UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

RADM William S. Stokes
Director, National Toxicology Program Interagency Center for the Evaluation of Alternative Animal Methods
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park
North Carolina 27709

February 23, 2011

Dear Dr. Stokes:

I write to respond to Dr. Birnbaum's September 2, 2010 letter providing test method recommendations from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). The United States Environmental Protection Agency (EPA) supports the development of alternative test methods that will replace, reduce or refine the uses of animals for assessing ocular hazard, as long as such methods afford humans with equivalent protection as currently provided by animal testing.

We concur with the ICCVAM recommendation for a balanced pain management plan. We understand these recommended procedures include the routine use of topical anesthetics, systemic analgesics, and humane endpoints, and that these methods should be used when the Draize rabbit eye test is required for regulatory safety testing purposes.

ICCVAM also recommends that the Cytosensor Microphysiometer (CM) test method be used as a screening test for a subset of substances (i.e., water-soluble surfactant chemicals and certain types of surfactant-containing formulations) that may cause permanent or severe eye injuries (EPA Toxicity Category I; DANGER). ICCVAM also recommended that the CM test method can be used to determine if a limited type of substances will not cause sufficient injury to require hazard labeling for eye irritation (EPA Toxicity Category IV; CAUTION). This in essence replaces animals for the subset of substances that can be conducted with the CM test method. We endorse these ICCVAM recommendations.

ICCVAM's third recommendation is that additional studies be performed to characterize the usefulness and limitations of a non-animal testing strategy that employs three *in vitro* test methods to assess the eye irritation potential of antimicrobial cleaning products: 1) Bovine Corneal Opacity And Permeability (BCOP) Test Method Protocol; 2) Cytosensor

Microphysiometer (CM) Test Method Protocol and 3) the EpiOcular® (EO) Test Method Protocol.

As you know, EPA is currently using these test methods in a pilot program for eye irritation for certain water-soluble surfactant chemicals or surfactant-containing antimicrobial products with cleaning claims. The ICCVAM recommendations are consistent with the pilot, which currently allows use of the CM for Toxicity Category III and IV. The Toxicity Category III determination is a bit beyond the ICCVAM recommendation for CM, but we have concluded that over prediction is protective for hazard determination. In addition we will add a caveat that allows the CM to be used for Toxicity Category I (permanent or severe ocular damage).

The fourth ICCVAM recommendation proposes that the low volume rabbit eye test (LVET) should not be used for regulatory testing due to performance issues when compared to the Draize rabbit eye test. ICCVAM also recommends: "...that retrospective LVET data can be used in a weight-of-evidence approach to classify ocular hazards provided that the validity of each type of evidence used for such assessments is adequately characterized." We appreciate the ICCVAM recommendations and note that the EPA currently uses the LVET results as part of the weight of evidence to support our risk assessments.

With respect to bringing to our attention your thoughts on the potential impact of GHS we will take them into account as appropriate in evaluating the potential application of GHS to chemicals within EPA's scope of regulation. Thank you for the opportunity to present our position on these important issues.

Sincerely,

/s/

John R. Fowle III. Ph.D., D.A.B.T.
ICCVAM Coordinator, US EPA