USING THE MONOCYTE ACTIVATION TEST AS A STANDALONE RELEASE TEST FOR MEDICAL DEVICES

September 18-19, 2018
Porter Neuroscience Building, Bethesda, MD
Co-organized by NICEATM and the PETA International Science Consortium

Monocyte activation tests (MAT) are widely available but infrequently used in place of animal-based pyrogen tests that are required or recommended by regulatory agencies before marketing medical devices. This workshop will explore how the FDA's Medical Device Development Tools (MDDT) Program can definitively qualify the use of MAT as a standalone release test for a specific medical device context of use. Critical to the planning and execution of this workshop will be input from key players including FDA Center for Devices and Radiological Health (CDRH), the U.S. Pharmacopeia (USP), the International Organization for Standardization (ISO), MAT experts, and medical device companies conducting pyrogenicity testing.

AGENDA

September 18

9:00-9:15	Welcome
9:15-9:45	Speaker: Thomas Hartung, Johns Hopkins Center for Alternatives to Animal Testing *Overview of the MAT and comparison to the rabbit pyrogen test and other pyrogen detection tests e.g., the mechanism by which the MAT detects pyrogens, applicability of the MAT to detect endotoxins and non-endotoxin pyrogens in medical devices and extracts, MAT patent status, and limits or gaps in mechanisms of detection.*
9:45-10:15	Speaker: Molly Ghosh, FDA CDRH Biocompatibility Standards Task Group *FDA CDRH requirements to accept the MAT as a replacement for the rabbit pyrogen test and/or bacterial endotoxin test to meet medical device biocompatibility and sterility testing requirements, and the role of the MDDT Program in meeting these requirements. Include discussion of how narrowly context of use must be defined for industry consortia planning an MDDT proposal.*
10:15-10:30	Break
10:30-11:00	Speaker: Anita Sawyer, International Organization for Standardization Technical Committee 194, Biological and clinical evaluation of medical devices

ISO 10993 and pyrogen testing recommendations, material mediated pyrogens, and pending revision of ISO TC 194 report on currently available pyrogen tests.

11:00-11:30 Speaker: Radhakrishna Tirumalai, United States Pharmacopoeia
Summary of recent revision to USP General Chapter <151> ("Pyrogens") to allow use of in vitro pyrogen tests, qualifying in vitro pyrogen tests according to General Chapter <1225> (Validation of Compendial Procedures), compatibility of USP requirements with the MDDT Program, sharing MAT data with USP.

11:30-12:30 Lunch

12:30-1:00 Speaker: Kelly Coleman, Medtronic
Information gaps on material mediated pyrogens, pyrogen test controls and other challenges and opportunities in validating the use of MAT to detect material mediated pyrogens.

1:00-3:00 Panel discussion: validating the MAT for the detection of material-mediated and other non-endotoxin pyrogens relevant for medical devices
A panel of MAT providers and experts will share their experiences with medical device and device extract testing, non-extract test preparations, available standards and controls, assay inhibition, and other topics that should be considered when using the MAT with medical devices. With reference to the FDA CDRH MDDT guidance, attendees and panelists will discuss the evidence needed to support qualification of MAT as a replacement for the RPT/BET, identify appropriate context of use limits, and summarize a proposed evidence plan.

Panelists:

Claire Briglia, Merck
Anja Fritsch, Confarma
Elizabeth Gonzalez, FDA CDRH
Jennifer Goode, FDA CDRH
Djik Maouyo, PyroDex Testing
Thierry Muller, Merck
Ruth Roeder, Microcoat Biotechnologie GmbH
Hilda Scharen-Guivel, FDA CDRH
Shabnam Solati, MAT BioTech B.V.
Walter Zwisler, Zwisler Laboratorium GmbH

Questions to address:

- How to address material-mediated pyrogens in an MDDT proposal?
  - The rabbit material-mediated pyrogenicity test is conducted with a saline extract of the entire device which is injected at 100% concentration. LAL testing is conducted using extracts of the device

in depyrogenated water, and used at 100% concentration in the test system. For MAT testing, if some dilution is needed for use in the cell system, how could this impact comparability across test systems?
- Does the test methodology need to be altered (e.g., longer incubation times) in order to better detect weak material-mediated pyrogens that may be present in an extract?

3:00-3:15	Break
3:15-4:15	Panel discussion: continued
	Questions to address:
	• How should devices be prepared for use with the MAT test system (e.g. extracts, whole devices (large vs. small), hydrogels, nanomaterials, etc.)? What devices can be grouped for MDDT validation studies? • Should inhibition/enhancement information be included as part of the test procedures? Are there specific chemicals that could be present in medical devices that may inhibit the MAT test?
4:15-4:45	Group questions after discussion *An opportunity to refine questions arising from the discussion that need consideration in the context of an MDDT proposal and evidence plan.*
5:00	Independently sponsored reception

September 19

9:00-11:00	Panel discussion: continued
	• What levels from MAT testing are clinically acceptable? How do those levels compare with traditional material-mediated pyrogen testing (0.5C temperature rise in rabbits per USP <151>) and traditional LAL testing for bioburden (i.e., in endotoxin units/device)? • Next steps for organizing industry consortia to further develop MDDT proposals to use MAT in place of other pyrogen tests, unmet needs and challenges in preparing an MAT evidence plan for MDDT proposals.
11:00-11:45	Summary of action items, next steps, and remaining questions.
11:45-12:00	Adjourn