Department of Energy
Office of Science
Washington, DC 20585

JAN 15 2009

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 is in response to a request from Dr. Samuel H. Wilson, Acting Director, National Institute of Environmental Health Sciences, dated October 23, 2008. Dr. Wilson requested the Department of Energy's review of the test method recommendations for five *in vitro* alternative test methods proposed for assessing the pyrogenic potential of regulated products. These recommendations are contained in a document entitled: *ICCVAM Test Method Evaluation Report (TMER): Validation Status of Five In Vitro Test Methods Proposed for Assessing Potential Pyrogenicity of Pharmaceuticals and Other Products* (NIH Publication No. 08-6392). This document presents the review of five test methods measuring cytokine levels (either IL-1β or IL-6) from human blood cells or a human monocytoid cell line as a biomarker of pyrogenic response.

This document was 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 Test Method Evaluation Report have been developed in a thorough, open, and technically defensible manner. This report and its underlying documentation has been reviewed vigorously and made available for general public comment. Both reviewer and public comments were considered and responded to carefully.

The Department of Energy is not one of the Federal agencies that promulgates regulations or guidelines regarding the assessment of pyrogenicity in regulated products 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,

Anna C. Palmisano
Associate Director of Science
for Biological and Environmental Research