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News

BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

Cosmetic products: an overview of International Regulatory Systems

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There has been significant growth in the global cosmetics trade in recent years, crossing geographical and generational borders, boosting new trends and new product demand. Novel market segments such as green-cosmetics, natural-cosmetics, and high-tech cosmetics are pushing the limits of Research & Development efforts and product launches. In chasing after efficacy and performance, R&D departments are blurring the border between the cosmetics and pharmaceutical industries as evidenced by new marketing expressions such as cosmeceutical, functional cosmetics and dermal-cosmetics.

Consumers' exposure to cosmetic products is generally higher than to pharmaceutical products, and cosmetovigilance is still on its growing curve. Accordingly, in an attempt to rule the growing cosmetics market, regional agencies have been working on a regulatory system to define rules and laws, enabling producers and importers to develop and trade safe products. In turn, government agencies are overseeing what is on the market. Overall, the main regulatory frameworks are in Europe, Japan, US, Canada, China, Brazil, Australia & New Zealand and the Middle East.

Some areas, for example the USA, use a voluntary registration system approach while others, mainly European and Japanese regulatory systems, require mandatory product filings prior to product marketing. The rules used to distinguish between pharmaceutical and cosmetics products may be significantly different in different countries.

To support global clients, Eurofins BioPharma Product Testing has structured a fully integrated programme to design and execute the set of tests required to develop, produce and launch cosmetic products complying with global regulatory systems through a full service package, including integrated regulatory assessment, dossier editing and preparation, safety and performance testing and clinical centres for performance testing partnering with a network of medical specialists. Among our experts, we have members of the Scientific Committee on Consumer Safety (SCCS) at the European Commission and the Japanese Cosmetic Centre, allowing first-hand updates on novel advancements in the field of cosmetic regulations.

For more information, visit: *www.Eurofins.com/consumer-product-testing/industries/cosmetics/*

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How similar is your biosimilar?

Pre-qualified GLP-compliant assays for biosimilars – fast track assays

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Large molecule generics, often referred to as biosimilars or follow-on biologics, are a major focus of drug development activities. As patents on many major biologics are expiring, it is estimated that $67B of the innovator drug sales will be open for biosimilar competition to 2019.

Biopharmaceutical companies developing biosimilars must prove that their version of the drug is similar to the original, or innovator molecule. In assessing the comparability of proposed biosimilar compounds to the innovator counterparts, regulatory agencies have stressed the "totality-of-evidence" approach, which relies on both structural and functional characterisation, as well as data from animal and clinical studies. Eurofins Bioanalytical Services has developed a suite of pre-qualified assay methods for biosimilars trastuzumab, adalimumab, bevacizumab, rituximab and cetuximab. These assays provide drug developers rapid access to clinical and characterisation data, and as core assays are pre-qualified, the development costs and time are typically half those of full validation using de novo methods.

Clinical Assays include pharmacokinetic (PK) and anti-drug antibody (ADA) assays. These tests are pre-qualified, using innovator standards and calibrators. Eurofins scientists consult with Sponsors who can provide additional biosimilar-specific reagents to further validate the assays to the specific needs of the study. Eurofins can follow both the "one assay" and "two assay" approach to provide flexibility for Sponsor study requirements.

Target binding and Fc receptor binding assays are performed using Biacore™ SPR systems using qualified reagents and methodology. Addition of the Sponsor supplied biosimilar enables rapid validation and analysis. C1q testing by ELISA and ADCC assays further expand the characterisation services available.

