eurofins

Pharma Services News

BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

N° 02 - June 2012

The personalized medicine revolution - keep up with the pace

By Sandra Hageman, Eurofins Global Central Laboratory, The Netherlands, and Dr. Brigitte Obermaier, Eurofins Medigenomix, Germany

Over the last decade, pharmacogenetics is increasingly used to predict variation in drug response, thereby aiming to improve the drug development process and to reduce risks in relation to adverse drug effects. Drugs are only effective for about 60% of all patients. Response rates in oncology are often even significantly lower. Besides, some patients show severe side effects while taking a drug. Variation in drug response is largely caused by genetic variations, mostly by single nucleotide polymorphisms (SNPs) and combinations of SNPs in relevant genes. Pharmacogenetics (PGx) allows drug therapy tailored to the individual which is foremost beneficial to the patient itself. The application of PGx will also benefit the general healthcare system and pharmaceutical companies alike.

Pharmacogenetics can be deployed for genetic profiling in the fields of pharmacokinetics (what the body does with the drug – Absorption, Distribution, Metabolism, Excretion), pharmacodynamics (what are the effects of the drug to the body) and stratification of patients in clinical trials. Typical examples of relevant genes include drug metabolising enzymes e.g. Cytochrome P450, drug transporters e.g. ABC transporters (ATP binding cassette), drug receptors e.g. HER2/neu receptor and signal transduction proteins e.g. GTP-binding proteins.

Eurofins Medigenomix in Ebersberg, Germany, is the competence center for genetic analyses of the Eurofins Pharma Services Group and supports pharmaceutical drug development with a comprehensive suite of services in pharmacogenetics and pharmacogenomics. Pharmacogenomics is the whole genome application of pharmacogenetics, which examines single gene interactions with drugs. These services include DNA/RNA extraction e.g. for DNA biobanking, genotyping, assay development and validation, transcriptome analysis and whole genome sequencing.

In 2010, Boehringer Ingelheim Pharma GmbH & C0. KG and Eurofins Medigenomix concluded a long-term service agreement in the area of DNA biobanking, as well as for pharmacogenetic and genomic services. Many thousands of blood samples are processed annually at Eurofins Medigenomix using a fully automated DNA extraction process. DNA samples are stored in Boehringer Ingelheim's central DNA bank. Equipped with the latest state-of-the-art technology platforms, Eurofins Medigenomix offers all tools to keep up with the personalised medicine revolution and can support pharma companies in the development of biomarkers and companion diagnostics.

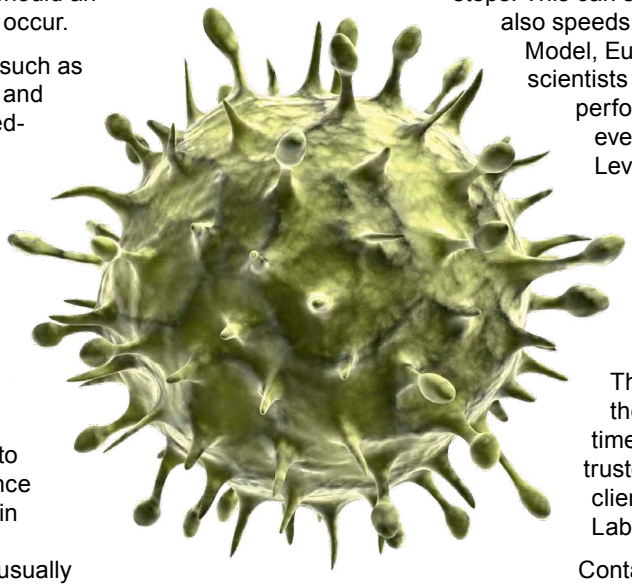
Contact: *pharmacogenetics@medigenomix.de*

Four viral clearance service models offer time and cost saving options

By Dr. Jeri Ann Boose, Director, Eurofins Lancaster Laboratories Biopharmaceutical Services, USA

Viral clearance studies help ensure that an acceptable level of safety has been achieved for biological products. The goal of these studies is to demonstrate that the manufacturing purification process has the potential to inactivate or remove a broad range of virus types should an unexpected viral contamination event occur.

Typically, individual purification steps such as chromatography, solution inactivation and virus removal filtration steps are scaled-down from manufacturing-scale to bench-scale. The starting material for each step is spiked with virus, and input and output samples are collected and quantitatively assayed for virus. The difference in virus quantity between the input and output samples represents the amount of virus cleared by the step.



As manufacturers cannot bring virus into their manufacturing facilities due to the risk of contamination, viral clearance studies are almost always performed in Eurofins Lancaster Laboratories' viral clearance suites. Sample generation usually involves the hands-on participation of the client.

