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BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

BioPharma Services News

N° 08 - June 2014

Eurofins BioPharma Product Testing provides harmonised US and EU support to global organisations

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Biopharmaceutical sponsors typically market products in multiple regions under different regulatory authorities, and therefore must identify, qualify and contract with both US and European laboratories. As the largest global network of harmonised BioPharma GMP product testing labs, Eurofins BioPharma Product Testing's (EBPT) expertise in bringing products to the market under both the US and EU regulatory environments allows global clients to work with just one organisation, utilising harmonised quality and IT/LIMS systems.

For example, Eurofins Lancaster Laboratories (ELLI) had been supporting a critical release testing programme in the US for a product in short supply, when the client requested support for their EU release testing. A risk-based analysis of the methods was performed. The more critical, higher-risk methods were transferred through parallel testing, in which samples were run at the Lancaster, US, site as the reference laboratory, and its Ireland site as the receiving laboratory. Subject matter experts (SMEs) from Lancaster travelled to Ireland to perform hands-on training of the technique-sensitive methods. All methods were successfully transferred, and the client can release product in both markets.

EBPT is taking another approach for method implementation for some of its large biologics programmes. One client required labs to be qualified in both the US and EU to support their monoclonal antibody stability and release programmes. Therefore, method implementation at EBPT US and Munich labs was accomplished through method co-validation. The protocol described testing of critical validation parameters such as intermediate precision and accuracy to be performed at both sites, allowing for simultaneous method implementation.

Also notable, after ELLI validated a variety of methods to support a client's NDA submission and release testing in the US, Eurofins' Milan lab was then able to support this client with their successful Marketing Authorisation Application (MAA) filing in the EU through seamless analytical method transfer (AMT) protocol development and collaboration.

Critical success factors of these method installation projects include strong project management, effective communication, extensive coordination among the US and EU laboratories and the client, collaborative protocol development, and SME driven training. All this results in shorter timelines and reduced costs to global clients.

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

Drug development: Bel/Novamann perspective

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The solid state of a drug is critically important in determining the drug's effectiveness for delivery. Poorly soluble compounds make up roughly 80% of drug candidates in the pharmaceutical industry. Instability, bitter taste, low permeability are examples of other unpleasant obstacles. The solid state treatment affording alternatively solid forms e.g. amorphous, polymorphs, solvates, solid dispersions, co-crystals, inclusion complex resolves these problems.

Eurofins Bel/Novamann R&D group has dealt with many significant projects on new solid forms due to their unique and compelling value intention. The R&D group offers the capacity, breadth of capabilities, innovator product expertise and global coverage to execute effectively on these complex programmes. Eurofins' experts have participated in the Structural Funds of EU. Clients have found state-of-the-art equipment, including XPS, DSC, XRPD, FTIR, LC-MS, ss-NMR and DVS for solid state characterisation. The R&D group has successfully generated co-crystals and inclusion complexes with natural products, including nutraceuticals.

Eurofins Bel/Novamann supports all aspects of drug testing, including dissolution, stability tests, and complete retesting (release). Also Eurofins Bel/Novamann has the infrastructure to support analysis of incoming product. When compendial methods and standards of impurities are not available, it is necessary to undertake method development/validation or integrate methods reported in pharmacopoeias with other tests. These BU laboratories are formed by experienced chemists focused on non-routine services individually tailored to the needs of clients.

Find more information, please visit *www.pharma.eurofins.com.*.

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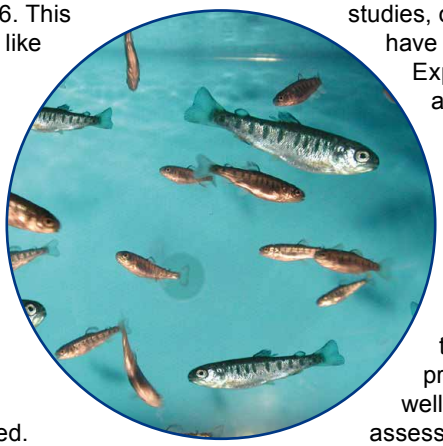
Environmental risk assessment for human pharmaceuticals New developments

By Dr. Ulrich Memmert, Eurofins Regulatory AG, UlrichMemmert@eurofins.com*
**: Affairs Group*

An Environmental Risk Assessment (ERA) is required for marketing authorisation of Human Medicinal Products by the European Medicines Agency (EMA) since 2006. This affects all new products (with some exemption like vitamins, amino acids, peptides, electrolytes, and herbal products) but also existing drugs if e.g. a new indication results in significant increase in their extent of use.



