United States Department of the Interior
U.S. GEOLOGICAL SURVEY
Reston, VA 20192

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Rear Admiral William S. Stokes, Executive Director
NTP Interagency Center for the Evaluation of
Alternative Toxicological Methods
National Institute of Environmental Health Sciences
National Institutes of Health
P.O. Box 12233, Mail Code EC-17
Research Triangle Park, North Carolina 27709

Dear Admiral Stokes:

Thank you for the opportunity to review and comment upon the reduced murine local lymph node assay (rLLNA) and the LLNA test method performance standards (NIH Publication Numbers 09-6439 and 09-7357). These documents were reviewed by Department of the Interior (DOI) scientists from the U.S. Geological Survey (USGS) and the U.S. Fish and Wildlife Service as part of our response to the Interagency Coordinating Committee on the Validations of Alternative Methods (ICCVAM).

Reviewers had laudatory comments about the documents. When only a "sensitizing" or "non-sensitizing" determination is required, the rLLNA can result in a 40% reduction in the number of mice used for a substance, and assay performance is nearly equal to that of the LLNA. This is consistent with the Animal Welfare Act's recommendation to reduce the number of animals used in biomedical or industrial applications. It was suggested that attention might be directed toward the intended use of the test substance and selection of test protocol. In the event that a severe acute reaction might occur in large numbers of people or animals following widespread use or exposure, it might be prudent to use the LLNA, which has a slightly lower false negative rate.

Although the DOI conducts ecotoxicological research and monitoring of fish and wildlife, it has very limited regulatory authority for chemicals and pharmaceuticals. At present, the DOI does not evaluate the potential of substances to cause contact dermatitis. Nonetheless, we do support testing methods that reduce the number of test subjects or that replace them altogether with in vitro assays. We are pleased to assist in such reviews and will gladly provide in depth comments on those test methods that are more closely allied to our mission.

Sincerely,

/s/

William H. Werkheiser
Regional Director, Eastern Region