

Update on the May 19-21, 2009 NICEATM-ICCVAM Independent Scientific Peer Review Panel on Alternative Ocular Safety Testing Methods and Strategies

An international independent scientific peer review panel (hereafter, “Panel”) met on May 19-21, 2009 to evaluate alternative test methods and approaches that may further reduce and refine the use of animals for ocular safety testing. The Panel was convened by the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).

Dr. Wallace Hayes of the Harvard School of Public Health chaired the public meeting of the Panel, composed of 22 scientists from the U.S., Japan, Canada, the Netherlands, Belgium, and Spain. The Panel represented a wide range of expertise, including human and veterinary ophthalmology, *in vitro* toxicology, biostatistics, anesthesiology, pathology, and regulatory toxicology. The Panel met at the headquarters of the U.S. Consumer Product Safety Commission in Bethesda, Maryland.

The Panel reviewed several proposed test methods and testing approaches nominated by the U.S. Environmental Protection Agency (EPA), including:

- Non-animal testing strategies using three *in vitro* test methods to assess the eye irritation potential of antimicrobial cleaning products for EPA ocular hazard classification and labeling purposes. The *in vitro* methods included the bovine corneal opacity and permeability (BCOP) assay, the Cytosensor Microphysiometer® (CM) assay, and the EpiOcular™ (EO) assays.
- Six individual *in vitro* test methods for identifying ocular irritants, including BCOP, CM, EO, isolated chicken eye, isolated rabbit eye, and the hen’s egg test – chorioallantoic membrane (HET-CAM) assays.
- The *in vivo* low volume eye test (LVET), proposed as an alternative to the current *in vivo* eye test.
- A proposal for the routine use of topical anesthetics, systemic analgesics, and humane endpoints to avoid or minimize pain and distress during required *in vivo* ocular irritation safety testing.

The Panel evaluated the validation status of each of the above proposed alternative test methods and approaches according to established Federal and international criteria.¹ The Panel also commented on draft ICCVAM recommendations regarding the usefulness and limitations of each proposed test method and approach.

The Panel agreed with ICCVAM’s proposal that topical anesthetics and systemic analgesics should routinely be used prior to any *in vivo* ocular irritancy testing. The Panel recommended an enhanced protocol of specific pain-relieving drugs and schedule of administration to effectively avoid or minimize discomfort. The Panel also agreed with most of the ocular lesions proposed as humane endpoints to end *in vivo* studies earlier.

¹ ICCVAM validation and acceptance criteria are provided in the document, *Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the ad hoc Interagency Coordinating Committee on the Validation of Alternative Methods*, available at http://iccvam.niehs.nih.gov/docs/about_docs/validate.pdf.

The Panel further recommended that more detailed observations of the eye should be routinely conducted to detect lesions that could be used to end such studies earlier.

The Panel did not make a final recommendation on the validity of the LVET because they were not able to review all existing data and information, including a background review document prepared by industry but not yet publicly available.

The Panel agreed with the draft ICCVAM recommendations that the BCOP and CM test methods could be used in limited circumstances as screening tests to identify some products and substances that would not require hazard labeling for eye irritation. The Panel did not support a similar draft recommendation for HET-CAM based on the lack of adequate data.

The Panel agreed with draft ICCVAM recommendations that the proposed non-animal testing strategies for hazard classification of antimicrobial cleaning products appear promising. However, the Panel concluded that there are insufficient data to demonstrate that the nonanimal testing strategies can accurately classify antimicrobial products in all four EPA ocular hazard categories.

The Panel recommended that studies to further characterize the *in vitro* test methods and testing strategies should be designed in coordination with ICCVAM. The Panel also encouraged stakeholders to submit validation and testing data to NICEATM to support the continued evaluation of the usefulness and limitations of these test methods and approaches.

Dr. Hayes will present a summary of the Panel's conclusions and recommendations to the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) at their public meeting on June 25-26, 2009 in Arlington, Virginia. The Panel's final report, including its conclusions and recommendations, will be published and available on the NICEATM-ICCVAM website in July at:

<http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm>

Information considered by the Panel during the meeting is also available on this page.

ICCVAM will consider the Panel's report along with all public and SACATM comments and prepare final test method recommendations that it will forward to Federal agencies. Prior to requiring, recommending, or encouraging the application of any new or revised toxicity test method, agencies must determine that the method is valid for its proposed use and that the method will provide for equivalent or improved protection of human health. The Panel's report and ICCVAM's evaluation will aid agencies in making these determinations. Agencies are required to respond to ICCVAM recommendations within 180 days.