eurofins | BioPharma Product Testing

EUROPEAN NEWSLETTER

TABLE OF CONTENTS

N°03 - JULY 2025

NEXT-GENERATION MAT VS. TRADITIONAL PYROGEN TESTS: FASTER, ETHICAL, AND MORE RELIABLE

Dr. Nicole Rieth, Business Unit Manager ATMP & Biologics
Dr. Frances Reichert, Technical Specialist Biologics, Eurofins BioPharma Product Testing Germany

Pyrogens – fever-inducing substances originating from bacteria, fungi, or viruses – pose significant health risks when present in injectable pharmaceuticals. As a critical quality control measure, pyrogen detection ensures patient safety. Historically, the Rabbit Pyrogen Test (RPT) has been the standard method for pyrogen detection. However, RPT presents ethical and sustainability concerns, alongside limitations in sensitivity and the lack of quantitative measurement. To address these issues, the Monocyte Activation Test (MAT) was introduced as an in vitro alternative, replicating the human immune response. Recognised in the European Pharmacopoeia (Chapter 2.6.30) since 2010, MAT is set to completely replace RPT by July 1, 2025.

Eurofins BioPharma Product Testing Europe has conducted extensive evaluations of various MAT kits, each utilising different human cell sources for immune response assessment. While these kits differ in their detection methods, the fundamental approach remains consistent: test samples are incubated with pyrogen-sensitive cells, such as THP-1 macrophages or peripheral blood mononuclear cells (PBMCs), leading to the release of measurable cytokines like IL-6 or TNF-alpha. Additionally, our teams had the opportunity to implement a next-generation MAT kit prior to its commercial launch. This advanced system incorporates a reporter gene cell line, enabling results within a single working day – a significant enhancement in efficiency while maintaining the high sensitivity and reliability of existing MAT technologies.

Why MAT is the Superior Choice for Pyrogen Testing

MAT offers multiple advantages over traditional methods, making it the preferred solution for pharmaceutical safety testing:

- Sensitive, reproducible, and semi-quantitative results
- Detection of both endotoxins (LPS) and non-endotoxin pyrogens (NEPs)
- Animal-free and ethically compliant
- Recognised by regulatory authorities (FDA, EMA)

As the regulatory transition deadline is approaching fast, pharmaceutical companies must adapt to this shift. Eurofins BioPharma Product Testing Europe, with its international team of experts, is at the forefront of this transformation, offering cutting-edge MAT solutions to support the industry's transition to more ethical and reliable pyrogen testing.

Making the Transition?

Get in touch today to discuss with our experts:
information@bpt.eurofinseu.com

Register now for our live webinar, Next-Generation MAT vs. Traditional Pyrogen Tests: Faster, Ethical, and More Reliable, on the 15th of July, 4-5pm CEST.

Register here

Also available on demand after July 15, contact us at: information@bpt.eurofinseu.com

ENHANCING POTENCY ASSAYS THROUGH SEMI-AUTOMATION: A CASE STUDY ON INCREASED CONSISTENCY AND REDUCED HANDS-ON TIME

Dr. Frances Reichert, Technical Specialist Biologics, Eurofins BioPharma Product Testing Germany

The Importance of Potency Assays in Biopharmaceuticals

Semi-automation in cell-based potency assays offers significant advantages in improving consistency and reducing hands-on time. Potency assays are essential for evaluating the biological activity of biopharmaceuticals and ensuring compliance with regulatory requirements like ICH Q6B. These assays must accurately reflect the drug's mode of action to yield reliable, physiologically relevant results, which are vital for quality control in pharmaceutical manufacturing.

Challanges with Traditional Cell-Based Bioassays

Cell-based bioassays typically involve living cells, multiple pipetting steps, and handling of small volumes, which can lead to inherent variability within assays, between analysts, and across different days. These challenges, coupled with low sample throughput, extensive analyst training, and health risks from repetitive manual pipetting, such as repetitive strain injury (RSI), can reduce efficiency and accuracy in manual bioassay methods.

Solutions

To overcome the limitations of manual bioassays, Eurofins BioPharma Product Testing implemented semi-automation using advanced instruments, including the Integra VIAFLO96, Integra ASSIST PLUS, and Hamilton Microlab STAR. These tools help streamline potency assays, improving consistency, enhancing sample throughput, and increasing overall efficiency, all while maintaining high standards of accuracy and reliability.

Case Study

In a case study evaluating a peptide agonist with the cAMP Hunter™ Bioassay Kit, the initial results using the semi-automated method showed high replicate variability and overestimated potency values compared to manual assays. However, after optimising pipetting speeds and reagent additions, the results significantly improved. Potency recoveries reached 103% and 93%, closely aligning with the expected 100% value, demonstrating the effectiveness of optimising automation protocols for consistent results.

The Future of Bioassay Automation

Semi-automation proved to be a valuable tool for potency assays, increasing throughput and reducing analyst time without sacrificing accuracy and precision. However, careful optimisation of automation methods is essential to ensure effective implementation. This case study highlights the potential of modular automation to improve bioassay efficiency, reduce manual workload, and ensure reliable quality control in biopharmaceutical manufacturing, pointing to a promising future for assay technologies.

