Make the change

Now is the time!

Meet regulatory requirements with the PyroMAT® Monocyte Activation Test (MAT)

Used to detect a broad range of pyrogens in medical products administered parenterally such as pharmaceuticals or biopharmaceuticals, the MAT gives an *in vitro* alternative to historical rabbit pyrogen test (RPT) according to the current regulatory guidelines.

The end of the RPT era in the European Pharmacopoeia (Ph. Eur.) has been implemented on July 1, 2025.
This represents a significant advancement for animal welfare, as no European Pharmacopoeia monograph will require the use of the RPT anymore. Instead, medicine developers must choose an appropriate *in vitro* method (e.g., the monocyte activation test) based on a risk assessment described in the new general chapter Ph. Eur. 5.1.13.

With **our Mono-Mac-6 cell-line based MAT,** we provide a robust, reliable and standardized method for *in vitro* pyrogen detection.

PyroMAT®: A cell-line based pyrogen test mimicking the human immune reaction

Pyrogens

- **Endotoxins**
  gram-negative bacteria
- **Non-Endotoxin Pyrogens (NEPs)**
  gram-positive bacteria, yeast & mold, viruses, particles of the environment (e.g. rubber, plastic, organic dust, packaging materials)

→ **Monocyte** →

Cytokines
IL-1β, IL-6, TNF-α, IFN-γ

↓

Detection of **IL-6** by ELISA test

The PyroMAT® kit is based on the Mono-Mac-6 (MM6) human monocytic cell line and uses interleukin-6 (IL-6) as a read-out.

Like in humans, once the MM6 cells come into contact with pyrogens from a contaminated sample, they produce cytokines such as interleukin-6 (IL-6), which can be quantified with an enzyme-linked immunosorbent assay (ELISA).

Go for simplicity

With a sensitivity of 0.05 EU*/mL, PyroMAT® System is a ready-to-use cell-line based MAT kit. A robust and easy way to perform pyrogen test.

*Endotoxin Units

Advantages of the MAT

Detection of the full range of pyrogens: patient safety is ensured if the full range of pyrogens is tested. Like the Rabbit Pyrogen Test (RPT), MAT is effective for detection of both Endotoxin and Non-Endotoxin Pyrogens (NEPs).

Extension of the range of products that can be tested: the most frequently applied methods, RPT and Bacterial Endotoxin Test (BET), are both limited in the product types they are able to test. The MAT offers more flexibility regarding its applications.

***In vitro* assay that mimics the human immune reaction:** for a robust predictive model that avoids animal consumption.

The method of choice to detect both endotoxin and non-endotoxin pyrogens, as described in Ph. Eur. 5.1.13.

Compliance with international regulations and guidelines: in line with ethical trends of industry and regulatory authorities to prevent and decrease the use of animal-based testing.

Cell line benefits

Qualified cells: in addition to being cited in the international validation of MAT, Mono-Mac-6 cells are qualified for the detection of all types of pyrogens by testing the expression of all surface Toll-Like Receptors (TLRs).

Standardized reactivity for reproduceable results Convenience of a ready-to-use cell line that prevents lab technician from laborious lab work and avoids the need for a cell culture laboratory.

Why is it important to detect endotoxin and non-endotoxin pyrogens?

Endotoxins, lipopolysaccharides from gram-negative bacteria, are the most common cause of pyrogenic reactions. However, non-endotoxin pyrogens, which have different structures, can also induce similar harmful effects. Standard tests for bacterial endotoxins may not detect non-endotoxin pyrogens, making it essential to employ comprehensive testing methods, such as the Monocyte Activation Test (MAT), which can identify both types of pyrogens.

Ensuring the detection of all pyrogenic substances is vital for maintaining the safety and efficacy of medicinal products and protecting public health.

HOW-TO WORKFLOW

Implementation of our Monocyte Activation Test (MAT), the PyroMAT® System

TRAINING
(recommended)

FEASIBILITY
Check that MAT is suitable for the sample (no interference)
In case of interference, method development with specific sample preparation can be tried to tackle the issue

COMPENDIAL?
Is the MAT method compendial in the reference regulatory guideline?

YES

PRODUCT SPECIFIC VALIDATION (PSV)
PSV is performed on 3 lots of sample to check:
- Acceptance criteria for validity of the endotoxin standard curve
- Test for interfering factors
- Detection of non-endotoxin contaminants
- Interference in the detection system

REGULATORY SUBMISSION

ROUTINE TEST

NO

FULL METHOD VALIDATION
Robustness, Accuracy, Precision, Specificity, Quantitation Limit, Linearity and Range of applicability.

