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BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

BioPharma Services News

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Biosimilars: An evolution in the biopharmaceutical industry

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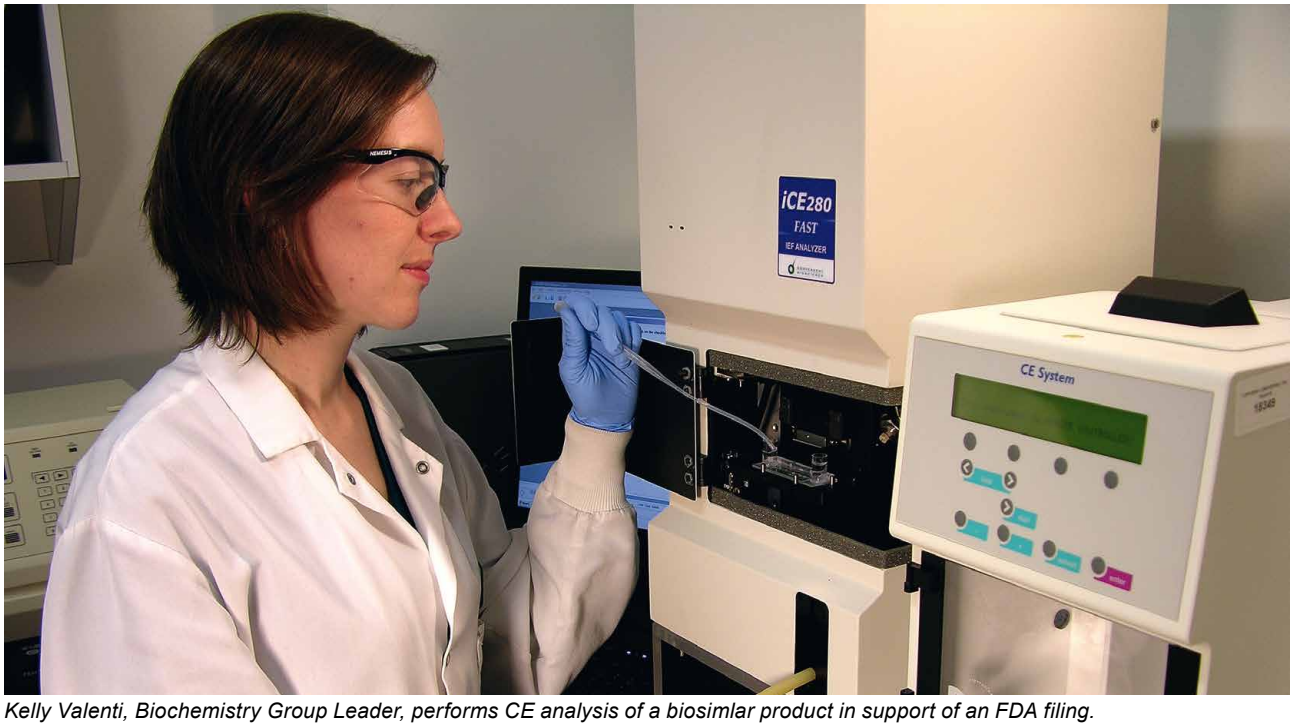
Patents for 12 blockbuster biologic compounds, generating a combined $67 billion in sales, will expire by 2020. In February 2012, the FDA released its long-awaited draft guidance on biosimilars, providing a regulatory framework for the approval of a biologic demonstrated to be similar to an already marketed product. The confluence of these two events has resulted in an evolution in the biopharmaceutical industry involving most players, but none more dramatically than a biopharmaceutical product testing laboratory.

Foremost in the FDA's approval process is the requirement for extensive testing and characterisation of the biosimilar to show that it is highly similar to the reference product. For innovator products, cGMP testing and extensive characterisation is loaded toward the back end of the drug development process after years of nonclinical and clinical studies. For biosimilars the extent of characterisation determines the need for additional nonclinical and clinical studies, thus moving testing to the front of the development process.

