	CEETOX	cat 1	No	No	3	0.955	1.687		23.277	7.239		2.094	0.659		.	.		.			2.094		I
101	CEETOX	cat 1	No	No	1	1.117	6.85		19.866	5.959		71.881	7.426		.	.		.			71.881		NI
101	CEETOX	cat 1	No	No	2	0.986	9.055		41.765	3.931		83.006	2.132		.	.		.			83.006		NI
101	CEETOX	cat 1	No	No	3	1.108	15.91		36.132	3.321		63.552	3.025		.	.		.			63.552		NI
102	CEETOX	cat 1	No	No	1	0.955	1.687		23.277	7.239		104.14	14.14		.	.		.			104.135		NI
102	CEETOX	cat 1	No	No	2	1.117	6.85		19.866	5.959		86.657	7.298		.	.		.			86.657		NI
102	CEETOX	cat 1	No	No	3	1.108	15.91		36.132	3.321		64.244	14.38		.	.		.			64.244		NI
103	CEETOX	cat 1	Yes	No	1	1.026	4.323		2.3871	0.22		1.332	0.149		.	.		0.2328	0.3353		1.25		I
103	CEETOX	cat 1	Yes	No	2	1.354	3.187		31.068	12.67		0.493	0.497		.	.		0	0		0.493		I
103	CEETOX	cat 1	Yes	No	3	1.017	7.024		26.217	4.983		0.95	0		.	.		13.387	0.5407		0		I
104	CEETOX	cat 1	Yes	No	1	1.026	4.323		2.3871	0.22		80.741	2.631		.	.		0.2815	0.2625		80.464		NI
104	CEETOX	cat 1	Yes	No	2	1.354	3.187		31.068	12.67		85.716	5.336		.	.		0.156	0.154		85.593		NI
104	CEETOX	cat 1	Yes	No	3	1.017	7.024		26.217	4.983		77.208	6.907		.	.		12.633	0		64.575		NI
105	CEETOX	cat 1	No	Yes	1	1.026	4.323		2.3871	0.22		1.185	0.442		0.6496	0.1		.			0.606		I
105	CEETOX	cat 1	No	Yes	2	1.354	3.187		31.068	12.67		1.121	0.238		0.4064	0.07		.			0.714		I
105	CEETOX	cat 1	No	Yes	3	1.017	7.024		26.217	4.983		0	0		0	0		.			0		I
1	L'OREAL	no cat	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.	0.1764		0	NQ	I
1	L'OREAL	no cat	Yes	No	2	1.215	6.134		65.417	5.374		1.475	0.214		.	.		0.1775	0.1764		1.315		I
1	L'OREAL	no cat	Yes	No	3	1.207	1.747		16.571	4.591		19.737	8.397		.	.		0.109	0.119		19.662		I
1	L'OREAL	no cat	Yes	No	4	0.954	5.639		25.157	6.823		8.134	4.728		.	.		0.0809	0.1154		8.125		I
2	L'OREAL	no cat	Yes	No	1	1.167	5.4		28.91	0.885		1.935	0.041		.	.		0	0		1.935		I
2	L'OREAL	no cat	Yes	No	2	1.171	5.113		44.435	13.63		2.021	0.247		.	.		0	0		2.021		I
2	L'OREAL	no cat	Yes	No	3	1.141	5.08		15.556	0.808		3.442	2.589		.	.		0	0		3.442		I
3	L'OREAL	no cat	No	No	1	1.167	5.4		28.91	0.885		1.164	0.112		.	.		.			1.164		I
3	L'OREAL	no cat	No	No	2	1.141	5.08		15.556	0.808		0.811	0.244		.	.		.			0.811		I
3	L'OREAL	no cat	No	No	3	1.158	6.507		37.465	0.834		0.831	0.094		.	.		.			0.831		I
4	L'OREAL	no cat	Yes	No	1	0.954	5.639		25.157	6.823		66.379	10.18		.	.		30.612	6.7693		35.767		I
4	L'OREAL	no cat	Yes	No	2	1.041	2.734		5.2453	0.719		64.189	7.059		.	.		28.101	6.2066		36.088		I
4	L'OREAL	no cat	Yes	No	3	1.112	4.848		7.1871	3.378		64.562	0.261		.	.		26.274	5.8127		38.288		I
5	L'OREAL	no cat	Yes	No	1	1.084	8.313		30.98	5.154		8.158	4.449		.	.		3.5418	2.571		4.705		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
5	L'OREAL	no cat	Yes	No	2	1.045	4.151		33.69	6.079		3.057	0.486		.	.		3.8017	2.6682		0		I
5	L'OREAL	no cat	Yes	No	3	1.171	5.113		44.435	13.63		7.728	3.467		.	.		3.4443	2.3804		4.284		I
6	L'OREAL	no cat	No	No	1	1.167	5.4		28.91	0.885		3.385	1.111		.	.		.			3.385		I
6	L'OREAL	no cat	No	No	2	1.141	5.08		15.556	0.808		14.357	2.922		.	.		.			14.357		I
6	L'OREAL	no cat	No	No	3	1.158	6.507		37.465	0.834		11.238	3.749		.	.		.			11.238		I
7	L'OREAL	no cat	Yes	No	1	1.167	5.4		28.91	0.885		4.71	3.057		.	.		0	0		4.71		I
7	L'OREAL	no cat	Yes	No	2	1.141	5.08		15.556	0.808		7.709	4.709		.	.		0	0		7.709		I
7	L'OREAL	no cat	Yes	No	3	1.011	5.403		48.7	2.057		0.852	0.052		.	.		0.366	0.2047		0.486		I
8	L'OREAL	no cat	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.			0	NQ	I
8	L'OREAL	no cat	No	No	2	1.215	6.134		65.417	5.374		23.297	3.211		.	.		.			23.297		I
8	L'OREAL	no cat	No	No	3	0.954	5.639		25.157	6.823		29.309	4.875		.	.		.			29.309		I
8	L'OREAL	no cat	No	No	4	1.041	2.734		5.2453	0.719		15.629	2.902		.	.		.			15.629		I
9	L'OREAL	no cat	Yes	No	1	1.084	8.313		30.98	5.154		30.968	4.386		.	.		0.0738	0.1278		30.946		I
9	L'OREAL	no cat	Yes	No	2	1.045	4.151		33.69	6.079		29.381	4.01		.	.		0.1484	0.1812		29.233		I
9	L'OREAL	no cat	Yes	No	3	1.171	5.113		44.435	13.63		19.755	4.426		.	.		0.185	0.1617		19.57		I
10	L'OREAL	no cat	No	No	1	1.158	1.866		26.395	0.521		1.164	0.299		.	.		.			1.164		I
10	L'OREAL	no cat	No	No	2	1.189	2.082		10.92	1.838		0.892	0.462		.	.		.			0.892		I
10	L'OREAL	no cat	No	No	3	1.118	0.919		31.095	4.839		1.364	0.857		.	.		.			1.364		I
11	L'OREAL	no cat	Yes	No	1	1.084	8.313		30.98	5.154		74.86	4.774		.	.		0.0277	0.0479		74.86		NI
11	L'OREAL	no cat	Yes	No	2	1.045	4.151		33.69	6.079		69.28	9.957		.	.		0.0707	0.1225		69.28		NI
11	L'OREAL	no cat	Yes	No	3	1.171	5.113		44.435	13.63		49.103	3.64		.	.		0.0807	0.1397		49.103		I
12	L'OREAL	no cat	No	No	1	1.166	6.115		0.8351	0.175		83.587	2.695		.	.		.			83.587		NI
12	L'OREAL	no cat	No	No	2	1.403	1.696		30.786	9.616		96.308	7.132		.	.		.			96.308		NI
12	L'OREAL	no cat	No	No	3	1.161	3.337		40.266	4.053		93.549	7.368		.	.		.			93.549		NI
13	L'OREAL	no cat	No	No	1	1.144	6.145		1.6528	0.635		97.021	6.737		.	.		.			97.021		NI
13	L'OREAL	no cat	No	No	2	1.071	2.796		33.29	7.118		96.48	7.74		.	.		.			96.48		NI
13	L'OREAL	no cat	No	No	3	1.161	3.337		40.266	4.053		85.999	3.523		.	.		.			85.999		NI
14	L'OREAL	no cat	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.			0	NQ	I
14	L'OREAL	no cat	No	No	2	1.215	6.134		65.417	5.374		87.512	1.371		.	.		.			87.512		NI
14	L'OREAL	no cat	No	No	3	1.22	1.963		28.513	4.792		89.487	2.908		.	.		.			89.487		NI
14	L'OREAL	no cat	No	No	4	0.954	5.639		25.157	6.823		99.569	5.871		.	.		.			99.569		NI
15	L'OREAL	no cat	No	No	1	1.166	6.115		0.8351	0.175		94.101	5.025		.	.		.			94.101		NI
15	L'OREAL	no cat	No	No	2	1.071	2.796		33.29	7.118		96.315	8.799		.	.		.			96.315		NI
15	L'OREAL	no cat	No	No	3	1.161	3.337		40.266	4.053		89.673	1.305		.	.		.			89.673		NI
16	L'OREAL	no cat	Yes	No	1	1.084	8.313		30.98	5.154		95.291	0.3		.	.		0.0343	0.0595		95.291		NI
16	L'OREAL	no cat	Yes	No	2	1.045	4.151		33.69	6.079		103.48	3.869		.	.		0.0729	0.1262		103.479		NI
16	L'OREAL	no cat	Yes	No	3	1.171	5.113		44.435	13.63		97.837	5.769		.	.		0.0949	0.1643		97.822		NI
17	L'OREAL	no cat	No	No	1	1.041	2.734		5.2453	0.719		86.429	5.045		.	.		.			86.429		NI
17	L'OREAL	no cat	No	No	2	1.118	0.451		21.723	7.774		90.337	8.516		.	.		.			90.337		NI
17	L'OREAL	no cat	No	No	3	1.158	1.866		26.395	0.521		79.685	2.503		.	.		.			79.685		NI
18	L'OREAL	no cat	No	No	1	1.166	6.115		0.8351	0.175		92.052	4.652		.	.		.			92.052		NI
18	L'OREAL	no cat	No	No	2	1.071	2.796		33.29	7.118		103.48	1.503		.	.		.			103.483		NI
18	L'OREAL	no cat	No	No	3	1.161	3.337		40.266	4.053		93.9	4.43		.	.		.			93.9		NI
19	L'OREAL	no cat	No	No	1	1.166	6.115		0.8351	0.175		98.734	6.043		.	.		.			98.734		NI
19	L'OREAL	no cat	No	No	2	1.403	1.696		30.786	9.616		107.25	3.553		.	.		.			107.249		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
19	L'OREAL	no cat	No	No	3	1.161	3.337		40.266	4.053		94.252	5.002		.	.		.			94.252		NI
20	L'OREAL	no cat	Yes	No	1	1.166	6.115		0.8351	0.175		42.034	17.14		.	.		62.469	9.0062		0		I
20	L'OREAL	no cat	Yes	No	2	1.403	1.696		30.786	9.616		39.73	7.303		.	.		51.865	7.4832		0		I
20	L'OREAL	no cat	Yes	No	3	1.117	3.017		25.194	7.837		36.964	8.234		.	.		64.616	9.3985		0		I
21	L'OREAL	no cat	Yes	No	1	1.158	1.866		26.395	0.521		66.573	5.018		.	.		0	0		66.573		NI
21	L'OREAL	no cat	Yes	No	2	1.189	2.082		10.92	1.838		63.627	1.167		.	.		0	0		63.627		NI
21	L'OREAL	no cat	Yes	No	3	1.119	2.182		18.851	9.32		68.993	2.341		.	.		0	0		68.993		NI
22	L'OREAL	no cat	No	No	1	1.189	2.082		10.92	1.838		1.122	0.795		.	.		.			1.122		I
22	L'OREAL	no cat	No	No	2	1.169	2.795		24.645	3.859		1.078	0.041		.	.		.			1.078		I
22	L'OREAL	no cat	No	No	3	1.151	3.882		20.444	5.887		1.053	0.093		.	.		.			1.053		I
23	L'OREAL	no cat	Yes	No	1	1.184	2.242		14.222	1.597		31.458	0.801		.	.		1.544	1.481		29.914		I
23	L'OREAL	no cat	Yes	No	2	1.162	3.08		44.054	2.436		30.198	4.072		.	.		1.5456	1.5087		28.653		I
23	L'OREAL	no cat	Yes	No	3	1.137	0.244		13.707	2.66		2.305	0.295		.	.		1.8358	1.5429		0.471		I
24	L'OREAL	no cat	Yes	No	1	1.118	0.919		31.095	4.839		0.834	0.503		.	.		0	0		0.834		I
24	L'OREAL	no cat	Yes	No	2	1.214	2.527		46.43	0.591		0.376	0.029		.	.		0	0		0.376		I
24	L'OREAL	no cat	Yes	No	3	1.362	3.038		40.51	0.668		0.549	0.122		.	.		0	0		0.549		I
25	L'OREAL	no cat	Yes	No	1	1.143	5.763		29.636	4.03		99.551	3.464		.	.		0	0		99.551		NI
25	L'OREAL	no cat	Yes	No	2	1.403	1.696		30.786	9.616		94.438	5.306		.	.		0	0		94.438		NI
25	L'OREAL	no cat	Yes	No	3	1.122	1.609		27.629	3.813		68.744	3.113		.	.		0	0		68.744		NI
26	L'OREAL	no cat	No	No	1	1.143	5.763		29.636	4.03		2.301	0.232		.	.		.			2.301		I
26	L'OREAL	no cat	No	No	2	1.117	3.017		25.194	7.837		3.034	0.721		.	.		.			3.034		I
26	L'OREAL	no cat	No	No	3	1.122	1.609		27.629	3.813		2.465	0.25		.	.		.			2.465		I
28	L'OREAL	no cat	No	No	1	1.167	5.4		28.91	0.885		94.743	7.359		.	.		.			94.743		NI
28	L'OREAL	no cat	No	No	2	1.141	5.08		15.556	0.808		90.959	4.122		.	.		.			90.959		NI
28	L'OREAL	no cat	No	No	3	1.158	6.507		37.465	0.834		88.244	1		.	.		.			88.244		NI
29	L'OREAL	no cat	No	No	1	1.166	6.115		0.8351	0.175		95.089	3.501		.	.		.			95.089		NI
29	L'OREAL	no cat	No	No	2	1.117	3.017		25.194	7.837		87.727	6.059		.	.		.			87.727		NI
29	L'OREAL	no cat	No	No	3	1.122	1.609		27.629	3.813		90.097	6.403		.	.		.			90.097		NI
30	L'OREAL	no cat	No	No	1	1.184	2.242		14.222	1.597		66.935	6.926		.	.		.			66.935		NI
30	L'OREAL	no cat	No	No	2	1.362	3.038		40.51	0.668		79.054	2.62		.	.		.			79.054		NI
30	L'OREAL	no cat	No	No	3	1.162	3.08		44.054	2.436		79.691	2.811		.	.		.			79.691		NI
31	L'OREAL	no cat	No	No	1	1.184	2.242		14.222	1.597		97.316	1.203		.	.		.			97.316		NI
31	L'OREAL	no cat	No	No	2	1.214	2.527		46.43	0.591		92.574	5.721		.	.		.			92.574		NI
31	L'OREAL	no cat	No	No	3	1.362	3.038		40.51	0.668		84.829	3.375		.	.		.			84.829		NI
32	L'OREAL	no cat	Yes	Yes	1	1.041	2.734		5.2453	0.719		5.727	0.418		1.1592	0.29		1.5371	0.8863		3.031		I
32	L'OREAL	no cat	Yes	Yes	2	1.112	4.848		7.1871	3.378		4.092	0.839		0.5473	0.18		1.375	0.83		2.17		I
32	L'OREAL	no cat	Yes	Yes	3	1.118	0.451		21.723	7.774		4.088	1.179		0.4412	0.07		1.4309	0.8322		2.216		I
33	L'OREAL	no cat	Yes	Yes	1	1.189	2.082		10.92	1.838		89.051	4.561		0.5427	0.18		0.0388	0.0672		88.508		NI
33	L'OREAL	no cat	Yes	Yes	2	1.118	0.919		31.095	4.839		92.322	4.602		0.255	0.15		0.0383	0.0663		92.067		NI
33	L'OREAL	no cat	Yes	Yes	3	1.119	2.182		18.851	9.32		104.93	8.24		0.554	0.06		0.0357	0.0619		104.371		NI
34	L'OREAL	no cat	Yes	Yes	1	1.189	2.082		10.92	1.838		66.769	5.409		3.4945	0.25		6.2317	0.3237		57.043		NI
34	L'OREAL	no cat	Yes	Yes	2	1.118	0.919		31.095	4.839		65.19	4.432		3.7771	0.7		6.6178	0.3442		54.796		NI
34	L'OREAL	no cat	Yes	Yes	3	1.119	2.182		18.851	9.32		77.936	15.22		5.8184	0.96		6.5973	0.3383		65.52		NI
35	L'OREAL	no cat	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.	1.5527		0	NQ	I
35	L'OREAL	no cat	Yes	No	2	1.215	6.134		65.417	5.374		85.967	5.533		.	.		1.3707	1.5527		84.596		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
35	L'OREAL	no cat	Yes	No	3	1.22	1.963		28.513	4.792		90.61	6.236		.	.		1.3488	1.5372		89.262		NI
35	L'OREAL	no cat	Yes	No	4	1.041	2.734		5.2453	0.719		97.907	2.867		.	.		1.6331	1.801		96.274		NI
36	L'OREAL	no cat	No	No	1	1.084	8.313		30.98	5.154		102.43	3.705		.	.		.			102.433		NI
36	L'OREAL	no cat	No	No	2	1.045	4.151		33.69	6.079		110.47	6.695		.	.		.			110.467		NI
36	L'OREAL	no cat	No	No	3	1.22	1.963		28.513	4.792		101.13	4.186		.	.		.			101.127		NI
37	L'OREAL	no cat	No	No	1	1.169	2.795		24.645	3.859		85.737	4.406		.	.		.			85.737		NI
37	L'OREAL	no cat	No	No	2	1.151	3.882		20.444	5.887		83.006	3.173		.	.		.			83.006		NI
37	L'OREAL	no cat	No	No	3	1.214	2.527		46.43	0.591		90.159	2.26		.	.		.			90.159		NI
38	L'OREAL	no cat	No	No	1	1.166	6.115		0.8351	0.175		96.268	3.966		.	.		.			96.268		NI
38	L'OREAL	no cat	No	No	2	1.403	1.696		30.786	9.616		100.86	2.793		.	.		.			100.858		NI
38	L'OREAL	no cat	No	No	3	1.161	3.337		40.266	4.053		97.064	10.56		.	.		.			97.064		NI
39	L'OREAL	no cat	No	No	1	1.166	6.115		0.8351	0.175		97.729	3.933		.	.		.			97.729		NI
39	L'OREAL	no cat	No	No	2	1.403	1.696		30.786	9.616		94.618	8.101		.	.		.			94.618		NI
39	L'OREAL	no cat	No	No	3	1.161	3.337		40.266	4.053		94.391	0.442		.	.		.			94.391		NI
40	L'OREAL	no cat	No	No	1	1.144	6.145		1.6528	0.635		94.782	3.001		.	.		.			94.782		NI
40	L'OREAL	no cat	No	No	2	1.071	2.796		33.29	7.118		74.376	7.79		.	.		.			74.376		NI
40	L'OREAL	no cat	No	No	3	1.161	3.337		40.266	4.053		94.18	14.4		.	.		.			94.18		NI
41	L'OREAL	no cat	No	No	1	1.169	2.795		24.645	3.859		92.756	3.146		.	.		.			92.756		NI
41	L'OREAL	no cat	No	No	2	1.151	3.882		20.444	5.887		95.925	5.298		.	.		.			95.925		NI
41	L'OREAL	no cat	No	No	3	1.119	2.182		18.851	9.32		96.776	2.828		.	.		.			96.776		NI
42	L'OREAL	no cat	Yes	No	1	1.169	2.795		24.645	3.859		74.057	3.067		.	.		0	0		74.057		NI
42	L'OREAL	no cat	Yes	No	2	1.151	3.882		20.444	5.887		79.115	1.958		.	.		0.0043	0.0075		79.115		NI
42	L'OREAL	no cat	Yes	No	3	1.119	2.182		18.851	9.32		76.238	1.867		.	.		0.0581	0.0604		76.233		NI
43	L'OREAL	no cat	No	No	1	1.151	3.882		20.444	5.887		94.581	4.906		.	.		.			94.581		NI
43	L'OREAL	no cat	No	No	2	1.184	2.242		14.222	1.597		95.517	0.247		.	.		.			95.517		NI
43	L'OREAL	no cat	No	No	3	1.214	2.527		46.43	0.591		93.62	2.342		.	.		.			93.62		NI
44	L'OREAL	no cat	No	No	1	1.169	2.795		24.645	3.859		94.234	4.922		.	.		.			94.234		NI
44	L'OREAL	no cat	No	No	2	1.151	3.882		20.444	5.887		87.078	0.931		.	.		.			87.078		NI
44	L'OREAL	no cat	No	No	3	1.214	2.527		46.43	0.591		89.017	0.72		.	.		.			89.017		NI
45	L'OREAL	no cat	No	No	1	1.169	2.795		24.645	3.859		89.716	2.714		.	.		.			89.716		NI
45	L'OREAL	no cat	No	No	2	1.151	3.882		20.444	5.887		91.837	4.49		.	.		.			91.837		NI
45	L'OREAL	no cat	No	No	3	1.119	2.182		18.851	9.32		98.091	3.935		.	.		.			98.091		NI
46	L'OREAL	no cat	No	No	1	1.151	3.882		20.444	5.887		54.131	8.582		.	.		.			54.131		NI
46	L'OREAL	no cat	No	No	2	1.184	2.242		14.222	1.597		93.096	6.064		.	.		.			93.096		NI
46	L'OREAL	no cat	No	No	3	1.214	2.527		46.43	0.591		84.614	3.815		.	.		.			84.614		NI
47	L'OREAL	no cat	No	No	1	1.169	2.795		24.645	3.859		49.016	11.12		.	.		.			49.016		I
47	L'OREAL	no cat	No	No	2	1.151	3.882		20.444	5.887		43.114	7.459		.	.		.			43.114		I
47	L'OREAL	no cat	No	No	3	1.214	2.527		46.43	0.591		30.902	4.799		.	.		.			30.902		I
48	L'OREAL	no cat	No	No	1	1.184	2.242		14.222	1.597		5.735	0.542		.	.		.			5.735		I
48	L'OREAL	no cat	No	No	2	1.362	3.038		40.51	0.668		3.445	0.145		.	.		.			3.445		I
48	L'OREAL	no cat	No	No	3	1.162	3.08		44.054	2.436		3.726	0.179		.	.		.			3.726		I
49	L'OREAL	no cat	Yes	No	1	1.143	5.763		29.636	4.03		88.067	1.818		.	.		0	0		88.067		NI
49	L'OREAL	no cat	Yes	No	2	1.403	1.696		30.786	9.616		88.544	3.95		.	.		0	0		88.544		NI
49	L'OREAL	no cat	Yes	No	3	1.122	1.609		27.629	3.813		79.082	1.477		.	.		0	0		79.082		NI
50	L'OREAL	no cat	No	No	1	1.071	2.796		33.29	7.118		100.5	2.787		.	.		.			100.5		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
50	L'OREAL	no cat	No	No	2	1.117	3.017		25.194	7.837		88.364	6.963		.	.		.			88.364		NI
50	L'OREAL	no cat	No	No	3	1.122	1.609		27.629	3.813		91.708	4.236		.	.		.			91.708		NI
51	L'OREAL	no cat	No	No	1	1.143	5.763		29.636	4.03		102.08	5.554		.	.		.			102.081		NI
51	L'OREAL	no cat	No	No	2	1.117	3.017		25.194	7.837		96.865	6.475		.	.		.			96.865		NI
51	L'OREAL	no cat	No	No	3	1.122	1.609		27.629	3.813		66.853	8.417		.	.		.			66.853		NI
52	L'OREAL	no cat	No	No	1	1.143	5.763		29.636	4.03		101.97	3.353		.	.		.			101.972		NI
52	L'OREAL	no cat	No	No	2	1.117	3.017		25.194	7.837		98.199	5.073		.	.		.			98.199		NI
52	L'OREAL	no cat	No	No	3	1.122	1.609		27.629	3.813		98.939	5.337		.	.		.			98.939		NI
53	L'OREAL	no cat	No	No	1	1.143	5.763		29.636	4.03		104.08	3.779		.	.		.			104.078		NI
53	L'OREAL	no cat	No	No	2	1.117	3.017		25.194	7.837		87.664	2.052		.	.		.			87.664		NI
53	L'OREAL	no cat	No	No	3	1.122	1.609		27.629	3.813		108.42	5.453		.	.		.			108.423		NI
54	L'OREAL	cat 2B	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.			0	NQ	I
54	L'OREAL	cat 2B	No	No	2	1.215	6.134		65.417	5.374		0.555	0.015		.	.		.			0.555		I
54	L'OREAL	cat 2B	No	No	3	1.22	1.963		28.513	4.792		0.413	0.028		.	.		.			0.413		I
54	L'OREAL	cat 2B	No	No	4	0.954	5.639		25.157	6.823		0.468	0.034		.	.		.			0.468		I
55	L'OREAL	cat 2B	Yes	No	1	1.118	0.919		31.095	4.839		0.92	0.048		.	.		0	0		0.92		I
55	L'OREAL	cat 2B	Yes	No	2	1.362	3.038		40.51	0.668		0.962	0.094		.	.		0	0		0.962		I
55	L'OREAL	cat 2B	Yes	No	3	1.162	3.08		44.054	2.436		0.984	0.056		.	.		0.0487	0.0844		0.982		I
56	L'OREAL	cat 2B	No	No	1	1.118	0.919		31.095	4.839		0.664	0.132		.	.		.			0.664		I
56	L'OREAL	cat 2B	No	No	2	1.362	3.038		40.51	0.668		0.645	0.093		.	.		.			0.645		I
56	L'OREAL	cat 2B	No	No	3	1.162	3.08		44.054	2.436		0.727	0.329		.	.		.			0.727		I
57	L'OREAL	cat 2B	No	No	1	1.158	1.866		26.395	0.521		0.692	0.127		.	.		.			0.692		I
57	L'OREAL	cat 2B	No	No	2	1.189	2.082		10.92	1.838		1.101	0.163		.	.		.			1.101		I
57	L'OREAL	cat 2B	No	No	3	1.118	0.919		31.095	4.839		0.286	0.027		.	.		.			0.286		I
58	L'OREAL	cat 2B	Yes	No	1	1.118	0.919		31.095	4.839		0.388	0.116		.	.		0	0		0.388		I
58	L'OREAL	cat 2B	Yes	No	2	1.214	2.527		46.43	0.591		0.239	0.01		.	.		0	0		0.239		I
58	L'OREAL	cat 2B	Yes	No	3	1.362	3.038		40.51	0.668		0.41	0.028		.	.		0	0		0.41		I
59	L'OREAL	cat 2B	Yes	No	1	1.184	2.242		14.222	1.597		21.196	4.499		.	.		0	0		21.196		I
59	L'OREAL	cat 2B	Yes	No	2	1.362	3.038		40.51	0.668		0.575	0.069		.	.		0	0		0.575		I
59	L'OREAL	cat 2B	Yes	No	3	1.162	3.08		44.054	2.436		20.027	9.052		.	.		0	0		20.027		I
60	L'OREAL	cat 2B	No	No	1	1.166	6.115		0.8351	0.175		0.429	0.07		.	.		.			0.429		I
60	L'OREAL	cat 2B	No	No	2	1.117	3.017		25.194	7.837		0.566	0.047		.	.		.			0.566		I
60	L'OREAL	cat 2B	No	No	3	1.161	3.337		40.266	4.053		0.775	0.212		.	.		.			0.775		I
61	L'OREAL	cat 2B	No	Yes	1	1.084	8.313		30.98	5.154		70.04	1.064		0.2767	0.04		.			69.764		NI
61	L'OREAL	cat 2B	No	Yes	2	1.045	4.151		33.69	6.079		86.21	1.466		0.4642	0.14		.			85.746		NI
61	L'OREAL	cat 2B	No	Yes	3	1.158	6.507		37.465	0.834		71.661	8.38		0.3542	0.04		.			71.307		NI
62	L'OREAL	cat 2B	No	No	1	1.151	3.882		20.444	5.887		93.212	5.778		.	.		.			93.212		NI
62	L'OREAL	cat 2B	No	No	2	1.214	2.527		46.43	0.591		88.27	6.142		.	.		.			88.27		NI
62	L'OREAL	cat 2B	No	No	3	1.362	3.038		40.51	0.668		86.195	3.253		.	.		.			86.195		NI
63	L'OREAL	cat 2B	No	No	1	1.184	2.242		14.222	1.597		88.452	0.533		.	.		.			88.452		NI
63	L'OREAL	cat 2B	No	No	2	1.362	3.038		40.51	0.668		86.32	5.561		.	.		.			86.32		NI
63	L'OREAL	cat 2B	No	No	3	1.162	3.08		44.054	2.436		88.642	2.966		.	.		.			88.642		NI
64	L'OREAL	cat 2B	No	No	1	1.158	1.866		26.395	0.521		73.271	0.159		.	.		.			73.271		NI
64	L'OREAL	cat 2B	No	No	2	1.189	2.082		10.92	1.838		68.532	1.769		.	.		.			68.532		NI
64	L'OREAL	cat 2B	No	No	3	1.151	3.882		20.444	5.887		78.342	0.9		.	.		.			78.342		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
65	L'OREAL	cat 2B	No	No	1	1.184	2.242		14.222	1.597		13.391	7.957		.	.		.			13.391		I
65	L'OREAL	cat 2B	No	No	2	1.162	3.08		44.054	2.436		68.057	1.931		.	.		.			68.057		NI
65	L'OREAL	cat 2B	No	No	3	1.137	0.244		13.707	2.66		44.987	24.05	NQ	.	.		.			44.987	NQ	I
65	L'OREAL	cat 2B	No	No	4	1.143	5.763		29.636	4.03		92.491	10.74		.	.		.			92.491		NI
66	L'OREAL	cat 2B	No	No	1	1.184	2.242		14.222	1.597		62.22	10.37		.	.		.			62.22		NI
66	L'OREAL	cat 2B	No	No	2	1.214	2.527		46.43	0.591		18.556	4.2		.	.		.			18.556		I
66	L'OREAL	cat 2B	No	No	3	1.362	3.038		40.51	0.668		3.315	1.986		.	.		.			3.315		I
67	L'OREAL	cat 2A	Yes	No	1	1.167	5.4		28.91	0.885		1.387	1.045		.	.		0	0		1.387		I
67	L'OREAL	cat 2A	Yes	No	2	1.141	5.08		15.556	0.808		0.958	0.852		.	.		0	0		0.958		I
67	L'OREAL	cat 2A	Yes	No	3	1.011	5.403		48.7	2.057		2.201	0.986		.	.		0	0		2.201		I
68	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	1	1.167	5.4		28.91	0.885		0.975	0.358		.	.		.			0.975		I
68	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	2	1.141	5.08		15.556	0.808		0.332	0.046		.	.		.			0.332		I
68	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	3	1.158	6.507		37.465	0.834		0.497	0.14		.	.		.			0.497		I
69	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	1	1.084	8.313		30.98	5.154		0.45	0.083		.	.		.			0.45		I
69	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	2	1.045	4.151		33.69	6.079		0.549	0.047		.	.		.			0.549		I
69	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	3	1.158	6.507		37.465	0.834		1.867	1.989		.	.		.			1.867		I
70	L'OREAL	cat 2A	No	No	1	1.118	0.919		31.095	4.839		0.796	0.029		.	.		.			0.796		I
70	L'OREAL	cat 2A	No	No	2	1.362	3.038		40.51	0.668		1.007	0.054		.	.		.			1.007		I
70	L'OREAL	cat 2A	No	No	3	1.162	3.08		44.054	2.436		0.975	0.017		.	.		.			0.975		I
71	L'OREAL	cat 2A (ICCVAM:cat2B)	Yes	No	1	1.118	0.451		21.723	7.774		1.204	0.255		.	.		0	0		1.204		I
71	L'OREAL	cat 2A (ICCVAM:cat2B)	Yes	No	2	1.158	1.866		26.395	0.521		0.645	0.179		.	.		0	0		0.645		I
71	L'OREAL	cat 2A (ICCVAM:cat2B)	Yes	No	3	1.119	2.182		18.851	9.32		0.684	0.036		.	.		0	0		0.684		I
72	L'OREAL	cat 2A (ICCVAM:cat2B)	Yes	No	1	1.184	2.242		14.222	1.597		3.996	0.853		.	.		0.7901	0.7575		3.208		I
72	L'OREAL	cat 2A (ICCVAM:cat2B)	Yes	No	2	1.162	3.08		44.054	2.436		1.444	0.817		.	.		0.8775	0.7747		0.582		I
72	L'OREAL	cat 2A (ICCVAM:cat2B)	Yes	No	3	1.137	0.244		13.707	2.66		3.085	1.12		.	.		1.0484	0.7922		2.037		I
73	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	1	1.141	5.08		15.556	0.808		95.425	3.203		.	.		.			95.425		NI
73	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	2	1.22	1.963		28.513	4.792		88.386	5.818		.	.		.			88.386		NI
73	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	3	0.954	5.639		25.157	6.823		97.272	4.536		.	.		.			97.272		NI
74	L'OREAL	cat 2A	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	0.02		.	0.1713		0	NQ	I
74	L'OREAL	cat 2A	Yes	Yes	2	1.215	6.134		65.417	5.374		89.152	1.886		0.8903	0.02		0.6957	0.1713		87.566		NI
74	L'OREAL	cat 2A	Yes	Yes	3	0.954	5.639		25.157	6.823		108.16	3.756		1.3621	0.02		0.9343	0.2167		105.86		NI

