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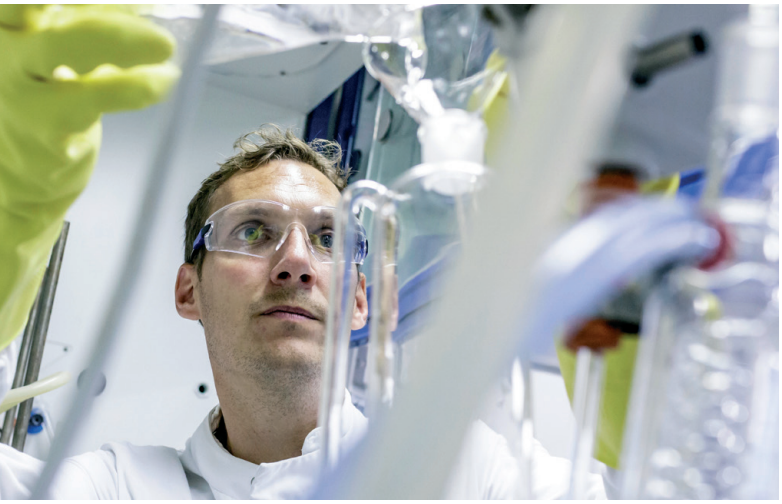
News

BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES



Eurofins offers Integrated Drug Discovery programme options

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When considering using the services of a Contract Research Organisation (CRO) to work on a drug discovery project, companies have to decide on their outsourcing strategy. Some prefer to use a wide variety of different suppliers, seeking the best specialists for different components of the drug discovery process. Others prefer to work with CRO providers who can integrate the services and provide integrated drug discovery (IDD), where a multi-disciplinary project team's drug discovery experience is brought on behalf of the client's drug discovery project. Eurofins Pharma Discovery Services can offer customers both of these options.

There are multiple advantages to customers of working with an IDD provider. Contractually, IDD typically operates under a single Master Services Agreement (MSA) with work orders governing the research to be carried out, thereby keeping to a minimum the contractual burden on the company. Additionally, a project manager within the CRO will manage the CRO's multi-disciplinary operations, therefore reducing the project management required at the outsourcing company, compared to working with multiple different suppliers.

The drug discovery companies that were acquired by Eurofins each offer different services in the drug discovery process. These companies were brought together in one subdivision - Eurofins Pharma Discovery Services - to offer a full portfolio of services to assist the customer in their drug discovery research. Joining Eurofins in December 2017, Eurofins Selcia Drug Discovery completed the portfolio of services. Selcia Drug Discovery has a 10-year track record of offering integrated drug discovery projects to customers, whereby experienced multidisciplinary drug hunters (employees who were from big Pharma) work as a project team supporting customers with innovative drug screening cascade and medicinal chemistry design, with the goal of identification of a pre-clinical drug candidate. Harnessing the combined capabilities of the Eurofins Pharma Discovery portfolio of services in these IDD projects allows Eurofins to enhance customers' outsourcing drug discovery experience and evolve with the market needs.
For more information visit: *www.selcia.com/drug-discovery*

ISO 18562 Standards reduce hazards for Medical Device Breathing Pathways

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All medical devices must be assessed for biocompatibility. Medical devices containing breathing gas pathways (e.g. ventilators, breathing tubes, and anesthesia equipment) have traditionally been evaluated as external communicating devices according to the ISO 10993 series of international standards. Unfortunately, this approach leads to testing that provides questionable benefits and may result in hazards being missed. Therefore, a new set of standards – ISO 18562 – was released in March 2017. This four-part series is specifically geared towards the biocompatibility evaluation of breathing gas pathways in healthcare applications. ISO 18562-1 outlines the overall risk management process for the biocompatibility evaluation, while parts two through four each address a specific type of hazard.

To support its clients, Eurofins now offers the full spectrum of testing required by the ISO 18562 series of standards to assess these three hazards. The first hazard is the emission of particulate matter. To evaluate this hazard, a particle counter is used to detect any particles in gas passing through the device.

ISO 18562-3 addresses the second hazard of volatile organic compounds (VOCs) emitted from the gas pathway. As air passes through the device, the VOCs are collected on a thermal desorption tube. These VOCs are then analysed by gas chromatography mass spectrometry (GC/MS) to identify and quantify them.