TESTING FOR ELEMENTAL IMPURITIES IN PHARMACEUTICAL PRODUCTS

Sharon McGeachie, Scientist and SME for ICP-MS, Eurofins BioPharma Product Testing UK

ICP-MS is a powerful analytical technique that detects and quantifies trace elements by ionising a sample in an argon plasma and separating ions via a mass spectrometer. The process involves sample aerosol generation, ion extraction, ion beam focusing, mass filtering through a quadrupole, and detection by electron multiplication.

The theory and components of ICP-MS, including the nebuliser, spray chamber, torch, plasma, interface cones, ion optics, quadrupole mass analyser, and detector, are crucial for accurate elemental analysis.

The ICH Q3D guideline needs to be adhered to when testing for trace elements, which standardises the risk assessment and control of elemental impurities in drug products. This guideline applies to new and finished pharmaceuticals and classifies 24 elements based on toxicity and likelihood of occurrence into types 1, 2A, 2B, and 3.

The guideline outlines acceptable daily exposure (PDE) levels based on toxicity data and specifies evaluation through risk assessment, which includes identifying potential sources, measuring impurity levels, and deciding on control measures. Four assessment options (option 1, 2a, 2b, and 3) offer flexible paths depending on the formulation and daily dosage.

In this case study, we illustrate real-world applications by showing the successful validation of lead testing for a compliant drug product

Why:
Client A required ICP-MS analysis to determine what was present within their sample to ensure compliance with ICH Q3D guidelines.

For whom:
This case study is designed for clients who are looking for elemental impurity testing in line with ICH Q3D requirements.

How:
We conducted a risk assessment screening on three batches of the product, producing a semi-quantitative elemental "fingerprint" for over 50 elements. The results indicated that Lead was present, close to the permitted concentration limit set by guidelines, while no other concerning elements were detected.

Since no measures could be taken to reduce lead levels, it is now essential to test all future batches after manufacture to accurately quantify the lead content. A GMP validation was also completed for the product, quantifying Lead against the specified guidelines.

Outcome:
Client A now has a fully validated method that can be used to test each manufactured batch of their product, ensuring that Lead levels are below the required limits and that the product is safe for patient consumption.

NEW CONSULTING SERVICE COMPLEMENTS TESTING CAPABILITIES AND PROVIDES CLIENTS WITH FULL RANGE OF REGULATORY COMPLIANCE SOLUTIONS

Linda Musitelli, Business Unit Manager, EBPT Consultancy Services, Eurofins Regulatory & Consultancy Services Italy

At Eurofins BioPharma Product Testing Consulting, we strive to provide our clients with comprehensive solutions that go beyond analytical testing. We provide expert consultancy services that complement our testing capabilities, enabling clients to meet regulatory compliance requirements, optimise processes, and ensure product safety and quality.

Regulatory and compliance challenges require an integrated approach. Companies operating in the biopharma sector must ensure that analytical results align with stringent regulatory requirements. Our consulting services bridge this gap by integrating world-class testing with regulatory strategy, facilitating compliance, and optimising operational efficiency through a comprehensive range of solutions, including:

- Regulatory Compliance and CMC Support: Expertise in dossier preparation, submission strategies, and post-approval compliance. This includes CMC documentation review to support drug development and lifecycle management (CTD, variations, regulatory intelligence).
- Facility and Equipment Qualification: Ensuring GMP compliance through structured validation plans and risk assessments (IQ, OQ, PQ protocols, regulatory compliance).
- Process Validation: Developing robust and reproducible manufacturing processes (E&L strategy, USP 1663-1665, BPOG, cleaning validation, disinfectant qualification).
- Safety and Toxicological Assessments: Assessing impurities, performing PDE calculations, and ensuring safety compliance (ICH Q3A/Q3B, Q3D, nitrosamines, ICH M7, OEL, QSAR, in-silico prediction).
- Environmental Risk Assessment: Identifying and mitigating environmental risks associated with manufacturing activities.

The increasing complexity of regulatory frameworks demands a structured approach to compliance. From early-stage product development to market authorisation and post-approval modifications, Eurofins BPT Consulting provides tailored expertise to navigate the evolving landscape. Eurofins BPT Consulting's collaboration with Eurofins' network of laboratories ensures that testing and consultancy efforts are aligned, reducing delays and improving regulatory submission outcomes.

By integrating analytical excellence with regulatory insight, we support streamlined compliance, minimise uncertainties, and help clients bring safe, high-quality products to market.

Our combined approach offers:

- A single-source solution for testing and regulatory compliance.
- Faster and more efficient regulatory approvals.
- Enhanced product quality and safety assurance.
- Optimised operational efficiency and risk management.