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
74	L'OREAL	cat 2A	Yes	Yes	4	1.112	4.848		7.1871	3.378		81.22	6.072		0.4154	0.04		0.8007	0.186		80.004		NI
75	L'OREAL	cat 2A	No	No	1	1.084	8.313		30.98	5.154		1.133	0.546		.	.		.			1.133		I
75	L'OREAL	cat 2A	No	No	2	1.045	4.151		33.69	6.079		30.458	49.34	NQ	.	.		.			30.458	NQ	I
75	L'OREAL	cat 2A	No	No	3	1.167	5.4		28.91	0.885		1.274	0.088		.	.		.			1.274		I
75	L'OREAL	cat 2A	No	No	4	1.158	6.507		37.465	0.834		0.796	0.389		.	.		.			0.796		I
76	L'OREAL	cat 2A	No	No	1	0.954	5.639		25.157	6.823		80.058	5.567		.	.		.			80.058		NI
76	L'OREAL	cat 2A	No	No	2	1.041	2.734		5.2453	0.719		60.811	7.86		.	.		.			60.811		NI
76	L'OREAL	cat 2A	No	No	3	1.118	0.451		21.723	7.774		72.566	5.978		.	.		.			72.566		NI
77	L'OREAL	cat 2A	No	No	1	1.118	0.451		21.723	7.774		91.228	6.137		.	.		.			91.228		NI
77	L'OREAL	cat 2A	No	No	2	1.158	1.866		26.395	0.521		87.171	5.285		.	.		.			87.171		NI
77	L'OREAL	cat 2A	No	No	3	1.189	2.082		10.92	1.838		91.157	2.664		.	.		.			91.157		NI
78	L'OREAL	cat 2A	No	No	1	1.041	2.734		5.2453	0.719		87.471	4.774		.	.		.			87.471		NI
78	L'OREAL	cat 2A	No	No	2	1.118	0.451		21.723	7.774		84.321	5.653		.	.		.			84.321		NI
78	L'OREAL	cat 2A	No	No	3	1.158	1.866		26.395	0.521		86.183	2.436		.	.		.			86.183		NI
79	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	1	1.184	2.242		14.222	1.597		17.635	6.188		.	.		.			17.635		I
79	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	2	1.162	3.08		44.054	2.436		52.806	3.408		.	.		.			52.806		NI
79	L'OREAL	cat 2A (ICCVAM:cat2B)	No	No	3	1.137	0.244		13.707	2.66		47.748	14.38		.	.		.			47.748		I
80	L'OREAL	cat 1	Yes	No	1	1.084	8.313		30.98	5.154		23.428	0.447		.	.		37.755	3.6437		0		I
80	L'OREAL	cat 1	Yes	No	2	1.045	4.151		33.69	6.079		32.527	1.65		.	.		39.181	3.7813		0		I
80	L'OREAL	cat 1	Yes	No	3	1.171	5.113		44.435	13.63		34.372	3.732		.	.		34.956	3.3735		1.234		I
81	L'OREAL	cat 1	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.			0	NQ	I
81	L'OREAL	cat 1	No	No	2	1.215	6.134		65.417	5.374		0.97	0.177		.	.		.			0.97		I
81	L'OREAL	cat 1	No	No	3	1.22	1.963		28.513	4.792		0.488	0.06		.	.		.			0.488		I
81	L'OREAL	cat 1	No	No	4	0.954	5.639		25.157	6.823		0.611	0.218		.	.		.			0.611		I
82	L'OREAL	cat 1	No	No	1	1.166	6.115		0.8351	0.175		0.4	0.07		.	.		.			0.4		I
82	L'OREAL	cat 1	No	No	2	1.403	1.696		30.786	9.616		0.245	0.068		.	.		.			0.245		I
82	L'OREAL	cat 1	No	No	3	1.161	3.337		40.266	4.053		0.402	0.05		.	.		.			0.402		I
83	L'OREAL	cat 1	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.			0	NQ	I
83	L'OREAL	cat 1	Yes	No	2	1.215	6.134		65.417	5.374		0.948	0.623		.	.		0	0		0.948		I
83	L'OREAL	cat 1	Yes	No	3	1.207	1.747		16.571	4.591		0.605	0.104		.	.		0	0		0.605		I
83	L'OREAL	cat 1	Yes	No	4	0.954	5.639		25.157	6.823		0.285	0.055		.	.		0	0		0.285		I
84	L'OREAL	cat 1	No	No	1	1.144	6.145		1.6528	0.635		0.619	0.204		.	.		.			0.619		I
84	L'OREAL	cat 1	No	No	2	1.071	2.796		33.29	7.118		0.364	0.047		.	.		.			0.364		I
84	L'OREAL	cat 1	No	No	3	1.161	3.337		40.266	4.053		0.474	0.057		.	.		.			0.474		I
85	L'OREAL	cat 1	No	No	1	1.084	8.313		30.98	5.154		0.466	0.1		.	.		.			0.466		I
85	L'OREAL	cat 1	No	No	2	1.045	4.151		33.69	6.079		0.574	0.16		.	.		.			0.574		I
85	L'OREAL	cat 1	No	No	3	1.158	6.507		37.465	0.834		0.289	0.059		.	.		.			0.289		I
86	L'OREAL	cat 1	No	No	1	1.144	6.145		1.6528	0.635		11.368	3.74		.	.		.			11.368		I
86	L'OREAL	cat 1	No	No	2	1.071	2.796		33.29	7.118		4.311	2.6		.	.		.			4.311		I
86	L'OREAL	cat 1	No	No	3	1.117	3.017		25.194	7.837		7.567	1.57		.	.		.			7.567		I
87	L'OREAL	cat 1	Yes	No	1	1.167	5.4		28.91	0.885		1.51	0.416		.	.		0	0		1.51		I
87	L'OREAL	cat 1	Yes	No	2	1.141	5.08		15.556	0.808		2.171	0.805		.	.		0	0		2.171		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
87	L'OREAL	cat 1	Yes	No	3	1.011	5.403		48.7	2.057		1.09	0.772		.	.		0	0		1.09		I
88	L'OREAL	cat 1	Yes	No	1	1.144	6.145		1.6528	0.635		0.99	0.167		.	.		0	0		0.99		I
88	L'OREAL	cat 1	Yes	No	2	1.071	2.796		33.29	7.118		0.643	0.023		.	.		0	0		0.643		I
88	L'OREAL	cat 1	Yes	No	3	1.403	1.696		30.786	9.616		0.815	0.075		.	.		0	0		0.815		I
89	L'OREAL	cat 1	No	No	1	1.041	2.734		5.2453	0.719		1.561	0.099		.	.		.			1.561		I
89	L'OREAL	cat 1	No	No	2	1.118	0.451		21.723	7.774		1.167	0.092		.	.		.			1.167		I
89	L'OREAL	cat 1	No	No	3	1.158	1.866		26.395	0.521		1.518	0.218		.	.		.			1.518		I
90	L'OREAL	cat 1	Yes	No	1	1.118	0.919		31.095	4.839		4.283	3.194		.	.		0.5885	0.6127		3.771		I
90	L'OREAL	cat 1	Yes	No	2	1.169	2.795		24.645	3.859		25.713	16.81		.	.		0.5903	0.6058		25.183		I
90	L'OREAL	cat 1	Yes	No	3	1.119	2.182		18.851	9.32		4.368	2.397		.	.		0.6433	0.6525		3.774		I
91	L'OREAL	cat 1	Yes	No	1	1.041	2.734		5.2453	0.719		7.681	2.889		.	.		3.3063	2.8439		4.374		I
91	L'OREAL	cat 1	Yes	No	2	1.112	4.848		7.1871	3.378		11.323	12.35		.	.		3.0815	2.6633		8.384		I
91	L'OREAL	cat 1	Yes	No	3	1.118	0.451		21.723	7.774		15.202	3.507		.	.		3.0734	2.6474		12.128		I
92	L'OREAL	cat 1	Yes	No	1	1.143	5.763		29.636	4.03		0.62	0.083		.	.		0.0676	0.0595		0.56		I
92	L'OREAL	cat 1	Yes	No	2	1.403	1.696		30.786	9.616		7.056	3.478		.	.		0.0471	0.0418		7.02		I
92	L'OREAL	cat 1	Yes	No	3	1.122	1.609		27.629	3.813		4.02	0.927		.	.		0.0094	0.0138		4.02		I
93	L'OREAL	cat 1	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.			0	NQ	I
93	L'OREAL	cat 1	No	No	2	1.215	6.134		65.417	5.374		17.034	4.873		.	.		.			17.034		I
93	L'OREAL	cat 1	No	No	3	1.22	1.963		28.513	4.792		36.583	10.1		.	.		.			36.583		I
93	L'OREAL	cat 1	No	No	4	0.954	5.639		25.157	6.823		20.012	9.12		.	.		.			20.012		I
94	L'OREAL	cat 1	No	No	1	1.215	6.134		65.417	5.374	NQ	.	.		.	.		.			0	NQ	I
94	L'OREAL	cat 1	No	No	2	1.215	6.134		65.417	5.374		11.518	1.58		.	.		.			11.518		I
94	L'OREAL	cat 1	No	No	3	1.22	1.963		28.513	4.792		16.217	4.688		.	.		.			16.217		I
94	L'OREAL	cat 1	No	No	4	0.954	5.639		25.157	6.823		16.61	4.525		.	.		.			16.61		I
95	L'OREAL	cat 1	No	No	1	1.167	5.4		28.91	0.885		0.618	0.054		.	.		.			0.618		I
95	L'OREAL	cat 1	No	No	2	1.141	5.08		15.556	0.808		1.082	1.124		.	.		.			1.082		I
95	L'OREAL	cat 1	No	No	3	1.158	6.507		37.465	0.834		0.425	0.131		.	.		.			0.425		I
96	L'OREAL	cat 1	No	No	1	1.084	8.313		30.98	5.154		49.663	9.665		.	.		.			49.663		I
96	L'OREAL	cat 1	No	No	2	1.045	4.151		33.69	6.079		38.227	1.07		.	.		.			38.227		I
96	L'OREAL	cat 1	No	No	3	1.22	1.963		28.513	4.792		35.157	10.65		.	.		.			35.157		I
97	L'OREAL	cat 1	No	No	1	1.167	5.4		28.91	0.885		67.488	1.938		.	.		.			67.488		NI
97	L'OREAL	cat 1	No	No	2	1.158	6.507		37.465	0.834		63.442	4.753		.	.		.			63.442		NI
97	L'OREAL	cat 1	No	No	3	1.22	1.963		28.513	4.792		60.011	2.542		.	.		.			60.011		NI
98	L'OREAL	cat 1	No	Yes	1	1.144	6.145		1.6528	0.635		26.048	4.527		2.7313	1.01		.			23.317		I
98	L'OREAL	cat 1	No	Yes	2	1.071	2.796		33.29	7.118		50.143	11.9		3.6837	0.91		.			46.459		I
98	L'OREAL	cat 1	No	Yes	3	1.117	3.017		25.194	7.837		31.103	5.456		3.8408	3.92		.			27.262		I
99	L'OREAL	cat 1	No	No	1	1.158	1.866		26.395	0.521		1.235	0.19		.	.		.			1.235		I
99	L'OREAL	cat 1	No	No	2	1.189	2.082		10.92	1.838		1.237	0.097		.	.		.			1.237		I
99	L'OREAL	cat 1	No	No	3	1.169	2.795		24.645	3.859		1.332	0.18		.	.		.			1.332		I
100	L'OREAL	cat 1	No	No	1	1.143	5.763		29.636	4.03		1.31	0.331		.	.		.			1.31		I
100	L'OREAL	cat 1	No	No	2	1.117	3.017		25.194	7.837		0.762	0.094		.	.		.			0.762		I
100	L'OREAL	cat 1	No	No	3	1.122	1.609		27.629	3.813		1.297	0.27		.	.		.			1.297		I
101	L'OREAL	cat 1	No	Yes	1	1.144	6.145		1.6528	0.635		71.722	3.625		0.9022	1.03		.			70.82		NI
101	L'OREAL	cat 1	No	Yes	2	1.071	2.796		33.29	7.118		75.215	2.562		0.235	0.07		.			74.98		NI
101	L'OREAL	cat 1	No	Yes	3	1.117	3.017		25.194	7.837		45.83	6.411		0.9595	1.16		.			44.871		I

		GHS				NC			PC			Uncorrected viability			NSC			MTT			Final	Final	Classification
Chemical	Laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	viability	call	50% cutoff
102	L'OREAL	cat 1	No	No	1	1.144	6.145		1.6528	0.635		84.685	10.06		.	.		.			84.685		NI
102	L'OREAL	cat 1	No	No	2	1.071	2.796		33.29	7.118		86.882	4.908		.	.		.			86.882		NI
102	L'OREAL	cat 1	No	No	3	1.161	3.337		40.266	4.053		77.44	2.903		.	.		.			77.44		NI
103	L'OREAL	cat 1	No	No	1	1.041	2.734		5.2453	0.719		1.052	0.137		.	.		.			1.052		I
103	L'OREAL	cat 1	No	No	2	1.118	0.451		21.723	7.774		0.715	0.03		.	.		.			0.715		I
103	L'OREAL	cat 1	No	No	3	1.158	1.866		26.395	0.521		0.981	0.093		.	.		.			0.981		I
104	L'OREAL	cat 1	No	No	1	1.189	2.082		10.92	1.838		80.426	4.441		.	.		.			80.426		NI
104	L'OREAL	cat 1	No	No	2	1.169	2.795		24.645	3.859		97.452	1.021		.	.		.			97.452		NI
104	L'OREAL	cat 1	No	No	3	1.151	3.882		20.444	5.887		84.223	2.44		.	.		.			84.223		NI
105	L'OREAL	cat 1	No	No	1	0.954	5.639		25.157	6.823		2.122	0.311		.	.		.			2.122		I
105	L'OREAL	cat 1	No	No	2	1.041	2.734		5.2453	0.719		1.427	0.05		.	.		.			1.427		I
105	L'OREAL	cat 1	No	No	3	1.118	0.451		21.723	7.774		1.257	0.058		.	.		.			1.257		I

Chemical 106 and 107 are considered incompatible with the test method because of strong colour interference and so SkinEthic™ HCE shows a limitation for colours that strongly interfere with MTT using the current system of photometry. These two chemicals are excluded for the statistical analysis.

		GHS				NC			PC			Uncorrected viability			NSC	MTT	Final
Chemical	laboratory	classification	MTT	coloring	test	OD	std	Qual	Mean%	Std	Qual	Mean%	Std	Qual	Mean%	Mean%	viability
106	CARDAM	cat 1	No	Yes	1	1.051	9.0646	Qualified	10.0328	2.8859	Qualified	200.444	54.382	Non-qualified	327.467	.	0
106	CARDAM	cat 1	No	Yes	2	1.083	4.8929	Qualified	10.1424	3.1003	Qualified	154.682	17.55	Qualified	27.746	.	126.936
106	CARDAM	cat 1	No	Yes	3	0.887	9.2479	Qualified	23.7508	10	Qualified	113.977	6.54	Qualified	72.133	.	41.843
106	CARDAM	cat 1	No	Yes	4	0.992	2.2742	Qualified	10.2611	2.6287	Qualified	112.74	13.573	Qualified	60.074	.	52.666
107	CARDAM	cat 1	No	Yes	1	1.083	4.8929	Qualified	10.1424	3.1003	Qualified	64.612	5.791	Qualified	17.377	.	47.235
107	CARDAM	cat 1	No	Yes	2	0.887	9.2479	Qualified	23.7508	10	Qualified	78.085	6.733	Qualified	34.252	.	43.833
107	CARDAM	cat 1	No	Yes	3	0.992	2.2742	Qualified	10.2611	2.6287	Qualified	66.187	14.918	Qualified	14.221	.	51.966
106	CEETOX	cat 1	Yes	Yes	1	0.986	9.0546	Qualified	41.7653	3.9306	Qualified	99.256	15.703	Qualified	29.202	349.239	0
106	CEETOX	cat 1	No	No	2	0.872	8.0336	Qualified	61.3649	6.3574	Non-qualified	.	.	Qualified	.	.	0
106	CEETOX	cat 1	Yes	Yes	3	0.997	8.8887	Qualified	9.1441	3.4044	Qualified	64.878	5.08	Qualified	24.841	345.353	0
107	CEETOX	cat 1	No	No	1	1.102	4.8262	Qualified	52.1174	3.4029	Non-qualified	.	.	Qualified	.	.	0
107	CEETOX	cat 1	Yes	Yes	2	0.99	7.2609	Qualified	33.1202	5.3244	Qualified	79.418	4.38	Qualified	14.137	76.809	0
107	CEETOX	cat 1	Yes	Yes	3	1.117	6.8498	Qualified	19.8657	5.9588	Qualified	74.672	3.45	Qualified	10.582	52.94	0
107	CEETOX	cat 1	Yes	Yes	4	1.108	15.906	Qualified	36.1324	3.3205	Qualified	80.873	13.806	Qualified	19.293	273.529	0
106	L'OREAL	cat 1	Yes	Yes	1	1.144	6.1445	Qualified	1.6528	0.6346	Qualified	66.395	13.785	Qualified	39.766	131.889	0
106	L'OREAL	cat 1	Yes	Yes	2	1.143	5.763	Qualified	29.6358	4.0301	Qualified	98.699	8.198	Qualified	119.582	132.049	0
106	L'OREAL	cat 1	Yes	Yes	3	1.117	3.0174	Qualified	25.1936	7.8366	Qualified	77.497	25.978	Qualified	43.393	135.025	0
106	L'OREAL	cat 1	Yes	Yes	4	1.161	3.3371	Qualified	40.2656	4.053	Qualified	111.753	23.189	Qualified	36.871	129.859	0
106	L'OREAL	cat 1	Yes	Yes	5	1.122	1.6091	Qualified	27.629	3.8131	Qualified	63.933	2.988	Qualified	13.115	134.401	0
107	L'OREAL	cat 1	Yes	Yes	1	1.166	6.1154	Qualified	0.8351	0.1747	Qualified	61.132	6.824	Qualified	11.175	29.452	20.504
107	L'OREAL	cat 1	Yes	Yes	2	1.403	1.6958	Qualified	30.7863	9.6157	Qualified	56.792	5.412	Qualified	8.189	24.55	24.053
107	L'OREAL	cat 1	Yes	Yes	3	1.117	3.0174	Qualified	25.1936	7.8366	Qualified	80.784	2.301	Qualified	11.687	30.789	38.308

Appendix VII Performance criteria

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Institute for Health and Consumer Protection
European Centre for the Validation of Alternative Methods (ECVAM)

Eye Irritation Validation Study (EIVS)
Guidance on Eye Irritation Validation Study (EIVS) Conduct for the Reconstructed Human Tissue (RhT) Assays and Performance Criteria to Assess the Scientific Validity of SkinEthic™ HCE and EpiOcular™ EIT

Version	Author	Reviewer	Approver	Date of approval
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Document history

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2	08/02/2011	João Barroso	Footnotes 3, 4, 5 and 6 were updated to include WLR, BLR, sensitivity and specificity of EpiOcular™ EIT calculated from pre-validation data considering both classification cut-offs of 50% and 60%.

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Institute for Health and Consumer Protection
European Centre for the Validation of Alternative Methods (ECVAM)

GUIDANCE ON EYE IRRITATION VALIDATION STUDY (EIVS) CONDUCT FOR THE RECONSTRUCTED HUMAN TISSUE (RhT) ASSAYS AND PERFORMANCE CRITERIA TO ASSESS THE SCIENTIFIC VALIDITY OF SkinEthic™ HCE AND EpiOcular™ EIT

Disclaimer: The Validation Management Group (VMG) of the Eye Irritation Validation Study (EIVS) proposes in this document a guidance on the conduct of certain aspects of EIVS, as well as "test method performance criteria" that describe the performance deemed by the VMG as necessary for a test method to be scientifically valid and considered for regulatory acceptance. Nevertheless, the EIVS VMG recognises that regulatory authorities ultimately make the determination of what is considered adequate performance for their relevant regulatory decisions.

1. DEFINITIONS

EpiOcular™ model/construct: A reconstructed human tissue (RhT) construct produced by MatTek Corporation, consisting of a non-keratinized multilayered epithelium prepared from non-transformed, human-derived epidermal keratinocytes.

SkinEthic™ Human Corneal Epithelium (HCE) model/construct: A RhT construct produced by SkinEthic™ Laboratories, consisting of a a multilayered epithelium prepared from immortalized human corneal epithelial cells.

EpiOcular™ Eye Irritation Test (EIT): A test method to predict eye irritation, employing the EpiOcular™ RhT construct as test system and a protocol defining different exposure and post-exposure incubations for liquids and solids (i.e., liquids: 30 min exposure followed by 120 min post-treatment incubation, and solids: 90 min exposure followed by 18 hours post-treatment incubation).

SkinEthic™ HCE Short-time Exposure (SE): A test method to predict eye irritation, employing the SkinEthic™ HCE RhT construct as test system and a short-time exposure of test chemicals (i.e., 10 min exposure without post-treatment incubation).

SkinEthic™ HCE Long-time Exposure (LE): A test method to predict eye irritation, employing the SkinEthic™ HCE RhT construct as test system and a long-time exposure of test chemicals (i.e., 1 h exposure followed by 16 h post-treatment incubation).

Eye irritation Peptide Reactivity Assay (EPRA): A test method to predict chemical reactivity, defined as the electrophilic potential of the chemical to react with cysteine or lysine containing peptides.

SkinEthic™ HCE test strategy/method: A test strategy to predict eye irritation, consisting of three separate assays (i.e., EPRA, SkinEthic™ HCE SE, and SkinEthic™ HCE LE). In the SkinEthic™ HCE test strategy, chemical reactivity, as determined by the EPRA, is used to decide if a chemical is tested with SkinEthic™ HCE SE (reactive chemicals) or SkinEthic™ HCE LE (non-reactive or inclusive chemicals).

Negative control (NC): A reference test chemical that does not induce a cytotoxic effect in the treated tissues (i.e., does not reduce their viability). It is used to verify if the viability of the tissues used for testing, as quantified by the MTT assay, is within a defined acceptance range of optical density (OD) (i.e., SkinEthic™ HCE SE/LE: $0.7 \leq OD_{NC} < 1.5$; EpiOcular™ EIT: $OD_{NC} > 1.0$).

Positive control (PC): A reference test chemical known to induce a cytotoxic effect in the treated tissues (i.e., SkinEthic™ HCE SE/LE: < 50% viability; EpiOcular™ EIT: < 50% viability), as quantified by using the MTT assay. It is used to verify if the tissue batch used for testing is responding to the reference chemical within a defined acceptance range of % viability (relative to NC). It should be noted that the positive control does not need to be an *in vivo* irritant chemical (based on the Draize eye irritation test).

Test chemical: Any chemical (substance or mixture) being tested as a single entity.

Test: A single test chemical concurrently tested in a minimum of two/three tissue replicates as defined in the corresponding SOP. A "test" for a test chemical is defined when the cytotoxic effect by using MTT is quantitatively measured. A reported technical issue before the viability measurement is not considered as a "test" for the test chemical (see section 2.2.3).

Run: A run consists of multiple tests with different test chemicals (one test per test chemical) conducted concurrently with a test with NC and a test with PC, tested by one operator, as defined in the corresponding SOP.

Qualified run: A run is qualified if it meets the test acceptance criteria for the NC and PC, as defined in the corresponding SOP. Otherwise, the run will be considered as non-qualified.

Qualified test: A test is qualified if it meets the criteria for an acceptable test, as defined in the corresponding SOP, and is within a qualified run. Otherwise, the test will be considered as non-qualified.

Test sequence: The total number of tests performed for a single test chemical in a single laboratory, which includes any re-testing. A test sequence may include both qualified and non-qualified tests. The first two tests having technical issues for each test chemical, tests included in the first two runs presenting technical issues, and tests included in the first six non-qualified runs are not considered as part of a test sequence.

Complete test sequence: A test sequence is considered complete if it contains three qualified tests. Otherwise, the test sequence will be considered as incomplete.

2. TESTING PROCEDURES

2.1 Testing Chemicals for the Eye Irritation Validation Study (EIVS)

In order to establish the reliability and relevance of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT during EIVS, **all test chemicals selected for the validation study (at least 104) should be tested with SkinEthic™ HCE SE, SkinEthic™ HCE LE and EpiOcular™ EIT in three laboratories**. SkinEthic™ HCE SE and SkinEthic™ HCE LE will be run in parallel in the same three laboratories, while three other laboratories will be responsible for running the EpiOcular™ EIT. In each laboratory, **all test chemicals should be tested in three independent qualified runs per test method performed with different production tissue batches and at sufficiently spaced time points** (at least one week apart), with the final objective of obtaining **three qualified tests per test chemical**. In each run, each test chemical, as well as the negative control (NC) and the positive control (PC) should be concurrently tested in a minimum of **three tissue replicates for SkinEthic™ HCE SE/LE and two tissue replicates for EpiOcular™ EIT (see note below), respectively**. Even if more than one test chemical is tested in the same run, one replicate set for each NC and PC is sufficient.

Any tissues pre-selection (before the testing, untreated tissues), procedural change or technical issue (during the testing, tissue treated) that may impact on test method reproducibility assessment, will be documented (see data reporting templates in the annexes to the SOPs) and reported to the core VMG.

Note on the number of replicates for the EpiOcular™ EIT:
The EpiOcular™ EIT has been developed using two concurrently tested tissue replicates on the basis of practical considerations in the technical procedures for conduct of this assay. The variability between two concurrently treated tissue replicates was found to be low in the 296 pairs of replicates produced by seven laboratories for a wide set of test chemicals during the pre-validation study of the EpiOcular™ EIT. Briefly, 99%, 95%, 90% and 74% of the 296 pairs of concurrently treated tissue replicates showed a difference of viability below 20%, 15%, 10% and 5%, repectively. Two independent biostatisticians evaluated the data and their conclusions led the VMG to consider the use of two tissue replicates for EpiOcular™ EIT in EIVS as sufficiently statistically and scientifically justified.

