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

Dear Dr. Stokes:

As requested by Dr. Samuel Wilson, Acting Director of National Institute of Environmental
Health Sciences, in his letter of October 23, 2008, the National Institute for Occupational Safety
and Health (NIOSH) is herein responding to you regarding in vitro test methods for assessing
pyrogenicity of pharmaceuticals and other products. These five methods were recommended by
the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).

NIOSH agrees that the recommended alternative methods can be considered for use on a case-by-
case basis to detect Gram-negative endotoxin in human parenteral drugs, as described in the
ICCVAM evaluation report. NIOSH acknowledges the requirement that each agency review
these recommended test methods and notify the ICCVAM regarding test methods for which these
alternative methods may be substituted. NIOSH is a research agency, has no regulatory testing
requirements, and does not perform testing for pyrogenicity of pharmaceuticals using the Rabbit
Pyrogen Test. Therefore, this agency has no methods for which the subject methods might be
substituted, and these methods are not applicable to the agency. However, NIOSH will inform
scientists via its Animal Care and Use Committee and will continue to encourage use or
consideration of alternative methods including these, in any animal-using tests that may be
conducted by this agency. NIOSH will attempt to identify and support research programs which
may contribute to future development of other alternative test methods.

NIOSH commends the efforts and accomplishments of ICCVAM in reviewing and evaluating
these alternative methods and other methods. We are proud of our participation on ICCVAM
during its activity as an interagency committee.

Thank you for the opportunity to respond for NIOSH about this achievement.

Sincerely,

/Signature/

Christine M. Branche, Ph.D.
Acting Director
NIOSH