The assay sets can be run individually or as a package. Bioanalytical and characterisation packages are tailored to meet the distinct needs of biosimilars developers ensuring accuracy, adherence to standards and on-time delivery of critical data, no matter the size of project. For more information, visit: *http://www.eurofins.com/biopharma-services/bioanalysis/biosimilars/*

Eurofins Lancaster Laboratories delivers one-stop-shop for GMP biosimilar bioassay needs

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Development and validation of cell-based biopotency assays can be a rate-limiting step when building a package of lot release and stability QC tests for a biosimilar. In addition, procurement and qualification of critical reagents, assay cell banks, and critical supplies can be costly, time consuming, and unpredictable. Eurofins Lancaster Laboratories has developed and validated cell-based potency assays for use in testing biosimilars such as filgrastim / pegfilgrastim, etanercept, adalimumab, rituximab, bevacizumab, and infliximab. These assays are ready-to-use to test in-process, drug substance, and drug product biosimilar molecules for their effect on cell proliferation, apoptosis, and/or ADCC activity.

In the world of bioassays, one size does not always fit all. In addition to providing ready-to-use assays for biosimilars, Eurofins Lancaster Laboratories has a team of Ph.D. level scientists dedicated to bioassay method development. This team uses their experience to rapidly redevelop any of the ready-to-use methods into product-specific bioassays that meet the unique requirements of individual clients. In addition to proliferation/apoptosis assays and ADCC assays, the Bioassay Team also has extensive experience in developing and validating a wide variety of bioassays, including reporter gene, intracellular signaling, receptor binding, and CDC assays, as well as ELISA-based potency assays.

Once a method has been developed and validated, Eurofins Lancaster Laboratories also has extensive experience in performing cGMP testing, as well as providing ongoing support in maintaining and trouble-shooting bioassays. Reagents and cell banks used in ready-to-use assays are qualified and maintained by the team, which eliminates the need for clients to manage this aspect of working with a bioassay. This results in lower costs and a streamlined service experience for the client. This broad range of comprehensive experience and capabilities makes Eurofins Lancaster Laboratories the best one-stop-shop for biosimilar bioassay needs. For more information, visit: *www.EurofinsLancasterLabs.com*

Eurofins Medical Device Testing expands Extractables & Leachables capabilities in Germany

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The first step in conducting the biological evaluation of medical devices, as defined in the ISO 10993 standard series, is chemical characterisation. Eurofins Medical Device Testing, an industry leader in this area, with over 50 scientists in its global Extractables and Leachables (E&L) team, is strengthening its capabilities at its site in Munich, Germany.

An accurate chemical characterisation study can save companies time and money when assessing the biological safety of their medical devices. A thorough toxicological risk assessment of the results generated by an E&L study can reduce the need for subsequent *in vivo* tests when evaluating:

- New device or packaging designs
- Changes in raw materials suppliers
- Changes in manufacturing processes

For medical devices in direct or indirect contact with body tissues or fluids, ISO 10993-12 states that solvents of different polarity should be used. Therefore, we use a variety of extraction solvents for simulated use or exaggerated extractions for semi-volatile compounds before GC-MS/FID fingerprint analytics:

- Standard solvents: water, 0.9% saline solution, 5% ethanol in water, isopropanol and n-hexane
- Artificial body fluids, e.g. artificial sweat, gastric juice, urine or saliva
- Customised solvents as dictated by use, e.g. 20-50% ethanol in water, methyl methacrylate

Our specialists have extensive knowledge and expertise to plan and coordinate your studies. Our detailed reports have been used to support many successful regulatory submissions, around the world.

No matter how complex the construction of your medical device, or how exotic the material, our experts will find a way to prepare, extract and analyze it in full compliance with ISO 10933 Parts 12 and 18.

In addition to the GC-fingerprint analysis for semi-volatile organic compounds, Eurofins Medical Device Testing is currently increasing its analytical testing capacity in Munich with the addition of three new analytical techniques at that laboratory:

- Headspace GC/MS-FID for volatile organic compounds
- LC/MS (Q-TOF) for non-volatile organic compounds
- ICP/MS for elements and metals analysis

Eurofins Medical Device Testing's laboratory in Munich operates in compliance with GLP quality systems, and has been accredited to ISO 17025 for biocompatibility testing of medical devices. For 30 years, the team in Munich has been helping medical device companies bring a wide range of products to market. For more information visit: *www.Eurofins.com/Medical-Device*

Extractable studies: managing LC/MS unknown compounds with an internal database

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Unknown compound characterisation has always represented one of the most challenging aspects of analytical chemistry. In the Extractables & Leachables (E&L) field, characterisation of unknown extractables is necessary to provide high quality studies.

