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EUROPEAN NEWSLETTER

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ADVANCING AAV THERAPIES TO REGULATORY APPROVAL - SUPPORTING EU RELEASE

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The genetic medicine landscape continues to accelerate, with rapid advances across modalities, including lentiviral *ex vivo* therapies, CRISPR-based gene editing, and RNA/oligonucleotide technologies. Among these, *in vivo* AAV (Adeno-Associated Virus) gene replacement therapies represent the largest portion of late-stage clinical pipelines and the majority of gene therapies progressing toward regulatory approval. AAV vectors deliver a functional gene directly to patient cells using a replication-incompetent viral system – an approach that introduces unique analytical challenges due to biological complexity, lot-to-lot variability, and inherently small batch sizes.

Since 2017, approximately 10 AAV therapies have received FDA approval, with seven also approved by the EMA. While both agencies maintain rigorous review standards, their approaches to QC release requirements differ.

Critical Quality Attribute (CQA)	Characteristic	Analytical Method[1]
Identity	Confirm correct vector genome sequence	Sanger Sequencing
		Next Generation Sequencing (NGS)[2]
	Confirm correct capsid	Mass Spectrometry
		Capsid ELISA
		Western blot (automated and manual)
	Confirm Genetic Payload	qPCR
		ddPCR
Purity	Quantification of process Impurities	Host cell DNA by ddPCR
		Host cell protein by ELISA
		Residuals by HPLC
		Residuals by LCMS
		Residuals by ELISA
	Quantification of Product Related Impurities	% Empty vs Full Capsid by AUC
		% Empty vs Full Capsid by SEC-MALS
		Aggregates by DLS
		Aggregates by SEC-MALS
		Replication Competent AAV
		Purity by CE-SDS
Potency	Cell based assay to demonstrate biological activity related to the mechanism of action	Western blot (automated and manual)
		ELISA
		Cell based reported Assay
	Cell based assay to demonstrate transgene expression	TCID50 Infectivity Assay
Quantity	Determination of Strength or Dose	ddPCR
		qPCR
Safety	Sterility	Ph. Eur. 2.6.1
	Endotoxin	Ph. Eur. 2.6.14
	Mycoplasma	Mycoplasma qPCR[2]
	Advantage Agents	Cell based Replication Competent Testing
Stability	Visual Inspection	Ph. Eur. 2.9.20
	Colour	Ph. Eur. 2.2.2
	Clarity	Ph. Eur. 2.2.1
	pH	Ph. Eur. 2.2.3
	Osmolality	Ph. Eur. 2.2.35

[1] *Methods listed below are not fully comprehensive of EBPT Ireland's AAV Gene Therapy capabilities but give an overview of critical methods requested by the EMA. If information on additional methods are required please don't hesitate to reach out to EurofinsBPT-IE@bpt.eurofinseu.com.*

[2] *Note these methods are not currently offered at our Ireland site but are offered at other sites in our European network where testing for EU release can be wholly managed and coordinated by EBPT.*

The FDA typically applies a flexible, risk-based philosophy, whereas the EMA requires a more prescriptive, fully developed analytical package prior to commercialisation. In the EU, AAV gene therapies fall under the category of Advanced Therapy Medicinal Products (ATMPs) and, importantly, are not covered by any Mutual Recognition Agreements. As mandated by EU Directive 2001/83/EC, Article 51(1)(b), ATMPs must undergo in-country testing within an EU member state before market release.

To meet EMA expectations, manufacturers must apply orthogonal analytical strategies for each Critical Quality Attribute (CQA), including identity, potency, purity, quantity, safety, and stability. The accompanying table outlines these CQAs and the gold-standard analytical methods typically required.

At Eurofins BPT Ireland, we are exceptionally well positioned to support clients preparing AAV therapies for the European market, with extensive experience in the commercial release of AAV programmes and in generating data packages for regulatory filings. As shown in the accompanying table, our laboratory delivers the complete suite of QC methods required for both AAV drug substance and drug product, supported by deep technical expertise in method development, validation, transfer, and comparability assessments essential for EMA submissions. Leveraging our strong track record in producing robust regulatory-ready datasets, we help de-risk submissions and accelerate programme progression right through to commercial release.

