



National Institutes of Health
National Institute of
Environmental Health Sciences
NTP Interagency Center for the Evaluation
of Alternative Toxicological Methods
P. O. Box 12238
Research Triangle Park, NC 27709
<http://iccvam.niehs.nih.gov>

DATE: February 23, 2004

TO: Scientific Advisory Committee on Alternative Toxicological
Methods (SACATM)

FROM: Director, NTP Interagency Center for the Evaluation
of Alternative Toxicological Methods (NICEATM)

SUBJECT: Update on ICCVAM Nominations: Evaluation of *In Vitro*
Ocular Toxicity Test Methods

At its August 2003 meeting, the SACATM unanimously recommended that ICCVAM evaluate the validation status of screening test methods that could be used to identify severe (irreversible) ocular irritants and that ICCVAM carry out an appropriate workshop or expert meeting on these test methods as a high priority. The purpose of this memorandum is to provide you with an update on the status of this recommendation, which was processed as a test method nomination, and other ocular toxicity related nominations.

In October 2003, the U.S. Environmental Protection Agency (EPA) nominated several ocular toxicity test method related activities to ICCVAM (see Attachment 1). These included:

- 1) Evaluate the validation status of *in vitro* ocular toxicity test methods that have potential for screening chemicals for severe eye irritation/corrosion and that could offer significant animal welfare advantages. Four methods currently being used for this purpose and mentioned in the EPA nomination include:
 - a. Bovine Corneal Opacity and Permeability Assay (BCOP)
 - b. Isolated Rabbit Eye Assay (IRE)
 - c. Isolated Chicken Eye Assay (ICE)
 - d. Hen's Egg Test on Chorioallantoic Membrane Assay (HET-CAM)
- 2) Explore ways to obtain existing and/or generating, if necessary, good quality *in vivo* eye irritation/corrosion reference data to assess interlaboratory variability and support the validation of *in vitro* test methods;
- 3) Explore ways of alleviating pain and suffering from current *in vivo* ocular toxicity testing; and

4) Review the state of the science and the availability of *in vitro* test methods for assessing mild or moderate ocular irritants, with the goal of identifying research, development, and validation priorities that might advance the usefulness of such methods.

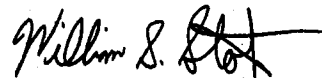
ICCVAM considered the SACATM and EPA nominations and recommended a high priority for all four nominated activities. ICCVAM recommended that the highest priority should be the review of the validation status of test methods that can be used to identify severe ocular irritants/corrosives, and the review of existing *in vivo* data to identify appropriate reference chemicals necessary to assess the performance of these test methods.

ICCVAM recommended that NICEATM and the ICCVAM Ocular Toxicity Working Group develop comprehensive Background Review Documents for each method and that an Expert Panel be convened to independently review the validation status of these methods and proposed standardized test method protocols. ICCVAM further recommended the collection and analysis of *in vivo* reference data necessary for review of *in vitro* ocular toxicity test methods. For the last two nominated activities, NICEATM and the ICCVAM OTWG will request and evaluate available data and information, and recommend appropriate review mechanisms, such as workshops, expert panel meetings, or independent peer review panel meetings.

NICEATM will be requesting public comment on these nominations via a *Federal Register* notice, and we will share these comments with you as they become available. We are also requesting, via the *Federal Register*, data and information relevant to all of the nominations. Finally, we are working closely with ECVAM in order to maximize collection and availability of data for these evaluations and to avoid duplication of efforts.

I have also included the report of a recent ECVAM workshop on eye irritation testing that you might find helpful (Attachment 2: Balls M, Berg N, Bruner LH, Curren RD, de Silva O, Earl LK, et al. 1999. Eye Irritation Testing: The Way Forward. The Report and Recommendations of ECVAM Workshop 34. ATLA 27, 53-77.)

At our March meeting, I will provide an update on the status of these four nominations and the proposed activities. We look forward to your comments and suggestions.



William S. Stokes, D.V.M., D.A.C.L.A.M.
CAPT, USPHS

Attachments

cc:
ICCVAM
ICCVAM OTWG