



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

April 24, 2008

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Samuel H. Wilson, Ph.D.
Acting Director
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Dear Dr. Wilson:

In your letter of October 25, 2007, you sent Administrator Stephen L. Johnson the report, *The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Test Method Evaluation Report: In Vitro Test Methods for Identifying Ocular Corrosives and Severe Irritants* (NIH Publication No.: 07-4517). He referred the letter to the Office of Science Coordination and Policy (OSCP) in EPA's Office of Prevention, Pesticides and Toxic Substances for a reply. The report contains ICCVAM recommendations for four *in vitro* test methods proposed for identifying substances that may cause ocular corrosion or severe ocular irritation. The test methods are the: (1) Bovine Corneal Opacity and Permeability (BCOP) assay, (2) the Isolated Chicken Eye (ICE) assay, (3) the Isolated Rabbit Eye (IRE) assay, and (4) the Hen's Egg Test-Chorioallantoic Membrane (HET-CAM) assay. EPA's response is as follows regarding the use of these alternative methods in the Office of Prevention, Pesticides and Toxic Substances (OPPTS). OPPTS administers the Agency programs responsible for the testing and regulation of pesticides [Office of Pesticide Programs (OPP)] and industrial chemicals [Office of Pollution Prevention and Toxics (OPPT)].

EPA was instrumental in having ICCVAM review the validation status of the BCOP, ICE, IRE and HET-CAM assays. The Agency was interested in an evaluation of these four *in vitro* methods for possible use in screening chemicals for severe eye irritation or corrosion and for potential utility as alternatives in relation to its existing test guidelines for acute eye irritation (OPPTS 870.2400-Acute Eye Irritation and OPPTS 870.1000 Acute Toxicity Testing – Background). ICCVAM agreed to initiate an assessment of the four *in vitro* ocular methods in response to a formal letter of nomination from the EPA issued in October 2003.

For the Agency's pesticide (OPP) and toxics programs (OPPT), EPA agrees with the ICCVAM recommendations that the BCOP and ICE *in vitro* methods have utility as screening level assays for the identification of ocular corrosivity (OPP Category I) for single component substances. For purposes of pesticide classification and labeling, although none of the four *in vitro* assays can serve as a full replacement for conventional *in vivo* ocular testing methods, positive results in the BCOP and ICE tests would obviate the need for further animal testing.

The toxics program would use data from the BCOP and the ICE methods to support screening level evaluation of severe eye irritation and/or ocular corrosivity and as a contribution to an overall weight of evidence analysis in the evaluation of industrial chemicals. We are hopeful that, if additional data are gathered on mixtures and formulations, these tests would have broader utility within OPPTS. In addition, the development of a standardized scoring scheme and a strategy for histopathological evaluation of corneal tissue show great promise for further classification refinements. EPA encourages the development of additional data to address these outstanding questions associated with the *in vitro* ocular methods analyzed by ICCVAM and looks forward to continuing to work with ICCVAM as these methods and others are enhanced and/or further optimized to support their regulatory utility.

EPA is currently considering amending our technical guidance to incorporate the BCOP and the ICE methods as screening assays for corrosive substances through our public Scientific Advisory Process.

Sincerely,



Elizabeth Resek
Acting Director
Office of Science Coordination and Policy

cc: Jim Jones
Charles Auer
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