Significant recent investment has further strengthened our gene therapy offering, including the expansion of our Biosafety Level 2 facilities and the addition of a purpose-built laboratory dedicated to AAV potency testing. We are also proud to be the first contract testing laboratory in Europe to offer GMP AUC, underscoring our leadership in advanced AAV characterisation and our commitment to expanding industry leading and life-enhancing capabilities.

With cutting-edge capabilities, regulatory expertise, and a proven record in supporting commercial release for global gene therapy programs, Eurofins BPT Ireland stands ready to help bring the next generation of transformative AAV therapies to patients across Europe. For more information contact us at: EurofinsBPT-IE@bpt.eurofinseu.com or visit: https://eurofins.ie/bpt.

ETHANOL UNDER THE BIOCIDAL PRODUCTS REGULATION: A DEFINING REGULATORY MILESTONE FOR THE EUROPEAN MARKET

Simone Bertolini, Senior Consultant, Team Leader Chemicals, Eurofins BioPharma Product Testing Italy

This whitepaper explores the regulatory outlook for ethanol as a biocidal active substance in the European Union, with particular emphasis on its evaluation under the Biocidal Products Regulation (BPR) and its potential harmonised classification under the Classification, Labelling and Packaging (CLP) Regulation. Ethanol is one of the most widely used active substances in disinfectants, notably for human hygiene, surface disinfection and food-contact applications (Product Types 1, 2 and 4), making its regulatory status critically important for public health and industry alike.

Despite its long history of use, ethanol is currently subject to heightened regulatory scrutiny. The key issue is the possible classification of ethanol as a carcinogenic, mutagenic or toxic for reproduction (CMR) substance under CLP. As CLP classification is based solely on intrinsic hazard rather than exposure scenarios, such a classification could occur even though biocidal uses primarily involve dermal exposure. If ethanol were classified as CMR category 1A or 1B, it would meet the exclusion criteria under the BPR and could only be approved via a time-limited derogation, subject to strict conditions. The whitepaper outlines the complex interplay between BPR approval and CLP classification processes, involving national authorities, ECHA scientific committees and final decisions by the European Commission. As of early 2026, the Biocidal Products Committee confirmed the safe use of ethanol for representative biocidal applications and did not support a CMR classification due to insufficient and non-relevant data. However, ongoing discussions at EU level mean that regulatory uncertainty remains.

Several future scenarios are examined, highlighting potential consequences such as restricted consumer access, increased regulatory burden, reformulation challenges and broader impacts across related legislation, including REACH, cosmetics regulation and worker protection rules. The paper underscores the importance for manufacturers and supply chain actors to proactively strengthen data packages, anticipate regulatory outcomes and prepare for market adaptation.

For more information contact us at: information@bpt.eurofinseu.com or read our whitepaper.

UNDERSTANDING THE NEW CHAPTER ON LEACHABLES ASSESSMENT FOR TOPICAL OPHTHALMIC DRUG PRODUCTS

Daniele Zarini, ERT, Senior Consultant and Team Leader, Eurofins BioPharma Product Testing Consulting Europe
Francesco Tessari, Technical Business Manager, Eurofins BioPharma Product Testing Italy

The recently released **USP <1664.3>** chapter represents an important extension of the U.S. Pharmacopeia Extractables and Leachables (E&L) framework, providing guidance specifically tailored to **topical ophthalmic drug products.** It applies to a wide range of formulations, including solutions, suspensions, emulsions and ointments, and addresses the unique E&L risks associated with these dosage forms. In particular, the chapter focuses on interactions between ophthalmic formulations, manufacturing equipment and container–closure systems over the full product shelf life.

Ophthalmic drug products present distinctive Leachables assessment challenges due to the extreme **sensitivity** of the ocular route of administration and the very low dosing volumes typically involved. Even trace levels of leachable compounds may pose a potential safety risk, requiring a **more refined and scientifically justified approach** than that used for many other dosage forms. At the same time, manufacturers must ensure that E&L programmes remain proportionate and efficient throughout development and commercialisation.

