U.S. Department of Labor

Assistant Secretary for
Occupational Safety and Health
Washington, D.C. 20210

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AUG - 5 2008

Dr. Samuel H. Wilson
Acting Director
National Institute of
Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709

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ICCVAM file
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Attached

Dear Dr. Wilson:

Thank you for your letter of February 28, 2008 to the Occupational Safety and Health Administration (OSHA) in which you forwarded two in vitro alternative test methods proposed for estimating starting doses for acute oral systemic toxicity tests from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) for our consideration.

The OSHA Hazard Communication standard (HCS) (29 CFR 1910.1200) requires manufacturers and importers to perform a hazard determination for the product(s) they manufacture or import to determine if, under the normal condition of use or in an emergency, workplace handling or use of their product(s) can or could result in employee exposure to a hazardous chemical(s). OSHA does not perform these hazard determinations for manufacturers; rather, it is up to the manufacturers and importers to consider all available scientific evidence concerning the hazardous effects of that chemical. No testing is required by the Agency and the evaluation may be based solely on the information currently available in the scientific literature.

The use of *in vitro* studies has not been specifically addressed in either the text of the HCS final rule (59 FR. 6126) or the preamble discussions. However, Appendix B states:

> The results of any studies which are designed and conducted according to established scientific principles, and which report statistically significant conclusions regarding the health effects of a chemical shall be a sufficient basis for a hazard determination and reported on any Material Safety Data Sheet (MSDS).

It is the manufacturer's responsibility to review all available scientific data when performing a hazard determination for the chemicals they produce. If the *in vitro* studies, conducted according to established scientific principles, report statistically significant conclusions regarding the health effects of a chemical, and if these are the only data available linking the hazard to the chemical exposure, results of these studies must be reported on the product's MSDS. It must be emphasized that the Agency does not encourage replacing *in vivo* tests with *in vitro* studies. In general, the Agency's policy on *in vitro* tests is that "*in vitro* studies, such as Ames tests, are useful pieces of information, but not definitive finding of hazards" (CPL 2-2.38D, Appendix C).

OSHA has actively participated in the ICCVAM and in the process for the validation of these test methods. OSHA believes that the independent review and validation process of the ICCVAM makes these determinations scientifically sound as required by Appendix B. Therefore, based on ICCVAM's independent review and validation of these methods, the Agency will accept any positive results from studies using these methods as a means of assessing ocular corrosion or ocular irritation, within the limitation of the tests methods. Although the Agency will accept any positive results from these tests as an indicator of acute systemic toxicity, the negative results would not rule out the possibility that the substance may be acutely toxic. Also, in the event of contradictory results from in vitro and in vivo studies, the Agency will rely on the values that are more protective of workers' health.

I hope that we have provided you with enough information to state the Agency's position on in vitro acute oral systemic toxicity alternative tests. If you require additional information, please feel to contact us.

Sincerely,

Edwin G. Foulke, Jr. /