The monocyte activation test (MAT) is a replacement for the rabbit pyrogen test (RPT) and the bacterial endotoxins test (BET)/limulus amoebocyte lysate (LAL) test. The MAT measures cytokine release from monocytes when human blood is exposed to a test substance. Cytokines released in the activation process are quantified by the enzyme-linked immunosorbent assay (ELISA).

**THE MONOCYTE ACTIVATION TEST FOR ASSESSING PYROGENICITY**

**ADVANTAGES OF THE MAT**

- Based on the human fever response, the MAT provides a more relevant prediction of pyrogenic activity than the RPT or BET/LAL.
- It can detect endotoxin and non-endotoxin pyrogens and is applicable to a greater variety of products than the RPT or BET/LAL (e.g. certain drugs and herbal formulations; see Hartung T. 2015. *ALTEX*. 32(2):79-100).
- It has a lower limit of detection and is more accurate as well as more cost-effective and efficient than the RPT.
- Five variants of the MAT have been standardised and validated.

**SELECT PUBLICATIONS**


**GUIDANCE**

- The European Pharmacopeia general method 2.6.30 Monocyte-activation test allows the MAT to serve as a full replacement for the RPT after product-specific validation.
- The US Pharmacopeia general chapter <151>, “Pyrogen Test”, allows use of a “validated, equivalent in vitro pyrogen or bacterial endotoxin test” in place of the in vivo RPT.
- The US FDA’s “Guidance for Industry: Pyrogen and Endotoxins Testing Questions and Answers” (2012) states that alternatives, specifically the MAT, may be used after product-specific validation for biological products, drugs, and devices, even when US Pharmacopeia monographs require the RPT. The FDA encourages companies to contact the agency to discuss alternative test methods (e.g. in “Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants and FDA’s guidance on its Pre-Submission Program and Meetings”).
- The MAT has been accepted into the US FDA’s Medical Device Development Tools (MDDT) programme and is undergoing review as a standalone release test for medical devices that can replace the use of the RPT and BET/LAL when satisfying biocompatibility and sterility testing requirements.
- The US FDA’s CDRH guidance (2016) states that the CDRH accepts validated methods equivalent to the RPT.
- In 2006 and 2007, respectively, ECVAM and ICCVAM endorsed the MAT for identifying Gram-negative endotoxins and recognised its capacity to detect a wider range of pyrogens. Considerable research has since supported its wider application.

Companies offering MAT kits or services include MAT Research, PyroDex, MilliporeSigma, and Microcoat Biotechnologie GmbH.

For more information, please see PISCLtd.org.uk/medical-device-pyrogen.