

Using the Monocyte Activation Test for Medical Devices

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Pyrogens are substances that can produce fever when present as contaminants in a drug or medical device; most pyrogens are biological substances derived from bacteria, fungi, and viruses. Material-mediated pyrogens (MMPs), while less common, may also be present. It's important that medical device products for implantation or other systemic exposure meet pyrogen limit specifications before they are marketed, and animal-based pyrogen tests (i.e., LAL and rabbit pyrogen tests) are often conducted to investigate the presence of pyrogens. Non-animal monocyte activation tests (MAT) are widely available but infrequently used. To review the MAT and discuss ongoing challenges to its widespread implementation, NICEATM and the PETA International Science Consortium (PISC) co-organized a September 2018 workshop. Workshop participants explored how the U.S. FDA's Medical Device Development Tools (MDDT) Program could be used to qualify the use of MAT as a standalone pyrogen test for specific medical device contexts of use. Attendees discussed practical aspects of pyrogen testing and the evidence needed to support qualification of MAT as a replacement for animal-based pyrogen tests. Scientists from the FDA Center for Devices and Radiological Health (CDRH) outlined important considerations for use of the MAT in assessment of medical device biocompatibility and sterility and the role of the MDDT Program for qualification of MAT. There was general agreement that the MAT likely could be qualified as acceptable for batch-release testing for microbial-based pyrogens. However, additional studies were recommended to demonstrate its ability to detect known MMPs. This testing would determine whether the MAT can be used for both biocompatibility and sterility or if other information on MMPs would be needed to address biocompatibility. Participants also discussed information gaps on MMPs, potential test controls, and other challenges and opportunities for implementing the use of MAT as a comprehensive pyrogen test. Funded in whole or in part with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.

Keywords: in vitro and alternatives; alternatives to animal testing; safety evaluation