



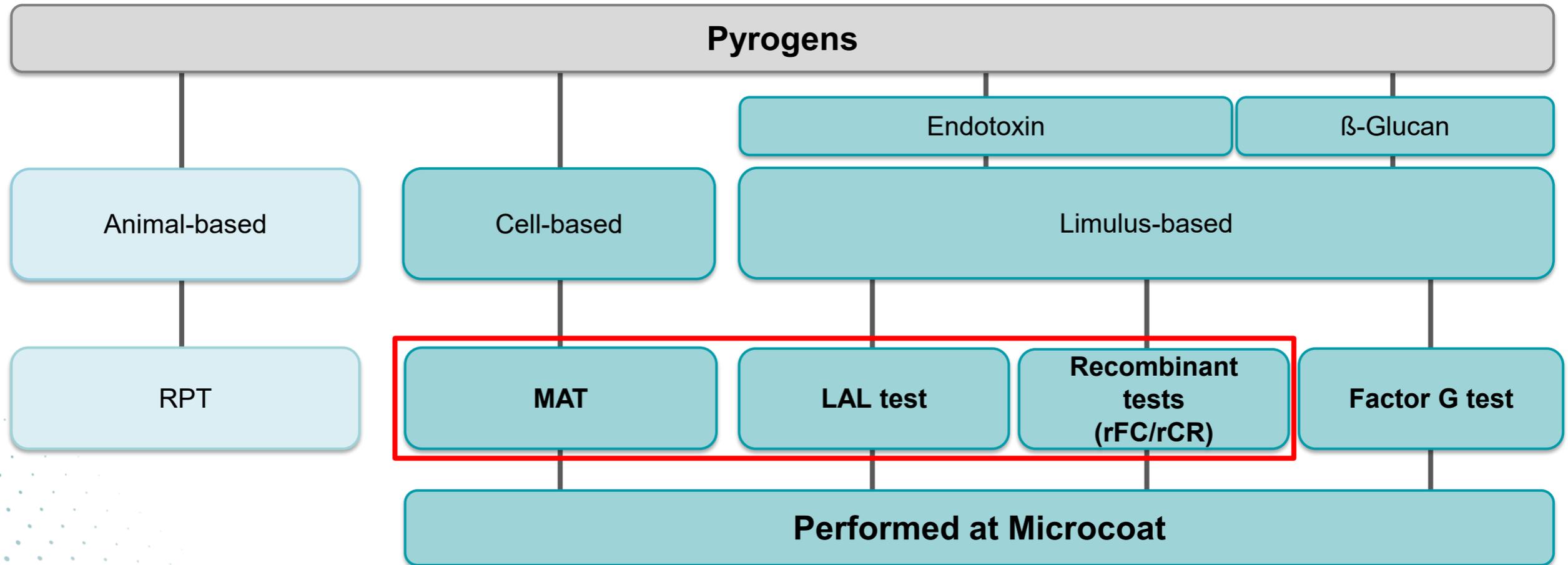
# **Navigating the Transition: Regulatory and Practical Perspectives on Implementing the Monocyte Activation Test**

