



20 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-I 7
Research Triangle Park, North Carolina 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 National Cancer Institute's (NCI) 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 (FMER): 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-1B or IL-6) from human blood cells or a human monocytoïd cell line as a biomarker of pyrogenic response.

This document was reviewed by staff in the NCI's Division of Cancer Biology and Toxicology and Pharmacology Branch. Based on this review, the NCI 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 NCI 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,

John E. Niederhuber, M.D.
Director
National Cancer Institute