



National Institutes of Health
National Institute of
Environmental Health Sciences
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MEMORANDUM

DATE: April 25, 2008

TO: The Record

FROM: Acting Director, NIEHS

SUBJECT: NIEHS Response to Test Recommendations on four *In Vitro* Test Methods for Identifying Ocular Corrosion or Severe Irritation from the Interagency Coordinating Committee on the Validation of Alternative Methods

On October 25, 2007, at the request of the Secretary of the Department of Health and Human Services, I forwarded toxicological test recommendations from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) to 14 Federal agencies for their consideration. The recommendations were developed and transmitted pursuant to Section 3(e)(4) of the ICCVAM Authorization Act of 2000 (42 U.S.C. 285l-3). Pursuant to Sections 4(a) and 4(d) of the ICCVAM Authorization Act, agencies are required to review ICCVAM test recommendations and notify ICCVAM in writing of their findings, including identification of relevant test methods for which the ICCVAM test recommendations may be added or substituted. This memorandum provides the NIEHS response to the ICCVAM test recommendations.

NIEHS has reviewed the ICCVAM test recommendations provided for 1) the Bovine Corneal Opacity and Permeability (BCOP) assay, 2) the Isolated Chicken Eye (ICE) assay, 3) the Isolated Rabbit Eye (IRE) assay, and 4) the Hens' Egg Test-Chorioallantoic Membrane (HET-CAM) assay. NIEHS agrees that the test methods should always be considered before using animals for ocular safety testing and that the methods should be used when determined appropriate. NIEHS also agrees that appropriate use of the methods can reduce animal use by avoiding the need to use animals for ocular safety testing when one of the *in vitro* test methods identifies substances as having the potential to cause permanent or serious eye damage. Such use will also provide for animal refinement in that substances that can cause serious damage will not have to be tested on animals.

NIEHS has determined that it does not currently use or specify any test methods for which the test recommendations may be added or substituted. Furthermore, NIEHS is not a regulatory agency and therefore does not promulgate regulatory testing requirements for which the recommendations may be applicable. While NIEHS does conduct toxicity testing as part of its National Toxicology Program activities, ocular safety testing is not normally performed. If, for some unforeseen reason, such data are required in the future, the NIEHS intends to follow the recommendations of the ICCVAM on this matter and use the recommended *in vitro* methods where appropriate.

NIEHS scientists and the NIEHS Institutional Animal Care and Use Committee (IACUC) have been informed about the availability of these four alternative test methods and advised that they should be considered when planning and reviewing animal studies involving ocular safety testing in order to minimize animal use and to avoid pain and distress. The IACUC has also been asked to ensure that these alternative methods are considered whenever applicable in accordance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals and applicable USDA Animal Welfare Act regulations.

NIEHS has also reviewed and agrees with the ICCVAM recommendations for optimization studies to potentially improve the accuracy and reproducibility of the current BCOP, ICE, IRE, and HET-CAM test method protocols for identifying severe ocular irritants and corrosives. NIEHS, through its National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), will coordinate selected test method optimization studies identified as high priority by ICCVAM with the goal of increasing test method performance and expanding the usefulness of the test methods. NICEATM has also created a comprehensive database of high quality *in vivo* reference data that can be used to select reference chemicals for future validation studies. NICEATM will continue to update this database as new data are received.

NIEHS remains committed to the development, validation, and regulatory acceptance of scientifically sound alternative testing methods that will provide improved protection of human and animal health and the environment, and that will provide for improved animal welfare.

/s/

Samuel H. Wilson, M.D.

cc:

Dr. William Stokes, Executive Director, ICCVAM
Dr. Marilyn Wind, Chair, ICCVAM