Leachables in condensate are the final hazard. During usage, water condenses inside the gas pathway. Compounds may then leach from the medical device into the condensate. Per ISO 18562-4, an aqueous extraction is first performed. Inductively coupled plasma optical emission spectroscopy (ICP-OES), direct injection GC/MS, and liquid chromatography mass spectrometry (LC/MS) are used to identify the leachables. Identification of these compounds is needed for a toxicologist to provide an accurate safety assessment. To identify the leachables, Eurofins' scientists use the Eurofins Extractables Index, its proprietary database of over 1,500 compounds, in conjunction with the Wiley/NIST databases.

Complete understanding of the requirements of ISO-18562 is important in order to save valuable resources when working to get a medical device to market. The analytical scientists and toxicologists at Eurofins are prepared to help clients meet this new testing requirement. For more information, visit: *www.eurofins.com/medical-device*

Don't get lost in EU Medical Device regulation harmonisation

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Harmonised standards (HS) are one of the key pillars of the European regulatory approach to medical devices. HSs are European standards developed by request of the European Commission to the European Standards Organisations (e.g. CEN). In line with the pivotal James Elliot legal case judgment, HSs are now seen as measures of European Union law, and the publication of an HS takes a form of an "official" European Commission decision.

The references of HSs are published in the Official Journal of the European Union, and the last publication in the medical device field is dated November 2017 with 159 standards cited for the Medical Device Directive, 37 for *In Vitro* Diagnostic and 36 for Active Implanted Medical Devices. More than 170 European standards were refused to be published due to a lack of compliance.

No standard is yet harmonised for the "new" Medical Device Regulation (MDR) because of a lack of an official mandate from the Commission to the European Standards Organisations to develop standards in compliance to MDR. The mandate is expected to be ready within the first half of this year, and it will be based on a step-wise approach with a prioritisation of standards.

The top priority topics are the quality management system (EN ISO 13485), risk management (EN ISO 14971), symbols and labelling (EN ISO 15223-1 and EN 15986), and good clinical practice (EN ISO 14155) with the aim of having these standards harmonised as soon as possible or at least by the end of the "transition period" (May 2020). Other horizontal standards (e.g. ISO 10993 series) are expected to have longer periods--in view of the Technical Committee work plans--to be harmonised. Semi-horizontal and product-specific standards will be last to be harmonised.

Having less than one year for the top priority standards from the mandate to the full implementation of MDR could be an issue. To meet the deadline and avert the risk of not having HSs, the Commission created a pool of technical consultants to support the entire cycle of the development of harmonised standards.

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

Engineering APIs to improve bioavailability–

Using the science of SSRD and PreForm to drive API development and improvement of drug product performance

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Therapeutic effectiveness of a drug depends upon its bioavailability - the fraction of an administered dose of an active pharmaceutical ingredient (API) that reaches the systemic circulation. Physicochemical characterisation of an API is a critical tool of an Investigational New Drug (IND), enabling development and the selection of the optimum drug candidate.

Solubility, dissolution and GI permeability are fundamental parameters that control rate and extent of drug absorption and its bioavailability. Optimising the parameters of the API through the selection and design of physical forms (polymorphs, salts, solvates, co-crystals, etc.) provides an opportunity to enhance drug bioavailability early in the development process. A systematic and extensive screening is recommended to discover and develop stable and formulation-suitable solid forms. Eurofins Alphora Solid State R&D and Drug Product Operations teams work together to provide scientifically sound development services from API solid form discovery through pre-formulation and a final dosage form.

Eurofins Alphora's high throughput screening (HTS) programmes for polymorph, solvate, salt, and co-crystal discovery allow experimentations using only minimum (mg) quantities of API, resulting in a significant reduction in cost, manpower and time. Integration of the HTS with an automated multi-sampler PXRD system provides rapid experimentation, exploring different crystallisation methods and conditions.

With the introduction of Pion µFlux and µDissolution technologies, Eurofins Alphora's Preformulation scientists can help to assess and rank order the solubility and drug absorption potential of APIs and finished products, thus optimising candidates far earlier in the development process. Furthermore, Eurofins Alphora Formulation Scientists have various techniques available to enhance the solubility and ultimately the bioavailability of the API through particle size reduction and amorphous dispersions. Collaboration between Eurofins Alphora's development teams help our clients achieve early clinical success in a more rapid and cost-effective way. For more information visit: *www.eurofins.com/cdmo*

Analytical considerations for administering drugs using food vehicles

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Administration of drugs using foods/liquids as a vehicle is needed for subjects with inadequate swallowing capabilities. This would include pediatric and geriatric patients, and those with physical impairments. Some drugs are specifically formulated for delivery in foods/liquids as sprinkles or small beads. This class of pharmaceutical compounds presents a unique challenge when determining the best analytical methodologies to use.