2.2 Re-conducting Tests/Runs ("Re-testing"/"Re-running")

It is possible that one or several tests pertaining to one or more test chemicals does/do not meet the test acceptance criteria as given in the corresponding SOP or is/are not acceptable for other reasons. It is also possible that acceptance criteria for the NC and/or PC, as defined in the corresponding SOP, are not met for one or more runs. In these cases, re-testing/re-running is allowed to complete missing data as described below. Importantly, each laboratory should not produce more than three qualified tests per test chemical, per test method, and re-testing/re-running is allowed only to try to accomplish the objective of producing three qualified tests per test chemical, per test method. Excess production of data and subsequent data selection are regarded as not appropriate. All tested tissues must be reported. The extent of unacceptable tests/runs will be documented and the basis for the likely cause of each will be provided.

2.2.1 Re-testing of test chemicals: If one or more test chemicals within a qualified run does/do not meet the test acceptance criteria (**non-qualified test(s)**), a maximum number of **two additional tests** per test chemical, per test method[1], per laboratory is/are admissible ("re-testing") to complement missing data. More precisely, since in case of re-testing also PC and NC have to be concurrently tested, a maximum number of two additional qualified runs may be conducted for each test chemical. Non-qualified tests have to be documented and reported.

2.2.2 Re-running runs: If a run does not meet the acceptance criteria for the NC and/or PC, as defined in the corresponding SOP (**non-qualified run**), **the full run must be repeated** for all test chemicals included in the non-qualified run. A maximum number of **six[2] additional runs** are admissible per laboratory, per test method[1] ("re-running") to complement missing data due to failure of NC or PC acceptance criteria. Non-qualified runs have to be documented and reported. None of the tests within the first six non-qualified runs obtained by a laboratory for each test method[1] should be considered for applying section 2.2.1, or for any calculations.

[1] SkinEthic™ HCE SE and SkinEthic™ HCE LE are considered as two separate and independent test methods when considering re-testing and re-running.

[2] This limit was defined by calculating the critical (smallest) number of repetitions that will result in a probability less then 5% assuming a binomial distribution with a failing rate of 10% and 30 runs in total.

After producing six non-qualified runs with one test method[1], a laboratory should stop testing and immediately inform the core VMG through the Coordinator Jan Lammers (jan.lammers@tno.nl), with the VMG Chair Stuart Freeman (stuart.j.freeman@talktalk.net) in copy (to take action in the absence of the Coordinator). The core VMG will then analyse in detail all the non-qualified runs obtained by the laboratory with that test method[1] to that point, looking at e.g., the consistency/inconsistency of the reason(s) leading to non-qualification and the time span between the non-qualified runs, in order to decide if the tests within further non-qualified runs should be considered as non-qualified tests. In such a case, further repetition of runs will be considered as re-testing for all test chemicals included in those runs.

Moreover, after producing three consecutive non-qualified runs with one test method[1], a laboratory should stop testing and immediately inform the core VMG through the Coordinator Jan Lammers (jan.lammers@tno.nl), with the VMG Chair Stuart Freeman (stuart.j.freeman@talktalk.net) in copy (to take action in the absence of the Coordinator). The core VMG will then investigate if the laboratory is having systematic technical problems, by looking at e.g., the consistency/inconsistency of the reason(s) leading to non-qualification.

If the core VMG identifies a systematic technical problem as the cause for non-qualified runs, the lead laboratory may be informed and involved in troubleshooting.

2.2.3 Re-testing/re-running for technical reasons: If a test/run fails because of **technical reasons** (technical issue) and the test/run was not finished (no viability measurement) **re-testing is allowed twice** for each test chemical in each laboratory, for each test method[1], and **re-running is also allowed twice** in each laboratory, for each test method[1], independently of the provisions described in sections 2.2.1 and 2.2.2. The reasons will be documented and reported to the core VMG.

Examples of technical issues include e.g. tissues that are mechanically damaged during the test or tissues for which some amount of test chemical is accidentally applied to the culture medium. If a technical issue occurs, all replicates of the corresponding test chemical should be withdrawn from any further step of the test procedure. It should be avoided that OD measurements of tissues with known unacceptable technical quality will be performed (including the remaining replicates of the test chemical).

Moreover, if **systematic technical issues** occur in one laboratory, leading to loss of data for more than one test chemical, **testing should be stopped** and the core VMG informed immediately through the Coordinator Jan Lammers (jan.lammers@tno.nl), with the VMG Chair Stuart Freeman (stuart.j.freeman@talktalk.net) in copy (to take action in the absence of the Coordinator), so that appropriate measures can be taken (e.g. the lead laboratory informed and involved in trying to solve a potential technical problem).

Tissues which feature obvious, visible damage (e.g. contamination or cuts in the epithelium) should be discarded and not used at all in order to avoid a posterior technical issue.

3. TEST ACCEPTANCE CRITERIA

The test acceptance criteria for test chemicals, NC, PC, Non Specific Color controls and Non Specific MTT reduction controls are described in the corresponding SOPs and have been approved by the VMG. For example regarding variability, these acceptance criteria were defined as follows: SkinEthic™ HCE SE/LE: SD > 18%; EpiOcular™ EIT: Range > 20%. Importantly, if during or

after completion of EIVS the predefined test acceptance criteria are found not to be appropriate due to failure of a high number of tests (non-qualified tests) and/or runs (non-qualified runs), the VMG may revise these criteria on the basis of the evaluation of the acquired data. All modifications have to be scientifically/statistically justified.

4. CALCULATION OF RELIABILITY (REPRODUCIBILITY) AND PREDICTIVE CAPACITY (ACCURACY)

The independent biostatistician assigned to the validation study will be responsible for calculating the reliability and predictive capacity values in EIVS, in accordance with the rules described below. The ECVAM biostatistician will perform an **independent review and quality assurance** on the calculations performed by the independent biostatistician.

While the reproducibility and predictive capacity of EpiOcular™ EIT will be evaluated in a single assessment (as described in sections 4.1-4.3) because each chemical will be tested in a single protocol (as a solid or a liquid), for SkinEthic™ HCE three independent assessments will be performed. Since all the selected test chemicals will be tested in both SkinEthic™ HCE SE and SkinEthic™ HCE LE, these two assays can be evaluated not only as part of a testing strategy with EPRA but also as independent test methods. Thus, the SkinEthic™ HCE testing strategy, the SkinEthic™ HCE SE and the SkinEthic™ HCE LE will all be independently evaluated for their reproducibility and predictive capacity as described in sections 4.1-4.3. Finally, the EPRA will be evaluated for its reproducibility according to sections 4.1 and 4.2 (see also Project Plan).

4.1 Within Laboratory Reproducibility (WLR)

For each laboratory, concordance of classifications and overall Standard Deviation will be calculated based only on qualified tests from test chemicals for which **at least two qualified tests** are available. The final report should state how many and which test chemicals per laboratory have none or only one qualified test (omitted from WLR calculations), as well as how many and which test chemicals per laboratory have two or three qualified tests (used for WLR calculations). In addition, the overall Standard Deviation associated with each laboratory will be calculated using all available test sequences, i.e. including both qualified and non-qualified tests.

4.2 Between Laboratory Reproducibility (BLR)

For the calculation of BLR the **final classification** for each test chemical in each participating laboratory should be obtained by using the **arithmetic mean value of viability over the different qualified tests** performed. Concordance of classifications between laboratories and overall Standard Deviation of the study will be calculated based only on qualified tests from test chemicals for which **at least one qualified test per laboratory** is available. The final report should state how many and which test chemicals do not have at least one qualified test per laboratory (omitted from BLR calculation), as well as how many and which test chemicals have 3, 4, 5, 6, 7, 8 or 9 qualified tests that can be used to calculate BLR (with at least one qualified test per laboratory). In addition, the overall Standard Deviation of the study will be calculated using all available test sequences, i.e. including both qualified and non-qualified tests.

4.3 Predictive Capacity (Accuracy)

All qualified tests for each test chemical will be used to calculate the predictive capacity values. The calculations will be based on the **individual predictions of each qualified test in each laboratory** and not on the arithmetic mean values of viability over the different qualified tests performed.

By using all qualified tests to calculate the predictive capacity values, the probability of obtaining 0% underprediction of Category 1 chemicals (0 out of about 200 tests), as requested in section 6.4 (see below), is extremely low due to the accepted fact that reproducibility of SkinEthic™ HCE SE/LE and EpiOcular™ EIT both within and between laboratories is not 100% (see section 6.3). Therefore, the rate of underprediction of Category 1 chemicals as No Category (Cat 1 → No Cat), will be calculated using the **mode of the *in vitro* predictions of all qualified tests** obtained in the three participating laboratories for each test chemical classified as UN GHS/EU CLP Category 1 based on *in vivo* Draize eye irritation data. This approach more closely reflects the real testing situation (post-validation). Thus, in a post-validation testing situation, a single qualified test obtained in one laboratory is usually sufficient to classify a test chemical, but if a borderline result, such as non-concordant replicate measurements and/or mean percent viability equal to 50±5%, is obtained, a second test may be considered, as well as a third one, in case of discordant results between the first two tests, in which case the **mode of the three classifications** is taken as the final decision.

5. STUDY QUALITY CRITERION

To limit the bias introduced in the calculations of reliability and predictive capacity due to the exclusion of the most variable tests (non-qualified tests) from some of the calculations (see section 4), and also to avoid further bias introduced by a reduction of the data used in some of the calculations (at least 104 test chemicals are needed to reach the statistical power defined for the study), the VMG decided to define a target value for the number of complete test sequences that should be available after re-testing as an objective to secure the quality of the study, i.e. to limit the amount of missing data due to the predefined test acceptance criteria (see section 3).

5.1 Target Number of Complete Test Sequences After Re-testing

In each participating laboratory, **at least 85%** of the test sequences (see definition in section 1) should contain **three qualified tests** (89 out of 104 test sequences, for 104 test chemicals).

If this criterion is not met, and before deciding that the required statistical power and study quality are not reached, the VMG may (i) investigate for potential reasons of misclassification, (ii) if deemed appropriate, revise the test acceptance criteria on the basis of the evaluation of the acquired data, as described in section 3 and/or (iii) request additional testing to complement the datasets.

6. PERFORMANCE CRITERIA TO ASSESS THE SCIENTIFIC VALIDITY OF THE TEST METHODS

Prior to the initiation of the validation study, the VMG defined test method performance criteria, which it considered appropriate for judging the performance of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT with the test chemicals selected for EIVS. The test method performance criteria described below provide some guidance on the target values which the VMG would ideally like to attain in EIVS in terms of test method performance (reliability and predictive capacity) for the SkinEthic™ HCE SE, LE and/or test strategy and for the EpiOcular™ EIT. One recommendation of a previous ESAC Peer Review Panel on cell-based assays was to receive guidance from the VMG to evaluate the performance of these cell-based assays. Therefore, within the framework of EIVS, the VMG also suggests the use of these test method performance criteria as a basis for the evaluation of the performance of the SkinEthic™ HCE LE, SE and test strategy and of the EpiOcular™ EIT by the ESAC Peer Review Panel after the completion of EIVS.

The test method performance criteria developed by the VMG for EIVS and described below took into account: (a) the background and specific objectives of the validation study (see EIVS Project Plan); (b) the requirements of regulatory authorities and industry when testing and classifying chemicals for eye irritation; (c) the within test variability in the *in vivo* Draize eye irritation data and the manner in which those data are currently used for classifying eye irritants according to UN GHS / EU CLP (UN, 2007; EC, 2008); (d) the standards of performance which are expected from the *in vitro* tests evaluated; (e) the way in which the *in vitro* tests are to be used (as a test within a tiered test strategy); and (f) the power of the design of the validation study.

It should be noted that the performance criteria on predictive capacity listed in section 6.4 should only be used to evaluate the validity of the SkinEthic™ HCE SE, LE and test test strategy and of the EpiOcular™ EIT as stand-alone test methods for the identification of chemicals not classified as eye irritants, in the framework of the Bottom-up/Top-down test strategy (please see the objective and goals of EIVS set out in the Project Plan). Therefore, even if the accuracy values obtained in EIVS for any of these RhT test methods are considered "definitely unacceptable" by the VMG as described in section 6.4, the test method(s) may still be useful for other purposes, e.g. the identification of chemicals not classified as eye irritants in combination with other appropriately validated test methods (i.e., use of more than one test method to identify the majority of non-classified chemicals). The EIVS VMG will consider these situations when evaluating the results of the validation study.

6.1 Flexibility Clause

Although the EIVS VMG is of the opinion that the definition of target values for test method performance prior to initiation of the experimental phase of a validation study is beneficial, bearing in mind the post-validation acceptance process, it also acknowledges that in a prospective validation study not all circumstances and possible outcomes can be considered beforehand. Thus, the following predefined and agreed target values are to be considered in the context of the practical study outcome. In case amendments are considered necessary, these will have to be scientifically justified.

6.2 Limitations of the Test Methods

The VMG also considers that it will be important to define the limitations of the test methods, and try to rationalize any apparent reasons for misclassifications before making a final recommendation about the scientific validity of the RhT test methods under evaluation. If potential reasons for misclassification strictly related to the test methods are identified, these should be considered for defining the limitations of the test method. If the estimated reliability and/or accuracy values of a test method can be improved by excluding identified limitations, these values should also be compared to the predefined test method performance criteria (sections 6.3-6.4).

6.3 Target Values for Reproducibility

Analysis of reproducibility will not be limited to the parameters described below. Other statistical tools, e.g. the overall Standard Deviation and Coefficient of Variation of the study calculated from all qualified tests as from all available tests (qualified and non-qualified), will also be considered before making a final decision on the reproducibility of the test methods.

6.3.1 Within one laboratory (and over time): The **concordance of classifications** (not classified / classified) for the set of chemicals tested during validation obtained in different, independent runs **within a single laboratory** should **ideally be equal or higher (≥) than 85%** for all participating laboratories[3].

6.3.2 Between laboratories: The **concordance of final classifications** (not classified / classified) for the set of chemicals tested during validation obtained **by the different participating laboratories** should **ideally be equal or higher (≥) than 80%**[4].

6.4 Target Values for Predictive Capacity (Accuracy)

The SkinEthic™ HCE SE, LE and test strategy and the EpiOcular™ EIT are being validated for their usefulness as stand-alone (independent) test methods to identify chemicals not classified as eye irritant (UN GHS/EU CLP No Category; "non-irritants") and their reliable discrimination from all classes of eye irritant chemicals as e.g. the initial step in a Bottom-Up approach (in the framework of a Bottom-Up/Top-Down test strategy, Scott L. *et al.*, 2010). The SkinEthic™ HCE test strategy and the EpiOcular™ EIT were developed for maximum sensitivity (ability to detect positives, with low rate of false negatives) rather than for optimal accuracy with balanced sensitivity and specificity (ability to detect negatives, with low rate of false positives). However, it was also sought to achieve a sufficiently high specificity in order to allow the identification of the highest number of chemicals not classified as irritant to the eye. By achievement of satisfactory

[3] The within laboratory reproducibility values obtained in the pre-validation of the SkinEthic™ HCE were of 90 to 100% concordance of classifications, and for EpiOcular™ EIT of 95 to 100% concordance of classifications (considering the classification cut-off of 60% viability) or of 90 to 100% concordance of classifications (considering the classification cut-off of 50% viability).

[4] The between laboratory reproducibility values obtained in the pre-validation of the SkinEthic™ HCE were of 95 to 100% concordance of classifications, and for EpiOcular™ EIT 100% concordance of classifications (considering the classification cut-off of 60% viability) or 96% concordance of classifications (considering the classification cut-off of 50% viability).

specificity, the SkinEthic™ HCE test strategy and the EpiOcular™ EIT would present stand-alone (independent) test methods for identification of "non-irritants".

Based on these premises, the EIVS VMG defined "definitely acceptable" and "definitely unacceptable" rates of overprediction and underprediction for determining the predictive performance of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT, which are outlined in Table 1. In particular, the following points were felt to be important to recommend the test methods as being sufficiently predictive to be considered as scientifically valid:

(a) About 10% false negatives should be "definitely acceptable" (sensitivity ≥ 90%), while more than 20% would be "definitely unacceptable"[5]. In previous validation studies for eye irritation led by ECVAM (Cytotoxicity and Cell-based assays) or ICCVAM (Organotypic assays) the Peer-Review Panels responsible for evaluating the validated test methods considered 0% false negatives as a test method performance criterion for acceptance of test methods to be used as an initial step in a Bottom-Up test strategy (identification of chemicals not classified as eye irritant). However, the Draize rabbit eye test shows the potential for up to 10% over classification of chemicals as UN GHS Cat. 2 (instead of UN GHS No Cat.) due solely to its within test variability (Zuang V. *et al.*, 2010). The actual rate of overprediction of the Draize test may be even higher when considering other factors like between laboratory variability and predictivity. Thus, the EIVS VMG is of the opinion that a False Negative rate up to 10% should be "definitely acceptable" for the UN GHS and EU CLP classification and labelling systems (UN, 2007; EC, 2008) for a test method to be considered useful for the identification of chemicals not classified as eye irritants as a stand-alone test (inititial step in a Bottom-up approach). Nevertheless, the nature, severity, duration, and frequency of *in vivo* eye injuries (based on the Draize eye irritation test) for chemicals that produce false negative results from *in vitro* tests will be fully discussed and considered by the VMG in assessing the usefulness and limitations of the *in vitro* test methods for regulatory hazard classification and labelling purposes.

(b) Ideally, no ocular corrosives/severe eye irritants (Category 1) should be underpredicted as No Category, but more than 10% Cat 1 chemicals being underclassified as No Category would be "definitely unacceptable".

(c) About 40% false positives should be "definitely acceptable" (specificity ≥ 60%), while more than 50% would be "definitely unacceptable"[6]. Since the purpose of the test methods will be the identification of chemicals not classified as eye irritant (UN GHS/EU CLP No Category) as an initial step of a Bottom-Up test strategy (Scott L. *et al.* 2010), the VMG considered that it is acceptable to have a lower specificity than sensitivity (higher false positives than false negatives). Nevertheless, specificity should not be too low in order to allow for the correct identification of the majority of the chemicals not classified as irritant to the eye.

[5] During pre-validation, the EpiOcular™ EIT showed a sensitivity of 99% (considering the classification cut-off of 60% viability) or of 96% (considering the classification cut-off of 50% viability), while the SkinEthic™ HCE test strategy showed a sensitivity of 87%.

[6] During pre-validation, the EpiOcular™ EIT showed a specificity of 65% (considering the classification cut-off of 60% viability) or of 72% (considering the classification cut-off of 50% viability), while the SkinEthic™ HCE test strategy showed a specificity of 69%.

(d) About 25% of overall misclassifications would be "definitely acceptable" (overall accuracy ≥ 75%), while more than 35% would be "definitely unacceptable". Potential reasons for misclassification will be analysed in detail, including individual tissue score lesions of misclassified chemicals, which may be considered in future regulatory acceptance of the evaluated assays.

(e) Misclassification of borderline chemicals, identified from *in vivo* Draize eye irritation data and/or structure-activity relationship considerations, would be easier to justify compared to non-borderline chemicals.

If the "definitely acceptable" rates of overprediction and underprediction defined in Table 1 are not attained in the validation study, but the rates obtained are not considered "definitely unacceptable" (Table 1), the VMG will not decide on the recommendation about the scientific validity of the test method before all the validation data have been evaluated and discussed as explained (see sections 6.1 and 6.2). If the accuracy values of any of the RhT test methods (EpiOcular™ EIT, SkinEthic™ HCE SE, SkinEthic™ HCE LE and SkinEthic™ HCE test strategy) as obtained in EIVS are considered "definitely unacceptable" by the VMG for a stand-alone test method, even taking into account any possible limitations of the test methods, these may still be useful for other purposes, e.g. the identification of chemicals not classified as eye irritants in combination with other methods. The EIVS VMG will consider these situations when evaluating the results of the validation study.

Table 1. VMG accepted rates of overprediction and underprediction for the SkinEthic™ HCE SE, LE and test strategy and for the EpiOcular™ EIT, in the framework of EIVS

	False Negatives[a] (%)	Cat 1 → No Cat[b] (%)	False Positives[c] (%)	Overall misclassifications[d] (%)
"Definitely acceptable" rates	≤ 10	0	≤ 40	≤ 25
Further evaluations necessary before any recommendation is made	10 < FN ≤ 20	0 < Cat 1 FN ≤ 10	40 < FP ≤ 50	25 < OM ≤ 35
"Definitely unacceptable" rates	> 20	> 10	> 50	> 35

[a] equal to (1-Sensitivity)
[b] based on the mode of all qualified tests (see section 4.3)
[c] equal to (1-Specificity)
[d] equal to (1-Overall accuracy)

7. REFERENCES

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EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Institute for Health and Consumer Protection
European Centre for the Validation of Alternative Methods (ECVAM)

ADDENDUM TO THE GUIDANCE ON EYE IRRITATION VALIDATION STUDY (EIVS) CONDUCT FOR THE RECONSTRUCTED HUMAN TISSUE (RhT) ASSAYS AND PERFORMANCE CRITERIA TO ASSESS THE SCIENTIFIC VALIDITY OF SkinEthic™ HCE AND EpiOcular™ EIT

Instructions for the Testing of Direct MTT-Reducers and/or Coloured Test Chemicals

1. Controls for direct MTT-reducers and coloured test chemicals

Controls for direct MTT-reducers (freeze killed tissues with MTT) and/or coloured test chemicals (living tissues without MTT) must always be performed irrespectively of the results of the viability tests. Therefore, even though Non-Specific MTT-reduction (NSMTT) and/or Non-Specific Colour (NSC) corrections will have no effect for MTT reducers and/or coloured test chemicals that are already identified as irritant in the viability tests, NSMTT and NSC controls must still be acquired for these chemicals.

2. Test chemicals showing %NSMTT or %NSC > 50% in any of the control tests performed

A test cannot be considered as non-qualified based only on the %NSMTT or %NSC values. According to the current EpiOcular™ EIT and SkinEthic™ HCE protocols, a %NSMTT or %NSC > 50% may suggest that the chemical is incompatible with the test method, but does not per se disqualify the test where it was obtained. A test can only be considered as non-qualified based on the variability of the two (EpiOcular™ EIT) or three (SkinEthic™ HCE) tissue replicates used in the %viability measurements or controls, or if it is included in a non-qualified run, where either the positive control or the negative control did not meet the test acceptance criteria. Moreover, the %NSMTT and %NSC cut-offs for deciding whether a direct-MTT reducer or coloured test chemical is compatible with the test method (currently defined as 50%) may be revised post-hoc by the Validation Management Group (VMG) once the testing phase of the ECVAM/COLIPA Eye Irritation Validation Study (EIVS) is completed and relevant statistical analysis have been performed.

Therefore, the laboratories participating in EIVS should always try to obtain three qualified viability tests and controls for direct MTT-reducers and/or coloured test chemicals even if %NSC or %NSMTT are > 50%. It will be up to the VMG to decide whether the test chemical should be considered incompatible with the test method when analysing the data acquired by all participating laboratories.

3. Re-testing due to failure to meet test acceptance criteria

Re-testing due to failure to meet test acceptance criteria should always be performed up to the maximum number of re-tests allowed and as long as three qualified tests (a complete test sequence) have not been obtained. Importantly, **re-testing should continue** up to the maximum number of re-tests allowed **even when** it becomes clear that **a complete test sequence** (three qualified tests) **can no longer be obtained** (see below: cases 5, 9, 13 and 18). **This rule applies to all test chemicals** (including coloured, non-coloured, MTT-reducer and non-MTT-reducer chemicals) and is important because according to sections 4.1, 4.2 and 4.3 of the Guidance on EIVS Conduct and Performance Criteria, the Within Laboratory Reproducibility will be calculated for "test chemicals for which at least **two** qualified tests are available", the Between Laboratory Reproducibility will be calculated for "test chemicals for which at least **one** qualified test per laboratory is available", and the Predictive Capacity will be calculated using **all** qualified tests obtained for each test chemical. Therefore, the order of qualified/non-qualified results should not dictate whether to proceed with testing since this would artificially bias the evaluation of the robustness of the protocol.

Finally, no further testing of a chemical by a laboratory should be performed once three qualified tests have been obtained for a test method (see below: cases 1, 2, 3, 6, 7, 10, 11, 15 and 16). Excess production of data and subsequent data selection are regarded as not appropriate. All tested tissues must be reported.

3.1. Extra re-testing of NSMTT control tissues due to failure to meet the test acceptance criterion

NSMTT controls are tested independently from viability tests (and NSC controls) since they use freeze killed tissues, which can only be used after all tissues from the same batch have already been used in a previous week. Moreover, NSMTT controls for one test method[1] only need to be performed once in each laboratory, for each direct MTT-reducer test chemical. If a NSMTT control within a qualified run does not meet the test acceptance criterion (SkinEthic™ HCE SE/LE: $SD_{\%NSMTT} > 18\%$; EpiOcular™ EIT: $Range_{\%NSMTT} > 20\%$) (non-qualified NSMTT control test), a maximum number of two additional NSMTT control tests per direct MTT-reducer chemical, per test method[1], per laboratory are admissible ("re-testing") to try obtaining one qualified NSMTT control for that chemical. Each additional NSMTT control test must be acquired concurrently with the negative control. All non-qualified NSMTT control tests have to be documented and reported.

It is important to note that although only one qualified NSMTT control test needs to be performed in each laboratory for each test method[1] for each direct MTT-reducer test chemical, a different %NSMTT value must be calculated from the single NSMTT control OD to correct each qualified viability test obtained. The %NSMTT value used to correct a qualified viability test must be calculated relative to the negative control that was run concurrently to that specific viability test. Depending on the negative control OD value that is used to calculate %NSMTT, it is possible that the same NSMTT control may meet the test acceptance criterion for one (or two) viability test(s), but not for the other. Thus, **a NSMTT control only qualifies if it meets the test acceptance criterion for all the qualified viability tests it needs to correct.**

If more than one qualified NSMTT control test is obtained in one laboratory for the same test chemical with the same test method[1], the mean of the different corrected OD values obtained

[1] SkinEthic™ HCE SE and SkinEthic™ HCE LE are considered as two separate and independent test methods when considering re-testing and re-running.

for those NSMTT control tests (EpiOcular™ EIT: OD_{KC}; SkinEthic™ HCE SE/LE: OD_{KT}-OD_{KU}) should be used to calculate one single %NSMTT value per qualified viability test.

3.2. Extra re-testing of coloured test chemicals due to failure to meet the test acceptance criterion in NSC control tissues

For coloured chemicals, NSC controls must be run concurrently with every viability test since the same tissue batch must be used for a viability test and its NSC control. Therefore, a viability test that meets the test acceptance criterion (SkinEthic™ HCE SE/LE: $SD_{\%Viability} \leq 18\%$; EpiOcular™ EIT: $Range_{\%Viability} \leq 20\%$) may still not qualify if the concurrent NSC control does not meet its test acceptance criterion (SkinEthic™ HCE SE/LE: $SD_{\%NSC} > 18\%$; EpiOcular™ EIT: $Range_{\%NSC} > 20\%$) (see below: for example, cases 6, 7, 8 and 9). In order to compensate for the higher probability of obtaining a non-qualified test with a coloured chemical (where two separate test acceptance criteria must be met) as compared to a non-coloured chemical (where only one test acceptance criterion must be met), a maximum number of four additional tests per coloured chemical, per test method[1], per laboratory are admissible to try obtaining a complete test sequence. Thus, a total of seven tests may be performed with coloured test chemicals in order to try obtaining three qualified tests (where both the viability test and the NSC control qualify). This corresponds to two extra re-tests in addition to the two already permitted in the Guidance on EIVS Conduct and Performance Criteria. However, the sixth and seventh tests for coloured test chemicals can only be performed if in the first five tests there are no more than two tests with $SD_{\%Viability} > 18\%$ (SkinEthic™ HCE SE/LE) or with $Range_{\%Viability} > 20\%$ (EpiOcular™ EIT), and no more than two tests with $SD_{\%NSC} > 18\%$ (SkinEthic™ HCE SE/LE) or with $Range_{\%NSC} > 20\%$ (EpiOcular™ EIT) (see below: cases 4, 5, 8, 9, 12, 13 and 14 where a 6th and 7th test cannot be performed; and cases 15, 16, 17 and 18 where up to 7 tests must be performed to generate a complete test sequence). Each additional viability test and NSC control test must be acquired concurrently with the positive control and the negative control. All non-qualified tests (including viability tests and concurrent NSC controls) have to be documented and reported.

4. Re-running due to failure to meet test acceptance criteria for the positive or the negative control

4.1. Extra re-running in each laboratory due to failure to meet test acceptance criteria for the positive or the negative control

If a run does not meet the acceptance criteria for the negative control and/or positive control, as defined in the SkinEthic™ HCE and EpiOcular™ EIT protocols (non-qualified run), the full run must be repeated for all test chemicals included in the non-qualified run. A maximum number of eight[2] additional runs are admissible per laboratory, per test method[1] ("re-running") to complement missing data due to failure to meet the negative control or positive control acceptance criteria. Thus, in addition to the six re-runs already foreseen in the Guidance on EIVS Conduct and Performance Criteria, two extra re-runs are now permitted. This amendment is proposed because the total number of runs required to generate three tests per test chemical in one laboratory is higher than the 30 initially predicted, which did not consider the need to run NSMTT and NSC controls. Assuming that 1/3 of the chemicals (about 35) will

[2] This limit was defined by calculating the critical (smallest) number of repetitions that will result in a probability less then 5% assuming a binomial distribution with a failing rate of 10% and 40 runs in total.

require controls in three runs, an extra 10 runs will be required to generate three tests per test chemical plus controls in one laboratory. These extra 10 runs justify the two extra re-runs now permitted. Non-qualified runs have to be documented and reported. None of the tests within the first eight non-qualified runs obtained by a laboratory for each test method[1] should be considered non-qualified, nor should they be used for any calculations.