02-Dec-2025

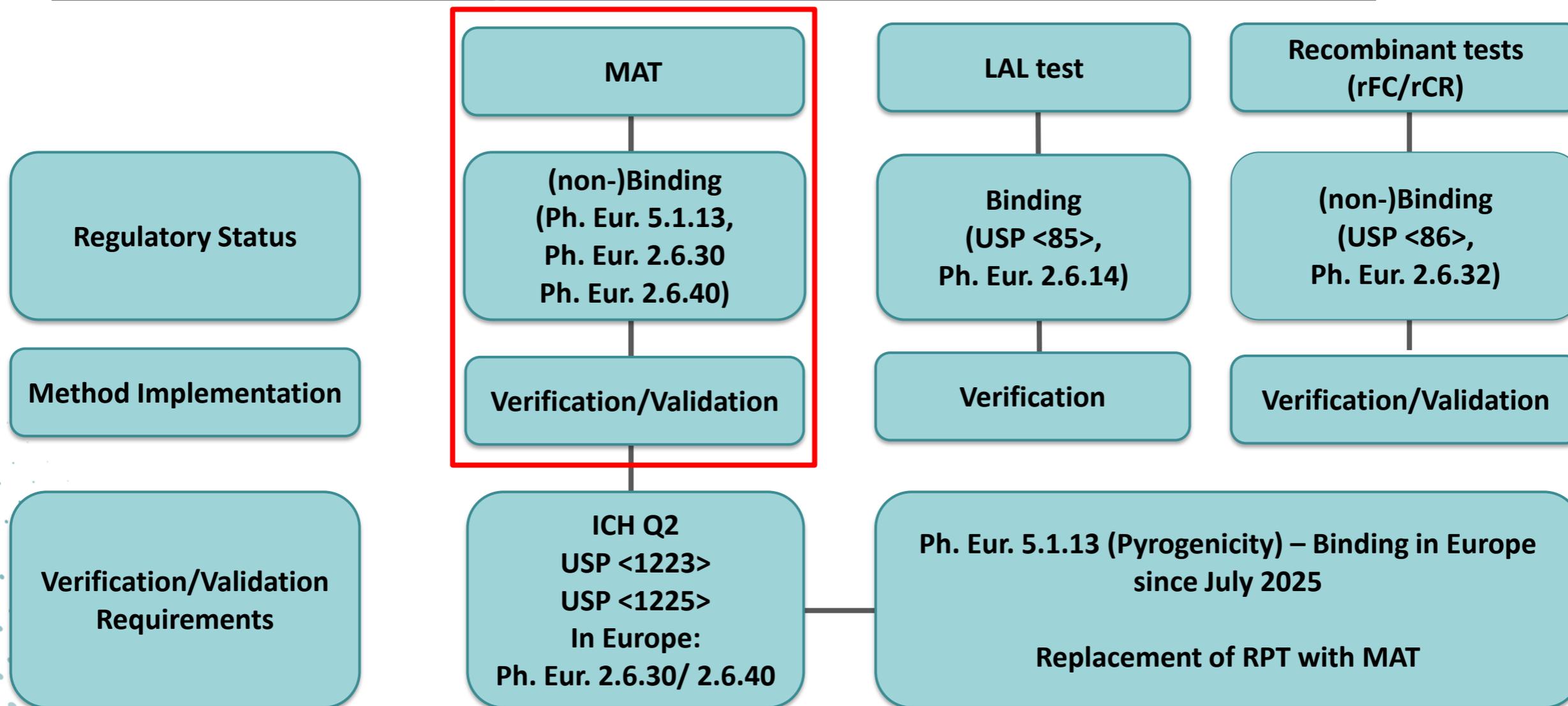
Dr. Bernhard Illes

Microcoat Biotechnologie GmbH

# Pyrogen and Endotoxin Testing - Overview

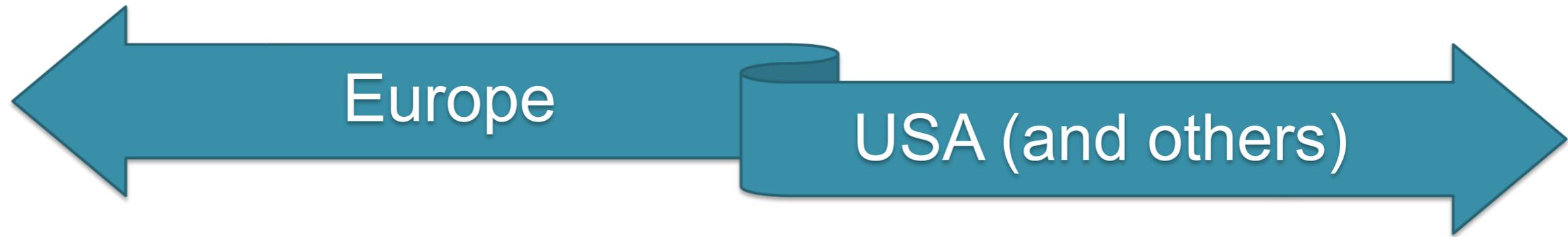


# Pyrogen and Endotoxin Testing - Implementation



## MAT Implementation

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MAT is part of **binding chapters** of EP  
(European Pharmacopoeia Chapters 2.6.30 and 2.6.40)

