



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

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

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

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

14 On the basis of the individual predictions of the four participating testing laboratories for the
15 12 Reference Chemicals (three tests per Reference Chemical per laboratory)¹, the following
16 Predictive Capacity was observed (Table 1):

17
18 ***Table 1: Predictive Capacity (Specificity, Sensitivity and Overall Accuracy) of the EST1000***
19 ***skin corrosion test method***

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

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25 This study showed that 11 out of 12 Reference Chemicals of the OECD TG 431 were
26 correctly predicted by EST1000 in all four laboratories when considering the final prediction
27 of each laboratory derived from the mode of the individual laboratory predictions (the mode
28 of 3 test predictions per Reference Chemical per laboratory). In the study, only one chemical,
29 *Tetrachloroethylene*, was incorrectly predicted by three laboratories as a skin corrosive (false
30 positive prediction), with the fourth laboratory making a correct prediction as non-corrosive.
31 Predictions were also variable within and between laboratories for the substance *Eugenol*
32 without however affecting the final decision based on the modes of individual laboratory
33 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).



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

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42 Joachim Kreysa
43 Head of Unit
44 In-Vitro Methods Unit
45 European Centre for the Validation of Alternative Methods
46 Ispra, 12 June 2009



47 **REFERENCES**

- 48 1. OECD Test Guideline (Nr. 431) for the testing of chemicals – In vitro skin Corrosion:
49 human skin model test. OECD 2004.
- 50 2. ESAC Peer Review Panel Consensus Report on the EST1000 in vitro test method for
51 assessing skin corrosion in vitro. 2009
- 52 3. ESAC Statement on the scientific validity of the EpiSkin test (an in vitro test fro skin
53 corrosivity). 1998. <http://ecvam.jrc.it/>
- 54 4. ESAC Statement on the application of the EpiDerm human skin model fro skin
55 corrosivity testing. 2000. <http://ecvam.jrc.it/>
- 56 5. ESAC Statement on the application of the SkinEthic human skin model for skin
57 corrosivity testing. 2006. <http://ecvam.jrc.it/>



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

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

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66 Ms Argelia Castaño (Spain)
67 Ms Maija Dambrova (Latvia)
68 Ms Alison Gray (ESTIV)
69 Ms Katalin Horvath (Hungary)
70 Ms Maggy Jennings (Eurogroup for Animals)
71 Ms Dagmar Jírová (Czech Republic)
72 Mr Roman Kolar (Eurogroup for Animals)
73 Ms Elisabeth Knudsen (Denmark)
74 Mr Manfred Liebsch (Germany)
75 Mr Gianni Dal Negro (EFPIA)
76 Mr. Walter Pfaller (Austria)
77 Mr Tõnu Püssa (Estonia)
78 Mr Jon Richmond (UK)
79 Ms Vera Rogiers (ECOPA)
80 Mr Hasso Seibert (ESF, acting as co-moderator at the meeting)
81 Ms Annalaura Stamatì (Italy)
82 Mr Jan van der Valk (The Netherlands)
83 Mr Carl Westmoreland (COLIPA, acting as moderator at the meeting)

84

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

88 **Commission services**

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

94

95 **Observers**

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

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102 **NOTE**

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Ispra, 21 September 2010

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

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