5. Re-testing due to technical issues

5.1. Extra re-testing of NSMTT control tissues due to technical issues

A NSMTT control test for a direct MTT-reducer test chemical may be repeated twice (re-tested) to replace NSMTT control tests that failed due to technical reasons (technical issue) and that were not finished (OD measurement not performed). These two re-tests are allowed in each laboratory and for each test method[1], independently of the re-testing allowed due to failure to meet the test acceptance criterion (see section 3.1 above). A NSMTT control that fails due to technical reasons does not disqualify viability tests or NSC controls since, as explained above, NSMTT controls are independent from viability tests and NSC controls (see section 3.1). All technical issues must be documented and reported to the core VMG.

5.2. Extra re-testing of coloured test chemicals due to technical issues in NSC control tissues

A coloured test chemical may be re-tested twice (including viability test and NSC control) to replace tests that failed due to a technical issue in NSC controls and that were not finished (OD measurement not performed for either the viability tissues or the NSC control tissues). Thus, four re-tests (including viability test and NSC control) due to 2 technical issues in viability tissues and 2 technical issues in NSC control tissues are allowed per coloured test chemical in each laboratory, for each test method[1], independently of the re-testing allowed due to failure to meet test acceptance criteria (see section 3.2 above). Each time a coloured test chemical is re-tested due to technical reasons, both the viability test and the NSC control must be re-tested concurrently since, as explained above, the same tissue batch must be used for the viability test and its NSC control (see section 3.1). All technical issues must be documented and reported to the core VMG.

		Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7
Case 1 (Complete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off				
	SD/range %NSC	< cut-off	< cut-off	< cut-off				
	Qualified Test	**YES**	**YES**	**YES**				
A 4th and 5th test is not required since all 3 first tests qualified.								
Case 2 (Complete Test Sequence)	SD/range %Viab.	< cut-off	> cut-off	< cut-off	< cut-off			
	SD/range %NSC	< cut-off	< cut-off	< cut-off	< cut-off			
	Qualified Test	**YES**	**No**	**YES**	**YES**			
A 5th, 6th and 7th test is not required since 3 qualified tests were obtained in 4 tests.								
Case 3 (Complete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	> cut-off	< cut-off	< cut-off		
	SD/range %NSC	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**YES**	**No**	**YES**	**YES**		
A 6th and 7th test is not required since 3 qualified tests were obtained in 5 tests.								
Case 4 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	> cut-off	< cut-off	> cut-off		
	SD/range %NSC	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**YES**	**No**	**YES**	**No**		
A 6th and 7th test cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %Viability above the cut-off.								
Case 5 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	< cut-off	> cut-off	*		
	SD/range %NSC	< cut-off	< cut-off	< cut-off	< cut-off	*		
	Qualified Test	**No**	**No**	**YES**	**No**	*		
A 6th and 7th tests cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %Viability above the cut-off. * A 5th test must be performed even though a complete test sequence (one containing 3 qualified tests) can no longer be obtained in 5 tests.								

		Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7
Case 6 (Complete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off	< cut-off			
	SD/range %NSC	< cut-off	< cut-off	> cut-off	< cut-off			
	Qualified Test	**YES**	**YES**	**No**	**YES**			
A 5th, 6th and 7th test is not required since 3 qualified tests were obtained in 4 tests.								
Case 7 (Complete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	SD/range %NSC	< cut-off	> cut-off	< cut-off	> cut-off	< cut-off		
	Qualified Test	**YES**	**No**	**YES**	**No**	**YES**		
A 6th and 7th test is not required since 3 qualified tests were obtained in 5 tests.								
Case 8 (Incomplete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	SD/range %NSC	> cut-off	> cut-off	< cut-off	< cut-off	> cut-off		
	Qualified Test	**No**	**No**	**YES**	**YES**	**No**		
A 6th and 7th test cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %NSC above the cut-off.								
Case 9 (Incomplete Test Sequence)	SD/range %Viab.	< cut-off	< cut-off	< cut-off	*	*		
	SD/range %NSC	> cut-off	> cut-off	> cut-off	*	*		
	Qualified Test	**No**	**No**	**No**	*	*		
A 6th and 7th test cannot be performed under the revised rules for re-testing since there are already 3 tests with SD or range of %NSC above the cut-off in the first 3 tests. * A 4th and 5th test must be performed even though a complete test sequence (one containing 3 qualified tests) can no longer be obtained in 5 tests.								

		Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7
Case 10 (Complete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	< cut-off	< cut-off	< cut-off		
	SD/range %NSC	< cut-off	> cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**No**	**YES**	**YES**	**YES**		
A 6th and 7th test is not required since 3 qualified tests were obtained in 5 tests.								
Case 11 (Complete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off		
	SD/range %NSC	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**No**	**YES**	**YES**	**YES**		
A 6th and 7th test is not required since 3 qualified tests were obtained in 5 tests.								
Case 12 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	< cut-off	< cut-off	> cut-off		
	SD/range %NSC	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off		
	Qualified Test	**No**	**No**	**YES**	**YES**	**No**		
A 6th and 7th test cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %Viability above the cut-off.								
Case 13 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	> cut-off	*	*		
	SD/range %NSC	> cut-off	< cut-off	< cut-off	*	*		
	Qualified Test	**No**	**No**	**No**	*	*		
A 6th and 7th test cannot be performed under the revised rules for re-testing since there are already 3 tests with SD or range of %Viability above the cut-off in the first 3 tests. * A 4th and 5th test must be performed even though a complete test sequence (one containing 3 qualified tests) can no longer be obtained in 5 tests.								
Case 14 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	> cut-off	< cut-off	> cut-off		
	SD/range %NSC	> cut-off	< cut-off	< cut-off	< cut-off	> cut-off		
	Qualified Test	**No**	**YES**	**No**	**YES**	**No**		
A 6th and 7th test cannot be performed under the revised rules for re-testing since within the first 5 tests there are 3 tests with SD or range of %Viability above the cut-off.								

		Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test 7
Case 15 (Complete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	> cut-off	< cut-off	< cut-off	< cut-off	
	SD/range %NSC	> cut-off	< cut-off	< cut-off	< cut-off	> cut-off	< cut-off	
	Qualified Test	**No**	**YES**	**No**	**YES**	**No**	**YES**	
A 6th test must be acquired under the revised rules for re-testing to try obtaining 3 qualified tests, since within the first 5 tests there are only 2 tests with SD or range of %Viability above the cut-off and only 2 tests with SD or range of %NSC above the cut-off. A 7th test is not required since 3 qualified tests were obtained in 6 tests.								
Case 16 (Complete Test Sequence)	SD/range %Viab.	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off	< cut-off	< cut-off
	SD/range %NSC	< cut-off	< cut-off	> cut-off	> cut-off	< cut-off	< cut-off	< cut-off
	Qualified Test	**No**	**No**	**No**	**No**	**YES**	**YES**	**YES**
A 6th and 7th test must be acquired under the revised rules for re-testing to try obtaining 3 qualified tests, since within the first 5 tests there are only 2 tests with SD or range of %Viability above the cut-off and only 2 tests with SD or range of %NSC above the cut-off.								
Case 17 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	< cut-off	< cut-off	< cut-off	> cut-off	< cut-off
	SD/range %NSC	< cut-off	< cut-off	> cut-off	> cut-off	< cut-off	< cut-off	> cut-off
	Qualified Test	**No**	**YES**	**No**	**No**	**YES**	**No**	**No**
A 6th and 7th test must be acquired under the revised rules for re-testing to try obtaining 3 qualified tests, since within the first 5 tests there is only 1 test with SD or range of %Viability above the cut-off and only 2 tests with SD or range of %NSC above the cut-off.								
Case 18 (Incomplete Test Sequence)	SD/range %Viab.	> cut-off	< cut-off	< cut-off	< cut-off	> cut-off	> cut-off	*
	SD/range %NSC	< cut-off	< cut-off	> cut-off	> cut-off	< cut-off	< cut-off	*
	Qualified Test	**No**	**YES**	**No**	**No**	**No**	**No**	*
A 6th and 7th test must be acquired under the revised rules for re-testing to try obtaining 3 qualified tests, since within the first 5 tests there are only 2 tests with SD or range of %Viability above the cut-off and only 2 tests with SD or range of %NSC above the cut-off. * A 7th test must be performed even though a complete test sequence (one containing 3 qualified tests) can no longer be obtained in 7 tests.								

Appendix VIII Project Plan

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Institute for Health and Consumer Protection
European Centre for the Validation of Alternative Methods (ECVAM)

Eye Irritation Validation Study (EIVS)
Validation of the SkinEthic™ HCE SE, LE and Test Strategy and of the EpiOcular™ EIT for the Prediction of Acute Eye Irritation
Project Plan

Version	Author	Reviewer	Approver	Date of approval
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Document history

Version	Date	Drafted by	Comments

EYE IRRITATION VALIDATION STUDY (EIVS)

PROJECT PLAN

Validation of the SkinEthic™ HCE SE, LE and Test Strategy and of the EpiOcular™ EIT for the Prediction of Acute Eye Irritation

1. Definitions

EpiOcular™ model/construct: A reconstructed human tissue (RhT) construct produced by MatTek Corporation, consisting of a non-keratinized multilayered epithelium prepared from non-transformed, human-derived epidermal keratinocytes.

SkinEthic™ Human Corneal Epithelium (HCE) model/construct: A RhT construct produced by SkinEthic™ Laboratories, consisting of a a multilayered epithelium prepared from immortalized human corneal epithelial cells.

EpiOcular™ Eye Irritation Test (EIT): A test method to predict eye irritation, employing the EpiOcular™ RhT construct as test system and a protocol defining different exposure and post-exposure incubations for liquids and solids (i.e., liquids: 30 min exposure followed by 120 min post-treatment incubation, and solids: 90 min exposure followed by 18 hours post-treatment incubation).

SkinEthic™ HCE Short-time Exposure (SE): A test method to predict eye irritation, employing the SkinEthic™ HCE RhT construct as test system and a short-time exposure of test chemicals (i.e., 10 min exposure without post-treatment incubation).

SkinEthic™ HCE Long-time Exposure (LE): A test method to predict eye irritation, employing the SkinEthic™ HCE RhT construct as test system and a long-time exposure of test chemicals (i.e., 1 h exposure followed by 16 h post-treatment incubation).

Eye irritation Peptide Reactivity Assay (EPRA): A test method to predict chemical reactivity, defined as the electrophilic potential of the chemical to react with cysteine or lysine containing peptides.

SkinEthic™ HCE test strategy/method: A test strategy to predict eye irritation, consisting of three separate assays (i.e., EPRA, SkinEthic™ HCE SE, and SkinEthic™ HCE LE). In the SkinEthic™ HCE test strategy, chemical reactivity, as determined by the EPRA, is used to decide if a chemical is tested with SkinEthic™ HCE SE (reactive chemicals) or SkinEthic™ HCE LE (non-reactive or inconclusive chemicals).

2. Study Objective

The objective of this study is to formally validate the SkinEthic™ HCE SE, LE and test strategy and the EpiOcular™ EIT by inter-laboratory ring trial study, to facilitate international acceptance in regulatory schemes for hazard assessment of chemicals. In particular, these test methods/strategy shall be incorporated into a tiered test strategy (so-called Bottom-Up/Top-Down test strategy, as defined in an ECVAM workshop held in 2005, Scott L. *et al.*, 2010) as e.g. the initial step in a Bottom-Up approach or the second step in a Top-Down Approach. The ultimate purpose of a tiered test strategy will be to replace the traditional *in vivo* Draize eye irritation test [Method B.5 of EC Regulation 440/2008 (EC, 2008a) or OECD TG 405 (OECD, 2002)].

3. Study Goals

The goal of the Eye Irritation Validation Study (EIVS) is to assess the relevance (predictive capacity) and reliability (reproducibility within and between laboratories) of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT, by testing a statistically significant number of coded test chemicals (substances and mixtures), supported by complete and quality assured *in vivo* Draize eye irritation data for comparative evaluation of results.

Specifically, EIVS will assess the validity of the SkinEthic™ HCE SE, LE and test strategy and of the EpiOcular™ EIT as stand-alone (independent) test methods to reliably discriminate chemicals not classified as eye irritant ("non-irritants") from all classes of eye irritant chemicals (in the framework of a Bottom-Up/Top-Down test strategy, Scott L. *et al.*, 2010), defined according to the United Nations Globally Harmonized System (GHS) of Classification and Labelling of Chemicals (UN GHS: No Category versus Category 1/Category 2A/Category 2B; UN, 2007) and as implemented in the European Commission Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (EU CLP: No Category versus Category 1/Category 2).

The SkinEthic™ HCE test strategy and the EpiOcular™ EIT were developed for maximum sensitivity (ability to detect positives, with low rate of false negatives) rather than for optimal overall accuracy with balanced sensitivity and specificity (ability to detect negatives, with low rate of false positives). Sensitivity had therefore a bigger weight than specificity and overall accuracy in their development. However, it was also sought to achieve a sufficiently high specificity and overall accuracy, in order to allow identification of the highest number of chemicals not classified as irritant to the eye. By achieving satisfactory specificity, the SkinEthic™ HCE test strategy and the EpiOcular™ EIT would represent stand-alone (independent) test methods for the identification of "non-irritants". Importantly, the test methods are not intended to differentiate between UN GHS/EU CLP Category 1 (irreversible effects) and UN GHS/EU CLP Category 2 (reversible effects). As proposed by the ECVAM workshop of February 2005, this differentiation would be left to another tier of the Bottom-Up/Top-Down test strategy (Scott L. *et al.*, 2010).

The EIVS will be undertaken in accordance with the principles and criteria documented in the OECD *Guidance Document on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment* (No. 34, OECD, 2005) and according to the Modular Approach to validation (Hartung T. *et al.*, 2004).

4. Test Methods

The SkinEthic™ HCE SE, LE and test strategy and the EpiOcular™ EIT have progressed through protocol optimisation and multi-laboratory assessment and will be evaluated in EIVS. The

SkinEthic™ HCE SE/LE and the EpiOcular™ EIT use as test systems reconstructed human tissue (RhT) constructs, and consist of a topical exposure of the neat test chemical to the epithelial surface of the tissue construct.

The EpiOcular™ tissue construct is a non-keratinized multilayered epithelium prepared from non-transformed, human-derived epidermal keratinocytes. It is intended to model the cornea epithelium with progressively stratified but not cornified cells. These cells are not transformed or transfected with genes to induce an extended life span in culture. The "tissue" is prepared in inserts with a porous membrane (MTI-003) through which the nutrients pass to the cells. A cell suspension is seeded into the MTI-003 membrane in specialized medium. After a period of initial cell proliferation, the medium is removed from the top of the tissue so that the epithelial surface is in direct contact with the air. This allows the test chemical to be directly applied to the epithelial surface in a fashion similar to how the corneal epithelium would be exposed *in vivo*. The ability to expose the tissue topically is essential to model the same kind of progressive injury expected *in vivo*. It also allows both solid and liquid test chemicals to be applied directly to the tissue. In the EpiOcular™ EIT, liquids and solids are treated with different exposure and post-exposure incubations (i.e., liquids: 30 min exposure followed by 120 min post-treatment incubation, and solids: 90 min exposure followed by 18 hours post-treatment incubation).

To construct SkinEthic™ HCE tissues, immortalized human corneal epithelial cells are cultured in a chemically defined medium and seeded on a polycarbonate membrane at the air–liquid interface. The tissue construct obtained is a multilayered epithelium resembling the *in vivo* corneal epithelium. As *in vivo*, columnar basal cells are present, including Wing cells. The model is characterized by the presence of specific ultra structural figures like intermediate filaments, mature hemi-desmosomes and desmosomes. Specific cytokeratins 64kD (K.3) have also been described (Nguyen D.H. *et al.*, 2003).

The SkinEthic™ HCE test strategy uses three separate assays, i.e. EPRA, SkinEthic™ HCE SE, and SkinEthic™ HCE LE. In this strategy, test chemicals are tested in a short-time exposure (SkinEthic™ HCE SE: 10 min exposure without post-treatment incubation) or a long-time exposure (SkinEthic™ HCE LE: 1 h exposure followed by 16 h post-treatment incubation) depending on their chemical reactivity (defined as the electrophilic potential to react with cysteine or lysine containing peptides), as measured by the Eye irritation Peptide Reactivity Assay (EPRA).

Following treatment with a test chemical as described above (using EpiOcular™ EIT, SkinEthic™ HCE SE or SkinEthic™ HCE LE), the relative tissue viability is determined against the negative control-treated constructs by the reduction of the vital dye MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide). Tissues treated with eye irritants (UN GHS/EU CLP Category 2 and Category 1) are expected to show a decrease in viability below a certain threshold in respect to the negative control.

5. Validation Management Group

The management structure of EIVS and the responsibilities of the different members are shown in Figure 1. The Validation Management Group (VMG), with supervisory role, comprises:

Core VMG

- Chair (Stuart Freeman)
- Co-chair (Valérie Zuang)
- COLIPA sponsor representative (Pauline McNamee; *alternate*: Penny Jones)
- ECVAM sponsor representative (João Barroso)
- TNO coordinator representative (Jan Lammers; *alternate*: Ruud Woutersen)
- TNO biostatistician (Carina de Jong-Rubingh)
- ECVAM biostatistician (André Kleensang until 30.09.2010)[1]
- Independent scientist (Chantra Eskes)
- Chemicals Selection Group (CSG) coordinator (Thomas Cole)

Representatives of the lead laboratories

- SkinEthic™ HCE test strategy lead laboratory: L'Oréal (Nathalie Alépée)
- EpiOcular™ EIT lead laboratory: Beiersdorf (Uwe Pfannenbecker)

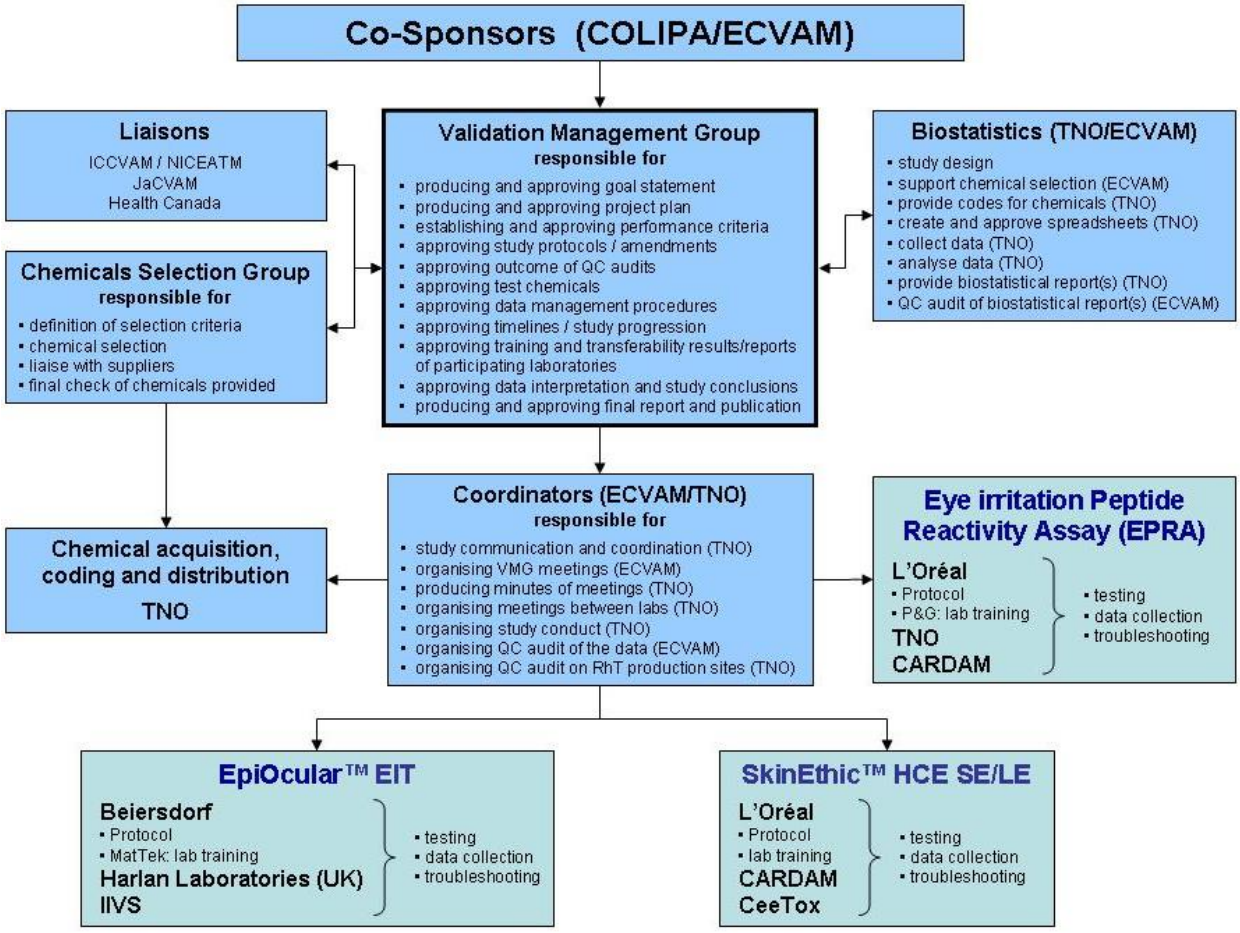
In addition, in the framework of the International Cooperation on Alternative Test Methods (ICATM), Liaisons from the USA, Japan and Canada are represented on the VMG namely:

- NICEATM (William Stokes; *alternates:* Warren Casey, David Allen, Elizabeth Lipscomb)
- ICCVAM (Jill Merrill)
- JaCVAM (Hajime Kojima)
- Health Canada (Alison McLaughlin)

Operational decisions will be taken by the core VMG only. Representation of the lead laboratories allows consultation on technical issues relating to the test systems and monitoring progress of experimental work, but will not be involved in discussions regarding the chemicals selection. The ICATM liaisons are invited to advise the VMG.

[1] From 30 September 2010, there will be no official representation from an ECVAM biostatistician in the VMG. Nevertheless, ECVAM will continue providing the planned biostatistical support to EIVS after this date.

Figure 1: Management Structure of the ECVAM Eye Irritation Validation Study



6. Study Coordination and Sponsorship

6.1. Overall study coordination

The overall study coordination will be conducted by ECVAM. This will include the organisation of all necessary VMG meetings and teleconferences, and the maintenance of a website where all EIVS documents not related to chemical selection are made available to VMG members and ICATM liaisons. ECVAM will also be responsible for organising the Quality Control audits on data collection, handling and analysis, as well as on the biostatistical reports produced by the TNO biostatistician.

6.2. Logistical coordination and communication

The TNO (Quality of Life) representative will coordinate the communication flow between all parties, draft minutes of VMG meetings and telephone conferences, organize meetings between laboratories, and organise the study conduct. TNO has also responsibility for logistics of test chemical acquisition, coding and distribution. Finally, the TNO representative will arrange quality control audits on the RhT production sites.

6.3. Study sponsorship

ECVAM and COLIPA will co-sponsor EIVS, with the main financial support being provided by COLIPA.

COLIPA will finance:

- conduct of the chemical reactivity assays
- lead and participating laboratories for the two test methods
- statistical support provided by TNO
- financial support of the independent chair of the VMG
- independent CRO responsible for the test chemicals purchase, coding and distribution to the laboratories
- overall logistical coordination of the study
- part of the independent QC audit on the RhT models production sites
- purchase cost of existing chemicals
- purchase of a proportion of the RhT tissues

ECVAM will finance:

- management and coordination of the study, including the organisation of all VMG meetings
- statistical support provided by ECVAM
- part of the independent QC audit on the RhT models production sites
- independent QC audit on data collection, handling and analysis
- independent QC audit of the biostatistical report(s)
- purchase of a proportion of the RhT tissues
- publication of the study

7. Chemicals Selection

7.1. Chemicals Selection Group (CSG)

The CSG is composed of the following members:

Tom Cole (ECVAM; coordinator)
João Barroso (ECVAM)
Chantra Eskes (independent scientist)
William Stokes (NICEATM)
Amanda Cockshott (HSE; UK Competent Authority)
Betty Hakkert (RIVM; NL Competent Authority)

The roles and responsibilities of the CSG are shown in Figure 1.

The members of Competent Authorities (Amanda Cockshott and Betty Hakkert) will give support in reviewing *in vivo* Draize eye irritation reports on CosIng ingredients provided by DG SANCO.

In the framework of the International Cooperation on Alternative Test Methods (ICATM), liaisons from NICEATM, ICCVAM, JaCVAM and Health Canada are invited to propose eligible test chemicals for selection, supported by quality assured *in vivo* Draize eye irritation data.

7.2. Chemicals selection

A principal criterion for selection of test chemicals is availability of supporting complete and quality assured *in vivo* Draize eye irritation data, for comparative evaluation of *in vitro* method predictive capacity. Complete *in vivo* Draize eye irritation data sets comprise severity and duration of ocular toxicity effects, registered over a 21 day observation period as irritation scores for corneal opacity, iritis and conjunctival chemosis/redness. Eligibility of test chemicals will be confirmed by compilation of *in vivo* Draize eye irritation data into a customised Excel template where algorithms generate systematic assignment of eye irritation EU DSD, UN GHS / EU CLP and US EPA classifications.

Intending to challenge performance of the *in vitro* tissue models, diverse chemicals will be sought that have not been previously tested during protocol R&D, optimisation and pre-validation. Therefore, in shortlisting chemicals from recognised sources (e.g., ECETOC, TSCA, ZEBET, NIHS Japan, EPA, etc.) those chemicals reported in the original test submissions will be avoided.

One potential source for screening eligible chemicals which will be considered by the CSG is the official European Commission inventory of cosmetic ingredients (CosIng). CosIng is supported by consolidated documentation (opinions) issued by the Scientific Committee on Consumer Safety (SCCS) with references to confidential *in vivo* Draize eye irritation studies archived by DG-SANCO. In collaboration with SCCS and DG-SANCO, *in vivo* Draize eye irritation data on CosIng chemicals will be reviewed, and sample material availability determined. For eligible chemicals, *in vivo* Draize eye irritation study sponsors will be requested to authorise use and eventual publication of eye irritation data and, in cases of proprietary production, to supply sample material for *in vitro* assay.

Proprietary new substances notified under Directive 67/548/EEC present another unique potential source, qualified by *in vivo* Draize eye irritation studies compliant with official guidelines and reviewed by Competent Authorities. Notification files (with summary *in vivo* Draize eye irritation data) archived in a confidential new chemicals database (NCD) accessible to authorised European Commission and Competent Authority personnel in the CSG, allow shortlisting of eligible candidates according to the notifier/producer. Under the auspices of the European Partnership for Alterative Approaches to Animal Testing (EPAA) affiliated companies will be invited to collaborate in determining availability of sample material, with release of supporting *in vivo* Draize eye irritation study reports. Initiative within cooperative companies to propose additional and/or alternative chemicals would also be welcomed.

A sample size calculation by the ECVAM biostatistician and the TNO biostatistician has shown that 104 test chemicals will be required for this validation study.

Ideally, chemical selection should achieve a balanced set of (i) irritancy (UN GHS/EU CLP categories 1 and 2 versus no category); (ii) physical state (liquids versus solids); and (iii) EPRA reactivity (reactive versus non-reactive). Acknowledging practicality of achieving a perfectly balanced set covering all three conditions, the VMG agreed the following limits: (i) an overall 50±5% split of UN GHS/EU CLP categories 1 and 2 versus no category, with a 50/50 split between category 1 and category 2, including adequate representation of UN GHS sub-categories 2A and 2B; (ii) an overall 50±10% split of solids versus liquids; and (iii) an overall 50±15% split

of reactive versus non-reactive chemicals (based on EPRA analyses). Similarly, the selection would aim for an even distribution of physical state (50±10% split of liquids versus solids) and EPRA reactivity (50±15% split of reactive versus non-reactive) among each irritancy sub-group (no category, category 2B, category 2A and category 1).

Significantly, since EPRA reactivity is not known in advance, the parameter cannot be applied as an eligibility criterion *a priori*. Thus, the VMG agreed to a wider limit of acceptance (50±15%) for the proportion of reactive versus non-reactive chemicals. In event of EPRA results demonstrating significant bias in reactivity distribution, this limit would have to be reconsidered.

The chemical selection would also aim for representation of a range of ocular toxicity effects, evident from distributions and persistence of irritation scores.

Final approval of the test chemicals proposed by the CSG is the responsibility of the core VMG. Respecting non-disclosure of chemical identities to the test facilities, the VMG lead laboratory representatives will not participate in the selection process.

The VMG recognises that commercial availability of selected test chemicals would facilitate future identification of performance standard reference chemicals, relevant to similar method catch-up studies (Performance Standards-based validation). Therefore, the CSG will limit the selection of proprietary chemicals and will aim at having at least ⅔ of commercially available chemicals (~70 chemicals) in their final chemical selection (at least 104 test chemicals), which present a balanced distribution of irritancy, physical state and reactivity similar to the overall set of selected test chemicals (see above). As such, ample scope for establishing a robust set of reference chemicals upon completion of EIVS shall be ensured.

