NICEATM and ICCVAM Evaluation of Five *In Vitro* Test Methods for Assessing Potential Pyrogenicity of Pharmaceuticals and Other Products

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In 2006, ECVAM submitted to NICEATM background review documents (BRDs) on five *in vitro* pyrogenicity test methods proposed as replacements for the Rabbit Pyrogen Test. These test methods are based on the measurement of proinflammatory cytokines released, from either fresh or cryopreserved human blood cells or a human monocytoid line, in response to the presence of Gram-negative endotoxin in parenteral pharmaceuticals. NICEATM and the ICCVAM/Pyrogenicity Working Group prepared a comprehensive draft BRD that included the available data for the five test methods and a separate document containing ICCVAM draft test method recommendations in terms of the proposed usefulness and limitations, standardized protocols, performance standards, and future studies. The BRDs and the ICCVAM draft recommendations were made available to the public and reviewed by an independent Peer Review Panel ('Panel'). The final Panel report and all public comments were provided to the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) for comment. ICCVAM will consider the Panel report, as well as any public and SACATM comments in finalizing the BRD and test method recommendations. ICCVAM will develop and forward final recommendations to relevant U.S. regulatory agencies for consideration and possible implementation, in accordance with the ICCVAM Authorization Act of 2000 (P.L. 106-545). Supported by NIEHS contract N01-ES-35504.