DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Toxicology Program (NTP); NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM); Availability of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Test Method Evaluation Report on *In Vitro* Ocular Toxicity Test Methods for Identifying Severe Irritants and Corrosives and Final *In Vitro* Ocular Test Method Background Review Documents; Notice of Transmittal of ICCVAM Test Method Recommendations to Federal Agencies

AGENCY: National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH).

ACTION: Availability of ICCVAM Test Method Evaluation Report and Final Background Review Documents.

SUMMARY: NICEATM announces availability of the *ICCVAM Test Method Evaluation Report: In Vitro Ocular Toxicity Test Methods for Identifying Severe Irritants and Corrosives* (NIH Publication 07–4517). The report describes four ocular toxicity test methods evaluated by ICCVAM: (1) The Bovine Corneal Opacity and Permeability [BCOP] test, (2) the Isolated Chicken Eye [ICE] test, (3) the Isolated Rabbit Eye [IRE] test, and (4) the Hen's Egg Test—Chorioallantoic Membrane [HET–CAM]. The report includes ICCVAM's (a) final test method recommendations on the use of these four *in vitro* test methods, (b) recommended test method protocols for future testing, (c) recommendations for further optimization and validation studies for these test methods, and (d) recommended reference substances for validation studies. The report recommends that the BCOP and ICE methods, with specific limitations for certain chemical classes and/or physical properties, can be used in a tiered testing strategy to determine ocular hazards, and substances that test positive can be classified as ocular corrosives or severe irritants without further testing in animals. The report also recommends that these *in vitro* test methods should be considered before using animals for ocular testing and used when determined appropriate.

NICEATM also announces availability of the final Background Review Documents (BRDs) for the BCOP, ICE, IRE, and HET–CAM test methods (NIH Publications 06–4512, 06–4513, 06–4514, and 06–4515, respectively). These BRDs provide the data and analyses used to assess the current validation status of these four test methods for identifying ocular corrosives and severe irritants.

Electronic copies of the ICCVAM Test Method Evaluation Report and the four BRDs are available from the NICEATM/ICCVAM Web site at *http://iccvam.niehs.nih.gov* or by contacting NICEATM (see **FOR FURTHER INFORMATION CONTACT**). The ICCVAM Test Method Evaluation Report and the final BRDs have been forwarded to U.S. Federal agencies for regulatory and other acceptance considerations where applicable. Responses will be posted on the ICCVAM/NICEATM Web site as they are received.

FOR FURTHER INFORMATION CONTACT: Dr. William S. Stokes, Director, NICEATM,

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SUPPLEMENTARY INFORMATION:

Background

In 2003, the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) and U.S. Environmental Protection Agency (EPA) recommended that ICCVAM review the validation status of screening test methods that could be used to identify severe and irreversible ocular effects. ICCVAM unanimously agreed that the four *in vitro* test methods (IRE, ICE, BCOP, and HET–CAM) nominated by EPA should have high priority for evaluation. On March 24, 2004, NICEATM published a **Federal Register** notice (Vol. 69, No. 57, pp. 13859–13861) requesting all available data on these four *in vitro* ocular irritancy test methods and corresponding data from in vivo rabbit eye test methods, as well as any human exposure data (obtained either from ethical human studies or by accidental exposure). NICEATM subsequently compiled data and information on each test method and released four draft BRDs for public comment on November 3, 2004 (**Federal Register**, Vol. 69, No. 212, pp. 64081–64082).

On January 11–12, 2005, NICEATM, on behalf of ICCVAM, convened an expert panel meeting to independently assess the validation status of these four test methods. The panel's report was released in March 2005 (**Federal Register**, Vol. 70, No. 53, pp 13513). Public comments at this meeting indicated that additional data on these *in vitro* test methods could be made available; therefore, the panel recommended that NICEATM obtain the additional data and reanalyze the accuracy and reliability of each test method. On February 28, 2005, NICEATM again solicited *in vitro* data on these four test methods and corresponding in vivo data (**Federal Register**, Vol. 70, No. 38, pp. 9661–9662). The revised analyses were published on July 26, 2005, as an addendum to the draft BRDs (**Federal Register**, Vol. 70, No. 142, pp. 43149).

NICEATM, on behalf of ICCVAM, reconvened the panel on September 19, 2005, to discuss the addendum to the draft BRDs (**Federal Register**, Vol. 70, No. 174, pp. 53676–53677). An addendum to the panel report was published in November 2005 (**Federal Register**, Vol. 70, No. 211, pp. 66451). At its December 2005 meeting, the SACATM discussed and provided comments on the panel report and addendum (**Federal Register**, Vol. 70, No. 216, pp. 68069–68070) (minutes from that meeting are available at *http://ntp.niehs.nih.gov/go/8202*).

ICCVAM considered the expert panel report and its addendum, public comments, SACATM comments, and the draft BRDs and their addendums in finalizing its recommendations on the validation status of these four test methods. The ICCVAM Test Method Evaluation Report includes the ICCVAM recommendations on the use of each test method, as well as recommended test method protocols, recommendations for further optimization and validation studies, recommended reference substances for future validation studies, the panel report and its addendum, and **Federal Register** notices. The four final BRDs, which provide the supporting documentation for this report, are available as separate documents. The ICCVAM Test Method Evaluation Report and the supporting final BRDs were forwarded to U.S. Federal agencies for their consideration for regulatory acceptance as required by the ICCVAM Authorization Act of 2000 (42 U.S.C. 285*l*–3). Agencies' responses to the test method recommendations will be posted on the ICCVAM/NICEATM Web site as they are received.

Background Information on ICCVAM, NICEATM, and SACATM

ICCVAM is an interagency committee composed of representatives from 15 Federal regulatory and research agencies that use, generate, or disseminate toxicological information. ICCVAM conducts technical evaluations of new, revised, and alternative methods with regulatory applicability and promotes the scientific validation and regulatory acceptance of toxicological test methods that more accurately assess the safety and hazards of chemicals and products and that refine, reduce, and replace animal use. The ICCVAM Authorization Act of 2000 established ICCVAM as a permanent interagency committee of the NIEHS under NICEATM. NICEATM administers ICCVAM and provides scientific and operational support for ICCVAM-related activities. NICEATM and ICCVAM work collaboratively to evaluate new and improved test methods applicable to the needs of U.S. Federal agencies. Additional information about ICCVAM and NICEATM can be found on their Web site (*http://iccvam.niehs.nih.gov*).

SACATM was established January 9, 2002, and is composed of scientists from the public and private sectors (**Federal Register**, Vol. 67, No. 49, page 11358). SACATM provides advice to the Director of the NIEHS, to ICCVAM, and to NICEATM regarding the statutorily mandated duties of ICCVAM and activities of NICEATM. Additional information about SACATM, including the charter, roster, and records of past meetings, can be found at *http://ntp.niehs.nih.gov/* see ''Advisory Board & Committees'' (or directly at *http://ntp.niehs.nih.gov/go/167*).

Dated: November 13, 2007.

Samuel H. Wilson,

Acting Director, National Institute of Environmental Health Sciences and National Toxicology Program.

[FR Doc. E7–22906 Filed 11–23–07; 8:45 am]

BILLING CODE 4140–01–P