8. Chemical Acquisition, Coding and Distribution

Independent coding and distribution of test chemicals will be contracted out by the sponsor COLIPA to TNO. TNO is certified according to ISO 9001 and GLP, and has proven experience of reliable services. TNO will purchase, code and supply existing chemicals, including cosmetic ingredients from the CosIng inventory. The CSG coordinator will ask companies producing new chemicals to send samples directly to TNO for coding and distribution. All test chemicals will be randomly coded. Each test chemical will have a code that is unique for each laboratory. The same code will be used for the SkinEthic™ HCE SE and for the SkinEthic™ HCE LE assays but otherwise distinct codes will also be used for each test method/assay (i.e., EpiOcular™ EIT, SkinEthic™ HCE SE/LE and EPRA) that is run in the same laboratory. The codes will be generated and provided by the TNO biostatistician. Expiry dates will be provided for all test chemicals. Furthermore, when available, a single Molecular Weight and a single purity for each coded test chemical will be provided to the laboratories performing the EPRA to allow preparation of Molar solutions, as required by the EPRA Protocol. This includes pure substances and mixtures. For mixtures, the single purity will be determined by the sum of the proportion of its components (excluding water), while the single Molecular Weight will be determined by considering the individual Molecular Weights of each component in the mixture (excluding water) and their individual proportions. In exceptional cases (e.g., complex mixtures or polymers) Molecular Weights and exact proportions of components may not be available.

Personnel responsible for chemical acquisition, coding and distribution shall be independent from those conducting the EPRA for EIVS.

9. Receipt and Handling of Chemicals

Coded test chemicals as well as a health and safety information package will be dispatched to the Safety Officer of each participating laboratory (see sections 10.1-10.3 and 11.4) in appropriate packaging, compliant with relevant regulatory requirements. The participating laboratories shall be notified by TNO when the test chemicals are shipped, shall make proper provision for their receipt, and promptly acknowledge that they have been received. Upon receipt at the laboratory, the test chemicals shall be stored in appropriate storage conditions as indicated in the unsealed accompanying documentation and must be stored for at least six months following submission of the final biostatistical report to the VMG.

The health and safety information package will include a sealed envelope for each test chemical identified by chemical code. Each envelope will contain a MSDS and a certificate of analysis for the respective test chemical. A sealed envelope shall be opened at the laboratory only in an emergency/need-to-know situation. At the end of EIVS, the Safety Officer shall return the health and safety information package with all unopened envelopes to the VMG (Logistics Coordinator). If a sealed envelope from the health and safety information package is opened by the laboratory, the Safety Officer shall immediately notify the VMG designated contact, i.e. the Logistics Coordinator (Jan Lammers, TNO).

The Study Director of each laboratory (see sections 10.1-10.3 and 11.1) shall receive essential information about the test chemicals (e.g. storage instructions). Upon receipt, each laboratory must complete and return the Test Chemical Receipt Report (Annex I).

Appropriate routine safety procedures shall be followed in handling the test chemicals unless otherwise specified in the unsealed documentation supplied at the time of chemical distribution. Laboratory personnel shall be instructed to treat all coded test chemicals as very hazardous and to dispose of laboratory waste as toxic waste.

10. Participating Laboratories

The laboratories participating in the study are defined as shown in Figure 1. The specific obligations and responsibilities of the participating laboratories will be specified in contracts between the sponsor COLIPA and the laboratories. These include, but are not limited to, the adherence to this project plan throughout the study, the adherence to the test method protocol, the adherence to the work program, assuring compliance with GLP-like principles, specifying and applying proper Quality Assurance procedures, and meeting the data submission deadlines. The participating laboratories shall have competence in performing the test method(s) and shall provide competent personnel, adequate facilities, equipment, supplies, and proper health and safety guidelines. The lead laboratories are further responsible for preparing detailed protocols for the EpiOcular™ EIT, SkinEthic™ HCE SE/LE and EPRA, and for providing training to the technical staff of the other testing facilities. The contracts between COLIPA and the laboratories should also clarify the ownership of results and the publication procedures.

The participating laboratories are allowed to freely communicate and meet during the training and transfer phases of EIVS. Such meetings will be organized by the lead laboratories and can occur without a formal approval by the VMG. However, during the testing phase, the participating laboratories and the personnel responsible for providing training on the test methods, will no longer contact each other regarding this validation study without the previous knowledge and approval by the VMG. All VMG approved meetings or other forms of communication between the participating laboratories during the testing phase will be organized by the Logistics Coordinator in collaboration with the lead laboratories.

10.1. Cys/Lys EPRA

Three laboratories will participate in EIVS for testing with the EPRA. These are:

- Lead laboratory – L'Oréal
  - Study Director: Nathalie Alépée
  - Safety Officer: Joan Eilstein
- Laboratory 1 – TNO
  - Study Director: Brigitte Buscher
  - Safety Officer: Hans Ram
- Laboratory 2 – CARDAM
  - Study Director: Griet Jacobs
  - Safety Officer: Frank Vander Plaetse / Katrien Smits

10.2. EpiOcular™ EIT

Three laboratories will participate in EIVS for testing with the EpiOcular™ EIT. These are:

- Lead laboratory – Beiersdorf
  - Study Director: Uwe Pfannenbecker
  - Safety Officer: Peter Klaws
- Laboratory 2 – Harlan Laboratories Ltd. (UK)
  - Study Director: Andrew Whittingham
  - Safety Officer: Christine Cauldwell
- Laboratory 3 – IIVS
  - Study Director: Hans Raabe
  - Safety Officer: Nathan Wilt

A reserve laboratory is also identified as Pierre-Fabre (Contact Person: Sandrine Bessou-Touya)

10.3. SkinEthic™ HCE SE/LE

Three laboratories will participate in EIVS for for testing with the SkinEthic™ HCE SE/LE. These are:

- Lead laboratory – L'Oréal
  - Study Director: Nathalie Alépée
  - Safety Officer: Samuel Blond
- Laboratory 2 – CARDAM
  - Study Director: An van Rompay
  - Safety Officer: Frank Vander Plaetse / An Jacobs
- Laboratory 3 – CeeTox Inc.
  - Study Director: Colleen Toole
  - Safety Officer: Karen Rutherford

A reserve laboratory is to be identified.

11. Laboratory Personnel

11.1. Study Directors

Each participating laboratory shall appoint a Study Director (see sections 10.1-10.3), a scientist of appropriate education, training, and experience in the field. The Study Director represents the single point of study control with ultimate responsibility for the overall technical conduct of the study, the documentation and reporting of the results, as well as GLP adherence or adherence to the minimum quality requirements (see section 14).

The Study Director is responsible for collecting the data of his/her laboratory and to send them to the Logistics Coordinator of the study (to be forwarded to the TNO biostatistician) according to the timelines established in the Project Plan (see section 17).

The Study Directors are also responsible for sending timely Study Reports to the contact person of the VMG, i.e. the Logistics Coordinator, who will monitor the progress of the study. Such reports should include all relevant experimental data as well as all deviations from the Project Plan and Test Method protocols.

The study directors will be the primary contact point for the communications between the VMG and the testing facilities unless otherwise requested.

11.2. Quality Assurance (QA) Officers

For participating laboratories that are GLP compliant the Quality Assurance Officer shall assure conformity with GLP requirements for all aspects of the study (facilities, equipment, personnel, methods, practices, records, controls, SOPs, Test Method protocol, final reports (for data integrity), and archives). The Quality Assurance Officer is entirely separate from and independent of the personnel engaged in the direction and conduct of the study.

Participating laboratories that are not GLP compliant, shall appoint an individual to assure that all records, documents, raw data and reports are available to the VMG if an inspection is requested, and ensure that the quality assurance provisions detailed in the section 14 (see below) have been implemented.

11.3. Experimental team

The conduct of the EpiOcular™ EIT, SkinEthic™ HCE SE/LE and EPRA requires personnel trained and competent in the specific techniques and general laboratory procedures. Each individual engaged in the conduct of, or responsible for, the supervision of a validation study shall have education, training, and experience, or combination thereof, to enable that individual to perform the assigned duties.

11.4. Safety Officers

A designated Safety Officer (not otherwise involved in the actual conduct of the validation study) at each participating laboratory (see sections 10.1-10.3) will receive the blinded (coded) test chemicals and shall transfer the test chemicals to the responsible person of the laboratory. Sealed Material Safety Data Sheets (MSDSs) will accompany the test chemicals and the Safety Officer shall retain the package until the completion of EIVS. Additional sealed MSDSs can be sent to the testing facilities upon request of the Safety Officer if this information needs to be kept in more than one location. At the end of the validation study, the Safety Officer shall return the unopened

packages to the Logistics Coordinator of the study. If any laboratory personnel should open the packages at any time during the validation study, the Safety Officer shall promptly notify the VMG through the Logistics Coordinator (Jan Lammers, TNO).

12. Study Design

12.1. Eye irritation Peptide Reactivity Assay ("chemical reactivity")

Chemical reactivity is defined in this validation study as the electrophilic potential to react with cysteine or lysine containing peptides.

The lead laboratory for the Cysteine/Lysine Eye Irritation Peptide Reactivity Assay (EPRA) is L'Oréal. Training of the other participating laboratories (TNO and CARDAM) in conducting the EPRA shall be provided by the test method developer (Procter & Gamble). The lead laboratory in collaboration with the test method developer will be responsible for issuing a final test method protocol. Upon completion of the training phase, participating laboratories shall test 5-10 test chemicals to demonstrate transferability of the assay and to confirm test method protocol adequacy. Importantly, training of TNO and CARDAM in conducting the EPRA and their respective transferability studies will not occur at the same time during EIVS because TNO will be involved in testing for chemical selection and for reliability assessment while CARDAM will only do testing for reliability assessment (see below). The trained participating laboratories will be responsible for issuing training and transfer reports upon completion of the transferability study. The results of the training phase and of the transferability study of a laboratory will be reviewed and approved by the VMG before that laboratory progresses with testing for EIVS (testing phase). If the transferability data do not meet test acceptance criteria, the VMG will work with the participating laboratory and the lead laboratory to identify the problems and make corrections where needed.

In a first stage of the EIVS testing phase, all eligible chemicals identified by the CSG will have their chemical reactivity determined based on the EPRA, in a blind study in a single laboratory (TNO), with a single test consisting of three replicate measurements. Since chemicals found eligible by the CSG will not all become available for EPRA testing at TNO at the same time (due to differences in the time required to gain access to *in vivo* Draize eye irritation study reports for different chemicals, and to differences in the time required to obtain commercially available and proprietary chemical samples), the selection of a final test chemical set will be phased, with subsets of 30-50 test chemicals being selected by the CSG in different stages, as the data from the EPRA analysis becomes available, and until the final amount of at least 104 test chemicals is reached. These chemical subsets shall be as balanced as possible considering the criteria described in section 7.2 (with some flexibility allowed) and, upon approval by the core VMG, they will be distributed to the participating laboratories for viability assessment. Importantly, the total chemical set of at least 104 test chemicals (considering all selected subsets) shall be well balanced and meet all the criteria defined in section 7.2.

Upon completion of the viability assessment study, a preliminary evaluation of the usefulness of the SkinEthic™ HCE test strategy composed of the EPRA, the SkinEthic™ HCE SE and the SkinEthic™ HCE LE assays will be performed using the reactivity data obtained by TNO for all the selected test chemicals (at least 104) and the viability data obtained with SkinEthic™ HCE SE and SkinEthic™ HCE LE for the same test chemicals. If by combining the three assays in a test strategy a better predictive capacity is obtained as compared to the SkinEthic™ HCE SE or the SkinEthic™ HCE LE assays alone, chemical reactivity data will be obtained for a subset of the full validation set, in three laboratories (L'Oréal, TNO and CARDAM), in a second step to assess the reliability of the EPRA. Each of these three laboratories will test each test chemical in this subset

in three independent tests (performed in separate runs) consisting of three replicate measurements each, in order to strictly determine reproducibility (WLR and BLR) of the EPRA. TNO, as one of the three laboratories, will be testing these chemicals in three new independent tests (performed in separate runs).

The definitive number and characteristics of the chemicals to be tested for reliability assessment of the EPRA will be decided on later by the VMG with the help of statistical power analysis performed by the biostatisticians, but at least 20 chemicals and up to the maximum number of chemicals that can be tested in two separate runs for one peptide will be tested. When selecting the subset of test chemicals to assess the reliability of the EPRA, preference will be given to test chemicals that classify differently in SkinEthic™ HCE SE and SkinEthic™ HCE LE, since this would allow the use of these data for calculating the predictive capacity of the SkinEthic™ HCE test strategy. However, if all of these cannot be included in the selection, the data of a single test acquired by TNO for the selected test chemicals (at least 104) will be used to determine the predictive capacity of the proposed SkinEthic™ HCE test strategy, and other chemicals may be chosen for reliability assessment.

12.2. Biological assays

The lead laboratories for the EpiOcular™ EIT and the SkinEthic™ HCE SE/LE are Beiersdorf and L'Oréal, respectively. Training of the participating laboratories in conducting the EpiOcular™ EIT or the SkinEthic™ HCE SE/LE assays shall be provided by the respective test method developer (MatTek Corporation for EpiOcular™ EIT and L'Oréal for SkinEthic™ HCE SE/LE). The lead laboratories in collaboration with the test method developers will be responsible for issuing final test method protocols. Upon completion of the training phase, participating laboratories shall test 5-10 chemicals to demonstrate transferability of the assay and to confirm test method protocol adequacy. The test method developers in collaboration with the participating laboratories will be responsible for issuing training and transfer reports upon completion of the transferability studies. The results of the training phase and of the transferability studies for a particular test method will be reviewed and approved by the VMG before progression of the study for that test method. If the transferability data do not meet test acceptance criteria, the VMG will work with the participating laboratory and the lead laboratory to identify the problems and make corrections where needed.

In the testing phase of EIVS, each of the test chemicals in the final chemical selection set (at least 104 test chemicals) will be tested in the three assays (EpiOcular™ EIT, SkinEthic™ HCE SE and SkinEthic™ HCE LE) in at least three independent tests (using different tissue batches and performed in separate runs) by each of three independent laboratories (see Document "Guidance on Study Conduct and Test Method Performance Criteria for EIVS"). Thus, each chemical will be tested with the two different exposure/post-treatment periods of the SkinEthic™ HCE SE/LE protocol (10 min and 1 h + 16 h post-treatment), and with one of the two EpiOcular™ EIT exposure procedures depending on the test chemical being solid or liquid (30 min + 120 min post-treatment, or 90 min + 18 h post-treatment). Importantly, the three laboratories participating in the validation of EpiOcular™ EIT will **not** be instructed on the physical state of the test chemicals. Therefore, each laboratory participating in the validation of the EpiOcular™ EIT shall decide on the physical state of each test chemical and the appropriate exposure procedure to use. Finally, each control and test chemical included in one run will be tested in two (EpiOcular™ EIT) or three (SkinEthic™ HCE SE/LE) replicate tissues.

The EIVS RhT testing phase will be conducted in two or more consecutive phases to allow for periodic opportunities to evaluate the frequency of technical errors and any other problems that might occur during testing. At least at the end of each RhT testing phase the Study Directors will forward the data acquired by their laboratories to the Logistics Coordinator after internal quality check (see Table 2 in section 17) who will provide it to the TNO biostatistician for immediate

preliminary analyses of Within Laboratory Reproducibility (WLR) and compliance with Study Quality criteria (number of complete/incomplete test sequences as described in the Performance Criteria). Once completed, these phased statistical analyses and their conclusions will be provided to the core VMG who will review them and determine if modifications to the protocol and/or study plan are warranted/appropriate in order to avoid future occurrences of identified issues. All participating laboratories should adhere to these testing phases and ideally complete testing of all chemicals in one phase (by obtaining three qualified tests per chemical) before testing chemicals of following phases. However, for practical reasons and in order to minimise the cost of the study, the participating laboratories may delay the testing of MTT reducers and/or colorants in order to test them all together in a later testing phase, provided delayed chemicals will not expire. Moreover, chemicals with short expiry dates included in later testing phases of the study may be moved to an earlier phase to avoid testing after the expiration date.

13. Data Collection, Handling, and Analysis

The Logistics Coordinator will collect the data from each participating laboratory via the Study Directors (see section 11.1) at least at the end of each RhT testing phase (see section 12.2 and Table 2 in section 17) and will forward it to the TNO biostatistician. The TNO biostatistician will organise the data in specific data collection software (MS EXCEL spreadsheets). The collected data shall be circulated to every participating laboratory for a quality check. At the end of each RhT testing phase a preliminary analysis of WLR and compliance with Study Quality criteria (see above) will be performed without decoding the test chemicals (to avoid breaking the code before completion of the study). Upon completion of the RhT testing phases by all participating laboratories and preliminary "blind" determination of WLR and Study Quality criteria for each laboratory, test chemicals will be decoded and the TNO biostatistician will do a complete statistical analysis of the data and provide a final biostatistical report to the VMG. The ECVAM biostatistician will do a quality control of the processes of data collection, handling and analysis, as well as of the final biostatistical report. The data management procedures and statistical tools that will be used for data analysis and included in the final biostatistical report will be described in a Statistical Analyses and Reporting Plan. This Plan shall be developed by the ECVAM and TNO biostatisticians before the end of the experimental phase of the study and shall be approved by the VMG before the biostatistical analyses begin.

Based on final data analysis, the VMG reserves the possibility to identify the most suitable test strategies for the identification of non classified chemicals from classified ones.

The VMG has the responsibility of producing the final report and publication of the study. These will include the results of the EIVS and the VMG conclusions/recommendations on the outcome of the study. VMG conclusions/recommendations will be supported by the Performance Criteria defined by the VMG prior to initiation of the testing phase of EIVS. The draft statistical report and the draft validation study report shall be circulated to every participating laboratory for review and comments prior to finalisation. The VMG should review all comments received and make revisions if deemed appropriate.

14. Quality Assurance, Good Laboratory Practice

14.1. Laboratories

Participating laboratories that are compliant with Good Laboratory Practices (GLP) will perform the studies in accordance with GLP standards (OECD, 1999). Non GLP-compliant laboratories shall use the OECD principles of GLP as guidelines for conducting the validation study. Any

deviations from these principles should be documented along with a discussion of their impact on the study results.

It is considered that the following requirements (Balls M. *et al.*, 1995) are essential for the mutual acceptance of information produced in the validation process:

- Qualified personnel, and appropriate facilities, equipment and materials shall be available for the timely and proper conduct of the study
- Records of the qualifications, training and experience, and a job description for each professional and technical individual involved in the study, shall be maintained.
- For each study, an individual with appropriate qualifications, training and experience shall be appointed to be responsible for its overall conduct and for any report issued (Study Director, see section 11.1).
- Instruments used for the generation of experimental data shall be inspected regularly, cleaned, maintained and calibrated according to established SOPs, if available, or to manufacturers' instructions. Records of these processes shall be kept, and made available for inspection on request.
- Reagents shall be labelled, as appropriate, to indicate their source, identity, concentration and stability. The labelling shall include the preparation and expiry dates, and specific storage conditions.
- All data generated during a study shall be recorded directly, promptly and legibly by the individual(s) responsible. These entries shall be attributable and dated.
- All changes to data shall be identified with the date and the identity of the individual responsible, and a reason for the change shall be documented at the time.

14.2. Tissue model suppliers

According to OECD GLP Consensus Document No.5 "*Compliance of Laboratory Suppliers with GLP Principles*" the responsibility for the quality and fitness for use of equipment and materials rests entirely with the management of the test facility (OECD, 1999).

The acceptability of equipment and materials in laboratories complying to GLP principles should therefore be guaranteed to any regulatory authority to whom studies are submitted. In some countries where GLP has been implemented, suppliers belong to national regulatory or voluntary accreditation schemes (for example, for laboratory animals) which can provide users with additional documentary evidence that they are using a test system of a defined quality.

The audits on the RhT tissue production sites (MatTek Corporation and EpiSkin Laboratories) will be carried out by TNO and ECVAM, and will focus on the procedures established to guarantee a defined quality of the tissue models, as defined in the audit protocol previously approved by the VMG.

15. Health and Safety

Each laboratory shall conform to all applicable statutes in effect at the time of this validation study. The designated Safety Officer (see sections 10.1-10.3 and 11.4) shall be the point of contact for health and safety issues.

16. Records and Archives

At the end of EIVS, the original raw (if applicable; not possible for GLP compliant laboratories) and processed data or copies thereof shall be submitted to ECVAM and COLIPA for storing and

archiving. In addition, other records relevant to EIVS (instrument logs, calibration records, facility logs, etc.) should be made available for inspection upon request by the VMG.

Raw and processed data or copies thereof (depending if the laboratory is or not GLP compliant) shall be stored and archived at the participating laboratory for at least five years after completion of EIVS. The data which are stored electronically shall be periodically copied, and backup files shall be produced and maintained.

17. Timelines

The following tables summarise the critical activities of the study and the estimated completion timelines. Timelines might need to be reviewed during the study.

Table 1. Study timelines

Critical activities	Timing (*finalisation)
Chemical eligibility / availability from suppliers	
o NCD	o 29 October 2010
o Existing	o VMG III 3-4 June 2009*
o CosIng	o 29 October 2010
o EPA	o 29 October 2010
Project Plan	
o Finalisation	o VMG VII 28-29 September 2010
o Approval by VMG	o 1 December 2010
Guidance on Study Conduct and Test Method Performance Criteria for EIVS	
o Finalisation	o VMG VII 28-29 September 2010
o Approval by VMG	o 1 December 2010
Study design approval by VMG	o 30 July 2009*
EPRA	
o Cut-off for EPRA	o VMG III 3-4 June 2009*
o EPRA updated/final Protocol approval	o 18 December 2009* (slightly revised and approved on VMG VII 28-29 September 2010)
o EPRA study plan	o VMG V 24-25 November 2009*
o # and identity of chemicals tested for reproducibility assessment of EPRA	o T.b.d. by July 2011
EPRA testing at TNO for chemicals selection	
o Training	o 3-4 June 2009*
o Transferability study	o 13 July-16 October 2009*
o Beginning of testing	o March 2010
EPRA reliability assessment	
o Training	o T.b.d. by March 2011
o Transferability study	o T.b.d. by March 2011
o Beginning of testing	o T.b.d. by July 2011

SkinEthic™ HCE SE/LE o Performance under UN GHS classification (TST data) o QA audit on RhT production site o Training o Transferability study o SkinEthic™ HCE SE/LE final Protocol approval o Beginning of testing (see Table 2)	 o VMG III 3-4 June 2009* o 19 March 2010* o 19-29 January 2010* o 8 February-9 April 2010* o 17 June 2010* o 21 June 2010*
EpiOcular™ EIT o QA audit on RhT production site o Insert to be used o Cut-off to be used o Training o Transferability study o Final Protocol approval o Beginning of testing (see Table 2)	 o 26 May 2010* o 9 September 2010* o 9 September 2010* o October-November 2010 o November 2010 o December 2010 o January 2011
CSG final chemical selection and Core VMG approval o 1st set (34 test chemicals) o 2nd set (46 test chemicals) o 3rd and final set (24-27 test chemicals)	 o 10 June 2010* o 8 September 2010* o 10 December 2010
Chemical coding and distribution	June 2010-January 2011
Participating laboratory contracts	December 2009-January 2011
Contract with SkinEthic Laboratories for the supply of SkinEthic™ HCE tissues	February 2010
Contract with MatTek corporation for the supply of EpiOcular™ tissues	April 2010
Delivery of final statistical report (biostatistician)	Within 2 months after completion of testing phase
Delivery of final study report (VMG)	Within 2 months after finalisation of the statistical report

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621 **Table 2. Testing and data collection timelines**

RhT testing phase	SkinEthic™ HCE SE/LE	EpiOcular™ EIT
1st Phase	**34 test chemicals (selected on 10/06/2010)** Starting date: 21 June 2010 Finishing date: February 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by February 2011	**~40 test chemicals (½ liquids, ½ solids)** Starting date: December 2010 Finishing date: March 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by March 2011
2nd Phase	**46 test chemicals (selected on 08/09/2010)** Starting date: October 2010 Finishing date: May 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by May 2011	**~40 test chemicals** Starting date: March 2011 Finishing date: May 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by May 2011
3rd Phase	**24-27 test chemicals** Starting date: March 2011 Finishing date: July 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by July 2011	**24-27 test chemicals** Starting date: May 2011 Finishing date: July 2011 Data collection by Study Directors and dispatch to Logistics Coordinator: by July 2011

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623 # 18. Documents and Data

624 1. ECVAM and/or the Logistics Coordinator, after consultation with the VMG, supplies EIVS
625 documentation 'in confidence' to participating laboratories. Unless and until ECVAM places these
626 documents in the public domain, they may not be published or communicated/distributed to other
627 third parties without the knowledge and consent of ECVAM after consultation with the VMG.

628 2. All study data generated by the contracted laboratories are the property of the European
629 Commission/ECVAM and COLIPA. These data may not be published, communicated or
630 circulated/distributed to third parties without the knowledge and consent of the European
631 Commission/ECVAM and COLIPA, and the knowledge of the VMG.

632 4. ECVAM and COLIPA reserve the right to be the first to promptly publish and communicate the
633 outcomes of the validation process.

634

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Annex I - Test Chemicals Receipt Report Template

Testing Facility:

Test Chemicals Received by:

Test Chemicals Receipt Date:

General Comments:

Test Chemical Code	Storage Conditions	Expiry date	Physical Appearance (colour physico-chemical state)	Container Appearance (vial and lid)	Deviations from description of the chemical	Was the envelope included in the health and safety information package received intact and unopened?	Other remarks
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	

Test Chemical Code	Storage Conditions	Expiry date	Physical Appearance (colour physico-chemical state)	Container Appearance (vial and lid)	Deviations from description of the chemical	Was the envelope included in the health and safety information package received intact and unopened?	Other remarks
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	

Test Chemical Code	Storage Conditions	Expiry date	Physical Appearance (colour physico-chemical state)	Container Appearance (vial and lid)	Deviations from description of the chemical	Was the envelope included in the health and safety information package received intact and unopened?	Other remarks
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	

Test Chemical Code	Storage Conditions	Expiry date	Physical Appearance (colour physico-chemical state)	Container Appearance (vial and lid)	Deviations from description of the chemical	Was the envelope included in the health and safety information package received intact and unopened?	Other remarks
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	
						YES ☐ / NO ☐	

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Appendix IX Post-validation analyses: 2 vs 3 tissues

Results reported by Joe Haseman (7-13-12) from NICEATM

Analysis of Short Time Exposure Data

This report addresses the following issue: The current testing paradigm for the short time exposure data is three runs, each with three samples. Within a run, the three samples are averaged, and if the average viability is greater than 50%, the run is considered "positive"; otherwise it is considered "negative".

The question of interest: What would be the impact of reducing the number of samples in a given run from three to two? More specifically, how often would averaging the viability of two samples and comparing it to 50% change the classification for that run relative to the classification based on averaging the viability of three samples?

To address this question, I considered all the runs for which I was given data and considered the consequence of using only two of the three observed samples as the basis for classification for that run. There are three possible pairs of samples (first and second; first and third; second and third). I then compared the classification for that run based on each pair with the classification based on the full three samples.

Obviously, if all three samples were <50% or all were >50%, then there would be no change in classification. Reducing the sample size could possibly change the classification only if there were some samples in the run that exceeded 50% and others that were less than 50%.

The rest of this report presents the results of this statistical analysis, but the bottom line is this: Reducing the number of samples from 3 to 2 for the short time exposure data will have almost no impact on the classification decision for a given run. The probability is less than 1% that such a reduction would change the classification for a given run. A companion report deals with the long time exposure data and reaches a similar conclusion.

General comments on the data and analysis:

(1) Approximately 90% of the chemicals had complete agreement among all the samples/runs evaluated with regard to classification (i.e., for a given chemical, all samples were either >50% or were <50% approximately 90% of the time, regardless of lab). This is outstanding consistency.

(2) Moreover, approximately 97% of the individual runs had complete agreement among the three samples with regard to classification. Again, the overall consistency of response was outstanding. Of the hundreds of runs evaluated, there were only a handful (detailed below) that produced any classification disagreement at all among the samples within the run, so it is only this few number of runs that could produce a possible classification inconsistency by reducing the sample size from 3 to 2.

(3) The 50% cutoff point is very reasonable.

(4) All chemicals had three runs.

(5) Unlike the case for the long time exposure chemicals (which had approximately a 50-50 mix of "positives' and "negatives"), the short time exposure data had far more "positives" than "negatives" (approximately 77% "positive" and 23% "negatives").

(6) The variability among runs was somewhat greater than the variability within a run among samples. There were a few cases at certain labs in which one run for a given chemical produced 3 samples with viability <50%, while a second run produced 3 samples with viability >50%. Thus, maintaining multiple runs is more important than maintaining multiple samples, but overall, even the reproducibility among runs was quite good.

(7) No single lab stood out as being clearly superior to the others with regard to reproducibility, although overall Cardam and L'Oreal did a slightly better job in this regard than did Ceetox.

(8) I received two sets of raw data, the first from Elizabeth Lipscomb and then later another dataset from ECVAM. The data appeared to be identical, although a handful of runs in the ECVAM data included a "correction" for something that was subtracted from the original viability value. For the analyses summarized in this report, I used the viability values that Elizabeth Lipscomb sent me. The ECVAM data also noted that certain chemicals were "excluded", and certain runs within a chemical were "non-qualified" because of excessive

variability among samples within the run. I noted all of these occurrences in this report, but I deleted them from my calculations. Among the more than 900 runs, there were very few (8 by my count) that were “non-qualified” because of excessive variability among samples within a run.

At some point, it would be a good idea to “decode” the chemicals to see if there was a consistency in classification of specific chemicals across labs. However, that was not the objective of this evaluation, which focused on reliability rather than on accuracy.

