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EUROPEAN NEWSLETTER

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THE POWER OF SPR BIACORE™ AND BLI OCTET® IN QC GMP METHODS

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Surface Plasmon Resonance (SPR) using the Biacore™ (Cytiva) platform and Bio-Layer Interferometry (BLI) using the Octet® (Sartorius AG) platform are powerful, label-free, optical biosensor technologies that produce real-time analysis of biomolecular interactions. Unlike traditional methods, such as ELISA, both SPR and BLI eliminate the need for labelling with fluorescent or enzymatic tags, allowing the direct assessment of kinetic parameters and binding affinity with high sensitivity and reproducibility.

In a comparative case study, assays were established on both platforms using the same ligand and a therapeutic monoclonal antibody as analyte. The reference standard representing 100% nominal potency was included in both setups.

In the first assay, varying concentrations of the analyte were evaluated for binding to human recombinant CD32 ligand. A linear regression model was fitted using PLA 3.0 software (Stegmann Systems) to determine the relative potency.

In the second assay, the association and dissociation of the analyte with the recombinant CD16a ligand were assessed using various concentrations of the reference standard and the sample. Binding affinities (KD values) were then calculated using instrument-specific software. Both technologies demonstrated high accuracy and precision in determining relative potency and binding affinities. This provides major advantages over label-based technologies such as ELISA. When comparing both technologies we found that SPR was more precise than BLI, making it particularly well-suited for applications requiring detailed kinetic resolution. In contrast, BLI technology has a shorter assay run time, making it advantageous for high-throughput screening workflows.

In summary, both SPR and BLI offer distinct benefits. Based on our experience, the rapid assay format of BLI is ideal for screening applications, while SPR provides precise kinetic and affinity data, and in some cases, higher sensitivity. Both technologies represent robust, label-free alternatives to traditional endpoint assays, enhancing the reliability and efficiency of biopharmaceutical characterisation and potency assessment.

For more information, visit: www.eurofins.de/advanced-spr-biacore-and-bli-octet-services-for-biopharmaceutical-analysis.pdf

NAVIGATING NITROSAMINE CHALLENGES - FROM RISK ASSESSMENT TO ENHANCED AMES TESTING AND ANALYTICS

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Understanding the evolving landscape and practical solutions for control

Nitrosamines have emerged as a critical concern in pharmaceutical development due to their potential carcinogenicity and the widespread contamination incidents involving drugs like sartans, ranitidine, and metformin. These events have prompted global regulatory bodies, including the EMA and FDA, to tighten guidelines and demand robust control strategies across the drug lifecycle.

Why Nitrosamines Matter

Nitrosamines can form unintentionally during manufacturing or storage through nitrosation reactions between precursor amines and nitrosating agents. Their mutagenic and genotoxic properties make them a serious safety issue, requiring proactive risk management and scientific rigor.

A Risk-Based Approach to Control

Controlling nitrosamine impurities begins with a structured risk assessment process:

- Identify potential sources of nitrosamine formation
- Evaluate formation mechanisms based on manufacturing and formulation factors
- Prioritise products for testing based on risk level

Cross-functional collaboration is key, bringing together regulatory, analytical, and toxicological expertise to ensure comprehensive risk mitigation.

Toxicological Evaluation and Regulatory Alignment

Determining Acceptable Intake (AI) limits involves using structure–activity relationship (SAR) models, literature data, and scientific justification. Transparent communication with regulators is essential to align on methodologies and ensure compliance.

Enhanced Ames Testing: A Smarter Way to Detect Mutagenicity

The Enhanced Ames Test, a refined version of OECD TG 471, is gaining traction as a preferred method for evaluating nitrosamine impurities. Recommended by ICH M7 (R2), it offers improved sensitivity through:

- Use of up to 30% rat and hamster liver S9 for metabolic activation
- Inclusion of nitrosamine-specific positive controlsA 30-minute pre-incubation step to enhance interaction between test compound and bacteria

While water remains the preferred solvent, alternatives like acetone, methanol, or DMSO may be used with caution to avoid interference.

Suspicion of presence? Analysis of your pharmaceutical products must be performed

If a risk is identified, Marketing Authorisation Holders (MAHs) must perform confirmatory testing (by screening or validated method) to verify or rule out the presence of nitrosamines. The results must be communicated as soon as possible. If the presence of nitrosamine(s) is confirmed, MAHs must implement effective risk mitigation measures by submitting a variation.

