

BioPharma Services
News
BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

Cost-effective, high-quality USP Reference Standards essential for compendial testing

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The United States Pharmacopeial Convention (USP) sets primary standards for quality control and assurance in pharmaceutical development and manufacturing. It is the only provider of the official Pharmacopoeia standards for the analysis of pharmaceutical ingredients, per USP and the National Formulary. These official standards help ensure that product testing will meet GMP compliance requirements, e.g. of the U.S. Food and Drug Administration.

Eurofins BioPharma Product Testing has added a new subsidiary, Eurofins PHAST, a USP Authorised Distributor and only official source for Reference Standards of the USP in Europe for compendial testing.

Official USP Reference Standards can help save time and resources in quality control in the pharmaceutical manufacturing process, from raw materials through product development to finished products. USP Reference Standards are used to demonstrate identity, strength, purity, and quality for medicines, dietary supplements, and food ingredients. When used according to the monograph, there is no longer a need to invest in the development of internal standards where equivalence must be proven to the authorities. USP Reference Standards are rigorously tested and evaluated by several independent regulatory, academic, and commercial laboratories to confirm accuracy and reproducibility.

In total, Eurofins PHAST offers more than 7,000 Reference Standards, of that, more than 3,700 USP Reference Standards and 2,800 European Pharmacopoeia Standards. With this comprehensive offering, Eurofins PHAST provides exactly the Reference Standards clients need in daily routine QC analyses. In addition, the cooperation with Eurofins PHAST offers the following benefits:

- **A step ahead in GMP compliance**
- **Always the official batch/lot deliverable**
- **Verified quality, early warning in case of recalls or changes**
- **Accepted by authorities, e.g. FDA**
- **Fast delivery to clients' sites:**
  - **EU-import from USA**
  - **Customs declaration**

For its customers, Eurofins PHAST has set up the website *www.reference-standards.com*. After registration and receiving the password, the delivery programme stored in a protected area can be viewed. The trilingual website (English, German, and French) also offers the option of requesting a PDF catalogue containing the available Reference Standards and its selling prices. If the Reference Standard you are looking for can not be found, please contact the sales team at: *reference-standards@phast.com*. Please note that only written orders can be accepted.

N°21 - October 2018

Eurofins CDMO: highly potent drug development from early stage

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High-potency drugs present numerous opportunities for improved drug selectivity, efficacy, and safety profiles and represent a growing area of global development focus for applications such as oncology and hormone-based treatments. Although this class of molecules offers numerous benefits to patients, they require particular care and attention in ensuring the safety for those involved in their manufacture and handling. Eurofins CDMO presents global offerings for the development of high-potency drugs, from API production to formulation and manufacture of clinical and commercial materials, including:

Drug substance (API)

Eurofins CDMO has significant experience in technology development of complex API molecules for scale-up manufacture. High Potency APIs (HPAPIs) are frequently structurally complex, requiring sophisticated process, manufacturing, and analytical methodologies. Particular challenges associated with HPAPIs relate to safe containment and handling practices and include:

- **Engineering, environmental, and cGMP controls in line with current guidance and best practices**
- **Dedicated equipment, including isolators and auxiliaries**
- **Equipment and instrument cleaning procedures, analytical methods & criteria**
- **Institutional training and general & product-specific SOPs**

In addition to establishing innovative synthetic routes, manufacturing processes and analytical controls, a Eurofins CDMO development programme will evaluate and implement appropriate toxicity control strategies for HPAPIs.

Drug Product (Finished Product)

In parallel, Eurofins CDMO provides a wide range of drug product development services for HPAPIs, from early development to clinical, and further to commercial supply. Eurofins CDMO has successfully developed, transferred, and supported the commercial manufacture and distribution of dry, liquid, and semi-solid finished product forms, for cytotoxics, hormones, and other high-potency products.