Only a **product-specific verification** of  
the method is necessary

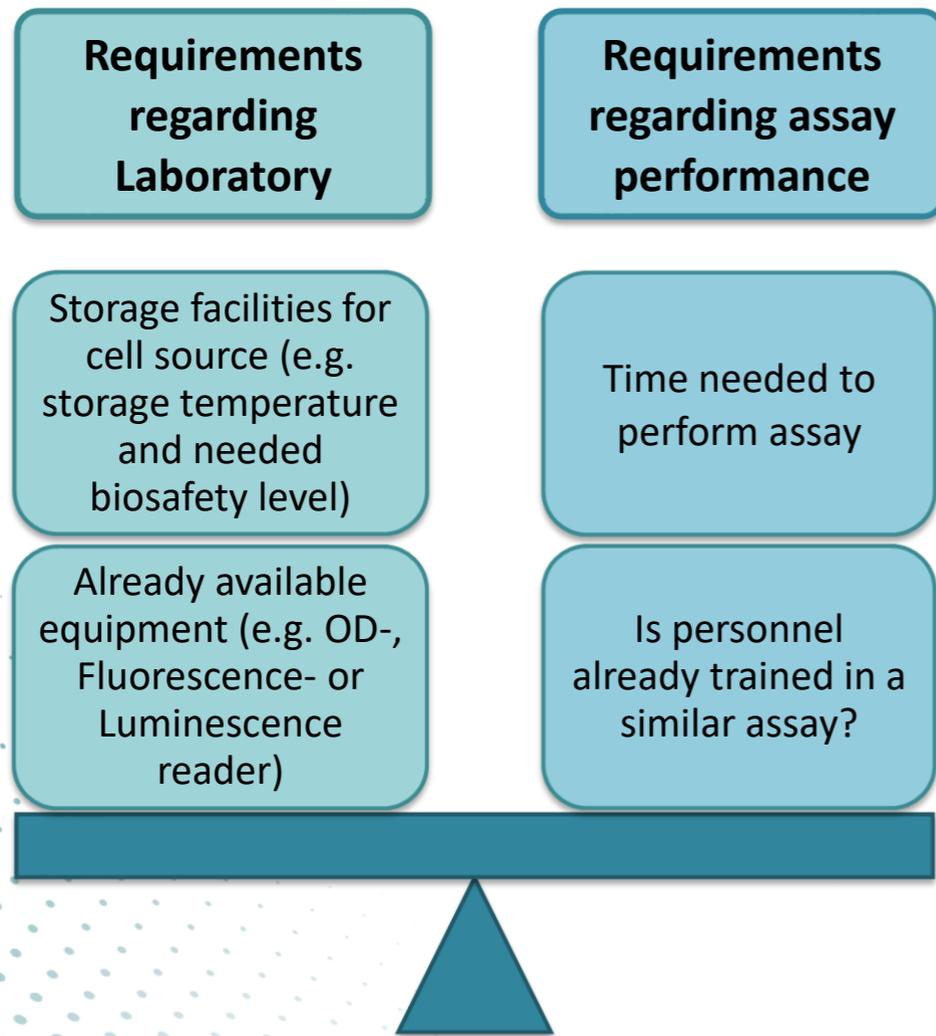
- Product-specific verification

MAT is not part of **binding chapters** of USP

A **complete validation** of the method as  
alternative method is necessary

- Generic Validation
- Product-specific verification  
(or combined generic and product-specific validation/  
verification)