Joe Haseman
7-13-12

Summary of Results for SE Protocol: Cardam

Number of usable chemicals: 104
Number of excluded chemicals: 2 (C53, and C58)
Non-qualified runs: C35, Run 2
C45, Run 1
C52, Runs 1 and 4
C83, Run 1
All chemicals had 3 runs
Total number of useable runs: 312
Total number of pairwise comparisons = 936
Bracketed data were excluded

Chemical Code	Run results (>50%)			Range of scores	Impact of reducing samples per per run from 3 to 2
C1	3/3	0/3	3/3	34.14 to 88.12	None
C101	3/3	3/3	3/3	74.19 to 102.58	None
C103	3/3	3/3	3/3	97.97 to 121.54	None
C104	3/3	3/3	3/3	72.51 to 106.79	None
C105	3/3	3/3	3/3	94.23 to 110.54	None
C106	3/3	3/3	3/3	83.11 to 98.71	None
C107	3/3	3/3	3/3	87.79 to 105.59	None
C108	3/3	3/3	3/3	86.59 to 102.52	None
C109	3/3	3/3	3/3	70.54 to 117.83	None
C11	0/3	0/3	0/3	0.12 to 19.01	None
C110	3/3	3/3	3/3	87.76 to 106.44	None
C112	3/3	3/3	3/3	83.57 to 109.81	None
C113	3/3	3/3	3/3	82.93 to 100.48	None
C114	3/3	3/3	3/3	87.94 to 114.66	None
C116	3/3	3/3	3/3	84.30 to 104.35	None
C119	0/3	0/3	0/3	20.75 to 45.78	None
C12	1/3	0/3	0/3	24.05 to 56.37 [---]	1/9
C120	3/3	3/3	3/3	85.54 to 105.20	None
C123	0/3	0/3	0/3	6.66 to 13.34	None
C124	3/3	3/3	3/3	82.12 to 123.05	None
C125	3/3	3/3	3/3	59.38 to 107.49	None
C127	3/3	3/3	3/3	58.16 to 102.30	None
C128	0/3	0/3	0/3	23.21 to 32.16	None
C129	3/3	3/3	3/3	87.02 to 121.48	None
C13	3/3	1/3	3/3	41.91 to 110.32 [+++]	1/9
C131	3/3	3/3	3/3	84.26 to 115.87	None
C132	3/3	3/3	3/3	59.00 to 90.81	None
C134	0/3	0/3	0/3	1.76 to 5.58	None
C135	0/3	0/3	2/3	32.52 to 63.37 [--+]	1/9
C136	3/3	3/3	3/3	61.01 to 79.77	None
C137	0/3	0/3	0/3	26.80 to 43.05	None
C138	0/3	0/3	0/3	3.27 to 4.93	None
C139	3/3	3/3	3/3	60.75 to 85.07	None
C14	3/3	3/3	3/3	93.06 to 110.29	None
C140	3/3	3/3	3/3	84.95 to 118.80	None
C141	3/3	3/3	3/3	84.55 to 124.83	None
C15	3/3	3/3	3/3	78.39 to 116.41	None
C16	3/3	3/3	3/3	84.16 to 120.66	None

C163		3/3	3/3	3/3	94.15 to 114.78	None
C164		3/3	3/3	3/3	83.36 to 105.49	None
C166		3/3	3/3	3/3	78.96 to 106.44	None
C170		3/3	3/3	3/3	70.86 to 95.07	None
C185		3/3	3/3	3/3	72.47 to 106.13	None
C19		3/3	3/3	3/3	53.53 to 84.86	None
C193		0/3	3/3	0/3	17.26 to 56.08	None
C195		3/3	3/3	3/3	97.47 to 110.93	None
C196		3/3	3/3	3/3	71.97 to 103.93	None
C2		3/3	3/3	3/3	96.82 to 129.00	None
C20		3/3	3/3	3/3	90.00 to 105.69	None
C21		0/3	0/3	0/3	14.77 to 30.35	None
C25		3/3	3/3	3/3	57.32 to 95.42	None
C26		0/3	0/3	0/3	0.26 to 5.22	None
C27		3/3	3/3	3/3	81.91 to 118.02	None
C28		3/3	3/3	3/3	95.05 to 116.42	None
C29		3/3	3/3	3/3	70.99 to 113.50	None
C3		3/3	0/3	3/3	37.49 to 63.02	None
C30		1/3	3/3	1/3	34.16 to 107.82 [-+-]	1/9
C33		0/3	0/3	0/3	1.22 to 7.88	None
C34		3/3	3/3	3/3	79.71 to 107.78	None
C35	3/3	[1/3]	0/3	0/3	6.31 to 75.29	None
C36		3/3	3/3	3/3	92.41 to 104.15	None
C37		3/3	3/3	3/3	88.08 to 118.30	None
C38		2/3	3/3	3/3	45.97 to 70.04 [+++]	None
C39		3/3	3/3	3/3	73.32 to 120.81	None
C4		3/3	3/3	3/3	93.21 to 115.11	None
C45	[3/3]	3/3	3/3	3/3	88.51 to 143.36	None
C46		3/3	3/3	3/3	57.91 to 105.31	None
C47		3/3	3/3	3/3	57.17 to 100.79	None
C48		0/3	0/3	0/3	3.17 to 16.52	None
C49		3/3	3/3	3/3	78.69 to 116.34	None
C50		0/3	0/3	0/3	22.95 to 42.83	None
C51		3/3	3/3	3/3	81.00 to 97.88	None
C52	[3/3]	3/3	3/3	[3/3]	3/3 120.20 to 188.94	None
[C53	3/3	3/3	3/3	3/3	66.72 to 117.40]	-
C54		3/3	3/3	3/3	88.22 to 123.44	None
C55		3/3	3/3	3/3	83.32 to 105.68	None
C56		3/3	3/3	3/3	87.26 to 137.29	None
[C58		3/3	3/3	3/3	82.79 to 132.92]	-
C6		0/3	0/3	0/3	18.99 to 38.64	None
C60		3/3	3/3	3/3	97.11 to 131.11	None
C62		0/3	0/3	0/3	4.89 to 11.27	None
C63		3/3	3/3	3/3	70.71 to 88.00	None
C64		0/3	0/3	0/3	2.00 to 4.97	None
C65		3/3	3/3	3/3	55.89 to 86.10	None
C66		3/3	3/3	3/3	56.43 to 87.90	None
C67		3/3	3/3	3/3	88.69 to 101.90	None
C70		3/3	3/3	3/3	78.05 to 107.99	None
C71		3/3	3/3	3/3	78.50 to 105.63	None
C75		0/3	0/3	0/3	0.91 to 3.27	None
C76		3/3	3/3	3/3	67.47 to 141.67	None
C77		3/3	3/3	3/3	81.71 to 108.82	None
C78		3/3	3/3	3/3	100.91 to 122.20	None
C79		3/3	3/3	3/3	86.86 to 114.39	None
C82		3/3	3/3	3/3	60.10 to 97.25	None
C83	[3/3]	3/3	3/3	3/3	74.80 to 113.41	None
C84		3/3	3/3	3/3	69.70 to 90.36	None
C85		3/3	3/3	3/3	71.85 to 109.15	None
C88		3/3	3/3	3/3	70.69 to 111.87	None
C9		3/3	3/3	3/3	78.89 to 107.07	None
C90		0/3	0/3	0/3	0.26 to 0.66	None
C91		0/3	0/3	0/3	0.58 to 13.73	None
C94		3/3	3/3	3/3	73.82 to 87.55	None
C96		3/3	3/3	3/3	71.36 to 111.21	None
C97		0/3	0/3	0/3	14.00 to 36.16	None
C98		0/3	0/3	0/3	7.32 to 12.52	None
C99		3/3	3/3	3/3	71.57 to 107.78	None

The likelihood that a reduction in sample size from 3 to 2 would change the classification for a run for Cardam is only 4/936 or 0.4%.

Revised Summary of Results for SE Protocol: L'Oreal

Number of usable chemicals: 102
Number of excluded chemicals: 4 (L6, L7, L58 and L100)
Non-qualified runs: L11, Runs 1 and 2
All chemicals had 3 runs
Total number of useable runs: 306
Total number of pairwise comparisons = 918
Bracketed data excluded

Chemical Code	Run results (>50%)	Range of scores	Impact of reducing samples per run from 3 to 2
L1	3/3 3/3 3/3	77.63 to 97.02	None
[L100 3/3 3/3 3/3 3/3 3/3		88.10 to 114.95]	-
L101	3/3 3/3 3/3	51.88 to 92.89	None
L102	3/3 3/3 3/3	84.75 to 95.31	None
L104	1/3 0/3 0/3	15.70 to 66.00 [+--]	1/9
L106	3/3 3/3 3/3	81.41 to 109.20	None
L107	3/3 3/3 3/3	76.85 to 103.71	None
L108	3/3 3/3 3/3	65.82 to 101.20	None
L109	3/3 3/3 3/3	75.35 to 93.49	None
L11 [1/3] [1/3] 0/3 0/3 0/3		2.49 to 20.74	None
L111	3/3 3/3 3/3	91.74 to 109.61	None
L112	3/3 3/3 3/3	86.06 to 104.46	None
L113	3/3 3/3 3/3	79.25 to 99.97	None
L114	3/3 3/3 3/3	70.01 to 101.79	None
L115	3/3 3/3 3/3	89.57 to 103.82	None
L118	3/3 3/3 3/3	83.32 to 101.86	None
L119	3/3 3/3 3/3	62.84 to 79.78	None
L12	3/3 3/3 3/3	79.10 to 99.99	None
L120	0/3 0/3 0/3	1.22 to 32.21	None
L122	3/3 3/3 3/3	86.60 to 101.87	None
L123	3/3 3/3 3/3	76.27 to 91.03	None
L125	0/3 0/3 0/3	11.91 to 28.32	None
L126	3/3 3/3 3/3	83.86 to 103.95	None
L127	3/3 3/3 3/3	84.45 to 95.62	None
L129	0/3 0/3 1/3	27.41 to 53.10 [---]	None
L13	3/3 3/3 3/3	72.37 to 86.69	None
L130	0/3 0/3 0/3	8.64 to 20.51	None
L131	3/3 3/3 3/3	60.28 to 86.71	None
L132	0/3 0/3 0/3	0.93 to 2.44	None
L133	3/3 3/3 3/3	55.61 to 82.01	None
L134	3/3 3/3 3/3	79.20 to 102.64	None
L136	3/3 3/3 3/3	70.75 to 96.30	None
L137	3/3 3/3 3/3	89.34 to 99.06	None
L139	0/3 0/3 0/3	4.44 to 9.39	None
L140	0/3 0/3 0/3	21.92 to 37.88	None
L144	3/3 3/3 3/3	82.84 to 109.65	None
L148	3/3 3/3 3/3	83.76 to 101.22	None
L15	3/3 3/3 3/3	64.98 to 106.13	None
L156	3/3 3/3 3/3	83.90 to 108.29	None
L16	3/3 3/3 3/3	78.52 to 97.18	None
L161	3/3 3/3 3/3	83.28 to 104.69	None
L164	0/3 3/3 3/3	18.88 to 71.25	None
L169	3/3 3/3 3/3	91.96 to 109.72	None
L17	3/3 3/3 3/3	72.21 to 88.47	None
L174	3/3 3/3 3/3	75.63 to 83.60	None
L18	3/3 3/3 3/3	89.41 to 98.43	None
L185	3/3 3/3 3/3	80.76 to 105.78	None
L20	3/3 3/3 3/3	84.56 to 102.45	None
L200	3/3 3/3 3/3	91.27 to 101.52	None
L23	2/3 3/3 3/3	45.75 to 84.83 [+++]	None
L24	3/3 3/3 3/3	53.01 to 77.98	None
L27	3/3 3/3 3/3	93.91 to 116.11	None
L28	3/3 3/3 3/3	67.13 to 111.24	None
L29	1/3 0/3 0/3	17.65 to 62.82 [+--]	1/9
L32	3/3 3/3 3/3	79.28 to 108.86	None
L33	0/3 0/3 0/3	3.00 to 5.42	None
L36	3/3 3/3 3/3	888.90 to 103.78	None
L37	0/3 0/3 0/3	11.08 to 32.83	None
L39	3/3 3/3 3/3	82.92 to 95.13	None

L4	3/3	2/3	3/3	49.96 to 78.37 [+++]	None
L42	3/3	3/3	3/3	52.07 to 79.95	None
L43	3/3	3/3	3/3	87.79 to 99.59	None
L45	0/3	0/3	0/3	1.95 to 17.41	None
L48	0/3	0/3	0/3	0.57 to 6.52	None
L5	3/3	3/3	3/3	79.22 to 97.95	None
L50	3/3	3/3	3/3	90.66 to 105.43	None
L51	3/3	3/3	3/3	77.40 to 95.84	None
L53	3/3	3/3	3/3	80.46 to 108.24	None
L55	3/3	3/3	3/3	102.65 to 123.46	None
L56	0/3	0/3	0/3	4.42 to 5.96	None
L57	3/3	2/3	3/3	46.95 to 68.54 [+++]	None
[L58	3/3	3/3	3/3	3/3 3/3	51.45 to 112.72] -
L59	3/3	3/3	3/3	78.56 to 105.22	None
[L6	3/3	3/3	3/3	3/3 3/3	89.35 to 178.31] -
L60	3/3	3/3	3/3	92.14 to 108.05	None
L61	3/3	3/3	3/3	87.83 to 95.37	None
L62	3/3	3/3	3/3	81.01 to 103.65	None
L64	3/3	3/3	3/3	85.09 to 105.38	None
L65	3/3	3/3	3/3	88.78 to 108.17	None
L66	3/3	3/3	3/3	77.01 to 102.83	None
L67	3/3	3/3	3/3	92.11 to 101.91	None
L68	0/3	0/3	0/3	1.14 to 1.69	None
[L7	3/3	3/3	3/3	73.43 to 115.91] -	
L70	0/3	0/3	0/3	0.68 to 10.00	None
L72	3/3	3/3	3/3	68.90 to 92.80	None
L73	3/3	3/3	3/3	76.03 to 111.97	None
L75	3/3	3/3	3/3	79.39 to 92.25	None
L76	3/3	3/3	3/3	82.38 to 102.14	None
L78	0/3	0/3	0/3	0.48 to 1.27	None
L79	3/3	3/3	3/3	84.12 to 109.33	None
L8	0/3	0/3	0/3	6.98 to 9.63	None
L80	0/3	0/3	0/3	2.69 to 7.67	None
L81	3/3	3/3	0/3	32.04 to 79.86	None
L82	0/3	0/3	0/3	1.75 to 4.68	None
L83	0/3	0/3	0/3	15.19 to 29.13	None
L85	1/3	0/3	1/3	26.68 to 58.01 [---]	None
L87	0/3	0/3	0/3	18.52 to 43.08	None
L9	0/3	0/3	0/3	21.66 to 34.22	None
L90	3/3	3/3	3/3	83.92 to 106.16	None
L91	3/3	3/3	3/3	54.96 to 97.66	None
L92	0/3	0/3	0/3	10.41 to 42.98	None
L94	3/3	3/3	3/3	75.79 to 87.39	None
L96	3/3	3/3	3/3	79.65 to 99.72	None
L97	3/3	3/3	3/3	69.00 to 83.24	None
L98	3/3	3/3	3/3	98.39 to 110.25	None
L99	3/3	3/3	3/3	102.28 to 134.49	None

The likelihood that a reduction in sample size from 3 to 2 would change the classification for a run for L'Oreal is only 2/918 or 0.2%.

Revised Summary of Results for SE Protocol: Ceetox

Number of usable chemicals: 102
Number of excluded chemicals: 4 (X32, X62, X81, X95)
Non-qualified runs: X19, Run 2
All chemicals had 3 useable runs
Total number of useable runs: 306
Total number of pairwise comparisons = 918
Bracketed data excluded

Chemical Code	Run results (>50%)			Range of scores	Impact of reducing samples per per run from 3 to 2
X1	3/3	3/3	3/3	85.69 to 100.66	None
X102	3/3	3/3	3/3	85.51 to 114.55	None
X103	3/3	3/3	3/3	84.68 to 105.20	None
X107	3/3	3/3	3/3	95.35 to 108.63	None
X108	3/3	3/3	3/3	85.59 to 114.25	None

X109		3/3	3/3	3/3	80.95 to 106.67	None
X11		3/3	3/3	3/3	85.20 to 107.54	None
X110		3/3	3/3	3/3	78.46 to 92.65	None
X111		3/3	3/3	3/3	85.20 to 107.54	None
X112		3/3	3/3	3/3	92.53 to 118.13	None
X113		3/3	3/3	3/3	87.44 to 106.66	None
X114		3/3	3/3	3/3	88.32 to 103.62	None
X115		3/3	3/3	3/3	92.60 to 107.49	None
X116		3/3	3/3	3/3	93.41 to 105.02	None
X117		0/3	0/3	0/3	2.14 to 5.34	None
X118		3/3	3/3	3/3	83.86 to 96.24	None
X119		0/3	0/3	0/3	17.27 to 47.26	None
X120		3/3	3/3	3/3	94.08 to 104.41	None
X121		0/3	0/3	0/3	4.89 to 13.61	None
X123		3/3	3/3	3/3	64.75 to 109.60	None
X125		3/3	3/3	3/3	83.93 to 109.59	None
X126		3/3	3/3	3/3	72.31 to 93.86	None
X127		0/3	0/3	0/3	19.63 to 44.28	None
X128		3/3	3/3	3/3	58.56 to 74.69	None
X129		3/3	3/3	3/3	72.65 to 97.77	None
X13		0/3	3/3	0/3	24.30 to 91.05	None
X131		3/3	3/3	3/3	72.00 to 85.24	None
X133		0/3	0/3	0/3	26.15 to 39.20	None
X134		3/3	3/3	3/3	88.46 to 111.52	None
X136		0/3	0/3	0/3	2.92 to 4.66	None
X138		3/3	3/3	3/3	76.85 to 98.66	None
X139		0/3	0/3	0/3	27.67 to 44.95	None
X14		0/3	0/3	0/3	5.12 to 7.36	None
X143		3/3	3/3	3/3	88.37 to 101.81	None
X157		3/3	3/3	3/3	87.71 to 111.22	None
X158		3/3	3/3	3/3	84.84 to 98.14	None
X16		3/3	3/3	3/3	82.47 to 111.99	None
X160		3/3	3/3	3/3	94.45 to 115.67	None
X165		3/3	3/3	3/3	71.63 to 92.89	None
X169		3/3	3/3	3/3	90.48 to 106.14	None
X173		3/3	3/3	3/3	94.26 to 121.71	None
X19	3/3	[2/3]	3/3	3/3	75.60 to 105.46	None
X190		3/3	3/3	3/3	91.10 to 105.51	None
X196		2/3	0/3	0/3	14.79 to 51.28 [---]	1/9
X2		3/3	3/3	3/3	87.43 to 101.47	None
X21		0/3	0/3	0/3	2.35 to 16.32	None
X22		3/3	3/3	3/3	79.82 to 108.71	None
X24		3/3	3/3	3/3	85.36 to 105.93	None
X25		3/3	3/3	0/3	14.79 to 67.98	None
X27		3/3	3/3	3/3	89.34 to 139.21	None
X28		3/3	3/3	3/3	70.69 to 91.89	None
X29		0/3	0/3	0/3	1.75 to 16.11	None
X3		3/3	1/3	1/3	21.06 to 90.05 [+--}	3/9
X30		1/3	0/3	0/3	33.78 to 51.16 [---}	None
X31		0/3	0/3	0/3	24.24 to 37.92	None
[X32		3/3	3/3	3/3	85.02 to 105.64]	-
X33		0/3	0/3	0/3	24.67 to 43.11	None
X36		3/3	3/3	3/3	54.99 to 73.43	None
X37		3/3	3/3	3/3	92.83 to 130.79	None
X38		3/3	3/3	3/3	76.04 to 87.21	None
X39		3/3	3/3	0/3	21.40 to 92.69	None
X40		3/3	3/3	3/3	76.28 to 90.67	None
X41		3/3	3/3	0/3	30.16 to 93.23	None
X42		0/3	0/3	0/3	3.73 to 10.09	None
X43		3/3	3/3	2/3	45.60 to 82.31 [+++]	None
X45		0/3	0/3	0/3	11.99 to 37.58	None
X46		3/3	3/3	3/3	83.51 to 99.37	None
X47		3/3	1/3	0/3	30.96 to 69.82 [+--]	None
X49		3/3	3/3	3/3	68.45 to 106.28	None
X5		3/3	3/3	3/3	76.18 to 94.94	None
X50		3/3	3/3	3/3	83.51 to 101.24	None
X51		0/3	0/3	0/3	1.31 to 6.31	None
X52		0/3	0/3	0/3	3.57 to 7.61	None
X53		3/3	3/3	3/3	90.51 to 109.75	None
X55		3/3	3/3	3/3	92.87 to 109.08	None
X56		0/3	0/3	0/3	0.68 to 2.26	None
X59		3/3	3/3	3/3	85.03 to 119.30	None
X6		3/3	3/3	3/3	69.89 to 94.73	None

X61	3/3	3/3	3/3	92.70 to 106.97	None
[X62	3/3	3/3	3/3	87.72 to 120..12]	-
X63	3/3	3/3	3/3	87.71 to 121.20	None
X64	3/3	3/3	3/3	58.89 to 87.77	None
X65	0/3	0/3	0/3	3.21 to 6.68	None
X66	3/3	3/3	3/3	71.90 to 89.39	None
X68	3/3	3/3	3/3	90.30 to 113.61	None
X7	3/3	3/3	3/3	94.15 to 131.17	None
X70	2/3	2/3	3/3	26.48 to 80.35 [-++]	1/9
X72	3/3	3/3	3/3	89.37 to 109.96	None
X73	0/3	0/3	0/3	3.94 to 21.98	None
X75	3/3	3/3	3/3	84.96 to 107.66	None
X77	3/3	3/3	3/3	91.81 to 113.68	None
X8	3/3	3/3	3/3	80.45 to 104.29	None
X80	3/3	3/3	3/3	76.07 to 103.97	None
[X81	3/3	3/3	3/3	61.99 to 80.22]	-
X82	3/3	3/3	3/3	80.22 to 92.19	None
X83	0/3	0/3	0/3	1.76 to 12.07	None
X84	1/3	3/3	3/3	47.05 to 106.58 [-++]	2/9
X86	3/3	3/3	3/3	83.94 to 107.60	None
X87	0/3	0/3	0/3	2.09 to 5.89	None
X89	3/3	3/3	3/3	79.70 to 95.24	None
X91	1/3	0/3	1/3	36.30 to 57.57 [---]	2/9
X93	3/3	3/3	3/3	69.56 to 90.86	None
X94	3/3	3/3	3/3	89.14 to 107.34	None
[X95	3/3	3/3	3/3	78.16 to 130.65]	-
X98	3/3	3/3	3/3	51.57 to 75.62	None
X99	3/3	3/3	3/3	88.69 to 116.50	None

The likelihood that a reduction in sample size from 3 to 2 would change the classification for a run for Ceetox is only 9/918 or 0.98%

Samples with less than complete agreement.

These are the only runs whose classifications could be altered by reducing the number of samples from 3 to 2

Lab	Chemical	Run	Sample			
			1	2	3	Mean
Cardam	C12	1	43.0	46.2	56.4	48.5
Cardam	C13	2	49.2	61.5	41.9	50.9
Cardam	C135	3	63.4	48.2	51.1	54.2
Cardam	C30	1	52.0	45.8	45.2	47.7
Cardam	C30	3	64.3	34.2	40.0	46.2
Cardam	C38	1	59.8	46.0	54.7	53.5
L'Oreal	L104	1	40.8	47.9	66.0	51.6
L'Oreal	L129	3	53.1	41.3	42.0	45.5
L'Oreal	L23	1	45.8	69.1	68.6	61.2
L'Oreal	L29	1	48.8	44.9	62.8	52.2
L'Oreal	L4	2	49.96	56.6	54.9	53.8
L'Oreal	L57	2	68.5	59.0	47.0	58.2
L'Oreal	L85	1	30.1	57.1	34.3	40.5
L'Oreal	L85	3	34.8	58.0	39.8	44.2
Ceetox	X196	1	31.5	50.4	51.3	44.4
Ceetox	X3	2	59.9	40.6	44.4	48.3
Ceetox	X3	3	21.1	47.4	53.0	40.5
Ceetox	X30	1	51.2	45.8	38.3	45.1
Ceetox	X43	3	61.7	56.5	45.6	54.6
Ceetox	X47	2	46.3	43.5	53.1	47.6
Ceetox	X70	1	54.4	52.3	26.5	44.4
Ceetox	X70	2	63.3	66.1	47.1	58.8
Ceetox	X84	1	47.1	47.0	55.1	49.7
Ceetox	X91	1	42.9	43.4	57.6	48.0
Ceetox	X91	3	42.6	46.6	52.7	47.3

SUMMARY PERFORMANCE BY LAB

	Cardam	L'Oreal	Ceetox
No. chemicals with adequate studies	104	102	102
No. chemicals with 100% sample agreement	95 (91%)	93 (91%)	90 (88%)
Positives	75	71	69
Negatives	20	22	21
No. adequate runs	312	306	306
No. runs with 100% agreement	306 (98%)	298 (97%)	295 (96%)
No. of possible pairs of samples among all runs	936	918	918
No. of pairs of that would give a classification different than the full 3 samples	4 (0.4%)	2 (0.2%)	9 (0.98%)

Analysis of Long Time Exposure Data

This report addresses the following issue: The current testing paradigm for the long time exposure data is three runs, each with three samples. Within a run, the three samples are averaged, and if the average viability is greater than 50%, the run is considered "positive"; otherwise it is considered "negative".

The question of interest: What would be the impact of reducing the number of samples in a given run from three to two? More specifically, how often would averaging the viability of two samples and comparing it to 50% change the classification for that run relative to the classification based on averaging the viability of three samples?

To address this question, I considered all the runs for which I was given data and considered the consequence of using only two of the three observed samples as the basis for classification for that run. There are three possible pairs of samples (first and second; first and third; second and third). I then compared the classification for that run based on each pair with the classification based on the full three samples.

Obviously, if all three samples were <50% or all were >50%, then there would be no change in classification. Reducing the sample size could possibly change the classification only if there were some samples in the run that exceeded 50% and others that were less than 50%.

The rest of this report presents the results of this statistical analysis, but the bottom line is this: Reducing the number of samples from 3 to 2 for the long time exposure data will have almost no impact on the classification decision for a given run. The probability is less than 1% that such a reduction would change the classification for a given run. A companion report deals with the short time exposure data and reaches a similar conclusion.

General comments on the data and analysis:

(1) More than 90% of the chemicals had complete agreement among all the samples/runs evaluated with regard to classification (i.e., for a given chemical, all samples were either >50% or were <50% more than 90% of the time, regardless of lab). This is outstanding consistency.

(2) Moreover, 97% of the individual runs had complete agreement among the three samples with regard to classification. Again, the overall consistency of response was outstanding. Of the hundreds of runs evaluated, there were only a handful (detailed below) that produced any classification disagreement at all among the samples within the run, so it is only this few number of runs that could produce a possible classification inconsistency by reducing the sample size from 3 to 2.

(3) The 50% cutoff point is very reasonable.

(4) Most (but not all) chemicals had 3 runs. Two chemicals (at Cardam) had 4 runs; three (at Ceetox) had 2 runs; one (at Ceetox) had a single run. All runs had three samples.

(5) There was approximately a 50-50 mix of "positives" and "negatives", which was good.

(6) The variability among runs was somewhat greater than the variability within a run among samples. There were a few cases at certain labs in which one run for a given chemical produced 3 samples with viability <50%, while a second run produced 3 samples with viability >50%. Thus, maintaining multiple runs is more important than maintaining multiple samples, but overall, even the reproducibility among runs was quite good.

(7) No single lab stood out as being clearly superior to the others with regard to reproducibility, although overall Cardam did a slightly better job in this regard than did the other two labs.

(8) I received two sets of raw data, the first from Elizabeth Lipscomb and then later another dataset from ECVAM. The data appeared to be identical, although a handful of runs in the ECVAM data included a "correction" for something that was subtracted from the original viability value. In one instance (noted in my report), I used these corrected values in my calculations, as it made a difference in the classification. In all other cases, I used the viability values that Elizabeth Lipscomb sent me. The ECVAM data also noted that certain chemicals were "excluded", and certain runs within a chemical were "non-qualified" because of excessive variability among samples within the run. I noted all of these occurrences in this report, but I deleted them from my calculations. Among the more than 900 runs, there were very few (8 by my count) that were "non-qualified" because of excessive variability among samples within a run.

At some point, it would be a good idea to "decode" the chemicals to see if there was a consistency in classification of specific chemicals across labs. However, that was not the objective of this evaluation, which focused on reliability rather than on accuracy.

