

ECVAM European Centre for the Validation of Alternative Methods

STATEMENT ON THE SCIENTIFIC VALIDITY OF LOCAL LYMPH NODE ASSAY FOR SKIN SENSITISATION TESTING

At its 14th meeting, held on 14 - 15 March 2000 at the European Centre for the Validation of Alternative Methods (ECVAM), Ispra, Italy, the ECVAM Scientific Advisory Committee (ESAC)¹ unanimously endorsed the following statement:

Following a review of scientific reports and publications on the local lymph node assay (LLNA), it is concluded that the LLNA is a scientifically validated test which can be used to assess the skin sensitisation potential of chemicals. The LLNA should be the preferred method, as it uses fewer animals and causes less pain and distress than the conventional guinea-pig methods. In some instances, and for scientific reasons, the conventional methods can be used.

The ESAC reviewed the final report of the independent peer review evaluation coordinated by ICCVAM² and NICEATM^{2,3} the report of the EMEA,^{2,4} the pre-report of the SCCNFP,^{2,5} and more-recent literature available since the original submission to ICCVAM.^{6,10}

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1. The ESAC was established by the European Commission, and is composed of representatives of the EU Member States, industry, academia and animal welfare, together with representatives of the relevant Commission services. The following members of the ESAC were present at the meeting on 14 - 15 March 2000:

Dr B Blaauboer (ERGATT)
Professor J Castell (Spain)
Dr B Garthoff (EFPIA)
Dr C Hendriksen (The Netherlands)
Professor V Rogiers (Belgium)
Dr O de Silva (COLIPA)
Professor O Svendsen (Denmark)
Dr M Viluksela (Finland)
Dr F Zucco (Eurogroup for Animal Welfare)

Dr P Botham (ECETOC)
Dr D Clark (UK)
Professor A Guillouzo (France)
Professor C Regan (Ireland)
Dr B Rusche (Eurogroup for Animal Welfare)
Professor H Spielmann (Germany)
Professor H Tritthart (Austria)
Professor E Walum (Sweden)

Mr A Aguilar (DG RTD)
Mme F Drion (DG SANCO)
Mr L Nørgaard (DG ENTR)
Mr E Sabbioni (ECVAM)
Mr A Worth (ECVAM)

Professor M Balls (ECVAM)
Ms S Louhimies (DG ENV)
Mr J Riego Sintes (ECB)
Mr F Sweeney (IHCP)

2. EMEA: European Agency for the Evaluation of Medicines and Products, London, UK; ICCVAM: Interagency Coordinating Committee on the Validation of Alternative Methods, Research Triangle Park, NC, USA; NICEATM: National Toxicology Program Center for the Evaluation of Alternative Biological Methods, NIEHS, Research Triangle Park, NC, USA; SCCNFP: Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers, DG SANCO, European Commission, Brussels, Belgium.

3. NIH (1999). The murine local lymph node assay. The results of an independent peer review evaluation coordinated by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and the National Toxicology Program Center for the Evaluation of Alternative Toxicological Methods (NICEATM). NIH Publication n.99-4494.
4. EMEA (2000). Report from the ad-hoc expert meeting on testing for immunohypersensitivity (11/01/2000). European Agency for the Evaluation of Medicinal Products.
5. SCCNFP (2000). Opinion adopted at the 11th plenary meeting, 17 February 2000. (http://europa.eu.int/comm/dg24/health/sc/sccp/outcome_en.html).
6. Basketter, D.A., Lea, L.J., Cooper, K., Stocks, J., Dickens, A., Pate, I., Dearman, R.J. & Kimber, I. (1999). Threshold for classification as a skin sensitizer in the local lymph node assay: a statistical evaluation. *Food and Chemical Toxicology* 37, 1-8.
7. Gerberick, G.F., Curse, L.W. & Ryan, C.A. (1999). Local lymph node assay: differentiation allergic and irritant responses using flow cytometry. *Methods* 19, 48-55.
8. Gerberick, G.F., Cruse, L.W., Miler, C.M. & Ridder, G.M. (1999). Selective modulation of B-cell activation markers CD86 and I-Ak on murine draining lymph node cells following allergen or irritant treatment. *Toxicology & Applied Pharmacology* 159, 142-151.
9. Lea, L.J., Warbrick, E.V., Dearman, R.J., Kimber, I. & Basketter, D.A. (1999). The impact of vehicle on assessment of relative skin sensitization potency of 1,4-dihydroquinone in the local lymph node assay. *American Journal of Contact Dermatitis* 10, 213-218.
10. Warbrick, E.V., Dearman, R.J., Lea, L.J., Basketter, D.A. & Kimber, I. (1999). Local lymph node assay responses to paraphenylenediamine: intra- and interlaboratory evaluations. *Journal of Applied Toxicology* 19, 255-260.

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