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

STATEMENT ON THE APPLICATION OF THE CFU-GM ASSAY FOR PREDICTING ACUTE NEUTROPENIA IN HUMANS

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 CFU-GM assay[2,3] for predicting acute neutropenia in humans as a substitute to using a second species, such as the dog, for this purpose. It should be noted that the test relies on the availability of mouse MTD data and is, therefore, not a full replacement method, but is intended to reduce the overall numbers of animals needed in toxicity testing. Performance standards for the assay should be developed to enable reasonable flexibility in the protocol used.

Thomas Hartung
Head of Unit
ECVAM
Institute for Health & Consumer Protection
Joint Research Centre
European Commission
Ispra

21 March 2006

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 Stammati (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)

2. Pessina, A., Albella, B., Bueren, J., Brantom, P., Casati, S., Gribaldo, L., Croera, C., Gagliardi, G., Foti, P., Parchment, R., Parent-Massin, D., Sibiril, Y., Schoeters, G. and Van Den Heuvel, R (2001) Prevalidation of a model for predicting acute neutropenia by Colony Forming Unit-Granulocyte/Macrophage (CFU-GM) assay. Toxicology in Vitro 15, 729-740.

3. Pessina A, Albella B, Bayo M, Bueren J, Brantom P, Casati S, Croera C, Gagliardi G, Foti P, Parchment R, Parent-Massin D, Schoeters G, Sibiril Y, Van Den Heuvel R, Gribaldo L. (2003) Application of the CFU-GM assay to predict acute drug-induced neutropenia: an international blind trial to validate a prediction model for the maximum tolerated dose (MTD) of myelosuppressive xenobiotics. Toxicological Sciences 75, 355-367.