Joe Haseman
7-13-12

Revised Summary of Results for LE Protocol: Cardam

Number of usable chemicals: 103
Number of excluded chemicals: 3 (C52, C53, and C58)
Non-qualified runs: C66, Run 1
C45, Run 3
All chemicals had 3 runs except C35 and C135 (4 runs)
Total number of useable runs: 311
Total number of pairwise comparisons = 933 (101 x 9) + (2 x 12)
Bracketed data were excluded

Chemical Code	Run results (>50%)	Range of scores	Impact of reducing samples per per run from 3 to 2
C1	0/3 0/3 0/3	0.04 to 1.87	None
C101	3/3 3/3 3/3	104.19 to 115.47	None
C103	3/3 3/3 3/3	83.83 to 104.44	None
C104	0/3 0/3 0/3	2.06 to 16.18	None
C105	3/3 3/3 3/3	89.82 to 104.85	None
C106	3/3 3/3 3/3	55.82 to 101.75	None
C107	3/3 3/3 3/3	86.02 to 106.30	None
C108	3/3 3/3 3/3	97.23 to 117.17	None
C109	3/3 3/3 3/3	73.96 to 126.20	None
C11	0/3 0/3 0/3	0.30 to 1.12	None
C110	3/3 3/3 3/3	90.77 to 120.39	None
C112	3/3 3/3 3/3	70.29 to 94.12	None
C113	3/3 3/3 3/3	72.00 to 108.34	None
C114	3/3 3/3 3/3	81.38 to 120.45	None
C116	3/3 3/3 3/3	69.36 to 107.87	None
C119	0/3 0/3 0/3	0.31 to 2.29	None
C12	0/3 0/3 0/3	0.21 to 2.36	None
C120	3/3 3/3 3/3	69.88 to 98.64	None
C123	0/3 0/3 0/3	0.62 to 1.80	None
C124	2/3 0/3 1/3	32.64 to 85.13 [+--]	None
C125	0/3 0/3 0/3	0.89 to 11.25	None
C127	0/3 0/3 0/3	3.28 to 12.72	None
C128	3/3 3/3 3/3	52.95 to 68.83	None

C129		3/3	3/3	3/3	93.14 to 118.97	None
C13		0/3	0/3	0/3	3.47 to 33.07	None
C131		3/3	3/3	3/3	70.04 to 94.01	None
C132		0/3	0/3	0/3	15.55 to 47.86	None
C134		0/3	0/3	0/3	0.66 to 1.06	None
C135	0/3	0/3	0/3	0/3	0.87 to 5.62	None
C136		3/3	3/3	3/3	55.67 to 72.98	None
C137		0/3	0/3	0/3	0.41 to 1.40	None
C138		0/3	0/3	0/3	0.58 to 1.09	None
C139		0/3	0/3	0/3	0.52 to 2.98	None
C14		3/3	3/3	3/3	88.09 to 119.20	None
C140		3/3	3/3	3/3	91.11 to 111.49	None
C141		3/3	3/3	3/3	87.98 to 114.53	None
C15		3/3	3/3	3/3	73.02 to 102.29	None
C16		3/3	3/3	3/3	77.45 to 108.15	None
C163		0/3	0/3	0/3	2.91 to 4.67	None
C164		3/3	3/3	3/3	88.39 to 119.58	None
C166	[2/3]	3/3	3/3	3/3	71.10 to 106.92	None
C170		0/3	0/3	0/3	5.19 to 9.52	None
C185		3/3	3/3	3/3	88.32 to 107.41	None
C19		0/3	0/3	0/3	0.47 to 2.94	None
C193		0/3	0/3	0/3	0.96 to 2.25	None
C195		3/3	3/3	2/3	37.32 to 86.20 [+++]	1/9
C196		3/3	3/3	3/3	102.89 to 128.94	None
C2		3/3	3/3	3/3	92.42 to 114.92	None
C20		3/3	3/3	3/3	91.02 to 123.19	None
C21		0/3	0/3	0/3	1.31 to 2.82	None
C25		0/3	0/3	0/3	1.03 to 1.51	None
C26		0/3	0/3	0/3	0.23 to 2.15	None
C27		3/3	3/3	3/3	71.13 to 103.15	None
C28		3/3	3/3	3/3	66.75 to 102.48	None
C29		0/3	0/3	0/3	2.93 to 19.06	None
C3		0/3	0/3	0/3	1.07 to 17.15	None
C30		3/3	3/3	3/3	76.78 to 115.22	None
C33		0/3	0/3	0/3	0.13 to 0.40	None
C34		3/3	3/3	3/3	87.40 to 217.81	None
C35	0/3	0/3	0/3	0/3	0.57 to 1.08	None
C36		3/3	1/3	3/3	46.32 to 78.88 [+-+]	1/9
C37		3/3	3/3	3/3	67.09 to 119.50	None
C38		0/3	0/3	0/3	6.57 to 10.65	None
C39		3/3	3/3	3/3	90.39 to 127.92	None
C4		3/3	3/3	3/3	83.45 to 107.84	None
C45	3/3	2/3	[2/3]	3/3	48.35 to 88.00 {+++}	None
C46		3/3	3/3	3/3	54.02 to 66.82	None
C47		0/3	0/3	0/3	0.74 to 1.46	None
C48		0/3	0/3	0/3	0.44 to 1.40	None
C49		3/3	3/3	3/3	59.10 to 104.02	None
C50		0/3	0/3	0/3	0.25 to 1.58	None
C51		0/3	0/3	0/3	1.42 to 27.25	None
[C52	3/3	3/3	3/3	3/3	101.68 to 236.55]	-
[C53		3/3	3/3	3/3	40.04 to 73.31]	-
C54		3/3	0/3	3/3	16.67 to 68.68	None
C55		3/3	3/3	3/3	75.59 to 102.00	None
C56		3/3	3/3	2/3	49.08 to 83.56 [+++]	None
[C58		3/3	3/3	3/3	44.43 to 79.54]	-
C6		0/3	0/3	0/3	28.51 to 44.49	None
C60		1/3	0/3	0/3	18.81 to 51.48 [---]	None
C62		0/3	0/3	0/3	0.84 to 1.60	None
C63		0/3	0/3	0/3	18.07 to 36.25	None
C64		0/3	0/3	0/3	0.22 to 2.12	None
C65		0/3	0/3	0/3	17.03 to 49.40	None
C66		0/3	0/3	0/3	0.24 to 1.10	None
C67		3/3	3/3	3/3	86.42 to 118.44	None
C70		3/3	3/3	3/3	53.38 to 81.18	None
C71		3/3	3/3	3/3	86.93 to 110.71	None
C75		0/3	0/3	0/3	0.15 to 0.84	None
C76		0/3	0/3	0/3	0.48 to 6.19	None
C77		0/3	0/3	0/3	0.24 to 0.62	None
C78		0/3	0/3	0/3	5.53 to 28.86	None
C79		3/3	3/3	3/3	65.96 to 114.18	None
C82		0/3	0/3	0/3	1.46 to 12.13	None
C83		3/3	3/3	3/3	67.77 to 98.02	None
C84		3/3	3/3	3/3	65.68 to 100.07	None

C85	3/3	3/3	3/3	71.99 to 108.77	None
C88	1/3	3/3	3/3	37.80 to 82.74 [-++]	None
C9	3/3	3/3	3/3	56.46 to 87.02	None
C90	0/3	0/3	0/3	0.16 to 0.88	None
C91	0/3	0/3	0/3	0.49 to 1.63	None
C94	0/3	0/3	0/3	9.56 to 39.37	None
C96	3/3	3/3	3/3	56.32 to 94.43	None
C97	0/3	0/3	0/3	0.30 to 1.25	None
C98	0/3	0/3	0/3	0.86 to 4.63	None
C99	0/3	0/3	0/3	1.89 to 12.43	None

The likelihood that a reduction in sample size from 3 to 2 would change the classification for a run for Cardam is only 2/933 or 0.2%

Revised Summary of Results for LE Protocol: L'Oreal

Number of usable chemicals: 105
Number of excluded chemicals: 1 (L6)
Non-qualified runs: L11, Run 2
L137, Run 3
All chemicals had 3 runs
Total number of useable runs: 315
Total number of pairwise comparisons = 945 (105 x 9)
Bracketed data excluded

Chemical Code	Run results (>50%)			Range of scores	Impact of reducing samples per per run from 3 to 2
L1	0/3	1/3	0/3	22.97 to 63.28 [---]	1/9
L100	3/3	3/3	3/3	51.06 to 82.79	None
L101	0/3	0/3	0/3	0.39 to 1.97	None
L102	3/3	3/3	3/3	75.54 to 114.39	None
L104	0/3	0/3	0/3	0.69 to 41.52	None
L106	3/3	3/3	3/3	89.14 to 101.98	None
L107	3/3	3/3	3/3	70.98 to 80.78	None
L108	3/3	3/3	3/3	87.61 to 102.59	None
L109	3/3	3/3	3/3	80.57 to 91.71	None
L11	0/3	[1/3]	0/3	0/3 0.35 to 21.54	None
L111	3/3	3/3	3/3	90.59 to 109.80	None
L112	3/3	3/3	3/3	86.01 to 99.77	None
L113	2/3	1/3	0/3	25.36 to 56.45 [---]	1/9
L114	2/3	3/3	3/3	48.25 to 93.01 [+++]	1/9
L115	3/3	3/3	3/3	90.14 to 99.84	None
L118	3/3	3/3	3/3	82.55 to 96.92	None
L119	0/3	0/3	0/3	0.33 to 1.33	None
L12	0/3	0/3	0/3	2.77 to 11.98	None
L120	0/3	0/3	0/3	0.23 to 0.52	None
L122	3/3	3/3	3/3	81.17 to 98.52	None
L123	3/3	0/3	0/3	1.75 to 73.97	None
L125	0/3	0/3	0/3	0.35 to 1.02	None
L126	3/3	3/3	3/3	80.51 to 91.60	None
L127	3/3	3/3	3/3	82.71 to 98.51	None
L129	0/3	0/3	0/3	3.30 to 6.36	None
L13	3/3	3/3	0/3	38.43 to 77.70	None
L130	0/3	0/3	0/3	0.77 to 1.05	None
L131	0/3	0/3	0/3	0.53 to 1.11	None
L132	0/3	0/3	0/3	0.87 to 1.05	None
L133	0/3	0/3	0/3	0.50 to 29.19	None
L134	3/3	3/3	3/3	59.25 to 81.90	None
L136	0/3	3/3	2/3	11.71 to 56.74 [-+-]	1/9
L137	0/3	3/3	[1/3]	3/3 7.86 to 100.90	None
L139	0/3	0/3	0/3	0.83 to 4.90	None
L140	0/3	0/3	0/3	2.07 to 34.00	None
L144	3/3	3/3	3/3	92.94 to 105.16	None
L148	3/3	3/3	3/3	83.64 to 102.26	None
L15	3/3	3/3	3/3	65.40 to 109.18	None
L156	3/3	3/3	3/3	61.21 to 105.75	None
L16	0/3	0/3	0/3	1.85 to 13.97	None
L161	3/3	3/3	3/3	66.11 to 100.53	None
L164	0/3	0/3	0/3	0.70 to 1.67	None
L169	3/3	3/3	3/3	77.48 to 91.57	None

L17	3/3	3/3	2/3	44.92 to 80.28 [++-]	1/9
L174	0/3	0/3	0/3	0.54 to 9.85	None
L18	3/3	3/3	3/3	97.64 to 107.96	None
L185	0/3	0/3	0/3	2.09 to 3.66	None
L20	0/3	0/3	0/3	16.57 to 33.67	None
L200	3/3	3/3	3/3	85.91 to 112.89	None
L23	0/3	0/3	0/3	0.24 to 0.72	None
L24	0/3	0/3	0/3	0.37 to 4.16	None
L27	3/3	3/3	3/3	92.91 to 107.80	None
L28	1/3	0/3	0/3	37.36 to 60.81 [---]	2/9
L29	0/3	0/3	0/3	2.65 to 25.46	None
L32	3/3	3/3	3/3	75.42 to 96.07	None
L33	0/3	0/3	0/3	0.62 to 1.18	None
L36	3/3	3/3	3/3	82.67 to 103.15	None
L37	0/3	0/3	0/3	0.31 to 0.85	None
L39	3/3	3/3	3/3	57.08 to 69.71	None
L4	3/3	3/3	3/3	52.22 to 85.82	None
L42	0/3	0/3	0/3	1.07 to 1.74	None
L43	0/3	0/3	0/3	1.65 to 6.41	None
L45	0/3	0/3	0/3	0.41 to 3.32	None
L48	0/3	0/3	0/3	0.28 to 1.31	None
L5	3/3	3/3	3/3	62.00 to 87.30	None
L50	3/3	3/3	3/3	87.25 to 104.73	None
L51	0/3	0/3	0/3	0.65 to 1.29	None
L53	3/3	3/3	3/3	86.19 to 102.09	None
L55	0/3	0/3	0/3	2.23 to 16.94	None
L56	0/3	0/3	0/3	0.69 to 1.20	None
L57	0/3	0/3	0/3	3.08 to 6.19	None
L58	2/3	0/3	0/3	22.28 to 52.96 [---]	1/9
L59	0/3	0/3	0/3	0.51 to 2.70	None
[L6	3/3	3/3	3/3	3/3 3/3 55.898 to 125.70]	-
L60	3/3	3/3	3/3	86.37 to 100.20	None
L61	3/3	3/3	3/3	78.00 to 90.51	None
L62	3/3	3/3	3/3	84.97 to 104.47	None
L64	3/3	3/3	3/3	77.59 to 97.11	None
L65	3/3	3/3	3/3	86.93 to 103.08	None
L66	0/3	0/3	0/3	0.80 to 12.49	None
L67	3/3	3/3	3/3	81.08 to 98.31	None
L68	0/3	0/3	0/3	0.27 to 2.37	None
L7	3/3	3/3	3/3	55.94 to 76.28	None
L70	0/3	0/3	0/3	0.46 to 1.47	None
L72	3/3	3/3	3/3	62.50 to 72.35	None
L73	3/3	3/3	3/3	83.66 to 101.89	None
L75	3/3	3/3	3/3	85.98 to 104.99	None
L76	3/3	3/3	3/3	80.61 to 102.54	None
L78	0/3	0/3	0/3	0.42 to 1.12	None
L79	3/3	3/3	3/3	66.53 to 79.26	None
L8	0/3	0/3	0/3	1.19 to 2.39	None
L80	0/3	0/3	0/3	0.20 to 0.48	None
L81	0/3	0/3	0/3	0.38 to 0.57	None
L82	0/3	0/3	0/3	0.22 to 1.67	None
L83	0/3	0/3	0/3	1.02 to 1.53	None
L85	3/3	3/3	3/3	80.21 to 100.91	None
L87	0/3	0/3	0/3	0.42 to 2.08	None
L9	0/3	0/3	0/3	22.92 to 38.66	None
L90	3/3	3/3	3/3	85.06 to 110.95	None
L91	0/3	0/3	0/3	11.86 to 44.42	None
L92	0/3	0/3	0/3	0.27 to 1.22	None
L94	0/3	0/3	0/3	1.33 to 26.40	None
L96	3/3	3/3	3/3	77.34 to 98.09	None
L97	0/3	0/3	0/3	10.19 to 21.83	None
L98	0/3	0/3	0/3	12.43 to 32.19	None
L99	3/3	3/3	3/3	60.87 to 95.51	None

The likelihood that a reduction in sample size from 3 to 2 would change the classification for a run for L'Oreal is only 8/945 or 0.8%

Revised Summary of Results for LE Protocol: Ceetox

Number of usable chemicals: 103
Number of excluded chemicals: 5 (X17, X31, X32, X62, X95)
Non-qualified runs: X47, Runs 1 and 2
X50, Run 2
X173, Run 3
All chemicals had 3 useable runs, except X37, X39, & X47 (2 runs) and X44 (1 run)
Total number of useable runs: 304
Total number of pairwise comparisons = 912 (99 x 9) + (3 x 6) + (1 x 3)
Bracketed data excluded

Chemical Code	Run results (>50%)			Range of scores	Impact of reducing samples per per run from 3 to 2
X1	3/3	3/3	3/3	94.02 to 102.29	None
X102	3/3	3/3	3/3	68.54 to 93.63	None
X103	3/3	3/3	3/3	92.94 to 101.91	None
X107	3/3	3/3	3/3	91.94 to 112.73	None
X108	3/3	3/3	3/3	72.06 to 88.66	None
X109	3/3	3/3	3/3	67.47 to 98.49	None
X11	3/3	3/3	3/3	84.85 to 112.44	None
X110	3/3	3/3	3/3	84.74 to 103.91	None
X111	0/3	2/3	3/3	37.63 to 64.33 [--+]	1/9
X112	3/3	3/3	3/3	89.18 to 108.01	None
X113	3/3	3/3	3/3	82.69 to 118.92	None
X114	3/3	3/3	3/3	79.27 to 110.81	None
X115	3/3	3/3	3/3	88.75 to 111.26	None
X116	3/3	3/3	3/3	94.39 to 103.51	None
X117	0/3	0/3	0/3	0.96 to 3.18	None
X118	0/3	0/3	0/3	16.08 to 31.72	None
X119	0/3	0/3	0/3	3.03 to 5.96	None
X120	3/3	3/3	3/3	82.38 to 109.38	None
X121	0/3	0/3	0/3	1.13 to 2.45	None
X123	3/3	3/3	3/3	68.49 to 98.37	None
X125	3/3	3/3	3/3	85.57 to 109.20	None
X126	0/3	0/3	1/3	18.48 to 59.77 [---]	1/9
X127	0/3	0/3	0/3	1.38 to 2.39	None
X128	0/3	0/3	0/3	1.23 to 2.13	None
X129	0/3	0/3	1/3	2.30 to 58.49 [---]	1/9
X13	3/3	3/3	3/3	71.80 to 110.46	None
X131	3/3	3/3	3/3	69.59 to 93.70	None
X133	0/3	0/3	0/3	0.62 to 3.67	None
X134	3/3	3/3	3/3	51.07 to 100.61	None
X136	0/3	0/3	0/3	0.88 to 1.75	None
X138	0/3	0/3	0/3	2.26 to 15.49	None
X139	3/3	3/3	3/3	50.84 to 61.79	None
X14	0/3	0/3	0/3	0.0 to 1.59	None
X143	3/3	3/3	3/3	75.93 to 108.45	None
X157	3/3	3/3	3/3	75.97 to 109.05	None
X158	3/3	3/3	3/3	74.03 to 107.32	None
X16	0/3	3/3	1/3	22.62 to 70.76 [-++]	1/9
X160	3/3	3/3	3/3	79.71 to 114.68	None
X165	0/3	0/3	0/3	4.28 to 13.98	None
X169	3/3	3/3	3/3	85.59 to 115.56	None
[X17	3/3	3/3	3/3	3/3	59.97 to 100.99]	-
X173	3/3	3/3	[3/3]	3/3	79.12 to 96.28	None
X19	3/3	3/3	3/3	91.18 to 112.30	None
X190	0/3	0/3	0/3	1.96 to 4.41	None
X196	0/3	0/3	0/3	1.48 to 2.79	None
X2	0/3	0/3	2/3	30.58 to 51.28 [---]	1/9
X21	0/3	0/3	0/3	1.01 to 1.85	None
X22	0/3	0/3	0/3	1.82 to 3.00	None
X24	3/3	3/3	3/3	75.14 to 102.04	None
X25	0/3	0/3	0/3	1.62 to 2.82	None

X27	3/3	3/3	3/3	63.10 to 111.81	None
X28	0/3	0/3	0/3	0.33 to 1.06	None
X29	0/3	0/3	0/3	1.03 to 2.90	None
X3	0/3	0/3	0/3	1.57 to 4.25	None
X30	0/3	0/3	0/3	0.99 to 4.58	None
[X31	3/3	3/3	3/3	41.98 to 64.57]	-
[X32	3/3	3/3	3/3	70.61 to 96.57]	-
X33	0/3	0/3	0/3	0.51 to 3.03	None
X36	0/3	0/3	0/3	1.08 to 1.40	None
X37	0/3	0/3		15.01 to 49.66	None
X38	3/3	3/3	3/3	51.62 to 91.32	None
X39	3/3	3/3		82.82 to 101.28	None
X40	3/3	3/3	3/3	71.71 to 97.67	None
X41	0/3	0/3	0/3	0.66 to 3.75	None
X42	0/3	0/3	0/3	1.31 to 2.50	None
X43	0/3	0/3	0/3	2.22 to 30.71	None
X44	3/3			66.41 to 87.18	None
X45	0/3	0/3	0/3	8.38 to 28.86	None
X46	3/3	3/3	3/3	70.31 to 91.69	None
X47	[2/3]	[3/3]	3/3	3/3	80.13 to 98.52	None
X49	3/3	3/3	3/3	55.49 to 66.72	None
X5	0/3	0/3	0/3	1.50 to 10.73	None
X50	3/3	[2/3]	3/3	3/3	50.28 to 90.97	None
X51	0/3	0/3	0/3	0.53 to 1.07	None
X52	0/3	0/3	0/3	0.96 to 1.64	None
X53	3/3	3/3	3/3	89.04 to 105.76	None
X55	3/3	3/3	3/3	83.25 to 118.34	None
X56	0/3	0/3	0/3	0.36 to 1.34	None
X59	3/3	3/3	3/3	86.74 to 117.13	None
X6	0/3	0/3	0/3	1.23 to 6.10	None
X61	3/3	3/3	3/3	88.88 to 118.44	None
[X62	3/3	3/3	3/3	54.62 to 72.86]	-
X63	0/3	0/3	0/3	15.94 to 46.50	None
X64	0/3	0/3	0/3	1.61 to 5.07	None
X65	0/3	0/3	0/3	0.85 to 1.71	None
X66	0/3	0/3	0/3	0.54 to 6.47	None
X68	0/3	0/3	0/3	0.0 to 12.93	None
X7	0/3	0/3	0/3	2.01 to 13.89	None
X70	2/3	3/3	3/3	47.84 to 81.69 [+++]	None
X72	3/3	3/3	3/3	94.63 to 109.40	None
X73	0/3	0/3	0/3	0.63 to 2.46	None
X75	3/3	3/3	2/3	47.64 to 113.89 [+++]	None
X77	3/3	3/3	3/3	95.04 to 132.51	None
X8	3/3	3/3	3/3	86.32 to 120.01	None
X80	3/3	3/3	3/3	60.50 to 85.39	None
X81	0/3	0/3	0/3	1.66 to 21.44	None
X82	3/3	3/3	3/3	54.81 to 87.66	None
X83	0/3	0/3	0/3	0.46 to 1.41	None
X84	3/3	3/3	3/3	67.98 to 97.20	None
X86	0/3	0/3	0/3	5.39 to 11.25	None
X87	0/3	0/3	0/3	0.09 to 1.46	None
X89	0/3	0/3	0/3	3.65 to 10.93	None
X91	0/3	0/3	0/3	11.25 to 37.33	None
X93	0/3	0/3	0/3	1.33 to 13.13	None
X94	3/3	3/3	3/3	85.33 to 109.59	None
[X95	3/3	3/3		61.07 to 116.44]	-
X98	0/3	0/3	0/3	0.38 to 1.29	None
X99	0/3	1/3	1/3	33.12 to 57.31 [--+]	2/9

The likelihood that a reduction in sample size from 3 to 2 would change the classification for a run for Ceetox is only 7/912 or 0.8%

Samples with less than complete agreement.

These are the only runs whose classifications could be altered by reducing the number of samples from 3 to 2

Lab	Chemical	Run	Sample			
			1	2	3	Mean
Cardam	C124	1	64.9	73.8	41.9	60.2
Cardam	C124	3	42.8	50.4	32.6	41.9
Cardam	C195	3	37.3	54.3	63.6	51.7

Cardam	C36	2	53.2	46.3	49.0	49.5
Cardam	C45	2	58.8	61.6	48.3	56.2
Cardam	C56	3	73.0	76.5	49.1	66.2
Cardam	C60	1	51.5	41.8	38.5	43.9
Cardam	C88	1	38.6	37.8	51.6	42.7
L-Oreal	L1	2*	59.6	43.4	36.4	46.5
L-Oreal	L113	1	36.2	56.5	54.4	49.0
L-Oreal	L113	2	38.3	39.3	51.7	43.1
L-Oreal	L114	1	64.0	48.2	50.2	54.1
L-Oreal	L136	3	53.5	58.3	31.4	47.7
L-Oreal	L17	3	44.9	51.5	50.9	49.1
L-Oreal	L28	1	43.7	60.8	44.5	49.7
L-Oreal	L58	1	53.0	22.3	50.9	42.1
Ceetox	X111	2	37.6	56.4	52.2	48.7
Ceetox	X126	3	48.0	38.3	59.8	48.7
Ceetox	X129	3	38.2	42.9	58.5	46.5
Ceetox	X16	3	47.4	47.5	70.8	55.2
Ceetox	X2	3	50.4	44.3	51.3	48.7
Ceetox	X70	1	58.9	47.8	53.4	53.4
Ceetox	X75	3	72.4	72.7	47.6	64.2
Ceetox	X99	2	35.7	47.6	53.5	45.6
Ceetox	X99	3	44.3	49.8	57.3	50.5

*corrected values used in this analysis

SUMMARY PERFORMANCE BY LAB

	Cardam	L'Oreal	Ceetox
No. chemicals with adequate studies	103	105	103
No. chemicals with 100% sample agreement	95 (92%))	95 (90%)	95 (92%)
Positives	47	46	48
Negatives	48	49	47
No. adequate runs	311	315	304
No. runs with 100% agreement	303 (97%)	307 (97%)	295 (97%)
No. of possible pairs of samples among all runs	933	945	912
No. of pairs of that would give a classification different than the full 3 samples	2 (0.2%)	8 (0.8%)	7 (0.8%)

Appendix X EPRA Results

Legend :

Chemical	EPRA code	name
1	41	1-bromohexane
2	42	1-methylpropyl benzene
3	43	2-ethoxyethyl methacrylate
4	44	iso-octylthioglycolate INCI name: ISOOCTYL THIOGLYCOLATE
5	45	4-(methylthio)-benzaldehyde
6	47	dipropyl disulphide
7	48	1-bromo-4-chlorobutane
8	51	1-bromo-octane
9	53	1,9-decadiene
10	54	2,2-dimethyl-3-pentanol
11	50	2-(2-ethoxyethoxy) ethanol INCI name: ETHOXYDIGLYCOL
12	61	bisphenol A, epichlorohydrin polymer, ethoxylated, propoxylated (53-57% aqueousemulsion)
13	62	bisphenol A, diethylene triamine, epichlorohydrin polymer, ethoxylated, propoxylated (56% aqueous emulsion)
14	63	dioctyl ether INCI name: DICAPRYLYL ETHER
15	64	dioctyl carbonate INCI name: DICAPRYLYL CARBONATE
16	65	2-propylheptyl octanoate INCI name: PROPYLHEPTYL CAPRYLATE
17	101	polyglyceryl-3 diisooctadecanoate INCI name: POLYGLYCERYL-3 DIISOSTEARATE
18	60	steareth-10 allyl ether/acrylates copolymer (30% aqueous) INCI name: STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER
19	113	dimethyl siloxane, mono dimethylvinylsiloxy- and mono trimethoxysiloxy-terminated (95%)
20	99	ricinoleic acid tin salt
21	100	1-ethyl-3-methylimidazolium ethylsulphate
22	103	3-phenoxybenzyl alcohol
23	123	ethyl thioglycolate INCI name: ETHYL THIOGLYCOLATE
24	134	glycidyl methacrylate
25	143	piperonyl butoxide INCI name: PIPERONYL BUTOXIDE
26	144	propiconazole
27	49	2-ethylhexylthioglycolate
28	67	4,4'-methylene bis-(2,6-di-tert-butylphenol)
29	136	tetradecyl tetradecanoate INCI name: MYRISTYL MYRISTATE
30	137	1,1-dimethylguanidine sulphate
31	138	potassium tetrafluoroborate
32	69	2,6-dihydroxy-3,4-dimethylpyridine INCI name: 2,6-DIHYDROXY-3,4-DIMETHYLPYRIDINE
33	70	2,2'-[[4-[(2-methoxyethyl)amino]-3-nitrophenyl]imino]bis-ethanol INCI name: HC BLUE NO. 11
34	71	2,2'-[[3-methyl-4-[(4-nitrophenyl)azo]phenyl]imino]bis-ethanol INCI name: DISPERSE RED 17
35	72	2,5,6-triamino-4-pyrimidinol sulphate INCI name: 2,5,6-TRIAMINO-4-PYRIMIDINOL SULFATE
36	73	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea INCI name: TRICLOCARBAN

Chemical	EPRA code	name
37	114	polyethylene glycol (PEG-40) hydrogenated castor oil INCI name: PEG-40 HYDROGENATED CASTOR OIL
38	74	2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) INCI name: METHYLENE BIS-BENZOTRIAZOLYL TETRAMETHYLBUTYLPHENOL
39	75	2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol] INCI name: BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE
40	76	acrylamidopropyltrimonium chloride/acrylamide copolymer
41	105	tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino) tribenzoate INCI name: ETHYLHEXYL TRIAZONE
42	106	trisodium mono-(5-(1,2-dihydroxyethyl)-4-oxido-2-oxo-2,5-dihydro-furan-3-yl) phosphate INCI name: SODIUM ASCORBYL PHOSPHATE
43	107	hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl) benzoate INCI name: DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE
44	108	[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl](6-iodoquinazolin-4-yl)amine
45	110	1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol
46	111	cellulose, 2-(2-hydroxy-3-(trimethylammonium)propoxy)ethyl ether chloride (91%) INCI name: POLYQUATERNIUM-10
47	115	3,4-dimethoxy benzaldehyde INCI name: VERATRALDEHYDE
48	126	sodium hydrogensulphite INCI name: SODIUM BISULFITE
49	153	propyl-4-hydroxybenzoate INCI name: PROPYLPARABEN
50	146	iodosulfuron-methyl-sodium
51	147	1,5-di(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene common name: Amitraz
52	149	2-anilino-4,6-dimethylpyrimidine common name: Pyrimethanil
53	150	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl[1,3,5]oxadiazinan-4-ylidene-N-nitroamine common name: Thiamethoxam
54	7	3-chloropropionitrile
55	117	2-methylpropanal INCI name: 2-METHYLPROPANAL
56	118	isopropyl acetoacetate
57	87	2-methyl-1-pentanol
58	128	1-(1-methyl-2-propoxyethoxy)propan-2-ol INCI name: PPG-2 PROPYL ETHER
59	129	ethyl-2-methyl acetoacetate
60	139	diethyl toluamide INCI name: DIETHYL TOLUAMIDE common name: DEET
61	39	2-hydroxy-1,4-naphthoquinone INCI name: LAWSONE
62	121	1,4-dibutoxy benzene
63	122	4-nitrobenzoic acid
64	98	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridine propionate
65	132	2,2-dimethyl-3-methylenebicyclo [2.2.1] heptane INCI name: CAMPHENE
66	133	sodium chloroacetate
67	3	gamma-butyrolactone INCI name: BUTYROLACTONE
68	5	cyclopentanol
69	15	alkyl (C10-16) glucoside sodium carboxylate (~ 30% aqueous) INCI name: SODIUM CARBOXYMETHYL

