European Commission
Joint Research Centre
Institute for Health & Consumer Protection
ECVAM Unit
21020 Ispra (VA)
Italy

Tel: +39 0332 785996
Fax: +39 0332 785336

ECVAM European Centre for the Validation of Alternative Methods

STATEMENT OF CONCERN ABOUT THE PROGRESS WITHIN THE OECD TOWARD DELETION OF THE ACUTE ORAL TOXICITY (LD50) TEST

At the 14th ESAC meeting, held on 14-15 March, 2000, the Non-Commission Members of the ECVAM Scientific Advisory Committee (ESAC)[1] were very concerned to hear that the OECD's timetable for the deletion of Guideline 401 (the LD50 test) was being threatened by the USA's position on one of the alternative methods, Guideline 425 (the Up-and-Down Procedure).

At the OECD Joint Meeting in February, the USA announced that a revised Guideline 425 would be subject to internal USA review through ICCVAM and a Scientific Advisory Panel, and that the outcome of these reviews would not be known until July 2000. As the OECD review of this and the other two alternative guidelines would need to start in May 2000, there is a real possibility of discrepancies arising between the two review processes, and hence the introduction of a further delay in the acceptance of the revised alternatives and the deletion of Guideline 401, which are currently scheduled for endorsement in November 2000, as agreed unanimously at the 29th Joint Meeting.

These ESAC Members were also concerned that, in reviewing only Guideline 425, the USA could in the future adopt a position of non-acceptance of the other two alternatives, Guideline 420 (the Fixed Dose Procedure) and Guideline 423 (the Acute Toxic Class Method).

Finally, these ESAC Members expressed their reservations about the animal welfare issues surrounding Guideline 425. Although a finalised version has not yet appeared from the USA Working Group on 425, the early indications are that it will consist of two parts, the first of which allows the calculation of an LD50 value, and a second to permit the calculation of the slope of the dose-response curve. The second part may require the use of between 15 and 20 animals (possibly more) and, as such, would result in the use of at least the same number of animals as with the LD50 test (Guideline 401), and also similar levels of morbidity and mortality

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

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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)
   Dr P Botham (ECETOC)
   Professor J Castell (Spain)
   Dr D Clark (UK)
   Dr B Garthoff (EFPIA)
   Professor A Guillouzo (France)
   Dr C Hendriksen (The Netherlands)
   Professor C Regan (Ireland)
   Professor V Rogiers (Belgium)
   Dr B Rusche (EUROGROUP for Animal Welfare)
   Dr O de Silva (COLIPA)
   Professor H Spielmann (Germany)
   Professor O Svendsen (Denmark)
   Professor H Tritthart (Austria)
   Dr M Viluksela (Finland)
   Professor E Walum (Sweden)
   Dr F Zucco (EUROGROUP for Animal Welfare)

   Mr A Aguilar (DG RTD)
   Mr M Balls (ECVAM - Chairman)
   Mme F Drion (DG SANCO)
   Ms S Louhimies (DG ENV)
   Mr L Nørgaard (DG ENTR)
   Mr J Riego Sintes (ECB)
   Mr E Sabbioni (ECVAM)
   Mr F McSweeney (IHCP)