USP <1664.3> addresses these challenges by building upon the principles established in the existing <1664> series while introducing safety-based thresholds specific to ophthalmic use. These thresholds support a risk-based determination of study scope, analytical sensitivity and overall programme complexity.

By clearly linking toxicological considerations with analytical expectations, the chapter provides practical direction for designing fit-for-purpose Leachables studies aligned with **regulatory expectations.**

The chapter also fits within a broader, evolving regulatory landscape. Alignment with frameworks such as ICH Q3E supports the development of globally acceptable, regulator-ready E&L strategies that balance patient safety with development efficiency. More broadly, USP <1664.3> reflects USP's ongoing efforts to promote harmonised, risk-based E&L practices across dosage forms. These efforts are further reinforced by the planned **revision of the USP <1664> subchapters across 2025 and 2026,** which aim to refine and clarify dosage form–specific expectations and strengthen consistency across the compendial framework.

For more information contact us at: information@bpt.eurofinseu.com or watch the webinar here: https://attendee.gotowebinar.com/recording/8396357227648986205

VIRAL SAFETY 2.0 - THE POWER OF NEXT-GENERATION SEQUENCING

Snehit Satish Mhatre, Senior Scientific Director, Eurofins BioPharma Product Testing Denmark

Traditional viral safety testing has long relied on *in vivo* and *in vitro* adventitious agent tests – methods that, while foundational, are limited by their narrow scope and lengthy turnaround times. As biopharmaceutical complexities increase, the industry has been transitioning toward viral safety, driven by the transformative power of Next-Generation Sequencing (NGS).

The challenge: risk and uncertainty

For clients, the limitations of legacy testing manifest as significant risks. Patients face the potential threat of "dark matter" viruses: emerging or cryptic contaminants that traditional assays fail to detect due to lack of specific primers or narrow host-cell susceptibility. For the client, these gaps translate into regulatory uncertainty and operational bottlenecks. A contamination event detected late in the manufacturing cycle can lead to catastrophic facility shutdowns, supply chain disruptions, and most importantly, compromised patient safety. Furthermore, the 28-day duration of traditional cell-based assays delays the delivery of life-saving therapies, particularly in the fast-paced field of Advanced Therapy Medicinal Products (ATMPs).

The solution: a client-centric NGS strategy

As a service provider, making NGS "client-centric" means evolving beyond mere data generation to provide actionable intelligence. By leveraging Metagenomic NGS (mNGS), Eurofins BPT offers a "catch-all" diagnostic tool that identifies known and unknown sequences simultaneously. To address client pain points, our approach focuses on:

- **Accelerated timelines:** reducing testing cycles from weeks to days, allowing for faster batch release.
- **Bioinformatic clarity:** translating complex genomic data into simplified, risk-based reports that ease the burden of regulatory filings.
- **Mitigation of false positives:** implementing robust bioinformatic pipelines to distinguish between environmental noise and genuine biological threats.

Ultimately, NGS is not just a technological upgrade; it is a commitment to a higher standard of care. By integrating NGS, Eurofins BPT provides clients with a proactive safety net, ensuring that the path from bench to bedside is swifter, more transparent, and uncompromisingly secure.

For more information, visit: Next-Generation Sequencing (NGS) - Eurofins Denmark

EUROFINS BIOPHARMA PRODUCT TESTING STRENGTHENS ITS PRESENCE IN SPAIN WITH THE OPENING OF A NEW LABORATORY IN MADRID

Ana Pascau, Microbiology Lab Manager, Eurofins BioPharma Product Testing Spain
Macarena Cuadros, Head of Quality Assurance and Qualified Person, Eurofins BioPharma Product Testing Spain
Elena Fariña, Site Manager, Eurofins BioPharma Product Testing Spain

Eurofins BioPharma Product Testing is pleased to announce the opening of its new laboratory in Madrid, further strengthening its footprint in Spain alongside its established BioPharma Product Testing site in Barcelona. This expansion reflects our continued commitment to supporting pharmaceutical and biotechnology manufacturers with high quality, local GMP testing services, backed by the strength of a global network.

