



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

Centers for Disease Control  
and Prevention (CDC)  
Atlanta GA 30333

SEP 5 2008

RADM 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, North Carolina 27709

Dear Dr. Stokes:

We recently received a letter from Dr. Samuel H. Wilson, Acting Director, National Institutes of Health (NIH), National Institute of Environmental Health Sciences (NIEHS), requesting that the Agency for Toxic Substances and Disease Registry (ATSDR) review the National Toxicology Program Interagency Center for the Evaluation of Alternative Methods – Interagency Coordinating Committee on the Validation of Alternative Methods' (ICCVAM) recommendations for two in vitro test methods proposed for acute toxicity testing. We have completed the review of the two ICCVAM publications "In Vitro Cytotoxicity Test Methods for Estimating Acute Oral Systemic Toxicity" (NIH Publication No: 07-4518) and "In Vitro Cytotoxicity Testing Methods for Estimating Starting Doses for Acute Systemic Toxicity Tests" (NIH Publication No: 07-4519).

First and foremost, I commend the work of ICCVAM toward reduction, refinement, and replacement of animals in toxicity testing. This is a tremendous challenge our society faces as new chemicals are being introduced into commerce at an ever increasing pace while the resources to test them are indeed limited. However, promoting advances in alternative methods and maintaining scientific quality without compromise of human, animal, and the environmental health should remain our goal.

Thank you for the opportunity to review and comment on these proposed test methods. The Centers for Disease Control and Prevention/ATSDR concurs with your recommendations regarding these methods and agrees that these test methods should be considered before using animals for acute oral toxicity testing. The methods should clearly be used where determined to be appropriate. In addition, data from the test methods should be used in a weight-of-evidence approach for determining starting doses for in vivo studies. The presented validation study conducted to characterize the accuracy and reliability of these tests was well organized and well managed by the

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National Toxicology Program (NTP). Thorough documentation with recommendations was provided regarding standardized protocols, means of improving the utility of the methods, and standards that can be applied in the future to similar methods and models.

Should you need any further information, please contact Dr. Moiz Mumtaz, Science Advisor, Division of Toxicology and Environmental Medicine (DTEM), the agency representative to ICCVAM, at (770) 488-3349, or Dr. Bruce Fowler, Associate Director of Science, DTEM, ATSDR, at (770) 488-7250.

Sincerely,

Julie Louise Gerberding, M.D., M.P.H.  
Director, Centers for Disease Control and  
Prevention, and  
Administrator, Agency for Toxic Substances and  
Disease Registry

cc:

Samuel H. Wilson, Acting Director, NIEHS  
Moiz Mumtaz, Ph.D., DTEM  
Bruce Fowler, Ph.D., DTEM