Over the past year, Eurofins Lancaster Laboratories has won many significant biosimilar testing programmes from new and existing clients due to its unique and compelling value proposition. Eurofins Lancaster Laboratories offers the extensive capacity, breadth of capabilities, innovator product expertise and global coverage to execute effectively on these very complex programmes. Clients have been pleased to find experts in Eurofins' Lancaster and Munich facilities to establish the often challenging cell based potency assays critical to these products. Clients have found state-of-the-art equipment, including CE, iCE, CD, LC-MS/MS, LC-TOF, MALDI-TOF, Q-TOF, TOF/TOF, and Orbitrap MS for orthogonal characterisation, including intact mass, peptide mapping, charge isoforms, carbohydrate sequencing, post translational modifications, and higher order structure.

This year, Eurofins Lancaster Laboratories has expanded its facilities, added extensive capital equipment, and attracted some of the brightest biochemists, cell biologists, and virologists to remain the first choice as a testing partner in this exciting, rapidly growing market.

For more information, visit *www.LancasterLabsPharm.com*



Kelly Valenti, Biochemistry Group Leader, performs CE analysis of a biosimlar product in support of an FDA filing.

Eurofins Cerep-Panlabs strengthens drug discovery services with GE Healthcare

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Eurofins Cerep-Panlabs, the world leader in discovery pharmacology testing services, has signed an agreement with GE Healthcare for the exclusive right to offer GE Healthcare's Cytiva™ Cardiomyocytes for drug discovery and early development cardio toxicity screening services.

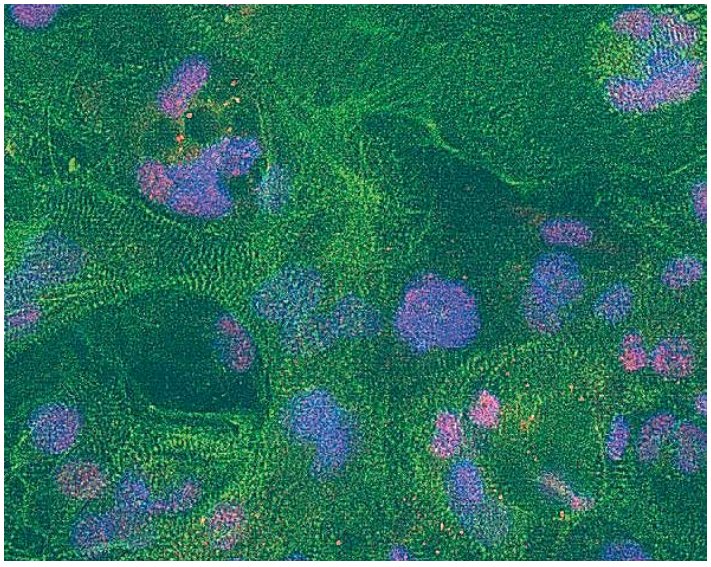
In drug development, up to three quarters of toxicity problems remain undetected until preclinical or later stages. Cardiotoxicity and hepatotoxicity are common causes of drug safety liabilities and withdrawal of drugs during development. The availability of more biologically relevant and predictive assays and cell models is key to helping improve the success rate and reducing the cost of the drug discovery and development process.

"This agreement gives Eurofins Cerep-Panlabs exclusivity in the CRO space to develop new assays for key indicators of cardiotoxicity using Cytiva cells for our clients," says Dr. Usha Warrior, Senior Director, Eurofins Cerep-Panlabs. "It also demonstrates our commitment to continuously developing the portfolio of services Eurofins Panlabs offers to help clients systematically reduce the risk in the drug discovery and development process."

GE Healthcare is pioneering the development of human cell-based models such as Cytiva Cardiomyocytes, which provide a biologically relevant alternative to current cell models and primary cells for predictive cardiotoxicity testing.

Eric Roman, General Manager of Research and Applied Markets, GE Healthcare Life Sciences, said: "The agreement with Eurofins Cerep-Panlabs will help realise our vision of bringing the benefits of human cell-based assays and models to pharmaceutical and cell science research. Cardiotoxicity is a common cause of late-stage drug failure, so it's vital that developers have access to the right tools to help reduce this high attrition rate and to help increase patient safety."

For more information visit *www.eurofinspanlabs.com*



High Content Analysis (HCA) screening with Cytiva™ Plus Cardiomyocytes

United, Cerep and Panlabs stand stronger

Jenny Thouvenin, Eurofins Cerep-Panlabs, pharma@eurofins.com

In the last quarter of 2012 and beginning of 2013, Eurofins acquired respectively Panlabs and Cerep – the two leaders in the field of molecular pharmacology testing services.