Accurate and meaningful toxicological assessments are not possible for unknown compounds, which are commonly treated as the most toxic compounds to provide a worst case assessment. Often, this level of risk does not correspond to the compound's actual toxicological risk. Therefore, a systematic approach to identify unknown extractables is needed to assign the correct degree of toxicological concern.

Unknown compound identification requires experienced analysts, high resolution instrumentation, and dedicated software able to quickly search historical data. Accordingly, Eurofins BioPharma Product Testing continues to invest in LC/MS and GC/MS databases to support their expertise and growth as an E&L service provider. For extractable compounds detected by LC/MS, Eurofins BioPharma Product Testing maintains a proprietary database of over 1,500 compounds.

The first step is to propose an identity using the databases. An attempt is made to confirm the identification by analysing the certified reference standard. If the standard is not commercially available, it may be possible to have it synthesised or to use a chemically-similar surrogate. If an identify cannot be proposed from this initial analysis, an MS/MS study is performed with high resolution mass spectrometers capable of accurate mass determination to at least three decimal places, such as LC-QTOFs and GC-QTOFs, to elucidate the structure based on the fragmentation pathways.

Through the years, Eurofins BioPharma Product Testing has developed the expertise needed to support all phases of an E&L study, including the characterisation of unknown compounds. Eurofins is continuously investing in state-of-the-art equipment to support clients in this critical area on their path to regulatory approval. For more information, visit *www.Eurofins.com/biopharma*

New opportunities for the evaluation of bio-distribution and pharmacokinetic studies of therapeutic products containing metal ions

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Several drugs containing metal ions are used in the treatment of severe medical conditions and illnesses. To determine drug dose, absorption, distribution, metabolism, and excretion of the metal ions for *in vivo* and clinical samples, new analytical technologies and tools have been developed for preclinical and clinical evaluation. The technologies allow for an evaluation of intended and unintended accumulation of metal ions in specific organs and body fluids.

With more than 15 years of experience developing and executing methods for metals analysis, Eurofins BioPharma Product Testing offers the complete range of metal testing services for preclinical and clinical samples, including method development and validation according to EMA or ICH guidelines, as well as testing of whole blood, serum, plasma, urine, tissues such as kidneys, heart, liver, spleen, bone marrow, etc.

Able to detect even minor differences in metal levels for specific samples, Eurofins BioPharma Product Testing can detect down to the ppb level, due to extensive possibilities for sample pre-treatment by microwaves and other sample preparation techniques in a specially designed high pressure room to safeguard samples from contaminating air particles.

In collaboration, *in vivo* research has been set up at partner lab, BSL BIOSERVICE in Munich, and samples are subsequently analysed at the Eurofins Biopharma Product Testing site in Copenhagen. BSL BIOSERVICE specialises in preclinical safety testing for drug candidates, including bio-distribution and pharmacokinetic studies. Eurofins Biopharma Product Testing Denmark is a Competence Centre for low level trace metal testing in the Biopharma Product Testing group and obtained GLP approval in November 2015 to support the regulatory requirements in pharmacokinetic studies.

Eurofins BioPharma Product Testing can help in the planning and execution of sample handling, selection of instrumentation and general instrument performance advice, optimised for specific testing needs. Eurofins BioPharma Product Testing's regulatory experience enables analysts to ask the right questions and determine the most appropriate testing approach, delivering service that meets client needs.

For more information visit: *www.Eurofins.dk/media/1229997/eurofins-metals-testing-in-clinical-and-preclinical-samples.pdf*

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