

**BioPharma Services**

News

BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

Charged Aerosol Detection

A powerful enabling tool for a CDMO in Biopharmaceutical Formulation and Development

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The biopharmaceutical industry has experienced an exponential growth in the number of site-directed drugs. These specifically targeted drugs are effective at lower doses and minimise or eliminate side effects. Site-directed delivery of DNA or RNA therapeutics often relies on nanoparticles to deliver their payload. Delivery to the cell nucleus typically involves the use of a solid lipid nanoparticle (SLN). The components of these lipid nanoparticles are critical to their effectiveness.

The analysis of nanoparticles is challenging as many of the components cannot be detected by traditional HPLC-UV. Eurofins Advantar scientists develop HPLC methods that employ a sensitive charged aerosol detector (CAD) to quantify these non-chromophoric components. For example, scientists use UHPLC-CAD method to measure multiple lipids and their degradation products (lyso-PC and free fatty acids) to support the analysis of a client's lipid nanoparticle drug product.

The useful application of HPLC-CAD goes well beyond the analysis of nanoparticles. Many antibiotics (gentamicin, streptomycin, tobramycin), including the broad spectrum anti-MRSA antibiotics in development cannot be measured by UV, but are perfect candidates for HPLC-CAD analysis. For example, Eurofins

Advantar manufactures and tests a topical antibiotic cream, paromomycin, for the US Army. This antibiotic cannot be measured by UV. Scientists have optimised and validated HPLC-CAD assays for the analysis of potency and purity in this drug product.

Carbohydrates in many drug products such as mannitol, sucrose and carboxymethyl cellulose can now be measured by HPLC-CAD. Polymers such as polyethylene glycol and dextrans are easily measured by HPLC-CAD. Even counter ions in drug products, such as sodium and potassium, can be measured by HPLC-CAD.

With experts in method development, formulation and 10 charged aerosol detectors at our site, Eurofins Advantar has been helping Biopharma clients advance their nucleic, antibiotic, and carbohydrate drug products to market. Offering non-sterile manufacturing services with a highly experienced staff in a 1,200 ft² manufacturing suite that includes an ISO 8 clean room, this FDA-inspected facility is ideal for GMP manufacturing of a wide range of non-sterile topical products, including clinical products. For more information visit: www.advantarlabs.com

Eurofins Medical Device Testing's new Package Testing Lab enhances global services

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Packaging and labelling play an important role in the delivery and use of medical devices, and documentation of packaging validations must be submitted in applications to regulatory agencies. Packaging materials and configurations are instrumental in protecting the product from damage during transportation from manufacture to point of use, as well as providing appropriate barrier protection. Package labelling is also a regulated element for medical devices; it is important for tracking product information, branding, and instructions-for-use. Labelling must be durable and remain legible until the point-of-use. Failures in readability have led to numerous product recalls.

Eurofins Medical Device Testing built a state-of-the-art Package Testing Lab to provide critical testing support to clients for both the protective properties of packaging, as well as the durability of their labelling. The Package Testing Laboratory provides additional capabilities to the Chemical Characterisation, Microbiology/Sterility, and Biocompatibility service offerings at the company's Lancaster, PA, site. Continually expanding comprehensive medical device testing capabilities among its network of 16 sites globally, Eurofins Medical Device Testing is further positioned to help clients navigate regulatory pathways in the US, EU and Asia Pacific. Eurofins Medical Device Package Testing offers:

Conditioning Accelerated Testing: With over 80,000 ft³ of monitored environmental chambers, clients can subject their products to a broad range of temperature and humidity conditions to assess the robustness of their packaging to withstand different conditions their product would undergo. Real-time shelf life studies can be performed concurrent with regulatory submissions using accelerated aging studies.

Isotopic fingerprinting: an efficient method to characterise pharmaceutical molecules

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The World Health Organisation estimates counterfeit pharmaceuticals at more than 10% of the global medicine market. The products most affected include both bulk ingredients, in which Active Pharmaceutical Ingredients (APIs) are produced and purchased in bulk for use in the manufacturing of finished pharmaceuticals, and the finished products themselves. The issues that are often



Distribution Testing: No matter how or where your product is shipped, Eurofins Medical Device Testing's state-of-the-art distribution testing equipment can simulate the stresses of shipping on products. Standard ASTM and ISTA distribution cycles, as well as custom programmes, can be performed that simulate stacking, manual handling, and vibrations associated with various forms of transport, as well as pressure changes that can be seen during air or mountainous product transportation.

Materials Testing: Materials Testing is used to verify the properties of packaging materials. The laboratory is equipped to perform a broad range of mechanical and material tests on raw materials and finished packaging designs, including tensile, torque, tear, burst, and bend testing. Understanding these properties vary between raw material suppliers, how they may change over time, or after exposure to sterilisation, is critical in properly designing effective packaging.

After any shelf-life testing or distribution simulations, further product testing is often required. Eurofins Medical Device Package Testing Lab is able to conduct a wide range of testing to ensure the product packaging has been properly designed such as: visual inspections, operational testing, product property testing, sterility testing, seal integrity testing, and label testing, including barcode verifications. For more information visit:

www.eurofins.com/medical-device

implicated in bulk ingredients are the infringement of patent and trademark rights.

Given the wide range of products and practices that come under the "counterfeit" umbrella, no single method is available for the identification and prevention of counterfeit medicines. Amongst the anti-counterfeiting technologies that have been developed are those based on stable isotope analyses, in which the unique chemical properties of a substance provide forensic evidence of its manufacturing process or the raw materials used.