Formerly in competition, Cerep and Panlabs have merged within the latest Eurofins' business line, Pharma Discovery Services, thus becoming a major partner in drug discovery services with a portfolio of hundreds of both *in vitro* and *in vivo* assays, offering the largest available pharmacological panel for drug screening and profiling.

After over 20 years as Chief Executive Officer at Cerep, Eurofins has entrusted Thierry Jean with the role of managing Eurofins Cerep-Panlabs, as a Senior Vice President.

The merger of both entities enhances valuable existing expertise, knowledge and skills. Moreover, with over 350 people in four operational sites worldwide: Poitiers (France); Seattle, WA (USA); Shanghai (China) and Taipei (Taiwan), Eurofins Cerep-Panlabs offers logistics and functional solutions to perform studies with the highest quality to meet customer needs.

From conventional binding assays, to cellular disease models (oncology and immunology, *in vitro* toxicology) or the highly valued epigenetic targets, Eurofins Cerep-Panlabs covers complete customer requirements in all therapeutic areas. The offer includes high throughput profiling and screening services as well as customised assay development.

While assay catalogues are being harmonised, the sales forces have already joined and contribute daily to the success of the business line. Currently Eurofins Cerep-Panlabs is developing new strategies to provide customers cost-effective assays and reduced turnaround times.

Another significant strength of combined entities will be the merger of the two proprietary databases, BioPrint® and Foresight™, allowing anticipation of adverse drug reactions and leading to the identification of most promising drug candidates at early stage.

For more information, please visit *www.eurofins.com*

Best Practices and Clinical Trial Logistics

By Dr. Antoine Balland, Eurofins Pharma Quality Control, AntoineBalland@eurofins.com

Clinical research today is defined through large legislative and regulatory guidelines, and its success depends on recruitment of patients, experimental drug manufacturing and distribution to the clinical investigation centres. The main texts are:

ICH E6 Guidelines for Good Clinical Practices (GCP): Defines the principles and guidelines applicable to all clinical studies of drugs, including pharmacokinetics and phase I, II, III, IV studies. The ICH E6 harmonises the various existing regulations (EU-USA-JAPAN).

European Directive 2001/20/EC: This guideline defines what a clinical study is and focuses on the protection of patients involved in clinical research. It also defines the exchanges of information between EU Member States through the database EUDRA CT (European database).

European Directive 2005/28/EC: This Directive completes 2001/20/EC but is more convenient. It redefines Good Clinical Practices for the design of studies and data monitoring.

European Directive 2003/94/EC: This establishes that experimental drugs should be produced according to Good Manufacturing Practices (GMP). All articles in this Directive are explained in GMP Annex 13.

GMP Annex 13: Procedures used in the manufacturing process must be adapted to the development of the product. The manufacturing of a new drug remains an experimental process. Complex data and manufacturing processes are still in the validation phase. Packaging (primary and secondary) is a critical step. The packaging must be customised, according to the protocol, the patient and test group.

Good Distribution Practices (GDP): Describes the process for reception, storage, shipping, tracking, returns management, destruction and batch recall of clinical drugs.

Since 2000, Eurofins Pharma Quality Control has been offering complete solutions to combine global and legal compliance (ICH, GCP, GMP, and GDP) and effectiveness of a clinical study, including:

• Therapeutic unit management: Import, Packaging, Labelling, Control, Batch Release, Stability Studies, Supply of Comparator, Randomisation, Returns Management, Reconcilliation, Destruction

• Multi temperature storage facilities, large volume (-80°C, -20°C, +5°C and +20°C)

• Distribution, refrigerated transport, validated insulated boxes

• Manufacturing of biological sampling kits

For more information, visit *www.eurofins.com*

Comparison of caffeine absorption between flow-through and static diffusion cells

By Christelle Gélis, Eurofins ADME Bioanalyses, skin@eurofins.com

Static cells (manually removing of receptor fluid) or dynamic cells (mimics blood flow and automatic sampling of receptor fluid) can be used to measure the *in vitro* absorption of chemicals through human skin to predict *in vivo* absorption.

Testing was performed by Eurofins ADME Bioanalyses for 14C-Caffeine absorption in order to compare the absorption results obtained from static and dynamic cells. The design was based on the publication, Regulatory Toxicology and Pharmacology[1].

