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BioPharma Services

News

BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

Changes to EU Medical Device Legislation: What you need to know

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On April 5, 2017, the European Parliament approved the New Regulations for Medical Devices (MD) and *in-vitro* diagnostic Medical Devices (IVD), proposed by the European Commission back in 2012. The final adopted text, Regulation (EU) 2017-745, was published in the *Official Journal* in May 2017. *(http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32017R0745)*

The two new Regulations replace the three existing Directives on MD. In detail, the EU Directive MD (93/42/EEC) and the EU Directive on active implantable MD (90/385/EEC) are replaced by the Regulation on Medical Devices (MDR). The Directive on IVD (98/79/EC) is also substituted by an up-to-date Regulation on the same topic.

While Directives require national implementation in every European country, the Regulations are directly enforced, overcoming issues caused by divergences in the national interpretation of the existing Directives.

The new Regulations aim to enhance patient safety through the introduction of numerous changes and improvements, involving both manufacturers and competent Authorities.

The definition of medical device is extended to groups of products without a medical purpose but similar to medical devices for their risk and characteristics (e.g. coloured contact lenses, facial dermal fillers).

The demonstration of medical device performance with stronger clinical evidence is another significant topic, as well as transparency of information for consumers through the new European database of MD (EUDAMED).

Safety improvements involve also the post-market surveillance, which obliges manufacturers to monitor products placed on the market, providing annual reports on their safety and performance. The Notified Bodies will have a strong authority in this subject by unannounced audits and samples controls.

Eurofins experts are happy to support manufacturers facing this changing regulation, providing testing and offering regulatory expertise during the entire medical device life cycle.

For more information visit:
www.eurofins.com/medical-device/

Optimising Cytomegalovirus (CMV) Outcomes with Personalised Testing

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According to the U.S. Centres for Disease Control and Prevention (CDC), CMV is a common virus that infects people of all ages. Over half of adults have been infected with CMV by age 40. Once CMV is in a person's body, it stays there for life and can reactivate. For most people CMV is not a concern, and may not even produce symptoms. However, for people with weakened immune systems, such as those who recently received a transplant, or babies infected with the virus before they are born, CMV can cause serious problems. In transplant recipients, the adverse outcomes from CMV disease are severe and can result in loss of the transplant and even death. For neonates, congenital CMV is a leading cause of permanent hearing loss and may cause brain, vision or developmental problems. Detecting and treating CMV early with antiviral medication can improve outcomes and prevent further damage from hearing and vision loss. Ruling out CMV can prevent unnecessary use of potent, harmful drugs.

Eurofins Viracor offers multiple CMV testing options to help improve patient outcomes. Viracor's CMV Quantitative Real-time PCR testing detects multiple targets of the virus, minimising the possibility of false negative results. Viracor recently validated saliva as an accepted specimen type for its CMV qPCR assay, to give physicians an easier, non-invasive, and accurate option for collecting specimens from neonates. Saliva is one of 19 specimen types Viracor accepts for CMV qPCR testing, giving physicians more options.

The risk of patients developing an antiviral-resistant strain of CMV with continued antiviral use in either prophylaxis or preemptive therapy regimens is rising. To aid in rapid detection of resistance, Viracor offers CMV Antiviral Resistance (AVR) Sequencing. Viracor also recently launched a CMV T Cell Immunity Panel to aid physicians in evaluating if the patient has a functional immune response to CMV, which may help the physician decide whether to continue or to stop using antivirals. For more information, please visit *www.Viracor-Eurofins.com*

Development and Qualification of a Characterisation Panel to Assess the Biological Activity of Golimumab (Simponi®)

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WHO, US FDA, and EU guidelines request the use of a variety of analytical methods for therapeutic monoclonal antibody biosimilar characterisation and comparison with reference products. In order to support clients with accelerating their biosimilar development programmes, Eurofins BioPharma Product Testing Munich has set up and qualified a characterisation panel for the biological activity of Golimumab (Simponi®) using the bioassay experience and expertise of its Potency Bioassay Team, which has provided cGMP bioassay testing and bioassay development services for more than 30 years.