In addition to their inherent toxicity, high-potency drugs frequently present formulation challenges requiring specific strategies, such as low aqueous solubility, poor bioavailability, food effects, and high inter-subject variability. Thanks to containment facilities and specialised technologies, Eurofins CDMO has set up specific tools for the formulation of high potency and poorly soluble entities based-upon their specific molecular characteristics and according to multivariate, design-of-experiment (DoE) approaches. With the benefit of more than 20 years of experience and a strong track record in development, Eurofins CDMO is the preferred partner to bring your challenging highly potent drug product to market within optimised timelines. For more information visit: *www.eurofins.com/biopharma-services/cdmo*

Protein formulation studies to optimise biopharma product's shelf-life

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Protein formulation studies begin with a thorough understanding of the clinical requirements for the biopharmaceutical product, including dosage form (liquid or lyophilised), concentration, pH, and long-term stability. The protein under development may lose activity over time or undergo degradation that limits its shelf life. Common pathways of protein degradation include aggregation, deamidation, oxidation, and loss of structural integrity. Based on the sponsor's required product characteristics and anticipated degradation pathways, multiple formulation candidates are prepared and screened in stability studies.

The optimal pH for a protein's stability can be determined in pH-stability screening studies with various buffer types and tested for degradation events (deamidation, aggregation, loss of activity, etc.). Antioxidants may be needed if the protein is susceptible to oxidation.

To minimise aggregation, polysorbates may be added to the formulation at low levels. The use of sugars and salts may be needed if the protein is to be formulated at high concentrations. If the dosage form requires ambient temperature storage or is not stable in a liquid formulation, Eurofins Advantar Laboratories can design a lyophilised formulation and lyophilisation cycle.

The formulation candidates are typically screened at real time and accelerated stability. The following analytical tools enable the collection of rapid and accurate results to identify the most stable formulation candidates. The formation of degradation products can be assessed by capillary electrophoresis (CE-SDS) on a SCIEX PA800 or by UPLC on an Agilent 1290. Dynamic light scattering (DLS) on a Wyatt Dynapro can be used as an early indicator of the on-set of aggregation. Size exclusion HPLC with a Wyatt multiangle light scattering detector (MALS) rapidly determines the molecular weight of protein aggregates. Protein deamidation and other events that change the charge of the protein can be monitored by capillary isoelectric focusing (cIEF) on a Protein Simple iCE system. ELISA experiments can be performed with Molecular Devices plate readers to evaluate the protein binding behavior.
For more information, visit: *www.eurofins.com/bpt*

Eurofins Lancaster Labs offers several options for container-closure integrity testing

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Container-closure integrity testing (CCIT) is required by the US and EU regulatory agencies in lieu of sterility testing to ensure a product's continued sterility, safety, and quality throughout shelf life. While sterility testing is important, it has limitations such as it is destructive to the sample, requires a product fill that is supportive of microbial growth, will only detect viable microorganisms present at the time of the test, and contamination can cause false positive results. Eurofins offers the full suite of USP <1207> probabilistic and deterministic technologies for CCIT, and provides consultation so that clients may choose the most appropriate and compatible CCIT methodology for each product-package system.

In addition to microbial immersion, dye immersion, and bubble emission testing, Eurofins offers full method development, validation, and routine testing services for the following USP <1207.2> deterministic methodologies. All deterministic technologies are non-destructive to the sample with the exception of Helium Leak Detection.

- **Pressure/Vacuum Decay measures a change in pressure over time, which correlates with leak size. This technology is suitable for use with rigid or flexible packages containing small molecule liquid or lyophilised products. The sensitivity is approximately 5 microns.**
- **High-Voltage Leak Detection (HVLD) uses an electrical current to detect leaks. This technology is suitable for use with large and small molecule liquid-filled parenteral drug products packaged in both vials and syringes. The sensitivity is approximately 2 microns.**
- **Oxygen Headspace Analysis measures the concentration of oxygen in the headspace of transparent rigid containers. A change in the oxygen concentration over time indicates a leak. This technology is suitable for use with lyophilised parenteral drug products or any product packaged with an alternate gas overlay, such as nitrogen or argon. The sensitivity is less than 0.2 microns.**
- **Helium Leak Detection quantitates the flow rate of helium tracer gas from defects in packaging. Helium is drawn through the defect by vacuum and detected using a mass spectrometer. This method is the most sensitive option, allowing for the detection of leak rates as small as 10^{-10} mbar·L/s.**

