EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

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

ESAC STATEMENT ON THE SCIENTIFIC VALIDITY OF AN IN-VITRO TEST METHOD FOR SKIN CORROSIVITY TESTING

Following its 30th meeting, held on 9 and 10 March 2009, the non-Commission members of the ECVAM Scientific Advisory Committee (ESAC) endorsed on 12 June 2009 by consensus and written procedure the following statement:

The Epidermal Skin Test 1000 (EST1000) method for skin corrosion testing can be used for reliably predicting the corrosive potential of chemical substances. It is considered meeting the Performance Standards as determined in the OECD test guideline TG 431 on in vitro skin corrosion testing using human skin model tests (Ref 1).

This conclusion is based on the results of an inter-laboratory study of the EST1000 human reconstructed epidermis (RhE) model that was reviewed by an independent ESAC Peer Review (Ref 2).

On the basis of the individual predictions of the four participating testing laboratories for the 12 Reference Chemicals (three tests per Reference Chemical per laboratory)[1], the following Predictive Capacity was observed (Table 1):

Table 1: *Predictive Capacity (Specificity, Sensitivity and Overall Accuracy) of the EST1000 skin corrosion test method*

Specificity (%)	84.7 (61/72)
Sensitivity (%)	100 (72/72)
Overall Accuracy (%)	92.4 (133/144)

This study showed that 11 out of 12 Reference Chemicals of the OECD TG 431 were correctly predicted by EST1000 in all four laboratories when considering the final prediction of each laboratory derived from the mode of the individual laboratory predictions (the mode of 3 test predictions per Reference Chemical per laboratory). In the study, only one chemical, *Tetrachloroethylene*, was incorrectly predicted by three laboratories as a skin corrosive (false positive prediction), with the forth laboratory making a correct prediction as non-corrosive. Predictions were also variable within and between laboratories for the substance *Eugenol* without however affecting the final decision based on the modes of individual laboratory predictions.

[1] Each of the 12 chemicals was tested three times in four laboratories. The total number of test results was therefore 144, with 72 results concerning actual negatives (n=6 chemicals) and 72 results concerning actual positives (n=6 chemicals).

However, all human skin models for skin corrosion assessment (EpiSkin, Ref 3; EpiDerm, Ref 4; and SkinEthic, Ref. 5) that were previously validated by ECAVM and that are considered meeting the OECD Performance Standards also displayed a higher extent of variability for these two chemical substances in comparison to the other 10 Reference Chemicals. Therefore the false positive prediction obtained for *Tetrachloroethylene* was regarded as acceptable.

Joachim Kreysa
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In-Vitro Methods Unit
European Centre for the Validation of Alternative Methods

Ispra, 12 June 2009

REFERENCES

1. OECD Test Guideline (Nr. 431) for the testing of chemicals – In vitro skin Corrosion: human skin model test. OECD 2004.

2. ESAC Peer Review Panel Consensus Report on the EST1000 in vitro test method for assessing skin corrosion in vitro. 2009

3. ESAC Statement on the scientific validity of the EpiSkin test (an in vitro test fro skin corrosivity). 1998. http://ecvam.jrc.it/

4. ESAC Statement on the application of the EpiDerm human skin model fro skin corrosivity testing. 2000. http://ecvam.jrc.it/

5. ESAC Statement on the application of the SkinEthic human skin model for skin corrosivity testing. 2006. http://ecvam.jrc.it/

The ESAC was established by the European Commission, and is composed of experts nominated by the EU Member States, and by industry, academia and animal welfare organisations. Representatives of the relevant Commission services, other international organisations, and partner validation bodies participate in its meetings.

This statement was endorsed by the following members of the ESAC:

Ms Argelia Castaño(Spain)
Ms Maija Dambrova (Latvia)
Ms Alison Gray (ESTIV)
Ms Katalin Horvath (Hungary)
Ms Maggy Jennings (Eurogroup for Animals)
Ms Dagmar Jírová (Czech Republic)
Mr Roman Kolar (Eurogroup for Animals)
Ms Elisabeth Knudsen (Denmark)
Mr Manfred Liebsch (Germany)
Mr Gianni Dal Negro (EFPIA)
Mr. Walter Pfaller (Austria)
Mr Tõnu Püssa (Estonia)
Mr Jon Richmond (UK)
Ms Vera Rogiers (ECOPA)
Mr Hasso Seibert (ESF, acting as co-moderator at the meeting)
Ms Annalaura Stammati (Italy)
Mr Jan van der Valk (The Netherlands)
Mr Carl Westmoreland (COLIPA, acting as moderator at the meeting)

The following Commission employees and observers were involved in the consultation process, both during the meeting and the following written procedure, but not in the endorsement itself:

Commission services
Mr Joachim Kreysa (DG JRC, Head of In Vitro Methods Unit/ECVAM, chairman)
Mr Claudius Griesinger (DG JRC, ESAC secretariat)
Ms Eimear Kelleher (DG JRC)
Ms Karin Kilian (DG SANCO)
Mr Juan Riego Sintes (DG JRC)

Observers
Mr Patric Amcoff (OECD)
Mr Hajime Kojima (JaCVAM, Japan)
Mr William Stokes (NICEATM/ICCVAM, USA)
Ms Marilyn Wind (ICCVAM/ U.S. Consumer Product Safety Commission, USA)

NOTE

Ispra, 21 September 2010

This statement was revised on 21 September 2010 in order to correct a mistake in the Specificity and Overall Accuracy values expressed in the document's Table 1.

Moreover, the Predictive Capacity (Specificity, Sensitivity and Overall Accuracy) of the EST1000 test method, as now presented in Table 1, was calculated on the basis of ***all individual laboratory predictions*** obtained. The rationale for calculating Predictive Capacity in this way is to regard the test results obtained in several laboratories during validation in the same manner as they would be considered during application of the test method *in realiter*: test results obtained in one laboratory, if meeting the acceptance criteria of the test method, would be taken as a basis for decision making on the hazard and/or risk of the chemical. This way of calculating Predictive Capacity is now (as of 2010) consistently applied by ECVAM in the key area of topical toxicity (including skin corrosion, skin irritation and eye irritation).