Golimumab (Simponi®) is a fully human monoclonal IgG1 antibody that inhibits binding of TNFα to its receptor TNFR. The characterisation panel addresses Fab functional activity using a cell based potency assay and Fab binding by a SPR binding assay to soluble TNFα as well as by a FACS binding assay to membranous TNFα. An ADCC and a CDC assay are available for characterisation of the Fc function of this therapeutic antibody. These cell based assays are supplemented by a panel of Biacore SPR binding kinetic assays for binding to FcγRI/CD64, FcγRIIA131R/CD32A, FcγRIIIA158V/CD16A, FcRn and binding to complement C1q ELISA/C1q SPR assay. The Biacore SPR assays are qualified as kinetic assays, and the cell-based assays are set up as potency assays. As these methods are used both for data generation for Quality Target Product Profile (QTPP) and for clone selection, the assays can be ordered in any combination as either GMP or non-GxP service.

Key Function	Assay (Read Out)
Fab functional assay	• Cell based Bioassay/neutralisation (Measurement of cell viability)
Binding to target antigen (Fab binding assays)	• Binding to soluble TNFα (SPR/Biacore) • Binding to membraneous TNFα (FACS)
Fc functional assays	• ADCC reporter gene assay (using Promega ADCC kit) • CDC assay
Fc binding assays	• Binding to FcγRI/CD64 (SPR/Biacore) • FcγRIIA131R/CD32A (SPR/Biacore) • FcγRIIIA158V/CD16A (SPR/Biacore) • FcRn (SPR/Biacore) • Binding to Complement (C1q ELISA/C1q SPR)

This assay panel can serve as a platform for other anti TNFα therapeutic monoclonal antibodies. Furthermore, the Characterisation Team has experience with the following Biacore SPR Fcγ receptor characterisation assays, which are established for therapeutic antibody innovator molecules and can be also set up for biosimilars: Binding to FcγRIIIA158F (CD16A), FcγRIIIB (CD16B), FcγRIIA131H (CD32A) and FcγRIIB/C (CD32B/C).

In addition, the Bioassay and Characterisation Assay teams of Eurofins Munich work on a variety of client specific innovator molecule bioassays using a diverse range of bioassay types (cell-based, ELISA, SPR, *in vivo*) and have experience with biosimilar molecules like Enbrel (Etanercept), Remicade (Infliximab), Humira (Adalimumab), Avastin (Bevacizumab), and Rituxan (Rituximab). For more information,visit *www.eurofins.com/biosimilars*

Eurofins Lancaster Laboratories PSS Insourcing Solutions® expands global reach at record pace

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More and more global biopharmaceutical companies are realizing the value of housing Eurofins Lancaster Laboratories PSS managed services to perform their testing and laboratory management for less limitations, restrictions, and co-employment hassles than if they hired temporary staff. It truly has the chemistry for an award-winning success.

Transforming a client's science into an outstanding service experience, Eurofins Lancaster Laboratories PSS has grown exponentially since its inception 15 years ago. Today, with approximately 1,500 employees worldwide, PSS delivers managed laboratory services at more than 65 client sites, providing services in 15 countries throughout North America, Europe, and Asia-Pacific.

On the horizon, the landscape is shifting beyond what has traditionally made this business model absolutely successful. What began as a simple service offering where PSS recruits, hires, trains and manages highly qualified scientists to perform laboratory testing services at the client's site, has blossomed to address more comprehensive client needs. Today PSS offers the most advanced, sophisticated biopharmaceutical managed laboratory testing services from early phase development to finished product testing, as well as comprehensive laboratory management, including:

- GMP Lean Laboratory Design and Validation
- Regulatory and Technical Training
- Lean Project Support/Management
- Upstream and Downstream Services

Another driver for this significant growth is the ever-changing employment legislation. For example, Germany is revising their laws regarding temps that includes employing temporary workers for 9 months at temp pay, and following that, they must compensate at a regular salary. If they are still employed at 18 months, the company must hire the temp full-time or let them go. And there are indications other countries may adopt a similar tack. PSS also solves the challenges associated with the EU Temporary Agency's Workers Directive 2008/104 since PSS is not a temporary service provider, rather laboratory managed services just as if clients sent samples to Eurofins' laboratories.

To that, as the industry grows wildly fond of relinquishing the hassles of co-employment headaches and replacing them with PSS Managed Services, some large biopharm firms have shared they wish to focus primarily on their large and small molecule pipelines, mitigate risks, and have declared a no-more-temps edict.