PRODUCT SPECIFIC VALIDATION (PSV)
PSV is performed on 3 lots of sample to check:
- Acceptance criteria for validity of the endotoxin standard curve
- Test for interfering factors
- Detection of non-endotoxin contaminants
- Interference in the detection system

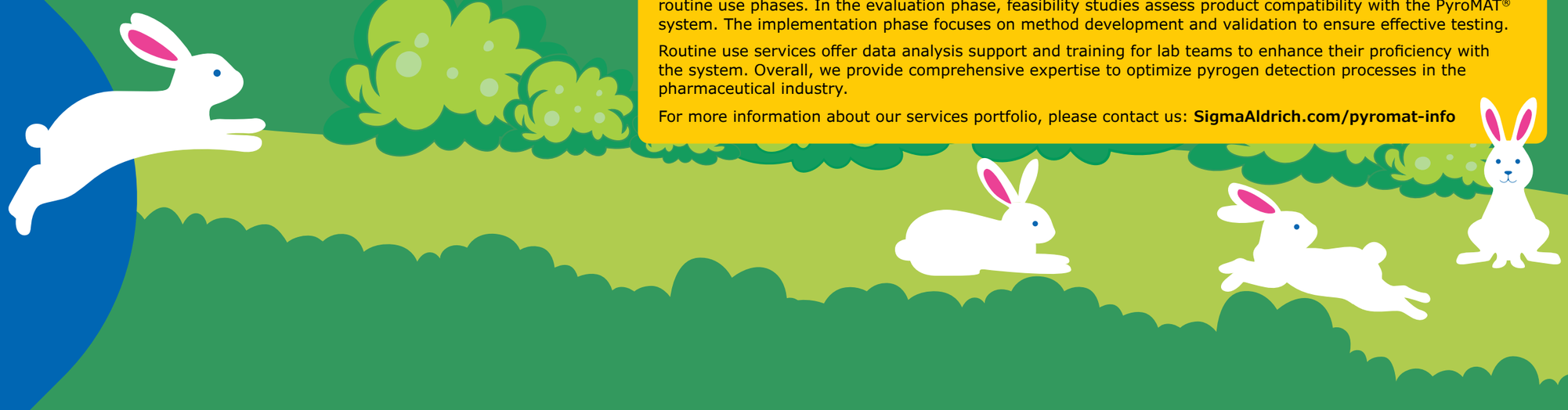
Services

Our services portfolio for the PyroMAT® Kit includes support during the evaluation, implementation, and routine use phases. In the evaluation phase, feasibility studies assess product compatibility with the PyroMAT® system. The implementation phase focuses on method development and validation to ensure effective testing.

Routine use services offer data analysis support and training for lab teams to enhance their proficiency with the system. Overall, we provide comprehensive expertise to optimize pyrogen detection processes in the pharmaceutical industry.

For more information about our services portfolio, please contact us: **SigmaAldrich.com/pyromat-info**

PyroMAT® System
All the advantages of the monocyte activation test combined with the benefits of using a continuous cell line.

