



MAY - 5 2009

RADM William S. Stokes
Director
National Toxicology Program
Interagency Center for the Evaluation
of Alternative Toxicological Methods
NIEHS
P.O. Box 12233, EC-17
Research Triangle Park, NC 27709

Dear RADM Stokes:

This letter is in response to Dr. Samuel H. Wilson's letter of October 23, 2008, to the Occupational Safety and Health Administration (OSHA) in which he forwarded five *in vitro* test methods for assessing potential pyrogenicity of pharmaceutical and other products proposed by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) for our consideration. Sections 4(a) and 4(d) of the ICCVAM Authorization Act requires agencies to review ICCVAM test method recommendations and notify ICCVAM in writing of their findings, including identification of relevant test methods for which the ICCVAM test recommendations may be added or substituted.

This document was reviewed by staff in OSHA's Directorate of Standards and Guidance. Based on this review, OSHA finds these recommendations are within the scope of the ICCVAM mission. We agree with ICCVAM that, although none of these test methods can be considered a complete replacement for the Rabbit Pyrogen Test (RPT) for the detection of Gram-negative endotoxin, they may be considered for use to detect Gram-negative endotoxin in human parenteral drugs on a case-by-case basis, subject to validation for each specific product to demonstrate equivalence to the RPT.

As you may know, OSHA does not require or enforce toxicity testing as a part of its regulatory activities. At this time, we have no relevant test methods for which the ICCVAM recommendations may be added or substituted. OSHA does, however, endorse the recommendations and the continued work to promote the development and use of alternative test methods.

Thank you for your valuable work in this field. We look forward to continued participation on the ICCVAM.

Sincerely,

/s/

Jordan Barab
Acting Assistant Secretary