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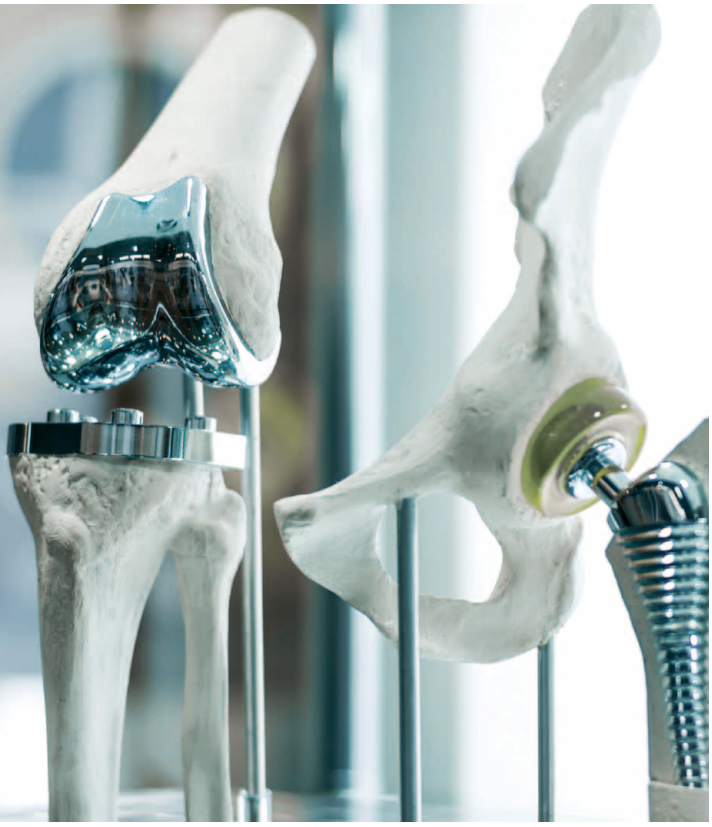
BioPharma Services

News

BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES



# A smart approach to chemical characterisation

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Medical devices must be safe and all risks associated with their use must be assessed. In fact, they can be made up of several constituents that could pose a biological risk to the patient during their clinical use. For this purpose, manufacturers often refer to the ISO 10993 series, the international standards to evaluate the biocompatibility of devices.

The approach to biological evaluation is changing: the new edition of ISO 10993-1 “Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process” was recently approved as final draft. Several aspects have been revised and, as a result, more emphasis is given to chemical characterisation, which now is a clear prerequisite for risk assessment.

A proper chemical characterisation should identify any compounds that may leach into the patient’s body from the medical device. By identifying these potential leachable compounds and evaluating their toxicological risk, certain *in vitro* and *in vivo* tests may be eliminated. Instead of indiscriminately performing all *in vitro* and *in vivo tests*, it is only necessary to perform those that are relevant based on the types of chemicals identified during chemical characterisation. For example, if only compounds were identified during chemical characterisation for which it is known that these do not have genotoxic properties, additional biocompatibility testing for genotoxicity would likely be deemed unnecessary.

Moreover, chemical characterisation data are useful in risk assessment to establish equivalency, in toxicological terms, of a proposed material to an existing clinically established material and to manage a change in a medical device.

Eurofins experts offer medical device manufacturers a structured approach to perform thoughtful, tailored and well-designed chemical characterisation in the context of biological safety evaluation of a medical device, thus providing a strategic biological evaluation. This approach may even eliminate unnecessary biocompatibility assays, thereby reducing the amount of *in vivo* tests as well as related time and costs. The more you know, the more you save! For more information, visit: *www.eurofins.com/medical-device*.

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# Eurofins provides custom synthesis & radiosynthesis capabilities

*James M. Schmidt, Senior Scientific Advisor, Custom Synthesis, jschmidt@eag.com*

Pharmaceutical companies often require the custom synthesis of test substances to support their research and development efforts. These include, but are not limited to reference standards, stable-labeled substances (esp. $^{2}H$, $^{13}C$, and $^{15}N$) for use as bio-analytical standards, or radiolabeled (esp. $^{14}C$ or $^{3}H$) material for use in preclinical animal studies or clinical studies in patients, to establish adsorption, distribution, and excretion patterns and mass balance and to profile and identify excreted and circulating parent compound and metabolites.