Located in Alcobendas, Madrid, the new laboratory has been purpose-built to support pharmaceutical manufacturing and R&D sites across the central region of Spain. With a total area of 266 m^2 and designed with future expansion in mind, the site enables faster response times, improved logistics, and enhanced sample stability, significantly reducing the risks associated with long-distance sample transport.

The Madrid laboratory complements the Barcelona site by focusing on critical facility support, validation activities, and microbiological quality control services. Key offerings include pharmaceutical water testing, environmental monitoring of cleanrooms, pharmaceutical gas testing, microbiological QC testing, and consulting services related to EU GMP Annex 1 and Contamination Control Strategies (CCS). Comprehensive on-site sampling services are available, allowing for rapid execution and water analysis within the first 24 hours.

As with the Barcelona laboratory, the new Madrid site operates under Eurofins BioPharma Product Testing' harmonised global quality system, fully aligned with GMP requirements. It benefits from validated IT systems, robust data integrity processes, and seamless access to Eurofins' centres of excellence for advanced microbial identification and specialist testing. Innovative solutions, including validated recombinant Factor C (rFC) endotoxin testing, further enhance the service portfolio.

Led by an experienced pharmaceutical leadership team, the Madrid laboratory combines strong local expertise with direct access to Eurofins BioPharma Product Testings global network of laboratories. Together, Barcelona and Madrid laboratories provide comprehensive, flexible, and reliable support to pharmaceutical companies across Spain, reinforcing our long-term commitment to the Spanish market and its promise of "Testing for Life".

STREAMLINING PHASE I & II TRIALS — END TO END, THE EUROFINS WAY

Florent Brun, Sales Director, Clinical trials and bioanalysis in the biopharmaceutical sector – Phase I clinical trials in France
Stephanie Burger-Prin, Marketing Director Europe, Eurofins BioPharma Product Testing

Launching an early phase clinical programme shouldn't mean juggling complexity.

Yet for many sponsors, Phase I–II development still involves multiple vendors, fragmented workflows, rising costs, and avoidable delays. Every handover introduces risk. Every misalignment slows progress.

Eurofins removes that burden.
We deliver a fully integrated, end to end clinical solution designed around one priority: **helping you move faster, with confidence, and with full control** — from first clinical batch to final study report.

One partner. One workflow. Total alignment.
Eurofins supports pharmaceutical and biotechnology companies across their Phase I and Phase II programmes through a single, coordinated network that connects **manufacturing, clinical supply, clinical operations, bioanalysis and data science.** By eliminating fragmentation, we simplify execution, reduce risk, and accelerate timelines — without compromising scientific rigour.

From IMP manufacturing to site delivery — seamlessly
Your programme begins with the **development, GMP manufacturing, quality control, stability studies and batch release** of Investigational Medicinal Products (IMPs). Once released, we take full ownership of the clinical supply chain, including **packaging, labelling, blinding, global distribution and ancillary supply,** ensuring investigator sites are ready, on time, every time.

