



STATEMENT ON THE VALIDITY OF IN-VITRO PYROGEN TESTS

At its 24th meeting, held on 20-21 March 2006 at the European Centre for the validation of alternative methods (ECVAM), Ispra, Italy, the non-Commission members of the ECVAM Scientific Advisory Committee (ESAC)¹ unanimously endorsed the following statement:

Following a review of scientific reports and peer reviewed publications on the following range of in-vitro pyrogen tests:

1. Human Whole Blood IL-1,
2. Human Whole Blood IL-6,
3. PBMC IL-6,
4. MM6 IL-6, and
5. Human Cryopreserved Whole Blood IL-1,

it is concluded that these tests have been scientifically validated for the detection of pyrogenicity mediated by Gram-negative endotoxins, and quantification of this pyrogen, in materials currently evaluated and characterized by rabbit pyrogen tests.

These methods have the potential to satisfy regulatory requirements for the detection and quantification of these pyrogens in these materials subject to product-specific validation.

The test methods have the capacity of detecting pyrogenicity produced by a wider range of pyrogens, but the evidence compiled for, and considered within this peer review and validation process, is not sufficient to state that full scientific validation of this wider domain of applicability has been demonstrated and confirmed.

Thus, the above test methods can currently be considered as full replacements for the evaluation of materials or products where the objective is to identify and evaluate pyrogenicity produced by Gram-negative endotoxins, but not for other pyrogens.

This endorsement takes account of the dossiers prepared for peer review; the views of independent experts who evaluated the dossiers against defined validation criteria; supplementary submissions made by the Management Team; and the considered view of the Peer Review Panel appointed to oversee the process.

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1. The ESAC was established by the European Commission, and is composed of nominees from the EU Members States, industry, academia and animal welfare, together with representatives of the relevant Commission services.

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

Prof Helmut Tritthart (Austria)
Dr Dagmar Jírová (Czech Republic)
Prof Elisabeth Knudsen (Denmark)
Dr Timo Ylikomi (Finland)
Prof André Guillouzo (France)
Dr Manfred Liebsch (Germany)
Dr Efstathios Nikolaidis (Greece)
Dr Katalin Horvath (Hungary)
Prof Michael Ryan (Ireland)
Dr Annalaura Stamatì (Italy)
Dr Mykolas Maurica (Lithuania)
Prof Eric Tschirhart (Luxembourg)
Dr Jan van der Valk (The Netherlands)
Dr Dariusz Sladowski (Poland)
Prof Milan Pogačnik (Slovenia)
Dr Argelia Castaño (Spain)
Dr Patric Amcoff (Sweden)
Dr Jon Richmond (UK)
Dr Odile de Silva (COLIPA)
Dr Julia Fentem (ECETOC)
Dr Nathalie Alépée (EFPIA)
Prof Robert Combes (ESTIV)
Dr Maggy Jennings (Eurogroup for Animal Welfare)
Mr Roman Kolar (Eurogroup for Animal Welfare)

The following Commission Services and Observer Organisations were involved in the consultation process, but not in the endorsement process itself.

Mr Thomas Hartung (ECVAM; chairman)
Mr Jens Linge (ECVAM; ESAC secretary)
Mr Juan Riego Sintes (ECB)
Ms Beatrice Lucaroni (DG Research, Unit F.5)
Mr Sylvain Bintein (DG Environment, Unit C.3)
Mr Sigfried Breier (DG Enterprise, Unit F.3)
Prof Dr Constantin Mircioiu (Romania)
Dr William Stokes (NICEATM, USA)
Prof Dr Vera Rogiers (ECOPA)