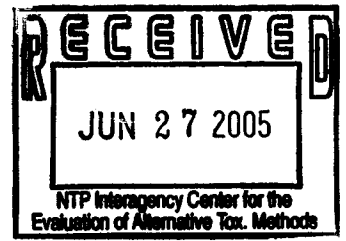




EUROPEAN COMMISSION
DIRECTORATE GENERAL JRC
JOINT RESEARCH CENTRE
Institute for Health and Consumer Protection
European Centre for the Validation of Alternative Methods (ECVAM)



VALIDATION OF IN VITRO PYROGENICITY TESTS BASED ON HUMAN MONOCYOID CELLS

Submission to ICCVAM Peer Review

Background information

In the first study, six in vitro pyrogen tests underwent validation. The study was financed by the European Commission with the 5th Framework Programme of DG Research (CONTRACT NO QLK3-CT-1999-00811) and recently published (Hoffmann et al, 2005; see below and included in the documentation package). Since two tests based on THP-1 cell lines did not meet the validation criteria, they are not included in the peer review.

During summer 2004, the University of Konstanz (Germany) carried out the catch-up validation of two tests using cryo-preserved blood (WBT-IL1) or blood cells (PBMC-IL6). The results are included in the peer review but have not yet been published.

Documents

Study related major publications (on CD in folder papers), which might not be included as hardcopy:

- Hoffmann et al (2005) International validation of novel pyrogen tests based on human monocytoid cells. *Journal of immunological methods*, 298, 161-173.
- Hartung et al (2002) Novel pyrogen tests based on the human fever reaction. *ECVAM Workshop Report 43. ATLA 29*, 99-123
- Schindler et al (2004) Cryopreservation of human whole blood for pyrogenicity testing. *Journal of Immunological Methods* 294, 89-100

ECVAM Validation guidelines (on CD in folder papers)

- Curren et al (1995) The Role of prevalidation in the development, validation and acceptance of Alternative Methods. *ECVAM Prevalidation Task Force Report 1. ATLA 23*, 211-217.
- Balls et al. (1995) Practical aspects of the validation of toxicity test procedures. *ECVAM Workshop Report 5. ATLA 23*, 129-147.
- Hartung et al (2004) A modular approach to the ECVAM principles on test validity. *ATLA 32*, 467-472.

Dossiers

- PBMC-IL6 (peripheral blood mononuclear cells; endpoint Interleukin-6 release)
- WBT-IL1-fresh (Whole blood test, endpoint Interleukin-1, fresh blood)
- WBT-IL1-cryo (Whole blood test, endpoint Interleukin-1, cryopreserved blood)
- WBT-IL6 (Whole blood test, endpoint Interleukin-6, fresh blood)
- MMc6-IL6 (MONO MAC 6, monocytoïd cell line; endpoint Interleukin-6)

You will find electronic versions of the dossiers and the SOPs on the CD in folder dossiers. The publications (see listed under point 14 of dossiers) are only included in the hardcopy).

Raw data

The CD includes the raw data of the labs which participated in the validation and catch-up validation study. The statistician, Sebastian Hoffmann, included a brief explanation.

Marlies Halder
23 June 2005