Example of static cell testing

The study was performed on an occlusive system on a simplest caffeine formulation at 4 mg/mL in ethanol/UHQ water (50/50, v/v) with application of 25 µL/cm² volume on a skin surface. The receptor fluid was NaCl 0.9%, and the receptor fluid was sampled at 1, 2, 4, 8 and 24-hour post-dosing. The skin surface was 2 cm² for static cell and 1 cm² for dynamic cell. Two donors and three cells per donor were used in this study. After 24 hours, the remaining formulation was washed using five cotton swabs dampened with ethanol/UHQ water (50/50, v/v) followed by one dry cotton swab.

The radioactivity was evaluated in skin excess (washing of remaining formulation and cleaning of donor compartment), strips, skin, remaining skin (corresponding to the skin non-exposed to the formulation), receptor fluid and cleaning of receptor compartment.

The caffeine absorbed corresponded to the caffeine recovered in skin and receptor fluid, including the cleaning of the receptor compartment.

The mean caffeine absorption obtained from static and dynamic cells were 19.2% ± 10.1% and 19.4% ± 8.1% respectively of the applied dose. No statistic difference was observed between the static and dynamic systems with the occlusive system. According to the data obtained in the literature, we can conclude that the dynamic and static systems were similar in terms of absorption.

While both have advantages, Eurofins can offer both systems and advise their customers to choose the best one in accordance to the objective of their studies.
For more information, visit *www.eurofinsadmebioanalyses.com*

1. "in vitro predictions of skin absorption of Caffeine, Testosterone and Benzoic acid: a multi-centre comparison study," JJM van de Sandt and al. Publication in Regulatory Toxicology and Pharmacology 39 (2004) 271-281.

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in brief

Biomarkers in Clinical Trials: a Central Laboratory perspective

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Pharmaceutical Research and Development has shifted its focus towards biomarker-mediated drug development that is aimed at preventing late stage diagnosis of unsuccessful drugs. As the use of novel biomarkers has become an integral part of the decision-making process in drug development, these biomarkers require detailed data to demonstrate the validity of their application.

A clear understanding of how the biomarker assay will be used during drug development is pivotal for allowing critical decision-making. This requires efficient coordination and clear communication between the translational and clinical drug development teams on one hand, and the test laboratory on the other hand. From a regulatory perspective, the translational and/or clinical drug development teams should be aware that the applied biomarker requires rigorous analytical assay validation in order to understand analytical limitations and, hence, inference of the correct conclusions. Depending on the purpose, the rigour of data documentation, record keeping and reporting, might need to be similar to that of methods for Drug PK support. As such, the purpose of the biomarker assay should be clearly defined, including expectations for application in clinical trials.

For use in drug development, biomarker assays (laboratory tests) are predominantly used to facilitate therapeutic and regulatory decision-making. Furthermore, supportive biomarker data may or may not be required for drug submission. Therefore a selected biomarker assay might require more rigorous assay validation than what is done for the “routine” laboratory tests. When a biomarker test is developed and validated for exploratory purposes, additional effort might be required to “upgrade” the assay for approval purposes.

The support by the Central Laboratory of many clinical studies with a broad variety of biomarker applications has become valuable in creating an environment for rationale decision-making on drug development. By clearly informing sponsors about the type of biomarkers being used and its potential analytical limitations, clinical laboratories have become a cornerstone in the drug development arena and are instrumental in accelerating drugs to market.
For more information, *visit www.centrallab.eurofins.com*

COMING EVENTS

EVENT	DATE & PLACE	MORE INFO	CONTACT
European Bioanalytical Forum	9-22 11 2013 Barcelona, Spain	*Speaker slot*	*clinicaltrials@eurofins.com*
AAPS Annual Meeting	10-14 11 2013 San Antonio, TX	*Booth #3223*	*GMP_US@eurofins.com*
PDA/FDA Advanced Technologies	13-14 11 2013 Bethesda, MD	*Booth #1*	*GMP_US@eurofins.com*
Partnerships in Clinical Trials	20-21 11 2013 Vienna, Austria	*Booth #447*	*clinicaltrials@eurofins.com*
WCBP	28-30 01 2014 Washington, DC	*Booth TBA*	*GMP_US@eurofins.com*

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