# Selection of MAT System and Implementation



## Points to be considered

- Conditions and characteristics of the laboratory
- Already available resources
- Effort and suitability of resources to be acquired
- Requirements regarding assay performance (e.g. particularities of sample)

➔ Continuous qualification of MAT and lab personnel possible by participation in proficiency testing

e.g. Microcoat MAT Proficiency Testing



# Selection of MAT System and Implementation

## MAT Kits\* or in-house MAT

- **HaemoMAT** from Haemochrom
- **MATR Kit** from MAT Research
- **PyroCell** from Lonza
- **MAT Biotech/ CTL MAT**
- PyroMAT and PyroDetect from Merck
- LumiMAT from Fujifilm WAKO
- MylcMAT from Mican
- NAT-MAT from Minerva biolabs
- instaCELL Pyrogen Detection Kit from accelerate
- HyperMAT from HyqualityDx

## Cell Sources\*

- PBMCs
- Whole Blood
- Monocytic Cell Lines
- Macrophages
- Others

## Positive Product Control (PPC)\*

- Endotoxin
- Lipoteichoic acid (LTA)
- Peptidoglycan (PGN)
- Flagellin
- Heat Killed *S. aureus* (HKSA)
- Other Non-Endotoxin Pyrogens

## Read-out systems\*

- Cytokine ELISA
- Cytokine HTRF
- Reporter Gene Assay
- Others

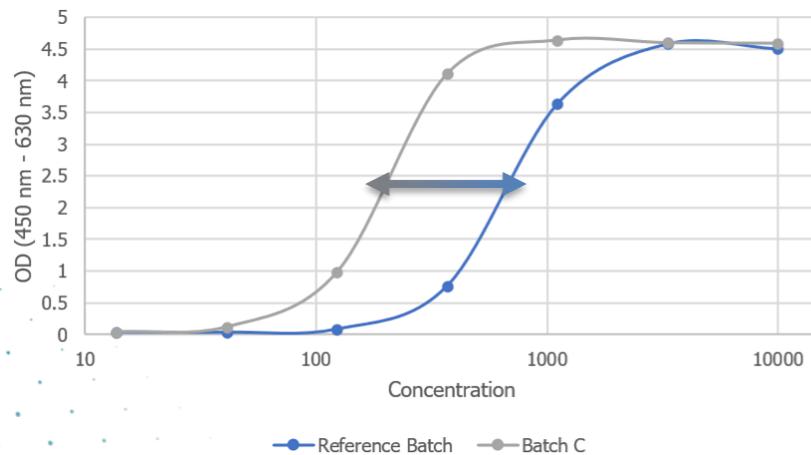
**Bold** = PBMC based MAT

\* = Lists do not claim to be complete in regard to available or possible options

# Case Study I: MAT Feasibility Study for Products with inherent Pyrogenicity - Method 2 – Reference Lot Approach

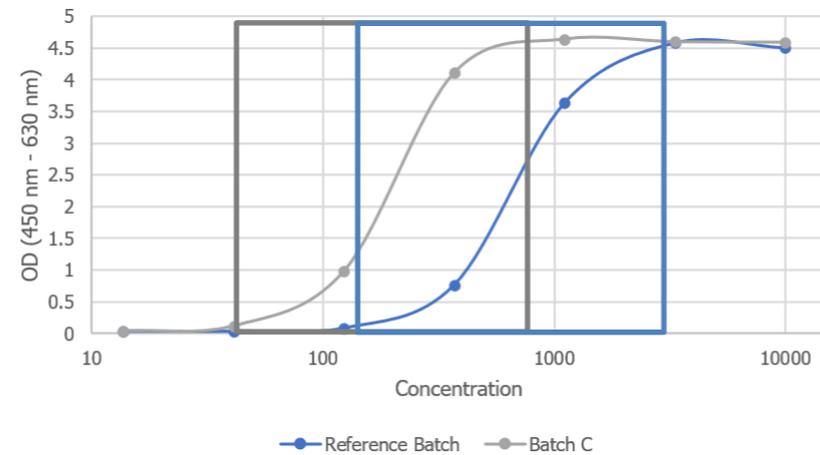
- Different data evaluation approaches are available