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Isotopic fingerprinting

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The two most commonly used methods for measuring stable isotope ratios are IRMS (Isotope Ratio Mass Spectrometry), which measures isotope ratios of several elements (C, H, N, O, S), and SNIF-NMR (Site-specific Natural Isotope Fractionation studied by Nuclear Magnetic Resonance spectroscopy), which provides information on different molecular sites simultaneously. Recent technological developments have made it possible to measure site-specific $^{13}\text{C}/^{12}\text{C}$ ratios directly using quantitative ^{13}C NMR, improving the ability to investigate the origin of active ingredients. This "isotopic" approach has been applied to the authentication of commonly used generic pharmaceuticals, such as ibuprofen and naproxen, demonstrating its potential to



provide evidence in cases of patent infringement or to help track a product along its supply chain.

As Eurofins Scientific was founded 30 years ago based on its patented SNIF-NMR technology, the Group has the scientific experience and expertise to support clients' most challenging testing projects.

For more information visit: www.eurofins.com

New scenarios for biological evaluation of medical devices with new ISO 10993-1 standard

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All medical devices, even when used appropriately, present a certain degree of risk to a patient. Manufacturers are required to weigh risks and benefits of a device. An essential tool for the evaluation of the potential biological risks is the ISO 10993 series of standard.

The ISO Technical Committee 194 is in charge of this series and is currently revising the main standard: ISO 10993-1 "Biological evaluation of medical devices, Part 1: Evaluation and testing within a risk management process." This part is an advanced stage as the draft (DIS) was approved for registration as final draft (FDIS) late last year. A lot of editorial and technical changes were made to the current document, and the most relevant are:

- *A brand-new Annex A "Endpoints to be addressed in a biological risk assessment" (the annex containing the*

very famous Table) was revised as normative, including new columns for specific endpoints in line with FDA requirements (physical and/or chemical information and material mediated pyrogenicity as well as columns for chronic toxicity, carcinogenicity, reproductive/developmental toxicity and degradation)

- *The Annex B was completely revised to include the provisions of ISO/TR 15499:2016 "Biological evaluation of medical devices—Guidance on the conduct of biological evaluation within a risk management process"*
- *New approach for the evaluation of transitory contacting devices*
- *Additional information on the evaluation of non-contacting devices, nanomaterials, absorbable materials and breathing gas pathways in healthcare applications (referenced in ISO 18562 series) was provided.*

The approach to biocompatibility is changing, moving towards an evaluation based upon review of relevant established scientific data, physico-chemical characterisation and *in vitro* testing, with *in vivo* testing only being carried out to fill gaps in our understanding. All device types (all device categories, with all types of contact, and all durations of contact) will require a chemical characterisation as a prerequisite for the risk assessment. The data coming from the chemical characterisation should be toxicologically assessed to elucidate the need for further tests to address the relevant biological endpoints for the device under evaluation.

Eurofins experts are happy to support manufacturers facing this change, providing testing and offering regulatory expertise during the entire medical device life cycle. For more information, visit: www.eurofins.com/medical-device/

Eurofins Lancaster Laboratories, Ireland, expands facility and introduces new training programme to support Bioanalytical and Molecular Cell Biology Testing

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Eurofins Lancaster Laboratories in Dungarvan, County Waterford, Ireland, is poised to meet the growing needs of clients with the completion of major building expansions and staff training initiatives. The expansion project will increase the capacity from 2,700m² to 9,000m² by Q3 2018, adding 4,400m² to its footprint with laboratories designated specifically to the Bioanalytics & Molecular Cell Biology to the existing laboratory. The development of an 1,800m² second site on the campus has allowed for expansion of Stability Storage capacity; additional laboratory space for Raw Materials, Microbiology Validation Studies, Training; and the introduction of a new Device Testing laboratory.

With an increased demand to support the full set of release testing of client biologic products, this expansion will increase the current Bioanalytical Testing area and introduce new technologies in Molecular Cell Biology such as Bioassay, ELISA and qPCR. This allows clients increased flexibility within the Eurofins network and ensures more agility with key testing capabilities available all at one site. To ensure sufficiently trained personnel on-site to support this Biologic growth phase in Dungarvan, Eurofins' technical leads engaged with the National Institute of Bioprocessing Research and Training (NIBRT), based on the campus of the University College of Dublin, to develop a Eurofins bespoke Bioanalytical & Molecular Cell Biology training programme.

The Eurofins / NIBRT Bioanalytical & Molecular Cell Biology Training Course has accomplished many of the below key objectives for its business and has introduced and developed the candidates' scientific knowledge of the Biopharmaceutical Industry from the early stages of developing a biologic drug product—from genetic engineering through to the production process—and the analytical requirements to assess the critical attributes of a Biologic product.

The NIBRT Facility has a small scale Biopharmaceutical production process that allows candidates to see the various stages in the upstream and downstream of a Biopharmaceutical production plant. The importance of each stage in the biological production lifecycle is reviewed with the candidates in detail and how the Bioanalytics and Molecular Cell Biology Analysis play a role in identifying the critical attributes of a Biologic product, enabling an in depth understanding of client products and production processes.

The training programme was such an immense success during the launch in September 2017, it is offered again at the NIBRT facility in April 2018 and will be shared with the Eurofins' network of Biologic laboratories.

These expansions and investment into bespoke Biologic training reinforces Eurofins commitment to enhancing services and quality and continuing to strengthen agility for customers.

For more information visit: www.eurofins.com/biopharma



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