During the past few years, several important questions arose on how to interpret some sections of the present ERA Guideline EMEA/CHMP/SWP/4447. For this reason, a Question and Answer (Q&A) document (EMA/CHMP/SWP/44609/2010) was finalised by EMA in 2011. Experience shows that with the implementation of the Q&A document, the ERA requirements were more strictly interpreted. For example, marketing research and prediction data cannot be further used for the refinement of the market penetration factor Fpen. Fpen can only be refined on the basis of European disease prevalence data when published by a reliable and independent source, e.g. a peer-reviewed scientific journal or the World Health Organisation (WHO).

Also other potential risk factors became more spotlighted. One of them is the PBT (persistent, bioaccumulative and toxic) assessment for drug substances. Others are the need for identification of degradation products in environmental studies, or the indication that the drug substance may have endocrine activity in the environment. Expertise is needed for the evaluation of available study results or for planning of study programmes to address these potential risks and for discussions with Competent Authorities.

Eurofins Regulatory AG in Switzerland has gained profiency and expertise in these areas in recent years. Several well-experienced experts are offering support for the environmental risk assessment, including project management and study monitoring, as well as expert judgement for e.g. PBT assessment for potential endocrine disrupting activity. Also data gap analysis, literature search and peer review of scientific literature are performed for the ERA of existing drugs. All environmental studies can be conducted at Eurofins laboratories. For more information on Eurofins' full range of services, including environmental studies and consulting work for the environmental risk assessment, visit *www.eurofins.com*.

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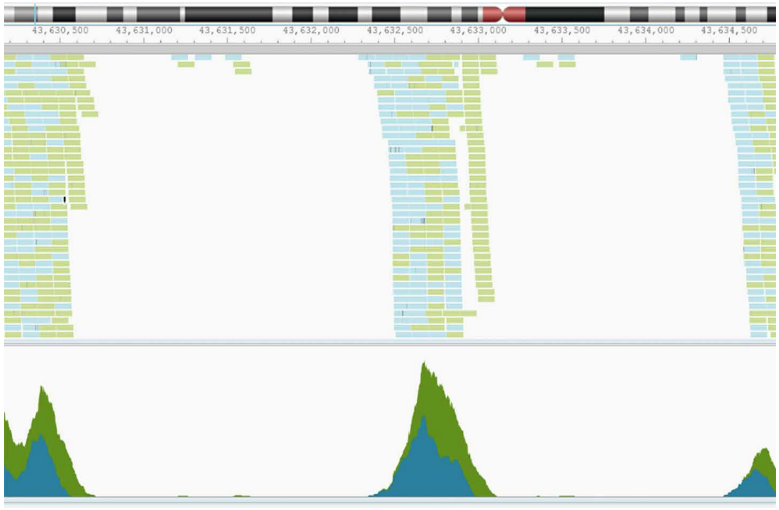
Exome Sequencing: Selective characterisation of the genome's complete coding region

By Dr. Katrin Mansperger, Pharmacogenomics, Eurofins Medigenomix, Germany

In humans, only 1-2 % of the genome is protein coding, the so-called exome. Exome sequencing is favoured over whole genome sequencing due to costs, efficiency and the easier interpretability of a much lower data volume compared to whole genome sequencing. It gains more and more clinical relevance in the determination of rare diseases as well as for cancer research and diagnostics. Furthermore, it's a very important screening tool for genetic variations e. g. involved in mental disorders such as schizophrenia and is therefore increasingly used as one genomic application in drug discovery. Exome analyses are frequently conducted as trio analyses with one patient plus healthy parents, who serve as controls to filter out benign variants. They are not only performed on behalf of companies or academic research organisations, but also gain more importance in diagnostic applications for individuals.



The most common technologies for exome analysis are based on in-solution hybridisation. They use a protocol that first generates a whole genome library, and then enriches the exome portion of the genome. The well-established kits for this kind of analysis are from NimbleGen, Agilent and Illumina. The exome enriched DNA is then primarily sequenced with Next Generation Sequencing systems from Ilumina, like Illumina HiSeq. This approach is typically selected for projects with large sample numbers. One limitation is the incomplete coverage for some genetic loci. More consistent sequence coverage can be achieved by using a PCR based exome capture approach offered by Ion Torrent. This approach allows a very fast and a more uniform exome analysis ideal for small to mid-size sample numbers.

Eurofins Genomics offers all the described technologies to guarantee an optimal solution for every exome sequencing project. Further, we offer DNA extraction from different kinds of samples like cell lines or FFPE, library construction, target enrichment and sequencing followed by data analysis using state-of-the-art bioinformatics pipelines. Which process fits best with the project needs will be discussed in detail with the client.

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A pioneer role of BSL BIOSERVICE in the in vitro alternative method and models development

By Hana Hofman-Hüther, BSL BIOSERVICE GmbH (a Eurofins partner laboratory), hhofman-huether@bioservice.com

The use of non-animal test methods, including in vitro studies, provides important tools to enhance our understanding of hazardous effects by chemicals and for predicting these effects on humans. The reduction of animals in toxicology research by encouragement of the development and validation of effective in vitro and alternative methods or models is one of the outmost concerns at BSL BIOSERVICE.

