



U.S. Department
of Transportation
**Pipeline and Hazardous
Materials Safety
Administration**



1200 New Jersey Ave., S.E.
Washington, DC 20590

APR -2 2009

Rear Admiral William S. Stokes
Executive Director, ICCVAM
National Institute of Environmental Health Sciences
P.O. Box 12233 (Mail Code EC-17)
Research Triangle Park, NC 27709

Dear Admiral Stokes:

Thank you for the letter to former Secretary Peters from Samuel H. Wilson, Acting Director, National Institute of Environmental Health Sciences which forwarded toxicological test method recommendations to the U.S. Department of Transportation (DOT) from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). The DOT is one of several Federal agencies that received the toxicological test method recommendations for consideration. The letter was referred to the Pipeline and Hazardous Material Safety Administration (PHMSA), the agency within DOT responsible for regulating the transport of hazardous materials in commerce and participation in ICCVAM. Mr. Wilson requested that we send the DOT response directly to you by April 22, 2009.

We reviewed the ICCVAM Test Method Evaluation Report. The report summarizes ICCVAM's evaluation of the validation status of five *in vitro* test methods proposed for assessing the potential pyrogenicity of pharmaceuticals and other products as potential replacements for the *in vivo* rabbit pyrogen test. The report also provides ICCVAM's recommendations for current uses and limitations for each test method, as well as recommendations for standardized protocols, future studies, and performance standards.

The DOT administers the Hazardous Materials Regulations and regulates the transportation of hazardous materials in commerce (HMR; 49 CFR Parts 171-180). The HMR include, among others, materials that meet the definition for Gas poisonous by inhalation (Division 2.3), Poisonous material (Division 6.1), and Corrosive material (Class 8).

Test methods for assessing the potential pyrogenicity of pharmaceuticals and other products are not applicable to the HMR.

If you have any further questions, please call me at (202) 366-0656.

Sincerely,



Theodore L. Willke
Associate Administrator for
Hazardous Materials Safety