**E**URL ECVAM  
**S**CIENTIFIC  
**A**DVISORY  
**C**OMMITTEE  
(**ESAC**)

**ESAC Sub-Group Report**

on the

**Scientific Validity of the**

**xxxTest Method**

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|  | V1.0 | | ESAC SG | First agreed draft of ESAC SG Report |
|  | Vx.x | | ESAC SG | xxx revised draft after commenting |
|  | Vx.x | | ESAC SG | Final approved draft of ESAC SG Report sent to ESAC for endorsement |

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**ESAC Sub-Group (SG)**

**Full title:** ESAC Sub-Group on the xxx Test Method

**Abbreviated title:** xxx

The ESAC SG was established in [date] by written procedure to assist in the production of an ESAC Opinion on the scientific validity of the xxx *in vitro* test method to assess xxx.

This report was prepared at the request of EURL ECVAM by the "ESAC Sub-Group xxx" (ESAC SG), which was charged with conducting a detailed scientific peer review of the [EURL ECVAM coordinated/external] validation study of the xxx *in vitro* test method. The basis for the scientific peer review was the EURL ECVAM Request for ESAC Advice approved by the ESAC by written procedure following the ESACxx plenary meeting of [Date] (ESAC request 20xx-xx).

The ESAC SG met at EURL ECVAM on xx-xx/xx/20xx to conduct its peer review. This ESAC SG Report was endorsed by the ESAC SG on xx/xx/20xx and represents its consensus view. The Report was endorsed by the ESAC on xx/xx/20xx.

**The ESAC SG had the following members:**

* xxx (ESAC Member, SG Chair)
* xxx (ESAC Member, SG Rapporteur)
* xxx (ESAC Member)
* xxx (ESAC SG Member)

***Invited experts***

* xxx (xxx)

***Observers***

* xxx (xxx)

**EURL ECVAM (Secretariat):**

* Dr. João BARROSO (ESAC Coordinator)
* xxx

**NOTE ON THIS REPORTING TEMPLATE**

The template follows the EURL ECVAM modular approach and allows at the same time for the description of the analysis and conclusions concerning more specific questions. The template was approved by the ESAC through written procedure on 29 October 2010.

The template can be used for various types of validation studies (*e.g.* prospective full studies, retrospective studies, performance-based studies). Depending on the study type and the objective of the study, not all sections may be relevant or applicable.

* **Explanatory notes to the paragraph titles (in green)** provide guidance on the type of information / analysis expected under each section. Depending on the purpose and scope of the study to be reviewed, some of the aspects mentioned in the explanatory notes may not be applicable or only be applicable to some extent. Moreover, the explanatory notes are not intended to represent an exhaustive list of possible issues to be addressed under the respective heading, but are thought to provide some guidance with respect to the considerations typically expected. **These notes are to be deleted in the final version of the ESAC WG Report.**
* **ESAC WGs are encouraged to provide, under each section first a brief summary view in bold** followed by more detailed comments.
* **Please use the font EC Square Sans Pro to draft the Report.**

**ABBREVIATIONS USED IN THE DOCUMENT**

* **BLR** Between-laboratory reproducibility
* **ESAC** EURL ECVAM Scientific Advisory Committee
* **ESAC WG** ESAC Working Group
* **EURL ECVAM** European Union Reference Laboratory for Alternatives to Animal Testing
* **GLP** Good Laboratory Practice
* **JRC** Joint Research Centre
* **OECD** Organisation for Economic Co-operation and Development
* **QA**  Quality Assurance
* **QC** Quality Control
* **SOP** Standard Operating Procedure
* **TG** Test Guideline
* **TGP** Test Guidelines Programme
* **VMG** Validation Management Group
* **VSR** Validation Study Report
* **WLR** Within-laboratory reproducibility
* **… …**

Formatting examples above

**1. Study objective and design**

**1.1 Analysis of the clarity of the study objective's definition**

*NOTE: (a) please summarise briefly in your own words the study objective as outlined in the Test Submission or Validation Study Report (VSR) and (b) provide an appraisal as to whether the study objective is clearly and comprehensibly defined in the Test Submission or VSR.*

