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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