Providing sponsors with accurate and timely proposals for radiolabeled synthesis and executing the programs to high quality standards requires experience and expertise on many aspects: advising customers on regulatory aspects (GMP vs. non-GMP), recommendations on synthesis routes and preferred position of the radiolabel on the molecule, biosynthetic approaches, advice on employing other (or multiple) isotopes, repurification and recharacterisation of existing materials, and much more.

From beginning to end, communication is key to a successful client-CRO relationship, and it's especially important for custom synthesis as the test substance supply is a critical material for the studies it supports. It all begins in the proposal process where we discuss the client's study design, material and timing needs, institutional knowledge on the chemistry, future supply needs, and more. Once a synthesis campaign is underway, the communication continues with frequent updates on progress.

Eurofins' recently acquired Columbia, Missouri location (EAG Laboratories) has been providing custom synthesis support for almost two decades, with special expertise in synthesis of radiolabeled materials. In addition to a synthesis R&D laboratory, the site maintains four Class 10,000 synthesis suites and the rigorous cGMP-compliant environment required to produce certified radiolabeled products suitable for human clinical trials. This team of developmental synthetic chemists is technically exceptional and is backed by a dedicated analytical and quality control scientific staff.

Likewise, recent acquisitions have now brought additional excellent custom synthesis support to the Eurofins family at the EAG-St Louis (MO, USA) and Selcia (Ongar, UK) laboratories. For more information, visit: *www.eag.com/services/synthesis/custom-synthesis-radiolabeling*.

# Bead-beating tissue homogenisation technology - *a powerful and high throughput sample prep tool for quantitation of analyte in bone, skin & lymph node*

*Bhavesh Patel, Director – Head DMPK-Bioanalysis, Eurofins Advinus Limited, BhaveshPatel3@eurofins.com*

Estimation of drug concentrations in tough tissues such as skin, lymph nodes, ocular tissues and bones is critical for many preclinical pharmacokinetic studies. For example, drug concentrations and exposure in bones is determined during development of drugs for osteoporosis, rheumatoid arthritis and bone cancer. Analyte extraction from these tough tissues, however, is plagued with inherent challenges. Traditionally, such extraction is accomplished using mechanical or manual homogenisers, mortar and pestle, and sonicators. Such sample preparation techniques require the tough tissues to be cryo-frozen to make them brittle as a first step followed by grinding. This procedure is prone to sample cross contamination. These procedures are time consuming and low throughput. Also, the mechanical processes involved result in elevated temperatures, which may be undesirable for the sample integrity.

The application of the bead-beater-blender resolves many of these challenges. The bead beater methodology involves grinding the tough biological samples with small beads in micro-centrifuge tubes for a brief period of about 15 minutes. Beads of different materials are available (stainless steel, zirconium, ceramic, etc.) and can be optimised based on the application. The device is cooled at 4 °C and insulated for noise. This simple approach enables fast and complete homogenisation of tissues as well as cultured cells. Simultaneously, 24 samples (0.3 g each) can be processed in individual microfuge tubes.

Using this platform, Eurofins Advinus has successfully developed robust sample preparation methods for these tough tissues. The newly procured "Bullet Blender Gold" agitates the sample tubes vigorously and provides uniform and reproducible homogenisation while preserving sample integrity. The platform has been used to efficiently extract drugs from skin, lymph nodes and tibia. All consumables involved in sample preparation are disposable; thus, the problems of cross contamination and sample loss are resolved. The effectiveness of this sample preparation procedure improves the quality and throughput of the results generated. For more information, visit: *www.advinus.com*.

# Eurofins BPT Toronto offers USP<81> antibiotic assay validation & routine testing capabilities

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The USP<81> chapter covers microbial assays for determining antibiotic activity (potency). The effectiveness of antibiotics can be determined by their ability to inhibit the growth of microorganisms under appropriate conditions. Experchem Laboratories Inc. joined the Eurofins family in June 2015 and has been rebranded as Eurofins BioPharma Product Testing Toronto. This acquisition has brought the capacity to test USP<81> for antibiotic products into the Eurofins BPT North American laboratory network.

USP<81> covers 29 antibiotics. Bacitracin, Gramicidin, Neomycin and Polymyxin B are the most common antibiotics used in OTC consumer products. There are two general techniques used to determine antibiotic activity. The cylinder plate method assay measures the dispersion of the antibiotic from a vertical cylinder through a solid agar petri plate. The growth of the specified microorganism is prevented in a circular zone surrounding the cylinder which contains the antibiotic solution. The second technique is called turbidimetric assay which involves mixing a solution of the antibiotic in a liquid media that is favourable for the specified microorganism growth in the absence of an antibiotic. Antibiotic potency is characterised by microbial growth inhibition and is calculated based on triplicate assays at different concentrations.