***(a) ESAC SG summary of the study objective as outlined in the Test Submission / Validation Study Report***

ENTER TEXT HERE

***(b) Appraisal of clarity of study objective as outlined in the Test Submission / Validation Study Report***

ENTER TEXT HERE

**1.2 Quality of the background provided concerning the purpose of the test method**

*NOTE: What is, according to the Test Submission or VSR, the overall purpose of the test method? Examples are a) scientific use (e.g. basic/applied research, b) screening for product development c) regulatory testing, etc.*

ENTER TEXT HERE

***(a) Analysis of the scientific rationale provided in the Test Submission / Validation Study Report***

*NOTE: Is the scientific rationale of the test method AND (consequently) for conducting the study clearly explained? Consider how the test method may contribute*

*(a) to the scientific understanding of the specified health/environmental effect or aspects of it?, i.e. does it provide relevant mechanistic information such as physiological pathways relevant for toxicity ("toxicity pathways") or other key physiological events leading to toxicity?*

*(b) to the prediction of the specified downstream health/environmental effect or aspects of it?*

*Moreover, does the Test Submission or VSR make sufficient reference to the relevant body of scientific literature?*

ENTER TEXT HERE

***(b) Analysis of the regulatory rationale provided in the Test Submission / Validation Study Report***

*NOTE: Is a regulatory rationale specified, i.e. a specific application of the test method for purposes of generating data with respect to regulatory requirements as specified in legislation or internationally agreed guidelines etc.? If so, how does the study and its objective and design relate to this regulatory rationale? Are the relevant regulatory documents appropriately referenced?*

ENTER TEXT HERE

**1.3 Appraisal of the appropriateness of the study design**

*NOTE: Is the study design appropriate in view of the stated objective of the study? This includes an analysis of the number of laboratories involved in the study, the organisation of study management including chemical selection, quality check of data, and independence of statistical analysis, i.e. was the statistician independent from the test method submitter/developer and, depending on the study, from the Validation Management Group (VMG). More technical aspects can also be considered such as an appraisal of the nature and number of test items used (details however to be provided in section 6, test materials), retesting in case of unqualified tests, pre-defined test acceptance criteria, etc.*

ENTER TEXT HERE

**1.4 Appropriateness of the statistical evaluation**

*NOTE: Consider whether the statistical approaches chosen are appropriate. This includes statistical calculations performed ex-ante such as sample size calculations as well as ex post statistical analysis of the data (e.g. for purposes of variability and predictive capacity). Is the choice of methods sufficiently justified?*

ENTER TEXT HERE

**2. Collection of existing data**

*NOTE: Validation studies typically make use of existing data, e.g. either as reference data (prospective studies) OR as reference data and testing data (retrospective study). Moreover, validation studies may use other information such as data in the literature, data banks, etc.*

**2.1 Existing data used as reference data**

*Which data sources were used for compiling the reference data associated with the test chemicals?*

ENTER TEXT HERE

**2.2 Existing data used as testing data**

*Point 2.2 only concerns retrospective validation studies or modular studies combining existing and newly generated data to assess an assay. Which data sources were used to collect existing testing data?*

ENTER TEXT HERE

**2.3 Search strategy for retrieving existing data**

*NOTE: Please describe and evaluate whether and how the search for existing data was planned, organised and conducted. In particular: has a search strategy been described and consistently applied?*

ENTER TEXT HERE

**2.4 Selection criteria applied to existing data**

*NOTE: Have consistent evaluation and decision criteria been pre-defined and applied in order to select the data and has the selection of data been explained in a transparent manner?*

ENTER TEXT HERE

**3. Quality aspects relating to data generated during the study**

**3.1 Quality assurance systems used when generating the data**

*NOTE: Have quality assurance systems such as GLP (Good Laboratory Practice), GIVIMP (Good In Vitro Method Practice) or GCCP (Good Cell Culture Practice) been used when generating the data?*

ENTER TEXT HERE

**3.2 Quality check of the generated data prior to analysis**

*NOTE: Have the generated data been checked for quality including correct formatting (-> data reporting) prior to analysis. Has the quality check been performed by a staff member independent from the laboratory staff generating the data?*

ENTER TEXT HERE

**4. Quality of data used for the purpose of the study (existing and newly generated)**

**4.1 Overall quality of the evaluated testing data (newly generated or existing)**

*NOTE: Please describe the quality of the* ***testing data****. This may concern data newly generated in the context of the study and/or existing data (e.g. in case of retrospective or modular studies).*