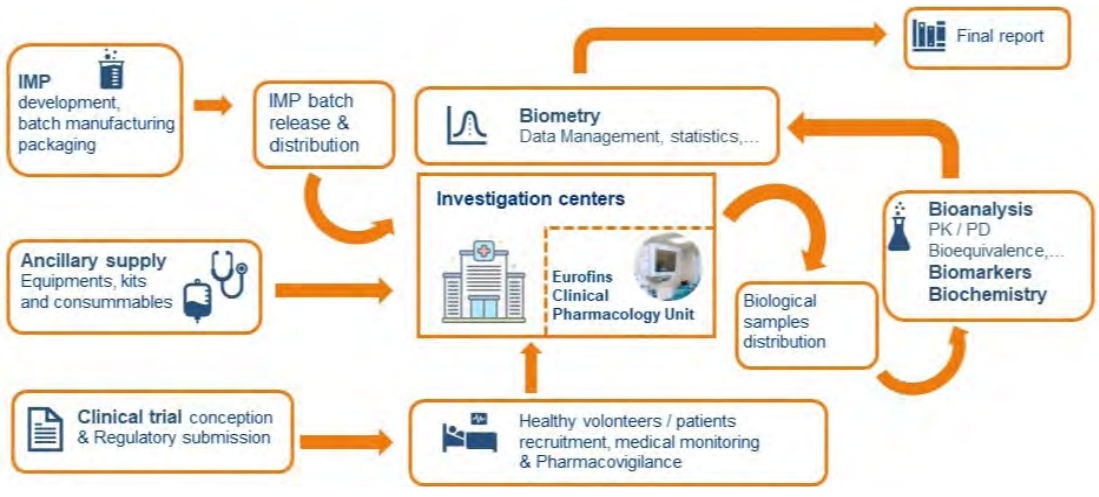
Built around your early phase strategy
Beyond execution, Eurofins supports you in shaping the right development strategy. Our teams contribute to **study design, feasibility assessments and regulatory submissions,** helping you make informed decisions early. **Volunteer and patient recruitment** is managed through established databases and trusted clinical partnerships to secure efficient enrolment and keep studies on track.

Proven Phase I excellence
At our dedicated pharmacology unit near Grenoble, **Eurofins Optimed** conducts the full spectrum of Phase I studies, including **First in Human, SAD/MAD, food effect and drug–drug interaction studies.** Throughout the study, our medical teams provide continuous **medical monitoring and pharmacovigilance,** ensuring participant safety and regulatory compliance at every stage.

Integrated bioanalysis and data insight
Clinical samples are centrally managed and transferred with full **temperature controlled traceability** to our analytical centres. At our **Eurofins ADME Bioanalysis facility in Vergèze,** we provide high quality bioanalysis for small and large molecules, including **pharmacokinetics, immunogenicity and biomarker assessments.**
To close the loop, our biostatistics experts deliver **data management, statistical analysis and PK/PD modelling,** transforming complex data into clear, decision ready insights to support milestones and regulatory filings.

The result: a streamlined, scientifically robust development pathway with fewer interfaces, greater visibility, and faster progress towards proof of concept.

With Eurofins, early clinical development becomes simpler, more predictable — and ultimately **brings innovative therapies to patients sooner.**



VIRAL CLEARANCE: PRINCIPLES, STUDY DESIGN AND BEST PRACTICES FOR ENSURING BIOLOGICS SAFETY

Elena Morelli, PhD - Study Director Virus Testing Laboratory at Eurofins BioPharma Product Testing Italy

Developing biologics - whether monoclonal antibodies, recombinant proteins, or advanced therapy medicinal products (ATMPs) - demands a robust and well designed viral clearance strategy. Today's manufacturers face increasing complexity: evolving regulatory expectations, diverse product modalities, and the need to demonstrate viral safety with high scientific rigor.

One of the most critical challenges lies in understanding viral removal and inactivation mechanisms within complex manufacturing processes. Designing representative scale down models that accurately reflect commercial conditions is equally demanding, particularly when working with innovative therapies or novel platforms. At the same time, ensuring alignment with regulatory guidelines such as ICH Q5A requires a deep understanding of study design fundamentals and best practices. When not addressed effectively, these challenges can lead to delays, data gaps, and increased development and regulatory risk.

Our approach is built around transforming these complexities into clear, actionable strategies. By combining science driven, risk based methodology, in depth process understanding, and strong regulatory expertise, we design viral clearance studies that are both fit for purpose and regulator ready. From early development through manufacturing, we support the definition of robust clearance claims, selection of appropriate model viruses, and execution of studies that demonstrate process reliability with confidence.

Beyond testing, we act as a strategic partner, helping clients anticipate risks, optimise study design, and ensure consistency across development stages. The result is reliable, scalable, and compliant data, enabling faster decision making and smoother regulatory interactions.

Ultimately, viral clearance is not just a regulatory requirement—it is a strategic pillar of biologics development, ensuring patient safety while accelerating the path from concept to clinic and beyond.

For more information contact us at: information@bpt.eurofinseu.com or watch the webinar here: https://attendee.gotowebinar.com/recording/4211203656405316954