To use the general method outlined in USP<81> a method validation must be performed for use on a finished product. During the validation, a maximum value for the confidence interval width is established, which is used in the calculation to estimate antibiotic potency. Any product containing one or more of the 29 antibiotics will require antibiotic assay to confirm potency using the USP<81> chapter. Common product matrices tested at Eurofins BPT Toronto include antibiotic ointments, creams, ophthalmic solutions, and feed additives. Eurofins BPT Toronto can explore other product matrices and help develop appropriate extraction protocols as needed. *For more information, visit: www.eurofins.ca*.

# Eurofins strengthens its alternative skin sensitisation testing portfolio for Cosmetics and Chemicals with GARD from SenzaGen

*Helge Gehrke, Head of In Vitro Pharmacology & Toxicology, Eurofins BioPharma Product Testing, HelgeGehrke@eurofins.com*

In March 2018, the full implementation of the EU animal testing ban for cosmetic products, which made necessary the fast implementation of solid *in vitro* tools for assessing the toxicological potential of cosmetic active ingredients and also finished formulations, has celebrated its 5th anniversary.

Eurofins laboratories are working to find the best solution for customers. For this reason Eurofins BPT Munich has signed a global licensing agreement with SenzaGen, which allows Eurofins to use the GARD™ test platform of SenzaGen for its future safety testing activities for Cosmetics and Chemicals.

GARD™ is a genome-based test, with higher accuracy than other available test methods that gives customers important safety information whether chemical substances are at risk of causing allergies in humans. Eurofins BPT Munich will include both GARD™ tests in its portfolio, GARDskin™ and the add-on test GARDpotency™, as a leading diagnostic tool in its chemical safety testing services to clients in the cosmetic, chemical and pharmaceutical industries worldwide.

GARDskin™, measures changes in gene expression of 200 genes relevant to skin sensitisation adverse outcome pathways (AOP). The high amount of data points measured by GARDskin™ gives a specific and high resolution result compared to tests measuring few data points.

GARD potency™ is an add-on application of the GARD™ platform able to provide the CLP categorisation of skin sensitisers Cat 1A for strong sensitisers, Cat 1B for moderate sensitisers, required by REACH regulation.

GARD™ has the potential to meet the increasing demands in the cosmetics, chemicals and pharmaceutical industries for reliable, *in vitro* testing methods to assess the allergy-inducing properties of chemical substances. The test is in the process of obtaining regulatory approval and inclusion in international test guidelines. For further information, *www.eurofins.com/cosmetics/safety-testing*.

# Eurofins Scientific earns CRO Award

*Lisa Bamford, Communications Manager, Eurofins Lancaster Laboratories, LisaBamford@eurofinsUS.com*

Eurofins has proudly been a winner of the CRO Leadership Award for five consecutive years. This year, Eurofins has been recognised for meeting or exceeding customer expectations in Capabilities, Compatibility, Quality and Reliability.

- **Capabilities - We support all functional areas of bio/pharmaceutical manufacturing and have locations worldwide.**
- **Compatibility - We are easy to work with and provide timely project communications.**
- **Quality - We ensure our data meets customers' data quality expectations and global regulatory compliance requirements.**
- **Reliability - We meet project timelines and milestones.**

"It is an outstanding honour for Eurofins to receive the CRO Leadership award for Capabilities, Compatibility, Quality and Reliability. This achievement is aligned with our mission to provide our customers with innovative and high quality scientific services, and we are delighted to know the bio/pharmaceutical industry continues to recognise Eurofins as a leader in these key areas," said Dr. Gilles Martin, Eurofins Founder & CEO.

From compound discovery and clinical research through manufacture and release of commercial product and post approval/marketing, Eurofins BioPharma Solutions provides seamless, end-to-end capabilities to help clients progress through the drug development cycle with a single, experienced provider. Eurofins supports all therapeutic areas within the Bio/Pharma industry & offers an integrated solution with the most comprehensive range of state-of-the-art analytical technologies with an expansive geographic reach.

For the 2018 CRO Leadership Awards, Life Science Leader magazine once again teamed up with Industry Standard Research (ISR) to determine the award recipients. More than 70 contract research organisations were assessed on 25+ performance metrics in ISR's annual CRO Quality Benchmarking survey. For more information, visit: *www.eurofins.com/biopharma-services/2018-cro-award-winner*.



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