Department of Energy
Washington, DC 20585

(received: June 2, 2008)

Rear Admiral William S. Stokes
Executive Director
Interagency Coordinating Committee on the
Validation of Alternative Methods
National Institute of Environmental Health Sciences
P.O. Box 12233
Mail Code EC-17
Research Triangle Park, NC 27709

Dear Admiral Stokes:

This letter is in response to a request from Dr. Samuel H. Wilson, Acting Director, National Institute of Environmental Health Sciences, in a letter dated February 28,2008. Dr. Wilson requested the Department of Energy's review of the test method recommendations for two *in vitro* alternative test methods proposed for estimating starting doses for acute oral systemic toxicity tests. These recommendations are contained in a document entitled: *ICCVAM Test Method Evaluation Report (TMER): In Vitro Cytotoxicity Test Methods for Estimating Starting Doses For Acute Oral Systemic Toxicity Testing* (NIH Publication No. 07-45 19). This document presents the review of two standardized in vitro neutral red uptake (NRU) test methods, using the ZEBET approach based on the Registry of Cytotoxicity (RC3) regression model. One test method used BALBIc 3T3 mouse fibroblasts (3T3) while the other used normal human epidermal keratinocytes (NHK).
These documents were reviewed by staff in the Department of Energy's Office of Science. Based on this review, the Department of Energy finds that the recommendations are consistent with the ICCVAM efforts to identify test protocols that "more accurately assess the safety and hazards of chemicals and products and that refine, reduce, or replace animal use." The Background Review Document and the Method Evaluation Report were developed in a thorough, open, and technically defensible manner. The findings are well documented and supported by the underlying science.

The Department of Energy is not one of the Federal agencies that promulgates regulations or guidelines regarding the testing of acute oral systemic toxicity and thus does not have relevant test methods for which the ICCVAM test recommendations may be added or substituted.

Thank you for the opportunity to review these documents and please accept our appreciation for the time, effort, and expertise that were taken to develop these recommendations and their supporting background review documents.

Sincerely,

(signed)
Anna Palmisano
Associate Director of Science
for Biological and Environmental Research