ENTER TEXT HERE

**4.2 Quality of the reference data for evaluating relevance[[1]](#footnote-1)**

*NOTE: What is the quality of the* ***reference data*** *used? Are the data and their quality sufficient in view of the study objective? To which extent has the quality of the reference data impacted on the conclusions drawn reg. performance of the assay studied?*

ENTER TEXT HERE

**4.3 Sufficiency of the evaluated data in view of the study objective**

*NOTE: Having considered the quality of the testing data (section 4.1) and reference data (section 4.2), consider here whether the quality of the entire data set was sufficient to draw robust conclusions?*

ENTER TEXT HERE

**5. Test definition (Module 1)**

*NOTE: Describe how well the test method has been defined in the Test Submission or VSR. This includes (a) test system (e.g. the cells or tissue used), (b) biological and/or mechanistic relevance of the test method for the target organ/species/system, etc., (c) test acceptance criteria, (d) the protocol, (e) prediction model(s). Consider whether the SOP(s) is/are sufficiently detailed and complete? Are the prediction models sufficiently well explained to be applied in the correct manner?*

**5.1 Quality and completeness of the overall test definition**

ENTER TEXT HERE

**5.2 Quality and completeness of the documentation concerning SOPs and prediction models**

ENTER TEXT HERE

**6. Test materials**

**6.1 Sufficiency of the number of evaluated test items in view of the study objective**

*NOTE: Is the number of test items sufficient in order to draw conclusions with respect to the objective of the study? If not, are there reasons for deviations and are these explained and justified?*

ENTER TEXT HERE

**6.2 Representativeness of the test items with respect to applicability**

*NOTE: Describe how suitable the selected test items are in order to gain – through empirical testing during the study – insight into the applicability domain / limitations of the test method.*

ENTER TEXT HERE

**7. Within-laboratory reproducibility (WLR) (Module 2)**

**7.1 Assessment of repeatability and reproducibility in the same laboratory**

*NOTE: How was variability, repeatability and reproducibility within laboratories assessed? Possible parameters to study are (a) intrinsic data variability, e.g. between replicates or runs; (b) concordance in predictions between replicates or runs. Regarding point (b), consider whether reproducibility and repeatability have been assessed separately. [****repeatability*** *= agreement of test results (same substance, identical conditions, e.g. equipment, operator etc.) while* ***reproducibility*** *= agreement of test results (same substance, same protocol, but not under identical conditions, e.g. different operator).*

ENTER TEXT HERE

**7.2 Conclusion on within-laboratory reproducibility as assessed by the study**

*NOTE: Are the conclusions on within-laboratory repeatability and reproducibility justified by the data as evaluated?*

ENTER TEXT HERE

**8. Transferability (Module 3)**

**8.1 Quality of design and analysis of the transfer phase**

*NOTE: Was the transfer phase appropriately planned, e.g. were there transfer instructions, training, minimum requirements, training SOP (if appropriate)? Were evaluation / decision criteria established beforehand defining successful transfer? If so, were these consistently applied during the analysis?*

ENTER TEXT HERE

**8.2 Conclusion on transferability to a naïve laboratory / naïve laboratories as assessed by the study**

*NOTE: Are the conclusions justified by the data generated? Have critical issues that may impact on transferability been identified?*

ENTER TEXT HERE

**9. Between-laboratory reproducibility (BLR) (Module 4)**

**9.1 Assessment of reproducibility in different laboratories**

*NOTE: How was variability and reproducibility between laboratories assessed? Possible parameters to study are (a) intrinsic data variability; (b) concordance in predictions between laboratories.*

ENTER TEXT HERE

**9.2 Conclusion on between-laboratory reproducibility as assessed by the study**

*NOTE: Are the conclusions justified by the data generated?*

ENTER TEXT HERE

**10. Predictive capacity and overall relevance (Module 5)**

**10.1 Adequacy of the assessment of the predictive capacity in view of the purpose**

*NOTE: How was the predictive capacity assessed? Were the reference data used in an appropriate manner? Are the conclusions justified based on the data evaluated and in view of the test method's purpose?*