Chemical	EPRA code	name
		C10-16 ALKYL GLUCOSIDE
70	131	methyl N,N,N-trimethyl-4-[(4,7,7-trimethyl-3-oxobicyclo[2.2.1]hept-2-ylidene)methyl]anilinium sulphate (30% aqueous) INCI name: CAMPHOR BENZALKONIUM METHOSULFATE
71	89	1-propoxy-2-propanol INCI name: PROPYLENE GLYCOL PROPYL ETHER
72	116	2,4,11,13-tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, di-D-gluconate (20% aqueous) INCI name: CHLORHEXIDINE DIGLUCONATE
73	32	3,3'-dithiopropionic acid
74	34	2-amino-3-hydroxy pyridine INCI name: 2-AMINO-3-HYDROXYPYRIDINE
75	36	sodium benzoate INCI name: SODIUM BENZOATE
76	94	6,7-dihydro-2,3-dimethyl-imidazo[1,2-a]pyridin-8(5H)-one
77	95	methyl (2E)-[2-(chloromethyl)phenyl](methoxyimino) acetate
78	96	(2R,3R)-3-((R)-1-(tert-butyldimethylsiloxy)ethyl)-4-oxoazetidin-2-yl acetate
79	119	ammonium nitrate INCI name: AMMONIUM NITRATE
80	1	methylthioglycolate INCI name: METHYL THIOGLYCOLATE
81	2	3-diethylaminopropionitrile
82	8	coco alkyl dimethyl betaine (~ 30% aqueous) INCI name: COCO-BETAINE
83	9	coco amidopropyl betaine (~ 30% aqueous) INCI name: COCAMIDOPROPYL BETAINE
84	10	sodium coco amphoacetate (~ 30% aqueous)
85	11	triethanol ammonium alkyl sulphate (~ 40% aqueous) INCI name: TEA-C12-14 ALKYL SULFATE
86	12	di-sodium alkyl ether sulfosuccinate (~ 30% aqueous) INCI name: DISODIUM LAURETH SULFOSUCCINATE
87	13	sodium alkyl ether sulphate (~ 30% aqueous) INCI name: SODIUM LAURETH SULFATE
88	14	bisphenol A, diethylene triamine, epichlorohydrin, polypropylene glycol diglycidyl ether, polymer (~ 60% aqueous)
89	81	ethoxylated (5 EO) alkyl (C10-14) alcohol
90	82	alkyl (C10-16) glucoside (~ 50% aqueous) INCI name: LAURYL GLUCOSIDE
91	80	(ethylenediaminepropyl)trimethoxysilane
92	152	tetraethylene glycol diacrylate
93	16	2,5-dimethyl-2,5-hexanediol
94	17	dodecanoic acid INCI name: LAURIC ACID
95	18	1,2,4-triazole sodium salt
96	19	1-naphthalene acetic acid
97	20	sodium oxalate INCI name: SODIUM OXALATE
98	21	4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromophenol] S,S-dioxide INCI name: TETRABROMOPHENOL BLUE
99	25	1,2-benzisothiazol-3(2H)-one INCI name: BENZISOTHIAZOLINONE
100	141	ethyl lauroyl arginate HCl INCI name: ETHYL LAUROYL ARGINATE HCL
101	30	2-[(4-aminophenyl)azo]-1,3-dimethyl-1H-imidazolium chloride INCI name: BASIC ORANGE 31
102	31	disodium 2,2'-([1,1'-biphenyl]-4,4'-diyldivinylene)bis(benzenesulphonate) INCI name: DISODIUM DISTYRYLBIPHENYL DISULFONATE
103	91	3,4-dimethyl-1H-pyrazole
104	93	N-(2-amino-4,6-dichloropyrimidin-5-yl) formamide

Chemical	EPRA code	name
105	97	1,2-dihydro-1,3,4,6-tetramethyl-2-oxo-pyrimidinium hydrogensulphate
106	24	4-((4-amino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl)-2-methylbenzenamine hydrochloride INCI name: BASIC VIOLET 2
107	90	xanthylium, 3,6-bis(diethylamino)-9-[2-(methoxycarbonyl)phenyl]-tetrafluoroborate

Results_EPRA_EIVS_first batch 030510 decoded (JBA).xls												
	IRRitant/Non-IRRitant			Lysine-peptide			Remarks	Cysteine-peptide			Remarks	
EPRA code	classification	State	Replicates	Depletion (%)	Mean depletion	SD		Depletion (%)	Mean depletion	SD		**Reactivity classification**
1	IRR	liquid	1	22.18				0.00				
Cat 1			2	23.19				0.00				
			3	27.12	24.16	2.6		4.14	1.38	2.4		**R**
2	IRR	liquid	1	24.36				83.48				
Cat 1			2	30.15				92.83				
			3	34.78	29.76	5.2		96.90	91.07	6.9		**R**
3	IRR	liquid	1	1.79				0.00				
Cat 2A			2	2.10				1.55				
			3	2.76	2.22	0.5		4.98	2.17	2.5		**NR**
4	IRR	liquid	1	0				9.46				
Cat 2A			2	0				13.51				
			3	0	0	0.0		18.62	13.86	4.6		**R**
5	IRR	liquid	1	0.00				0				
Cat 2A/B			2	0.00				3.45				
			3	0.00	0.00	0.0		12.02	5.16	6.2		**NR**
6	IRR	liquid	1	0.37				0.00				
Cat 2B			2	0.47				2.68				
			3	0.87	0.57	0.3		9.75	4.14	5.0		**NR**
7	IRR	liquid	1	81.72				90.89				
Cat 2B			2	86.47				96.91				
			3	89.79	85.99	4.1		99.15	95.65	4.3		**R**
8	IRR	liquid	1	1.83				0				
Cat 1			2	1.80				0				
			3	2.49	2.04	0.4		2.99	1.00	1.7		**NR**
9	IRR	liquid	1	2.27				0				
Cat 1			2	2.25				0				
			3	2.31	2.28	0.0		0				**NR**
10	IRR	liquid	1	0.54				-17.03				
Cat 1			2	0.95				-15.77				
			3	0.74	0.74	0.2		-16.11	-16.30	0.7	no interference	**repeat analysis cys**
11	IRR	liquid	1	94.39				1.15				
Cat 1			2	94.25				1.16				
			3	94.58	94.41	0.2		9.68	4.00	4.9		**R**

12	IRR	liquid	1	84.12			interference	2.01				
Cat 1			2	85.46			interference	4.42				
			3	86.46	85.35	1.2	interference	7.89	4.77	3.0		**N/A**
13	IRR	liquid	1	89.51			interference	-38.0			interference	
Cat 1			2	89.41			interference	-37.6			interference	
			3	89.72	89.55	0.2	interference	-37.7	-37.8	0.2	interference	**N/A**
15	IRR	liquid	1	<-10			interference	4.39			interference	
Cat 2A			2	<-10			interference	9.42			interference	
			3	<-10			interference	11.57	8.46	3.7	interference	**N/A**
16	IRR	solid	1	0.98				1.17				
Cat 1			2	1.24				0.00				
			3	1.01	1.08	0.1		6.03	2.40	3.2		**NR**
17	IRR	solid	1	0.58				1.85				
Cat 1			2	0.08				4.20				
			3	0.42	0.36	0.3		6.66	4.24	2.4		**NR**
18	IRR	solid	1	2.50				0.38				
Cat 1			2	2.33				5.06				
			3	2.79	2.54	0.2		9.39	4.94	4.5		**NR**
19	IRR	solid	1	1.15				5.02				
Cat 1			2	1.09				5.21				
			3	1.70	1.31	0.3		8.33	6.19	1.9		**R or N/A?**
20	IRR	solid	1	0.30				0.00				
Cat 1			2	0.39				8.09				
			3	0.16	0.28	0.1	10 mM	9.01	5.70	5.0	10 mM	**NR or N/A??**
22	IRR	solid	1	0.00				-661.9			interference	
Cat 1			2	0.00				-665.1			interference	
			3	0.00	0.00	0.0		-651.8	-659.6	7.0	interference	**N/A**
24	IRR	solid	1	13.13				93.47				
Cat 1			2	20.58				96.31				
			3	20.95	18.22	4.4		96.89	95.56	1.8		**R**
26	IRR	solid	1	11.29				11.57				
Cat 1			2	13.40				18.68				
			3	14.46	13.05	1.6		20.72	16.99	4.8		**R**
27	IRR	solid	1	32.23				1.30				
Cat 1			2	30.28				6.72				
			3	34.03	32.18	1.9		7.33	5.12	3.3		**R**
32	IRR	solid	1	11.62			interference	96.93				

Cat 2A/B			2	12.58			interference	97.58				
			3	13.44	12.55	0.9	interference	97.84	97.45	0.5		**R**
34	IRR	solid	1	19.11				99.59				
Cat 2A			2	22.98				99.58				
			3	22.56	21.55	2.1		99.60	99.59	0.0		**R**
35	IRR	solid	1	33.43				100.00				
			2	41.12				100.00				
			3	48.04	40.86	7.3		100.00	100.00	0.0		**R**
36	IRR	solid	1	-104.00			interference	-747.1			interference	
Cat 2A			2	-106.71			interference	-732.3			interference	
			3	-108.24	-106.32	2.2	interference	-694.5	-724.6	27.2	interference	**N/A**
37	IRR	solid	1	21.17				100.00				
Cat 2A			2	23.27				100.00				
			3	30.19	24.87	4.7		100.00	100.00	0.0		**R**
39	IRR	solid	1	<-10			interference	18.94				
Cat 2B			2	<-10			interference	25.52				
			3	<-10			interference	26.92	23.79	4.3		**R**
40	NIRR	liquid	1	1.02				41.82				
No Cat			2	1.35				51.83				
			3	2.03	1.47	0.5		57.93	50.53	8.1		**R**
41	NIRR	liquid	1	0.46				16.31				
No Cat			2	0.66				19.52				
			3	0.51	0.54	0.1		27.22	21.02	5.6		**R**
42	NIRR	liquid	1	0				0.00				
No Cat			2	0.33				0.80				
			3	0.07	0.13	0.2		7.65	2.82	4.2		**NR**
43	NIRR	liquid	1	7.78				43.12				
No Cat			2	9.10				51.10				
			3	8.99	8.63	0.7		59.58	51.27	8.2		**R**
45	NIRR	liquid	1	23.38			interference	0				
No Cat			2	23.52			interference	0				
			3	23.61	23.51	0.1	interference	0	0	0		**N/A**
46	NIRR	liquid	1	2.70				20.24				
No Cat			2	0.63				25.81				
			3	0.00	1.11	1.4		33.94	26.66	6.9		**R**
47	NIRR	liquid	1	0				86.74				
No Cat			2	0.28				87.62				
			3	0.01	0.09	0.2		88.34	87.57	0.8		**R**

48	NIRR	liquid	1	1.48				30.85				
No Cat			2	2.13				42.79				
			3	2.41	2.01	0.5		51.47	41.70	10.4		**R**
49	NIRR	liquid	1	11.58				<-10				
No Cat			2	14.79				<-10				
			3	17.05	14.47	2.7		<-10	<-10		No co-elution observed	**R**
50	NIRR	liquid	1	0.22				0.00				
No Cat			2	0.69				0.00				
			3	0.30	0.40	0.3		0.00	0.00	0.0		**NR**
51	NIRR	liquid	1	0				0.37				
No Cat			2	0				0.53				
			3	0	0.00	0.0		3.43	1.45	1.7		**NR**
52	NIRR	liquid	1	0				3.15				
No Cat			2	0				2.09				
			3	0	0	0.0		5.41	3.55	1.7		**NR**
53	NIRR	liquid	1	0.43				0.00				
No Cat			2	0.14				2.92				
			3	0.30	0.29	0.1		7.36	3.43	3.7		**NR**
55	NIRR	liquid	1	0.25				0.00				
No Cat			2	1.19				2.58				
			3	0.20	0.54	0.6		7.50	3.36	3.8		**NR**
56	NIRR	liquid	1	0.64				0.00				
No Cat			2	0.91				3.00				
			3	0.74	0.76	0.1		5.79	2.93	2.9		**NR**
57	NIRR	liquid	1	0.37				0.28				
No Cat			2	0.44				2.42				
			3	0.73	0.51	0.2		7.25	3.32	3.6		**NR**
58	NIRR	liquid	1	0.05				0				
No Cat			2	0.16				0				
			3	0.56	0.26	0.3		5.93	1.98	3.4		**NR**
59	NIRR	liquid	1	0				7.01				
No Cat			2	0.47				15.03				
			3	0.00	0.16	0.3		11.39	11.14	4.0		**R**
63	NIRR	liquid	1	0.00				0.70				
No Cat			2	0.00				4.38				
			3	0.00	0.00	0.0		5.16	3.41	2.4		**NR**

64	NIRR	liquid	1	0				0.47				
No Cat			2	0				3.64				
			3	0	0.00	0.0		4.32	2.81	2.1		**NR**
65	NIRR	liquid	1	0				0.00				
No Cat			2	0				0.00				
			3	0	0	0.0		0.00	0.00	0.0		**NR**
67	NIRR	solid	1	0.00				1.69				
No Cat			2	0.00				3.48				
			3	0.00	0.00	0.0		8.09	4.42	3.3		**NR**
68	NIRR	solid	1	1.70				98.11				
No Cat			2	1.59				97.57				
			3	1.54	1.61	0.1	insoluble	98.44	98.04	0.4	insoluble	**R**
72	NIRR	solid	1	13.60				99.82				
No Cat			2	13.34				100.00				
			3	12.98	13.30	0.3	insoluble	100.00	99.94	0.1	insoluble	**R**
73	NIRR	solid	1	1.25				0.00				
No Cat			2	1.52				2.79				
			3	2.10	1.62	0.4		7.67	3.49	3.9		**NR**
77	NIRR	solid	1	2.38								
No Cat			2	1.80								
			3	1.53	1.90	0.4	insoluble				insoluble	**repeat analysis cys**
Results_EPRA_EIVS_second batch 310810 decoded (JBA).xls												
21	IRR	solid	1	100.00				42.16			dissolved in 50 % DMSO/acetonitrile	
			2	88.03				50.21			peptide concentration In ref control was <0.45 mM (0.31 mM)	
			3	88.19	92.07	6.9	interference (1.4 % rel. to Ref Control)	57.18	49.85	7.5		**R**
23	IRR	solid	1	42.59				100.00				
			2	40.96				100.00				
			3	38.85	40.80	1.9		100.00	100.00	0.0		**R**
25	IRR	solid	1				interference	100.00				

			2				interference	100.00				
			3				interference	100.00	100.00	0.0		**R**
44	NIRR	liquid	1	9.90				-15.97				
			2	12.19				-15.12				
			3	14.04	12.05	2.1	interference (5 % relative to REF control)	-18.45	-16.52	1.7	no interference in Co-elution control	**R**
54	NIRR	liquid	1	1.22				0.00				
			2	1.81				1.01				
			3	1.62	1.55	0.3		5.58	2.20	3.0		**NR**
69	NIRR	solid	1	5.72				100.00				
			2	0.12				100.00				
			3	6.09	3.97	3.3		100.00	100.00	0.0	interference	**N/A**
70	NIRR	solid	1	91.04			interference	70.66				
			2	89.65			interference	84.22				
			3	88.84	89.84	1.1	interference	93.22	82.70	11.4		**R**
71	NIRR	solid	1	36.86				62.28				
			2	26.07				70.27				
			3	22.49	28.47	7.5		80.58	71.04	9.2		**R**
78	IRR	liquid	1	3.79				0.00				
			2	3.98				0.00				
			3	3.80	3.86	0.1	interference (1.2 %)	3.97	1.32	2.3		**NR**
80	IRR	liquid	1	0.00				0.37				
			2	0.00				1.00				
			3	0.00	0.00	0.0		1.97	1.12	0.8		**NR**
81	IRR	liquid	1	0.97				0.00				
			2	1.63				1.47				
			3	1.57	1.39	0.4		5.34	2.27	2.8		**NR**
82	IRR	liquid	1	0.00				0.00				
			2	0.00				0.57				
			3	0.00	0.00	0.0	10 mM	3.40	1.32	1.8	10 mM	**N/A**
87	IRR	liquid	1	1.41				1.22				
			2	1.69				2.97				
			3	2.18	1.76	0.4		4.56	2.92	1.7		**NR**
89	IRR	liquid	1	1.54				0.00				
			2	1.89				1.51				
			3	1.76	1.73	0.2		7.27	2.92	3.8		**NR**

90	IRR	solid	1	2.74				91.31				
			2	2.54				99.50				
			3	2.43	2.57	0.2		99.86	96.89	4.8		**R**
91	IRR	solid	1	0.00				1.92				
			2	0.00				4.41				
			3	0.18	0.06	0.1	interference (3 % rel. to Ref Control C)	5.10	3.81	1.7		**NR**
92	IRR	solid	1				interference	0.00				
			2				interference	0.00				
			3				interference	0.00	0.00			**N/A**
93	IRR	solid	1	12.37				81.16			dissolved in 50 % DMSO/acetonitrile	
			2	22.36				80.30			peptide concentration In ref control was 0.31 mM	
			3	24.04	19.59	6.3		79.57	80.34	0.8	interference (2.4 %)	**R**
94	IRR	solid	1	2.26				0.00				
			2	1.93				1.74				
			3	1.87	2.02	0.2		2.55	1.43	1.3		**NR**
95	IRR	solid	1	18.85				53.89				
			2	24.39				62.42				
			3	28.47	23.90	4.8		70.54	62.28	8.3		**R**
96	IRR	solid	1	30.82				98.96				
			2	28.65				99.08				
			3	29.47	29.65	1.1		99.18	99.07	0.1		**R**
97	IRR	solid	1	41.27				37.02				
			2	38.94				47.31				
			3	37.63	39.28	1.8		55.62	46.65	9.3		**R**
98	IRR	solid	1	0.72				84.93				
			2	0.49				91.05				
			3	0.32	0.51	0.2		94.45	90.14	4.8		**R**
100	NIRR	liquid	1	0.01				2.71				
			2	0.95				4.06				
			3	0.23	0.40	0.5		10.42	5.73	4.1		**NR**
101	NIRR	liquid	1	0				0.00				

			2	0				0.00				
			3	0	0	0		3.54	1.18	2.0		**NR**
102	NIRR	liquid	1	6.27				0.00				
			2	6.26				3.23				
			3	7.23	6.59	0.6	interference (2 % rel. to Ref Control C)	7.61	3.61	3.8		**R**
103	NIRR	liquid	1	1.51				0.00				
			2	1.32				1.98				
			3	1.67	1.50	0.2		3.38	1.78	1.7		**NR**
105	NIRR	solid	1	0.17				5.45				
			2	0.00				5.87				
			3	0.00	0.06	0.1		2.52	4.61	1.8		**NR**
106	NIRR	solid	1	0.96				100?			injection error?	
			2	0.99				8.28				
			3	0.36	0.77	0.4		11.34	9.81	2.2	mean depletion without replicate 1	**R**
107	NIRR	solid	1	0.00				1.41				
			2	0.00				5.77				
			3	0.00	0.00	0.0		12.34	6.51	5.5		**R**
108	NIRR	solid	1	1.50				0.22				
			2	1.45				4.35				
			3	1.62	1.53	0.1	10 mM	9.60	4.72	4.7	10 mM	**NR at 10 mM**
110	NIRR	solid	1	0.01				4.57				
			2	0.00				2.33				
			3	0.00	0.00	0.0		2.08	2.99	1.4		**NR**
111	NIRR	solid	1	2.87				0.00				
			2	2.75				0.00				
			3	2.32	2.64	0.3	10 mM	0.00	0.00	0.0	10 mM	**N/A**
113	NIRR	liquid	1	-10.85				0.00				
			2	-10.74				0.00				
			3	-11.33	-11.0	0.3	no interference observed	0.00	0.00	0		**N/A**
114	NIRR	solid	1	0.74				5.28				
			2	0.27				8.10				
			3	0.46	0.49	0.2		13.01	8.80	3.9		**R**
115	NIRR	solid	1	29.08				-2033.76			interference at 9	

											min	
			2	28.43				3.38			interference at 9.7 min	
			3	27.42	28.31	0.8		95.58	-644.93	1203.6	interference at 9.7 min	**R**
116	IRR	liquid	1	0.00				6.10				
			2	0.00				10.96				
			3	0.00	0.00	0.0	interference (4 %)	10.87	9.31	2.8		**R**
117	IRR	liquid	1	7.03				14.57				
			2	6.68				17.97				
			3	6.83	6.84	0.2		21.03	17.86	3.2		**R**
118	IRR	liquid	1	2.29				4.82				
			2	0.00				10.34				
			3	0.00	0.76	1.3		8.54	7.90	2.8		**R**
119	IRR	solid	1	1.59				0.00				
			2	0.42				0.83				
			3	0.00	0.67	0.8		4.55	1.80	2.4		**NR**
121	IRR	solid	1	0.00				4.58				
			2	0.00				8.99				
			3	0.00	0.00	0.0		10.28	7.95	3.0		**R**
122	IRR	solid	1	4.48				2.10				
			2	5.74				7.45				
			3	4.81	5.01	0.7		10.02	6.52	4.0		**R**
123	NIRR	liquid	1	-17.02				2.37				
			2	-12.55				3.20				
			3	-3.41	-10.99	6.9	interference!	7.73	4.43	2.9		**N/A**
126	NIRR	solid	1	2.46				0.00				
			2	2.04				0.00				
			3	2.92	2.47	0.4		17.86	5.95	10.3		**NR**
128	IRR	liquid	1	0.29				11.19				
			2	0.12				5.08				
			3	0.08	0.16	0.1		10.35	8.88	3.3		**R**
129	IRR	liquid	1	1.57				0.27				
			2	1.51				0.00				
			3	1.83	1.64	0.2		5.78	2.02	3.3		**NR**
130	IRR	liquid	1	11.13				6.99				
			2	10.59				4.73				
			3	9.79	10.50	0.7		8.61	6.78	1.9		**R**

131	IRR	liquid	1	0.23				4.14				
			2	0.00				9.44				
			3	0.09	0.11	0.1		13.72	9.10	4.8		**R**
132	IRR	solid	1	0.00				1.35				
			2	0.00				8.17				
			3	0.00	0.00	0.0		8.40	5.97	4.0		**R**
133	IRR	solid	1	0.19				28.18				
			2	0.20				39.60				
			3	0.66	0.35	0.3		41.61	36.46	7.2		**R**
134	NIRR	liquid	1	23.32			interference				interference	
			2	23.43			interference				interference	
			3	21.59	22.78	1.0	interference				interference	**N/A**
137	NIRR	solid	1	0.00				0.00				
			2	0.00				0.00				
			3	0.04	0.01	0.0		0.04	0.01	0.0		**NR**
138	NIRR	solid	1	0.12			10 mM	17.43				
			2	0.05				5.68				
			3	0.00	0.06	0.1		7.45	10.19	6.3		**R**
10	IRR	liquid	1	*0.54*			*result obtained in April 2010*	-17.03			same result as in April 2010	
*			2	*0.95*			*result obtained in April 2010*	-16.67			no interference observed	
*			3	*0.74*	*0.74*	*0.20*	*result obtained in April 2010*	-16.08	-16.59	0.48	before the run	**N/A**
14	IRR	liquid	1	4.10				0				
*			2	2.07				0				
*			3	2.23	2.80	1.13		0	0	0		**NR**
30	IRR	solid	1	1.17				0.0				
*			2	0.32				1.2				
*			3	0.34	0.61	0.48		3.2	1.4	1.6		**NR**
31	IRR	solid	1	0.41			10 mM; interference during the run	0.0			10 mM	
*			2	0.18			10 mM; interference during the	5.6			10 mM	

							run					
*			3	0.00	0.20	0.20	10 mM; interference during the run	5.8	3.8	3.3	10 mM	**N/A**
33	IRR	solid	1	-334.8			interference	98.09				
*			2	-413.1			interference	98.14				
*			3	-422.9	-390.3	48.3	interference	98.05	98.09	0.05		**R**
60	NIRR	liquid	1	3.07				52.78				
*			2	1.45				54.83				
*			3	3.64	2.72	1.14		65.87	57.83	7.04		**R**
61	NIRR	liquid	1	0.43				12.82				
*			2	1.89				17.23				
*			3	1.29	1.20	0.74		20.94	17.00	4.06		**R**
62	NIRR	liquid	1	0.00				4.2			10 mM	
*			2	0.00				11.2			Ref control (50 % DMSO) not accepted	
*			3	0.00	0.00	0.00	10 mM	15.3	10.2	5.6	also not after repeat analysis (mean conc< 0.45 mM)	**N/A**
											(Same as for test chemical Tetrabromophenol Blue)	
74	NIRR	solid	1	0.0			insoluble	0.0			insoluble	
*			2	0.8			insoluble	0.4			insoluble	
*			3	1.0	0.6	0.5	insoluble	6.9	2.4	3.9	insoluble	**N/A**
75	NIRR	solid	1	0.92				0.00				
*			2	0.00				0.00				
*			3	0.54	0.49	0.46		2.47	0.82	1.43		**NR**
76	NIRR	solid	1	0.20			10 mM	0			10 mM	
*			2	2.51			10 mM	0			10 mM	
*			3	2.06	1.59	1.23	10 mM	0	0	0	10 mM	**N/A**
83	NIRR	liquid	1	0.91				0				
*			2	0.80				0				
*			3	1.46	1.06	0.35		0	0	0		**NR**
99	NIRR	liquid	1	1.69				0.00				
*			2	1.88				0.00				
*			3	2.71	2.10	0.54		3.09	1.03	1.79		**NR**

113	NIRR	liquid	1	27.86			see also result in run 13	*0.00*			*result obtained in August 2010*	
*			2	-11.64			no interference observed	*0.00*			*result obtained in August 2010*	
*			3	-11.41	1.60	22.74	before the run	*0.00*	*0.00*	*0*	*result obtained in August 2010*	**N/A**
136	NIRR	solid	1	0.0			insoluble	0.0			insoluble	
*			2	1.4			insoluble	5.2			insoluble	
*			3	0.0	0.5	0.8	insoluble	12.2	5.8	6.1	insoluble	**N/A**
139	IRR	liquid	1	5.01				0.0				
*			2	5.19				0.2				
*			3	6.06	5.42	0.56		5.1	1.8	2.9		**NR**
141	IRR	solid	1	0.00				0.00				
*			2	0.00				4.29				
*			3	0.52	0.17	0.30		4.04	2.78	2.41		**NR**
142	IRR	solid	1	0.34				1.5				
*			2	0.00				5.6				
*			3	0.32	0.22	0.19		11.6	6.2	5.0		**R**
143	NIRR	liquid	1	0.42				0.62				
*			2	0.00				0.71				
*			3	0.71	0.38	0.36		1.12	0.82	0.27		**NR**
144	NIRR	liquid	1	0.14				0.0				
*			2	0.18				2.5				
*			3	0.70	0.34	0.32		6.3	2.9	3.2		**NR**
145	NIRR	solid	1	2.01				8.60				
*			2	1.36				1.78				
*			3	0.78	1.38	0.62		2.27	4.22	3.81		**NR**
146	NIRR	solid	1	4.60				99.08				
*			2	6.40				99.13				
*			3	4.78	5.26	0.99		99.35	99.19	0.14		**R**
147	NIRR	solid	1	6.68				4.3				
*			2	5.16				5.6				
*			3	6.99	6.27	0.98		10.1	6.6	3.1		**R**
148	NIRR	solid	1	1.76				0			mean depletion -5 %	
*			2	1.21				0			interference 7 % relative to Ref Control	

*			3	1.72	1.56	0.31		0	0	0		**NR**
149	NIRR	solid	1	0.83				0.0				
*			2	0.00				3.5				
*			3	0.33	0.39	0.42		6.5	3.3	3.2		**NR**
150	NIRR	solid	1	73.22			interference	5.41				
*			2	71.82			interference	8.26				
*			3	73.12	72.72	0.78	interference	10.86	8.18	2.73		**R**
151	IRR	liquid	1	0.71				0.0				
new			2	0.54				0.0				
*			3	0.74	0.66	0.11		0.0	0.0	0.0		**NR**
152	IRR	liquid	1				interference	99.2				
new			2				interference	99.2				
*			3				interference	99.1	99.2	0.1		**R**
153	NIRR	solid	1	1.17				3.2				
new			2	0.48				1.8				
*			3	0.59	0.75	0.37		5.3	3.4	1.8		**NR**
Results_EPRA_EIVS_third batch 070342011(JBA).xls												
10	IRR	liquid	1	0.54				-17.03				
Cat 1			2	0.95				-15.77				
			3	0.74	0.74	0.2		-16.11	-16.30	0.7	no interference	**repeat analysis cys**
21	IRR	solid	1	100.00				42.16			dissolved in 50 % DMSO/acetonitrile	
			2	88.03				50.21			peptide concentration In ref control was <0.45 mM (0.31 mM)	
			3	88.19	92.07	6.9	interference (1.4 % rel. to Ref Control)	57.18	49.85	7.5		**R**
113	NIRR	liquid	1	-10.85				0.00				
			2	-10.74				0.00				
			3	-11.33	-11.0	0.3	no interference observed	0.00	0.00	0		**N/A**
Results_EPRA_EIVS_extra analyses 18042011.xls												

10			1	-				-14.7			dissolved in water	
			2	-				-16.0				
			3	-				-14.0	-14.9	1.0	no signal in co-elution control during the run	
14			1	99.5			pure chemical; not diluted	-730.7			pure chemical; not diluted	
			2	99.6			depletion related to peptide in acetonitrile	-766.3			depletion related to peptide in acetonitrile	**R**
			3	97.8	99.0	1.0	signal in Co-elution control increasing with time	-764.5	-753.8	20.055631	huge signal in co-eluition control	**(pure chemical)**
99			1	38.7			pure chemical; not diluted	30.9			pure chemical; not diluted	
			2	52.3			not completely dissolved	20.9			not completely dissolved	**R**
			3	53.9	48.3	8.4	depletion related to peptide in acetonitrile	29.5	27.1	5.4	depletion related to peptide in acetonitrile	**(pure chemical)**
							hardly any signal in co-elution control during the run				no signal in co-elution control during the run	
113			1	-10.7			dissolved in IPA	-				
			2	-6.0				-				
			3	-6.7	-7.8	2.5	low signal in co-elution control (<10 %) during the run	-				

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