To address this, BSL BIOSERVICE offers a variety of cell-based alternative methods or models under GLP to examine the hazardous effects of chemicals, herbals, cosmetic and food ingredients or medical devices. The suitable test design is chosen depending on the material of the product and the aim of the study.

BSL BIOSERVICE is establishing a method to assess the potential of a substance to cause a skin allergy in humans that incorporates a tissue model, a 3-dimensional human cell skin model that replicates key characteristics of normal human skin. RHE IL-18 potency test is a part of a validation project sponsored by industry (including BSL BIOSERVICE) and involving nine partners and four skin models (Gibbs et al. 2014). It will replace the use of guinea pigs, rats or mice, which would have been injected with a substance or had it applied to their shaved skin to determine an allergic response. Skin or Eye models are also being used to replace rabbits that have traditionally been used to evaluate chemicals for their ability to corrode or irritate the skin or eye.

Thus, in vitro 3D human tissue equivalents have made significant contributions to the reduction of animal use in industrial product development and regulatory testing, of which two are accepted from a regulatory standpoint as full replacement methods for testing dermal corrosion and irritation. Other models/methods are recommended as components of tiered testing strategies.

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

Ensuring safety of cosmetic products: evaluation of packaging-content interactions

By Davide Tartaglione, Eurofins BioPharma Product Testing Italy, DavideTartaglione@eurofins.com

Assurance of consumer health is one of the main focuses of Cosmetic Regulation (EU 1223/2009). According to Annex I, the assessor should evaluate the safety of the product through an in-depth toxicological assessment. He/she should also take into account any impurities, traces and information on packaging, "including its interaction with the product, its barrier properties and substance migration from/to the packaging material." A correct choice of container ensures that the characteristics of the products are maintained through its shelf life, without any modification of performance and safety.

As no specific guidelines have been issued on this topic by now, main knowledge comes from food contact material regulation and guidelines where interaction/compatibility with packaging is strictly regulated.

Accelerated stability in a climate chamber is a useful tool as it simulates long-term storage, while rapidly allowing detection of unwanted interactions. Appropriate controls for inert packaging, such as glass containers, should always be carried out.

In general, alterations in the formulation, appearance, colour, odour, pH and appearance/functionality of the package are assessed. Adsorption/absorption, leaching, permeation and chemical reaction should also be evaluated on a case-by-case analysis, depending on nature of package and formulation. Specific attention is given to potential leaching of substances that can arise in toxicological concern. For example plastics can release phthalates as degradation products or additives, heavy metals as manufacturing process catalysts, additives such as antioxidants or polymerisation stoppers and nitrosamines and aldehydes as degradation products could also be eventually monitored. A wide range of analytical techniques, from wet chemistry to HPLC to mass spectroscopy, are employed for this scope.

Eurofins specialists will be happy to support you in defining the best study design suitable for your product and your needs.

For more information, please visit *www.pharma.eurofins.com* or contact *GMP_EU@eurofins.com*.

COMING EVENTS

EVENT	DATE & PLACE	MORE INFO	CONTACT
54° SIMPOSIO AFI	11-13.06.2014, Rimini, Italy	*Booth 39-41*	*GMP_EU@eurofins.com*
Viral Safety for Biologics	24-25.06.2014, Cologne, Germany	*Contact us*	*GMP_EU@eurofins.com*
Contract Pharma	18.09.2014, New Brunswick, NJ, USA	*Contact us*	*GMP_US@eurofins.com*
BioProcess International	20-23.10.2014, Boston, MA, USA	*Contact us*	*GMP_US@eurofins.com*
PDA Pharmaceutical Microbiology	20-22.10.2014, Bethesda, MD, USA	*Contact us*	*GMP_US@eurofins.com*
Well Characterized Biologicals	03-04.11.2014, Washington, DC, USA	*Contact us*	*GMP_US@eurofins.com*
Outsourcing in Clinical Trials Europe	21-22.05.2014, Brussels, Belgium	*Booth 8*	*clinicaltrials@eurofins.com*
PCMG 10th Annual Meeting	04-06.06.2014, Lisbon, Portugal	*Attend only*	*clinicaltrials@eurofins.com*
DIA 2014 50th Annual Meeting	15-19.06.2014 San Diego, CA, USA	*Booth 2635*	*clinicaltrials@eurofins.com*
Outsourcing in Clinical Trials Nordic Countries	10-11. 09.2014, Copenhagen, Denmark	*Booth 18*	*clinicaltrials@eurofins.com*
Outsourcing in Clinical Trials New England	07-08.10.2014 Boston, MA, USA	*Booth 28*	*clinicaltrials@eurofins.com*
Partnerships in Clinical Trials	05-06.11.2014, Barcelona, Spain	*Booth 711*	*clinicaltrials@eurofins.com*

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