Eurofins BioPharma Product Testing uses its experience in chromatography coupled by mass spectrometry detection (LC-MS/MS/GC-MS/MS/head space GCMS) at your service. With over 100 developments completed since 2020, our project managers provide services from screening to routine GMP testing of your finished products and active ingredients.

From Insight to Action

Navigating nitrosamine challenges requires more than compliance, it demands innovation, collaboration, and a deep understanding of both chemistry and regulation. At Eurofins Biopharma Product Testing, we support clients with end-to-end solutions, from risk assessment to validated analytical methods and enhanced mutagenicity testing.

EUROFINS BPT ITALY OFFERS ENHANCED ACCESS TO VIRAL CLEARANCE STUDIES

Giulia Sbarufatti, Business Unit Manager Virus Testing - Eurofins BioPharma Product Testing - Italy

Eurofins BioPharma Product Testing (BPT) Italy has officialy launched Viral Clearance Services at its Milan site, further expanding the Eurofins BPT network's global footprint in viral safety services.

Since 2009, the Virus Testing Unit in Milan has supported biopharmaceutical companies with viral inactivation studies (e.g., low pH and solvent/detergent treatments) on their products. In response to the growing development of biologic drugs and increasing awareness of viral safety requirements, the expansion into viral removal studies represents a significant enhancement of our analytical capabilities. This milestone strengthens both Eurofins BPT's global offering and its local presence in Europe.

What differentiates us is our flexible, client-focused approach, each study is tail ored to meet the specific needs and expectations of our clients. Additionally, our reduced backlog allows for faster project initiation, offering a critical time advantage in development timelines.

Clients can choose between two service models:

- A standard full-service model, in which Eurofins BPT conducts the entire study, including technology transfer and scaleddown process execution with virus spiking and detection.
- A hybrid-service model, where clients access our virus testing facility and use our purification equipment (e.g., ÄKTA systems or filtration setups), while our expert Virology Team manages all virological operations, including spiking, sampling, and virus detection.

The Virus Testing Unit operates within a GLP-compliant testing facility, supported by a comprehensive viral library (over 40 strains, including XMuLV, PRV, MVM, and Reo-3), a 450 m² laboratory, an ÄKTA Pure 25 system, and all necessary equipment for viral clearance studies.

For further information and details click here.

PFAS IN PHARMACEUTICALS: A SCIENTIFIC AND REGULATORY PERSPECTIVE

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PFAS (Per- and Polyfluoroalkyl Substances) are a large group of synthetic chemicals known for their extremely strong carbon-fluorine bonds. This bond gives PFAS exceptional thermal and chemical stability, making them resistant to degradation—hence the nickname "forever chemicals."

These substances are widely used across industries such as textiles, construction, cosmetics, and food. In the pharmaceutical sector, PFAS play a crucial role not only as active ingredients but also in manufacturing equipment, packaging, and excipients. Their amphipathic nature, thermal resistance (up to 150 °C), chemical inertness, good cleanability and vapour resistance make them ideal for a lot of purposes during drug manufacturing, research and development, and quality assurance processes. PFAS functional group contribute to optimising important drug parameters such as bioavailability, binding affinity to the therapeutic target and elimination through catabolism enhancing efficacy and safety of medicines.

However, their persistence in the environment raises serious concerns. PFAS accumulate in water, soil, and living organisms, including humans, and have been linked to adverse health effects. Managing their spread is complex and costly, with significant socio-economic and regulatory implications.

Since 2009, the Stockholm Convention has restricted certain PFAS, but finding viable alternatives remains a challenge. In 2020, EFSA set a group tolerable weekly intake of just 4.4 ng/kg body weight for four PFAS in food, underlining their toxicity even at trace levels.

Currently, there are no specific guidelines for PFAS in pharmaceuticals. A precautionary approach is essential, based on general risk management principles. And this is precisely where our expertise comes in: we support companies in assessing PFAS-related risks through tailored risk assessments. These include identifying contamination sources, evaluating human exposure, assessing toxicity, and characterising risk—steps that guide regulatory actions and mitigation strategies.