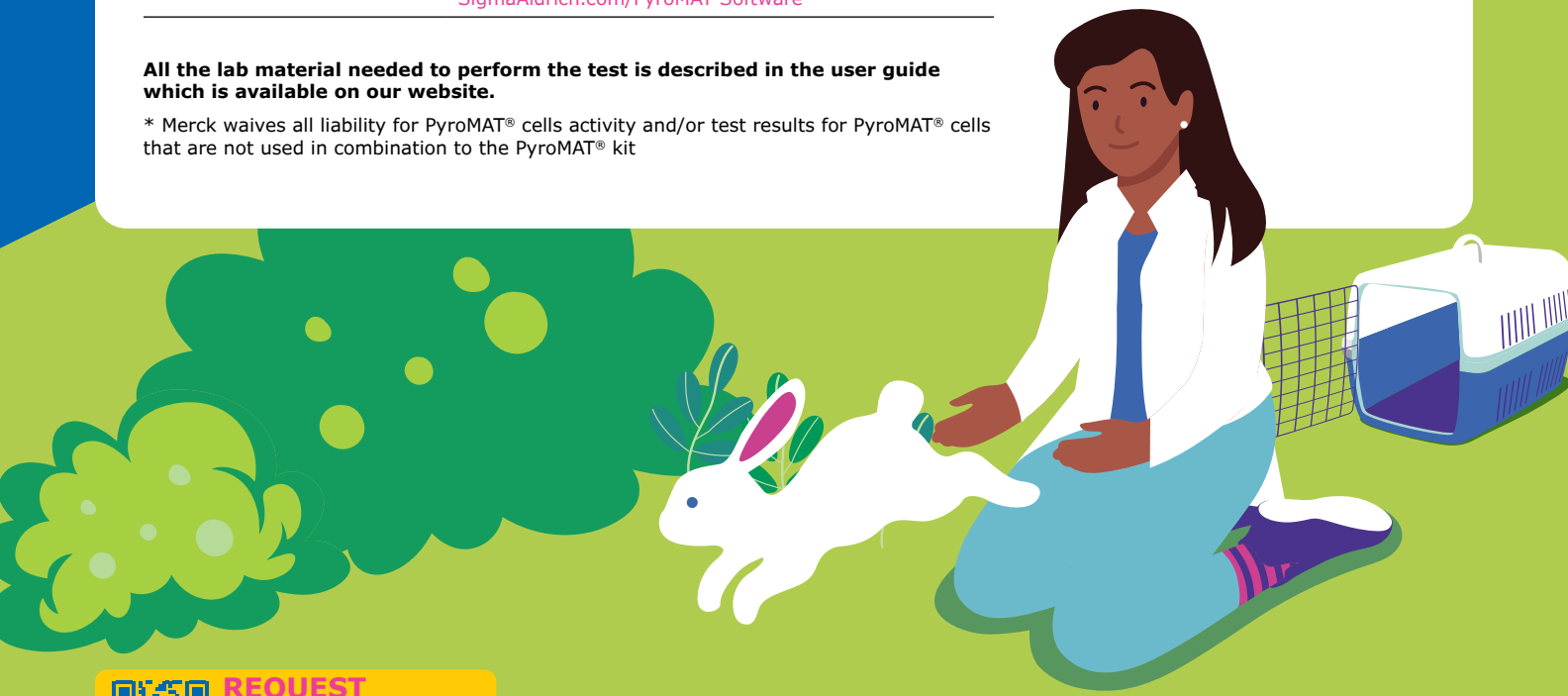


Ordering Information

	Product Description	Store at	Catalog Number
PyroMAT® kit*	The kit contains reagents for the incubation with the cells and includes the interleukin IL-6 ELISA control. Note: the PyroMAT® cells are not included and should be ordered separately.	2-8 °C	PYR0MATKIT
PyroMAT® cells*	Contains the cryopreserved Mono-Mac-6 cells for one test (2 x 1 mL)	-80 °C or below	PYR0MATCELLS
Reference Standard Endotoxin	International Reference Standard Endotoxin (RSE)—positive control of endotoxin, TLR-4 agonist	Lyophilized store at -20 °C, reconstituted at -40 °C or below	1.44161.0001
Non-Endotoxin Pyrogen control HKSA	NEP Control HKSA is a heatkilled preparation of *Staphylococcus aureus*, TLR-2 agonist. Gram-positive bacteria	Lyophilized store at 2-8 °C, reconstituted at -20 °C	MATHKSA
Non-Endotoxin Pyrogen control Flagellin	NEP Control Flagellin is a preparation of Flagellin from *Salmonella typhimurium*, TLR-5 agonist. Gram-positive and Gram-negative bacteria	Lyophilized store at -20 °C, reconstituted at -20 °C	MATFLAGELLIN
Non-Endotoxin Pyrogen control PAM3CSK4	NEP Control PAM3CSK4 is a synthetic triacylated lipopeptide, TLR-2/TLR-1 agonist. Gram-positive and Gram-negative bacteria	Lyophilized store at 2-8 °C, reconstituted at -20 °C	MATPAM3CSK4
Non-Endotoxin Pyrogen control Resiquimod	NEP Control Resiquimod R848 is an imidazoquinoline compound with anti-viral activity, TLR-7/TLR-8 agonist. Virus	Lyophilized store at -20 °C, reconstituted at -20 °C	MATRESIQUIM0D
Non-Endotoxin Pyrogen control FSL-1	NEP Control FSL-1 is a synthetic lipoprotein of *Mycoplasma salivarium*, TLR-2/TLR-6 agonist. Mycoplasma	Lyophilized store at 2-8 °C, reconstituted at -20 °C	MATFSL1
Software protocols	To analyze results according to European Pharmacopoeia (EP 07/2024 : 2.6.30 & 2.6.40). These analysis tools can be downloaded on SigmaAldrich.com/PyroMAT-Software		

All the lab material needed to perform the test is described in the user guide which is available on our website.

* Merck waives all liability for PyroMAT® cells activity and/or test results for PyroMAT® cells that are not used in combination to the PyroMAT® kit



REQUEST INFORMATION
SigmaAldrich.com/pyromat

Merck KGaA
Frankfurter Strasse 250
64293 Darmstadt, Germany

To Place an Order or Receive Technical Assistance

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Technical Service: **SigmaAldrich.com/techservice**

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