Historically, evaluation of suitable food types for use as a dosing vehicle included limited stability of a selected matrix where assay was the primary test method. Thus, the drug would be mixed with foods (i.e. apple sauce) and stored for a few hours prior to potency testing. The July 2018 FDA draft guidance, "*Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments*" provides specific suggestions for testing of drugs developed to be administered with a food vehicle. The intent of the guidance is to ensure consistency and standardisation for products developed for use with a food vehicle. Analytical recommendations discussed include: *in vitro*, method validation, stability, integrity, potency, impurity evaluation, and homogeneity.

- **Polymorphism** and bead integrity are suggested as part of integrity evaluations, but polymorph evaluation can be complex for drug products. If known polymorphisms are soluble in an aqueous environment, this may not be a critical issue. However, appropriate methodology would be developed to support a drug product if significant solubility differences exist between polymorphs.
- **Potency Assay** requires a validated method and assumes method qualification with food material matrices. Partially dissolved active pharmaceutical ingredients (APIs) in food vehicles will complicate the assay as the API is in two matrices. Homogeneity requires three to six equal portions of the food/DP mixture.
- **Stability** is evaluated at room and refrigerated temperatures over two hours. If potency testing shows loss of API, an impurity assessment is required using a stability indicating method and may require additional qualification with the prospective matrix.
- **Dissolution** testing is required if the API does not dissolve in the food matrix and is complicated if the API only partially dissolves.

The Guidance's decision tree is useful for determining the sample preparation and food vehicle qualifications. Overall, the Guidance adds definition and complexity to drug products for use with food vehicles. Product labeling may require "do not use with" text based on the food vehicle data if the drug product is shown to not be compatible with certain matrices.

With these unique analytical evaluations, a client's study design can be an important factor to ensure regulatory compliance and study success. Eurofins has experience with complex analytical programmes, including food vehicle administration. If the programme requires custom analytical design, Eurofins has the expertise to guide clients to the right fit for any regulatory and technical needs. For more information, visit: *www.EurofinsUS.com/BPT*

Eurofins expands Central Laboratory Shanghai facility

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In 2017, China became the world's second-largest national pharmaceutical market, due to its aging population and rising medical needs. In its ongoing commitment to adapt to emerging trends in the pharmaceutical industry, Eurofins Central Laboratory, a member of Eurofins BioPharma Services, has expanded its facility in Shanghai, China. Since 2015, the China National Drug Administration (CNDA), formerly China Food and Drug Administration (CFDA), has increased its focus on quality driven laboratory data, revising regulations, and creating new enforcement standards. In light of these events, companies have engaged international central lab providers, like Eurofins, to ensure quality data is produced to global standards. Eurofins Central Laboratory continuously monitors both data quality and laboratory operations in its Shanghai, China, facility in accordance with GCP, GLP, CAP and NGSP Level 1 accreditations. This focused effort on quality operations is reflected with the Shanghai location having successful CNDA inspections twice, with no major findings, in the last three years.

The expansion of the Shanghai facility is in response to the growth of clinical trials conducted in China, originating from both Eurofins' International and Intra-China client base. Also, this facility supports comprehensive Central Laboratory Services (safety, efficacy and biomarkers), BioAnalytical Services (Ligand Binding Assays, neutralising anti-bodies, plate based immunogenicity capabilities), and Kit Packing capabilities. Eurofins Central Laboratory deploys Lean, globally standardised processes, enabling high quality GMP and FDA/CNDA/EMA compliant specimen and transportation kits to be distributed worldwide. Each year, Eurofins Central Laboratory produces and ships approximately 800,000 specimen collection and transportation kits to investigator sites all over the world.

With 30 years of experience serving the pharmaceutical and biotech industry, Eurofins looks forward to providing dedicated services to this critical market and region, with continuously expanded analytical capabilities and service offerings. For more information, visit: *www.eurofinscentrallaboratory.com*

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