A control's analytical strategy can be implemented following the risk assessment. Its level of specificity is tailored to the required task, ranging from determining overall fluorine content using 19-NMR to quantitative determination of specific PFAS using LC/MS. LC/MS is considered the gold standard for PFAs analysis due to its exceptional sensitivity and specificity.

Certain key aspects must be considered in this analytical strategy, especially when using LC/MS, such as the risk of contamination due to the ubiquity of PFAs and the optimisation of the analytical process, including sample preparation.

Thanks to our expertise in analysing trace residues in pharmaceutical products and our use of advanced analytical techniques, our laboratories are ideally suited to developing new methods for this challenging area of PFAS analysis.

NEW: RAPID STERILITY TEST RESULTS IN FOUR DAYS

Sara Baroni, Marketing Specialist - Eurofins BioPharma Product Testing - Italy
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In recent years, the regulatory landscape has encouraged the adoption of rapid microbiological methods as alternatives to traditional sterility compendial tests, which currently require a minimum incubation time of 14 days. General chapters 5.1.6 of the European Pharmacopoeia and <1223> of the USP provide clear guidelines on the implementation of alternative methods, emphasising the possibility of selecting the most suitable technology based on the product type, provided it is properly validated and demonstrated to be comparable to traditional methods.

In response to this regulatory evolution and the growing demand to reduce release times, benefiting both patient safety and manufacturing companies, Eurofins BioPharma Product Testing (BPT) Italy has adopted a multi-technological approach, integrating rapid and automated methods to support clients in choosing the most suitable solution.

In addition to the classic compendial sterility test Ph. Eur. 2.6.1/USP <71>, Eurofins BPT Italy now offers the following innovative technologies in compliance with 21 CFR Part 11 and data integrity:

- RedOne® by Redberry (based on Solid Phase Cytometry): sterility test in four days. With high sensitivity and automation, it supports early decision-making in batch release processes.
- Celsis® by Charles River (based on ATP bioluminescence): rapid detection through ATP bioluminescence. This allows product release in a minimum of six days with significant optimisations for large sets of samples.
- BacT/ALERT 3D: automated test for cellular products, validated according to the specific chapter of the pharmacopoeia EP 2.6.27. It's suitable for cell-based preparations with high complexity or reduced shelf life.

The adoption of rapid and automated microbiological methods drastically reduces the time-to-results, prevents production blocks, optimises deviation management, and improves timely patient access to advanced therapies.

Eurofins BPT Italy is a strategic partner in the implementation of innovative solutions, in line with the principles of Quality by Design and Process Analytical Technology, promoted by the FDA and EMA.

MICROBIOLOGICAL ASSAY OF ANTIBIOTICS: METHODOLOGY, VALIDATION, AND REGULATORY COMPLIANCE

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The activity of an antibiotic is estimated by comparing the growth inhibition of sensitive microorganisms caused respectively by known concentrations of the antibiotic to be examined (theoretical potency of the finished product - sample) and a reference substance (SCR or USP standard with known potency).

Routine assay involves preparing the standard and the sample in order to obtain working solutions of the sample with a theoretical concentration equivalent to that of the standard. From these working solutions (sample and standard), the assay ranges for the standard and sample are prepared by dilution and deposited in the cups or cylinders. Antibiotic solutions diffuse into the seeded agar medium, creating inhibition diameters after incubation.

The European Pharmacopoeia, like the USP, specifies the solvent to be used to solubilise the antibiotic, the strain(s) to be used to inoculate the recommended medium, and the incubation temperature.

These inhibition diameters are imported into a Combistats sheet (EDQM statistical analysis software) to check titration conformity by statistical analysis. The potency or activity of the sample will be the combination of the results of 2 (or more) assays, expressed in IU, mg or other units of the sample, for the cup method according to the European Pharmacopoeia.

For the USP cylinder technique, the result is expressed as a combination of the results of 6 assays, expressed as a % of the 100% target value and calculated according to a USP calculation sheet. The Combistats or USP spreadsheets are checked against the examples given in the two Pharmacopoeias.

Each technique applied routinely will, beforehand, have undergone either a method validation or a method transfer in order to verify the feasibility of the technique under the laboratory's operating conditions.

In parallel, the physico-chemical quality of the antibiotic is assessed through tests such as identification, assay, dissolution, impurities, and water content, according to ICH Q6A and relevant pharmacopoeial monographs. This dual approach ensures efficacy, safety, and regulatory compliance.