Learn more about how Eurofins BioPharma Product Testing Consulting can support your projects at www.eurofins.it/consultancy-services/biopharma/

AAV-BASED GENE THERAPIES: A REVOLUTIONARY METHOD TO QUANTIFY EMPTY/(PARTIALLY) FILLED CAPSIDS

Kassiani Kytidou, Senior R&D Scientist
Sabine van der Sanden, Head of Department, Viral Safety & Cell Banking,
Eurofins BioPharma Product Testing Netherlands

Adeno-associated viruses (AAVs) are small, non-enveloped viruses with a single-stranded DNA genome. They are increasingly used as vehicles for gene transfer in gene therapies. AAV-based gene therapies have emerged as a novel therapeutic modality in the past few decades, with over 200 clinical trials and six EMA/FDA approved therapies. AAV-based clinical trials target five main therapeutic areas: blood disorders, eye disorders, central nervous system disorders, neuromuscular disorders, and additional disease areas that are still under clinical trials, showing promising results and the significant impact on the patient community.

AAVs are the most promising gene transfer viral vectors that show established long-term gene expression in different tissues. Constant improvements to recombinant AAV cassettes and capsids contribute to optimal gene delivery and successful therapeutic outcomes. However, inconsistency in AAV preparations during manufacturing processes leads to product heterogeneity and negatively affect the gene delivery. Additionally, impurities can influence bioavailability and biodistribution of the particles, potentially causing undesired immunogenic
reactions.

To ensure the quality and regulatory compliance of AAV preparations, fast, robust, reliable, and GMP-compliant analytical methods are needed. A revolutionary method using Mass Photometry (MP) is now being implemented for GMP-compliant measurement of empty, full, and partially filled AAV viral particles, to ensure that the product falls within the justified release specifications for the amount of empty or partially filled particles that can impact the therapeutic outcome, as directed by FDA/EMA guidelines. MP is a light scattering-based technique that detects individual, unlabelled molecules in dilute solutions. A single AAV particle, in contact with a glass coverslip, is exposed to a beam of light and produces a small, but measurable light scattering signal. This signal is directly proportional to the particle's mass. SamuxMP® from Refeyn Ltd. is a mass photometer tailored to the characterisation of AAV particles, using a method/software that is compliant with FDA 21 CFR 11 (US) and EU GMP Annex 11.

Using MP for AAV characterisation (empty/full/partially filled) has many advantages over the orthogonal techniques, such as analytical ultracentrifugation, transmission electron microscopy, and size exclusion chromatography coupled to multi-angle light scattering. These benefits include:

- lowing AAV packaging (measurements of all subpopulations) in three stages:
  - Vector development stage (packaging efficiency, manufacturability)
  - Manufacturing process: optimisation of purification process
  - Final QC testing
- Rapid analysis, requiring minimal sample amount (10-20 µL, 1E11 particles/mL) and sample preparation
- Easy measurement with a very low turnaround time (2 min)
- Applicable to all AAV serotypes without method adaptation

Eurofins BioPharma Product Testing Netherlands is now leading the implementation and development of this innovative method under GMP conditions, in accordance with ICH guidelines, to offer it as a new service to customers.

EUROFINS BIOPHARMA PRODUCT TESTING IRELAND ACHIEVES *MY GREEN LAB CERTIFICATION*

my green lab certification.

Eurofins BioPharma Product Testing Ireland is proud and excited to announce they received a My Green Lab Platinum Certification in May 2025.

Key areas of the laboratory under review for the certificate were process control, HPLC, CE and ICE, which undertook the journey starting in Q3 2024 and have now completed the reassessment in May 2025 with a hugely successful outcome.

My Green Lab Certification is a proven, scalable program that helps organisations achieve their sustainability goals. It offers tried-and-true methods rooted in science to dramatically reduce the environmental impact of laboratories without disrupting the critical work underway. Recognised by the United Nations Race to Zero campaign as a key measure of progress towards a zero-carbon future, My Green Lab Certification is considered the gold standard for laboratory sustainability best practices around the world.

"We are delighted to join a community of hundreds of laboratories that have been My Green Lab certified. A sincere thank you to all who contributed to this success, notably the sustainability team and area management who engaged and drove the process." – Jean Keating, Deputy Managing Director, Eurofins BioPharma Product Testing Dungarvan.

More information about this program can be found at www.mygreenlab.org/green-lab-certification

Our live and on-demand webinars

Understanding PFAS in Pharma: Risks, Regulations, and Readiness, 9th of July, 2-3 pm CEST

This webinar offers a concise and practical overview of PFAS — persistent and pervasive chemicals increasingly under regulatory scrutiny. Aimed at pharmaceutical professionals, the session will explore the fundamentals of PFAS, recent regulatory trends, and how a risk-based approach can support informed decision-making and compliance planning.

Register here

Navigating Nitrosamine Challenges: From Risk Assessment to Enhanced Ames Testing and Analytics, 21st of July, 11-12 am CEST

Our esteemed panel of experts will navigate through the regulatory frameworks established by the EMA and FDA, offering insights into risk assessment strategies, enhanced Ames test and cutting-edge analytical techniques crucial for Nitrosamine detection as well as OECD 471 adaptation, and detection strategies using LC-MS/MS and GC-MS.

Register here

Also available on demand, contact us at: information@bpt.eurofinseu.com