



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

Background information: Validation of Organotypic *in vitro* assays to identify severe eye irritation

Four tests have been evaluated:

Bovine Corneal Opacity & Permeability (BCOP) test;

Isolated Chicken Eye (ICE) test

Isolated Rabbit Eucleated Eye (REET, IRE) test

Hen's Egg Test – Chorio-Allantoic Membrane (HET-CAM) test

For sixty years, eye irritation of chemicals is tested by applying them to the eye of rabbits. The test was named after the U.S. FDA toxicologist as Draize-eye-test. In Europe, positive outcome from the BCOP, ICE, IRE and HET-CAM, four organotypic assays are accepted for labelling of severe eye irritation since 2004 after an assessment carried out by ECVAM on behalf of the National Coordinators for the Test Guideline Programme. However, EU Member States have requested these methods to be evaluated for their scientific validity before they can be included in Annex V of the Dangerous Substances Directive.

In autumn 2003, following a request from the EPA, the U.S. counterpart ICCVAM has initiated a retrospective evaluation to evaluate the current status of these four assays for identifying ocular corrosives and severe irritants. To favour harmonisation and avoid duplication of work, ECVAM and ICCVAM have agreed to work jointly in that area. As a consequence ECVAM has extensively collaborated to the ICCVAM retrospective evaluation by providing:

- relevant data from major validation studies,
- information on the European regulatory framework,
- comments from an ECVAM extended task force on eye irritation of experts on the test methods under evaluation,
- continuous consultation and internal observations.

The ECVAM peer-review proposes to endorse the BCOP and ICE test methods to be used for classification and labelling for severe eye irritation in the EU. They also recommend the early preparation of a guidance document on the use of these assays and the revision of the relevant technical annexes of EU Directives.

With regard to the IRE and HET-CAM assays, they propose further analysis and/or improvements before a final statement can be made.