ENTER TEXT HERE

**10.2 Overall relevance (biological relevance and accuracy) of the test method in view of the purpose**

*NOTE: Are the conclusions regarding biological/mechanistic relevance and relevance in terms of making accurate predictions/measurements for the specific toxicity effect justified by the evaluated data?*

ENTER TEXT HERE

**11. Applicability domain (Module 6)**

**11.1 Appropriateness of study design to conclude on applicability domain, limitations and exclusions**

*NOTE: When considering the objective of the study, was the study designed in a way to enable conclusions on the applicability domain, the limitations and possible exclusions (e.g. technical incompatibility of the test method with specific chemicals)?*

ENTER TEXT HERE

**11.2 Quality of the description of applicability domain, limitations, exclusions**

*NOTE: When considering the objective of the study and the data generated/analysed, have the applicability domain, the limitations and the exclusions of the method been sufficiently described?*

ENTER TEXT HERE

**12. Performance standards (Module 7)**

*NOTE: This section is only relevant in case Performance Standards have been suggested upon completion of a validation study.*

**12.1 Adequacy of the proposed Essential Test Method Components**

*NOTE: Are the proposed Essential Test Method Components adequate with respect to the key elements of the validated method as evidenced by existing information and testing data generated during the study?*

ENTER TEXT HERE

**12.2 Adequacy of the proposed Reference Chemicals**

*NOTE: Are the Reference Chemicals adequately mapping the accuracy values of the validated method? Do they provide a representative range of the applicability domain of the test substances used during validation? Do they map an appropriate range of toxicity effects of the particular health endpoint in question? Are they commercially available?*

ENTER TEXT HERE

**12.3 Adequacy of the proposed performance target values**

*NOTE: Are the performance target values, i.e. within- and between-laboratory reproducibility (typically assessed through concordance in predictions) and predictive capacity adequate considering the performance of the validated reference method(s)?*

ENTER TEXT HERE

**13. Readiness for standardised use**

**13.1 Assessment of the readiness for regulatory purposes**

*NOTE: Is the test method ready for regulatory purposes? If yes, why? If no – what impediments currently exclude application for regulatory purposes?*

ENTER TEXT HERE

**13.2 Assessment of the readiness for other uses**

*NOTE: Is the test method ready for other uses (e.g. screening purposes, testing to gain mechanistic insight, to generate supportive information for hazard/risk assessment).*

ENTER TEXT HERE

**13.3 Critical aspects impacting on standardised use**

*Note: What are the factors that may impact on standardised use (in regulatory or non-regulatory settings)?*

ENTER TEXT HERE

**13.4 Gap analysis**

*NOTE: Identify, if appropriate, gaps in the study design and/or conduct that may have impacted on the stated study objective or the conclusions drawn.*

ENTER TEXT HERE

**14. Other considerations**

*NOTE: Please address any other consideration you might have in relation to the proposed approach under this section.*

ENTER TEXT HERE

**15. Conclusions on the study**

*NOTE: This section should present a brief summary of the study results and conclusions as described in the Test Submission or VSR (subsection 15.1), discuss to which extent the conclusions drawn in the study reports are justified by the study results on their own (subsection 15.2) and evaluate to which extent the conclusions are plausible with respect to other information (subsection 15.3).*

**15.1 ESAC SG summary of the results and conclusions of the study**

ENTER TEXT HERE

**15.2 Extent to which study conclusions are justified by the study results alone**

ENTER TEXT HERE

**15.3 Extent to which conclusions are plausible in the context of existing information**

ENTER TEXT HERE

**16. Recommendations**

*Note: This section should provide recommendations on the test method (e.g. further work, possible use) and their constituting elements (e.g. test system, prediction model, SOP).*

**16.1 General recommendations**

ENTER TEXT HERE

**16.2 Specific recommendations (e.g. concerning improvement of SOPs)**

ENTER TEXT HERE

**17. References**

* xxx
* xxx

1. OECD guidance document Nr. 34 on validation defines relevance as follows: "Description of relationship of the test to the effect of interest and whether it is meaningful and useful for a particular purpose. It is the extent to which the test correctly measures or predicts the biological effect of interest. Relevance incorporates consideration of accuracy (concordance) of a test method." [↑](#footnote-ref-1)