A well-executed container-closure integrity study ensures that patients receive sterile, safe, and quality medications. For more information, visit: *www.Eurofins.com/Medical-Device.*

Inhalation testing enhances Eurofins BPT service portfolio for all drug delivery systems

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Inhalation drug products represent a significant and expanding portion of the overall pharmaceutical, biopharmaceutical, and generic markets. The Asthma and Chronic Obstructive Pulmonary Disease (COPD) markets alone are expected to exceed $50 billion annually by the year 2022. Beyond these respiratory diseases, inhalation delivery is also used for a variety of additional treatments: neurological disorders, poorly soluble drugs, nanoparticle delivery, etc., making it one of the fastest expanding delivery technologies.

Specialised drug-device combination products are used to deliver drugs directly to lungs: pressurised metered dose inhalers (pMDI), dry powder inhalers (DPI), and nebulisers. While the chemical testing (assay, related substances, etc.) of these products is very similar to those of the other delivery routes (parenteral, ophthalmic, oral, etc.), the inhalation performance testing of the devices is very specialised and technically challenging. The performance testing measures the ability to deliver the correct amount of the drug to the correct location in the lungs. Several specialised tests are used to properly monitor the performance: spray pattern, leak rate, dose content uniformity, through-life, shot weight, and most importantly aerodynamic particle size, which measures how deeply into the lung the drug is being delivered.

With the recent acquisition of the Eurofins BPT Columbia facility (previously EAG labs) located in Columbia, MO, Eurofins is now able to offer this testing to its customers. The Columbia facility has been performing inhalation testing for over 15 years on both developmental and commercial products. The expert technical team has decades of experience working on all types of inhalation devices. The facility includes two temperature and humidity controlled inhalation testing rooms along with all specialised instrumentation. This addition now means that Eurofins can provide analytical testing services for all drug delivery systems, which are utilised in the pharmaceutical market. Combined with the existing testing, synthesis, and manufacturing services, this further establishes Eurofins as the premier contract laboratory in the industry. For more information, visit: *www.eurofins.com/bpt*

Innovative, specialised testing from Viracor Eurofins helps biopharma companies and healthcare professionals improve patient care

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As a specialty laboratory with over 30 years of experience and more than 2,500 validated tests in the areas of molecular and infectious disease, allergy/hypersensitivity, and immune response monitoring, Viracor Eurofins helps biopharma companies and hospitals with innovative testing to support clinical trials and evolving clinical diagnostic needs.

One such example is a new cytomegalovirus (CMV) gene sequencing assay for resistance to letermovir, the most recent FDA-approved CMV antiviral for use in adult Hematopoietic Stem Cell Transplant (HSCT) patients. While there has been no resistance identified in treatment-naive patients, clinical trials have shown resistance can develop in UL56 after exposure for some HSCT patients. Laboratory testing is recommended to quickly confirm the occurrence of resistance, as treatment modification based solely on clinical suspicion may result in added toxicity and increased time and complexity in patient management, if resistance is present in the patient.

The CMV Resistance: Letermovir sequencing assay, made commercially available in May 2018, is designed to detect identified mutations in the UL56 genes of CMV. The use of genotypic sequencing offers a rapid turnaround time, a broad range of antiviral resistance information, and the ability to provide information concerning new drugs as they become available.*

The newest assay is available as a standalone test or as a complete panel that includes the other CMV antiviral drugs ganciclovir, foscarnet and cidofovir. The panel is designed to detect identified mutations in the UL54, UL56 and UL97 genes of CMV. These new assays add testing options that help physicians across the continuum of care for immunocompromised patients.

In addition to clinical testing innovations, Viracor Eurofins partners with biopharmaceutical companies to help with complex assay design/transfer, optimisation and validation of assays to support the needs of study protocols. For more information, visit *www.viracor-eurofins.com*.

Kotton, C. N., Kumar, D., Caliendo, A. M., Åsberg, A., Chou, S., Danziger-Isakov, L., & Humar, A. (2013). Updated International Consensus Guidelines on the Management of Cytomegalovirus in Solid-Organ Transplantation. Transplantation Journal, 96(4), 333-360. doi:10.1097/tp.0b013e31829df29d

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