## Parallel line analysis (PLA)

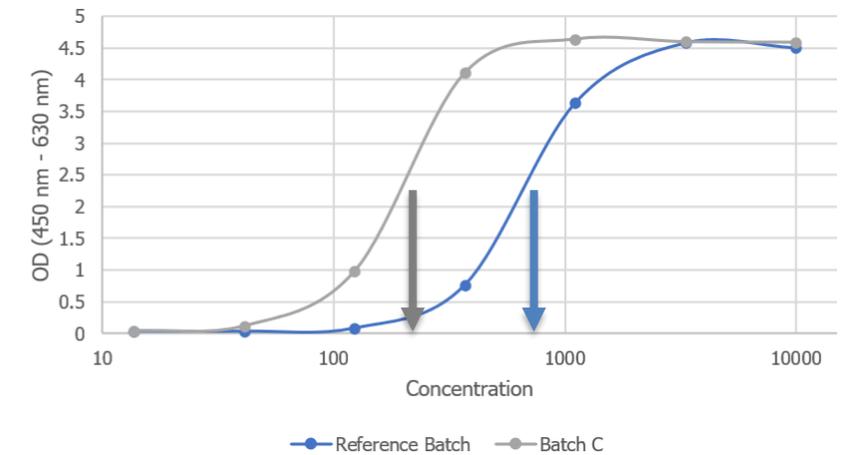


## Ratio of mean response

(based e.g. on OD values or back-calculated IL-6)



## Ratio of EC50 values



- other approaches for data evaluation might also be applicable based on the response to the product
- For vaccines with inherent pyrogenicity, PLA has to be used (Ph. Eur. 2.6.40)
- For vaccines without inherent Pyrogenicity Method 1 is used (Ph. Eur. 2.6.30)

## Case study II – Replacement of RPT by MAT



- ❖ Feasibility of MAT method was tested for different products
- ❖ MAT was generically validated according to USP <1225>, USP <1223>, ICH Q2(R1)\*, and Ph. Eur. 2.6.30
- ❖ Product-specific verification of MAT method on top of generic MAT validation
- ❖ Release testing of 3 PPQ batches → no pyrogens could be detected in the product
  - MAT method and results of release testing were submitted to FDA



\* Now ICH Q2(R2)

## Case study II – Replacement of RPT by MAT



### ➤ Request by FDA: Show equivalency of specific MAT system and RPT

- *„... provide data demonstrating that the XXX-MAT kit is better or equivalent in detecting non- endotoxin pyrogens (NEP) to RPT using a panel of NEP. This information may be provided by the vendor.“*
- *„We are asking for a one-time, non-product specific study, that compares the proposed XXX-MAT method with the RPT using a panel of non-endotoxin pyrogens (NEP). As indicated before, this study may be conducted by the vendor, or supported by data in the literature.“*

*from Sven Deutschmann, PharmaLab 2024*



## Case study II – Replacement of RPT by MAT



- Request by FDA: Show equivalency of specific MAT system and RPT
  - Equivalency/ Superiority of specific MAT system to RPT could be shown
    - Selection of relevant NEPs (inhouse contaminants)
    - Absence of Endotoxin in selected NEPs was shown
    - Sensitivity of RPT towards specific Pyrogens (RSE, LTA, PGN, Zymosan) from literature was compared to tested sensitivity in the MAT



