DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

April 22, 2008

Rear Admiral William S. Stokes
Executive Director, ICCVAM
NIEHS
PO Box 12233, Mail Code EC-17
Research Triangle Park, NC 27709

Dear Dr. Stokes:

FDA has reviewed the ICCVAM test method recommendations for four in vitro test methods proposed for identifying substances that may cause ocular corrosion or severe ocular irritation. The test methods are (1) the Bovine Corneal Opacity and Permeability (BCOP) assay, (2) the Isolated Chicken Eye (ICE) assay, (3) the Isolated Rabbit Eye (IRE), and (4) the Hen's Egg Test-Chorioallantoic Membrane (HET-CAM) assay. The recommendations were provided to the FDA in the report, *The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Test Method Evaluation report: In Vitro Test methods fro Identifying Ocular Corrosives and Severe Irritants (NIH Publication No. 07-4517).*

Two of the methods, the BCOP assay and the ICE assay, are recommended by ICCVAM to have sufficient performance to be used for hazard classifications, in appropriate circumstances and with certain limitations outlined in the report, as screening tests for the detection of ocular corrosives and severe irritants in a tiered-testing strategy, as part of weight-of-the-evidence approach. FDA concurs with this recommendation.

At the present time, HET-CAM and IRE are not recommended by ICCVAM as screening tests for the identification of ocular corrosives and severe irritants for regulatory classification purposes. FDA concurs with this recommendation.

FDA does not have any relevant test methods requirements for which the BCOP or the ICE assays could be added or substituted. FDA does not categorize its human pharmaceutical products by ocular hazard. Definitive studies are conducted in humans. However human drug sponsors may find the BCOP or the ICE assays useful as screens for the need for worker ocular protection before there are human data or before administering a pharmaceutical by the ocular route to animals. Inadvertent ocular exposure to dermal products could be also assessed by these two in vitro assays.

FDA does not prescribe specific test methods for cosmetics. Rather sponsors of cosmetic products have a general requirement to determine safety by those methods that they deem appropriate.

FDA will encourage manufacturers to use the BCOP and the ICE assays in the development phase of their products. FDA will also make its pharmacology/toxicology reviewers aware of these assays and the ICCVAM recommendations. The availability of these assays could be announced on an ICCVAM section of the FDA website along with the ICCVAM recommendations for these and other test methods.

Although FDA does not envision a lot of regulatory utility for these in vitro ocular corrosion assays in its present testing requirements, it applauds all attempts at reducing numbers of test animals used in regulatory testing.

If you need any further information, please do not hesitate to contact me.

Norris E. Alderson, PhD
FDA Associate Commissioner for Science