



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 SCIENTIFIC VALIDITY OF THE UPPER THRESHOLD
CONCENTRATION (UTC) STEP-DOWN APPROACH – A NEW
TESTING STRATEGY TO REDUCE THE USE OF FISH
IN ACUTE AQUATIC TOXICITY TESTING**

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:

The “Upper Threshold Concentration (UTC) Step Down Approach” first described by Hutschinson et al. (2003)² and later evaluated on a larger data base by ECVAM and ECB (Jeram et al., 2005)³ is a straightforward strategy making use of the fact that in acute aquatic toxicity tests fish are in many cases less sensitive than algae and daphnia⁴.

Hazard classification of acute aquatic toxicity of chemicals is based on the lowest toxic concentration obtained in algae, daphnia, or fish. Thus, the lowest mean growth inhibiting concentration in algae (EC₅₀), or the lowest mean immobilising concentration in daphnia (EC₅₀), or the lowest mean lethal concentration in fish (LC₅₀) is relevant for classification. The UTC approach therefore proposes a tiered testing strategy. In tier 1, tests on algae and daphnia are performed and the lowest EC₅₀ value obtained is defined as UTC. In tier 2, the UTC is applied to fish. If application of the UTC demonstrates no lethal effects on fish, testing is terminated and the chemical classified based on the result of algae or daphnia from tier 1. However, if mortality occurs at the UTC, a full LC₅₀ test in fish should be performed according to OECD Test Guideline 203, or Method C.1 of Annex V to *Directive 67/548/EEC*. In cases where the UTC from algae or daphnia exceeds 100 mg/L, in tier 2 a limit test in fish is performed at 100 mg/L.

Based on this proposed strategy, the potential reduction in numbers of fish ranged from 65.0% to 72.8%. The Committee therefore recommends that the UTC approach should be implemented as a valid strategy to significantly reduce the number of fish used in the assessment of acute aquatic toxicity for hazard classification.

This statement was prepared by the ECVAM Peer Review Panel⁵, an *ad hoc* group established by ECVAM with the remit of assessing the scientific validity of the strategy.

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 Stamatii (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. Hutchinson, T.H., Barrett, S., Buzby, M., Constable, D., Hartmann, A., Hayes, E., Huggett, D., Länge, R., Lillicrap, A.D., Straub, J.O., Thompson, R.S. (2003) A strategy to reduce the numbers of fish used in acute ecotoxicity testing of pharmaceuticals. *Environ. Toxicol. Chem.* 22, 3031-3036.
3. Jeram, S., Riego Sintes, J.M., Halder, M., Baraibar-Fentanes, J., Sokull-Klüttgen, B., Hutchinson, T.H. (2005) A strategy to reduce the use of fish in acute ecotoxicity testing of new chemical substances notified in the European Union. *Regulatory Toxicology and Pharmacology* 42, 218-224.
4. Weyers, A., Sokull-Klüttgen, B., Baraibar-Fentanes, J., Vollmer, G. (2000) Acute toxicity data: a comprehensive comparison of results of fish, *Daphnia* and algae tests with new substances notified in the EU. *Environ. Toxicol. Chem.* 19, 1931-1933.
5. The ECVAM Peer Review Panel on the “Step Down Approach” comprised the following members:

Dr Argelia Castaño (ESAC, Spain),
Dr Manfred Liebsch (ESAC, Germany)
Dr Mike Comber (Exxonmobile, Belgium)
Prof Michael Depledge (Environment Agency, UK)
Dr Marc Leonard (L'ORÉAL, France)
Dr Scott Bellanger (Procter & Gamble, USA)