

Monocyte Activation Test for pyrogen testing of biopharmaceutical products

Commonly used acronym: MAT

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Organisation

Name of the organisation Janssen Pharma of JNJ

Department Analytical Development

Country Belgium

Geographical Area Flemish Region

Partners and collaborations

Janssen Pharma of JNJ

SCOPE OF THE METHOD

| | |
|--|---|
| The Method relates to | Human health |
| The Method is situated in | Regulatory use - Routine production: Regulatory use - GMP process validation |
| Type of method | In vitro - Ex vivo |
| Species from which cells/tissues/organs are derived | Human blood |
| Type of cells/tissues/organs | Peripheral Blood Mononuclear Cells (PBMC) |
| Specify the type of cells/tissues/organs | Peripheral Blood Mononuclear Cells (PBMC) |

DESCRIPTION

Method keywords

PBMC

ELISA

endotoxins and non-endotoxin pyrogens

alternative to rabbit pyrogen test

IL-6

european pharmacopoeia

Scientific area keywords

pyrogenicity
Biopharmaceuticals

Method description

Pharmaceutical products intended for parenteral use must be free from pyrogenic (fever-inducing) contamination. Pyrogens comprise endotoxin from Gram-negative bacteria and non-endotoxin pyrogens (NEP) from Gram-positive bacteria, viruses, and fungi. The longstanding compendial test for pyrogens is the Rabbit Pyrogen Test (RPT) but in 2010 the Monocyte Activation Test (MAT) for pyrogenic and pro-inflammatory contaminants was introduced into the European Pharmacopoeia (Ph. Eur.) as a 'non-animal' replacement for the RPT. The developed MAT method was fully validated for GMP purposes according to Ph. Eur. MAT, Quantitative test, Method A to test for pyrogenic and pro-inflammatory substances in therapeutic monoclonal antibodies (mAb). The MAT uses cryo-preserved PBMC with an interleukin-6 (IL-6)-based ELISA readout. The method has been successfully approved by EMA in scope of commercial licensing applications (MAA) for several mAb-based drug products.

Lab equipment

- CO2 incubator;
- Washer;
- ELISA plate reader;
- SoftMax Pro.

Method status

Internally validated
Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

- *In vitro* test which replaces rabbit-based testing;
- (Semi-) Quantitative.

Challenges

- Extensive validation required;
- Requires well-characterized PBMCs.

Modifications

In case the drug product would interfere with an IL-6-based readout, other cytokines such as IL-1 beta may need to be explored and validated as alternative.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

Associated documents

[Daniels et al - ALTEX 2022 - MAT for therapeutic monoclonal antibodies.pdf](#)
[Daniels et al - Curr Res Tox 2024 - MAT Fit for purpose testing.pdf](#)

Links

[Validation of the monocyte activation test with three therapeutic monoclonal an...](#)
[Fit for purpose testing and independent GMP validation of the monocyte activati...](#)

Other remarks

Partners for this method: Sanquin (m.molenaar@sanquin.nl) & Janssen Pharma of JNJ (rdanie22@its.jnj.com)

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