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  - Equivalency/ Superiority of specific MAT system to RPT could be shown
    - Selection of relevant NEPs (inhouse contaminants)
    - Absence of Endotoxin in selected NEPs was shown
    - Sensitivity of RPT towards specific Pyrogens (RSE, LTA, PGN, Zymosan) from literature was compared to tested sensitivity in the MAT
  - BLA including MAT instead of RPT was **approved by FDA** (by now also for a second product)



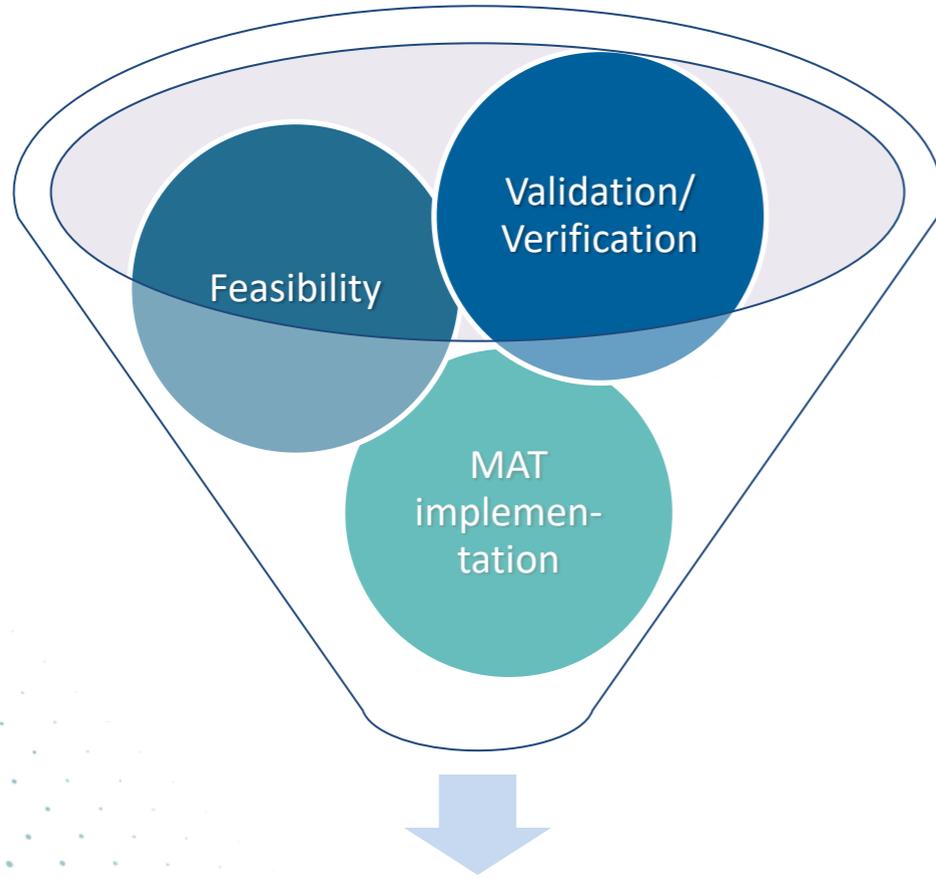
# Lessons learned - Take home message

## 10 years MAT in a contract lab in Germany

Past		Today
Logistics of cells was often inadequate → inoperable	→	No problem, logistics are under control → reliable cells available
Home brew kits require high maintenance (preps, qualification, costs,...)	→	Various vendors with excellent quality available
Lack of routine testing	→	Today, MAT is a routine test procedure
Limited knowledge	→	Experience (specific handling, data evaluation, statistics, etc.)
Limited comparability of tests	→	Increasing amounts of products and studies available (PTP)
Limited training opportunities	→	Training courses

➤ MAT accepted by authorities in Europe and US

**Thank you for your attention!**



**It is possible!**

**Change now and  
Go Alternative!**

**MAT as replacement of RPT**

# My Contact Details

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