One of Eurofins Lancaster Laboratories PSS secrets to success is the focus on people excellence. It's done by finding great people, taking great care of them, and creating excitement, engagement, and retention by providing full-time employment, comprehensive benefits as well as proactive training, development, and career advancement opportunities. Creating a culture of positivity and engagement through employee empowerment and recognition, allows PSS to attract, retain and motivate high-caliber employees to better serve clients at their sites.

At the heart of this evolution is a passion for forging long-term partnerships and friendships, delighting clients, and delivering tailored and valuable service solutions that are ultimately good for business and good for people. Believing this human element and connection will always achieve a successful outcome, the PSS teams are motivated to serve clients and improve and save lives together. And being the only managed service insourcing provider in the industry to receive 10 client strategic partnership awards in the last 9 years is demonstration of that success. For more information, visit *www.eurofins.com/biopharma*

New solutions for Endocrine Disrupters

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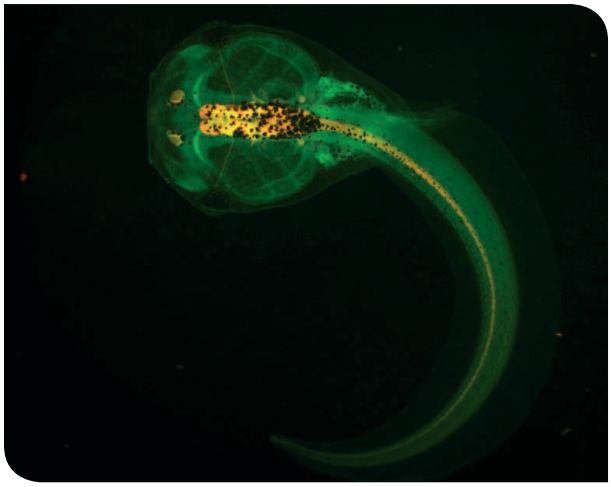
Some chemicals, known as endocrine disruptors, can have harmful effects on the body's endocrine (hormone) system. The endocrine system is a complex, interconnected system that enables regulation of growth, development and reproduction. Responses of the endocrine system act over longer periods than do those of the autonomic nervous system and affect all the tissues and organ systems of the body. Chemical substances suspected to be an Endocrine Disruptor on organisms are banned from formulations and products, which are made to be in contact with users and consumers, or which can end up in the environment. With this fact, Industries (Biopharma Industries included) have to detect endocrine properties of their products. This research has to be made as far upstream as possible to prevent the marketing of products that can have a negative impact on human health and adverse consequences for next generations (due to the impact on the hormonal system).

To date, there are more than 40 different ecological *in vitro* and *in vivo* mammalian assays included in the Organisation for Economic Co-operation and Development's (OECD) conceptual framework, and there are still additional assays being developed in other parts of the world despite the volume and complexity of existing test methods.

Within the Eurofins network of laboratories, Environmental and BioPharma Product Testing sites offer the full range of Endocrine Disruptors testing required by the different Industries (pharmaceutic, cosmetic, chemistry, etc.). Assessments of weight-of-evidence and expert statements, tailored for respective regulatory programmes, are helpful to know the endocrine disrupting properties of a substance. Eurofins experts recommend that studies are constructed carefully in order to meet global requirements and avoid redundant testing.

Eurofins Expertises Environnementales in France and Eurofins BioPharma Product Testing in Germany are able to measure the impact of products on the endocrine system. The Endocrine Test Strategy



includes *in vitro* and as well *in vivo* tests, which are able to evaluate the endocrine impact of the product.
In vitro Assays:

- Aromatase Assay
- ER TranscripAct (Human HeLa 9903) Assay
- H295R Steroidogenesis Assay
- Androgen Receptor Binding Assay
- Estrogen Receptor Binding Assay

In vivo Assays:

- Estrogenic scale: Fish to reveal estrogen disruption
- Thyroid scale: Amphibian larvae to reveal thyroid disruption
- Androgenic scale: Fish to reveal androgen disruption

By doing these tests, Eurofins takes into account the complete metabolic system with an enhanced sensitivity. Moreover, by using larvae of amphibian and fish models, Eurofins has representative organisms for biodiversity. For more information, visit *www.eurofins.com/contact-us/worldwide-interactive-map/*

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