The time clients spend in the viral clearance suite equates to time spent away from manufacturing. To alleviate this issue, Eurofins Lancaster Laboratories now offers four levels of service solutions. With the Level 1 Service Model, clients participate fully in the study. With the Level 2 Model, clients perform the more complicated processing steps, but Eurofins Lancaster Laboratories personnel assist by performing the less complicated steps. This can save the client's days in the lab and also speeds the reporting time. In the Level 3 Model, Eurofins Lancaster Laboratories scientists train on all client procedures and perform all the clearance steps, saving even more of the client's time. With the Level 4 Model, clients provide a complete description of the full-scale manufacturing process and Eurofins Lancaster Laboratories personnel develop and validate all scale-down models and generate all study samples.

These flexible service models enhance the client's experience with significant time and cost savings, fostering a trusted strategic partnership between the client and Eurofins Lancaster Laboratories.

Contact: *GMP_US@eurofins.com*

Release testing of biologics into the EU

By Mark Glass, Eurofins Lancaster Laboratories, Republic of Ireland

With the consolidation of global manufacturing and increased use of single-site manufacturing through Asia and the Americas, the importation of biological medicinal products is becoming a key supply chain route into the European Union.

Under Directive 2004/94/EC, commercial products must undergo complete retesting of the product specification before a qualified person can certify the batches and allow onward entry into the market place.

Biologic compounds are often temperature sensitive and have more complex analytical requirements within their product specification. Eurofins Pharma Products Testing Group supports all aspects of biologics products testing. With experience in temperature controlled sample shipping and QPs on-site at several locations, Eurofins has the infrastructure to support incoming product.

These methods must be validated and transferred with a technical agreement in place with the client. Often these methods originate at the site of manufacture and must be those included in the Marketing Authorisation Application (MAA). The testing facilities will also be listed in the MAA . Having a broad base of the required capabilities means the timelines for transfer can be managed effectively to ensure readiness for the testing and release of the all important commercial batches.

Contact: *GMP_EU@eurofins.com*

Purpose	Test	Method
General (Compendial)	Appearance	Visual
	pH	Ph.Eur.
	Osmolarity	Ph.Eur.
	Moisture	KFT
Identity	Isoelectric Point	CE, Gel, Strip
	Peptide Map	HPLC
	Western Blot	ELISA
Purity	Chromatographic Purity	HPLC
	Gel Purity	SDS Reduced & Non-Reduced
Potency	Protein Concentration	A280
	Binding Assay	ELISA
	Biological Activity	Cell Based Bioassay
Safety	Sterility	MF/DT
	Endotoxin	Kinetic
	Bioburden	Ph.Eur.
	Particulate Matter	Light Obscuration
Impurities	Specific to the Manufacturing Process	

Table 1: This shows typical product characteristics and test requirements.

Risk based set-up for Analytical Process Control & Monitoring Systems (APC&MS)

By Pablo Moreno, Eurofins Biolab, Italy

Pharmaceutical facilities are required to meet GMP and governing regulations during the entire production lifecycle so that performance verifications, control of processes and monitoring systems are part of the validation lifecycle.

A science risk based approach applied to APC&MS is essential for an appropriate set-up in terms of effectiveness and costs. Mastering numerous projects and with years of experience, Eurofins recommends the following key concepts:

1. Product and process understanding:
An understanding of the supported process is fundamental in determining system requirements, focusing on those aspects that are critical to patient safety and product quality. The final objective of this approach is also linked to the identification of Critical Quality Attributes (CQAs) and related Critical Process Parameters (CPPs).

2. Lifecycle approach within Quality Management System (QMS):
Adopting a system lifecycle approach entails defining activities in a systematic way from system conception to retirement. As experience is gained in system use, the QMS should enable continuous process and system improvements on periodic review and evaluation and root-cause analysis of failures.

3. Choose carefully Risk Assessment (RA) technique:
Since the main cost in development of a QRM system is linked to the time spent of high level human resources, the choice of the RA technique is a very critical point. Below is a comparative table for the most common RA and their applications on APC&MS.

4. Analytical techniques must focus the scope of APC&MS:
In some cases, compendial methods may not be the best choice for APC&MS. Therefore, it would be necessary to undertake method development/validation and/or integrate methods reported in pharmacopoeias with other specific analytical tests. With the industry's most regulatory compliant capabilities and expertise, Eurofins can support production plants in analysing their approach to APC&MS set-up and implement a validation and monitoring plan based on these findings.

Contact: *GMP_EU@eurofins.com*

RA technique	Type of risk evaluation				Notes for application on APC&MS
	Numeric evaluation?	Time required	Expertise required	Inductive or deductive	
FMEA (Failure modes and effects analysis)	Yes	Moderate	Moderate	Inductive	Preferred for processes well known and for review of risks because it allows to quantify risks from failure modes.
HACCP (Hazard Analysis and Critical Control Points)	No	Moderate	Moderate	Inductive	Preferred for the evaluation of critical control points. Risk identification departs from specific hazards (like microbiological contamination).
FTA (Fault tree analysis)	Yes (could be)	Extensive	Extensive	Deductive	Apply only for very complex situations, such as tailor made systems that use unconsolidated technologies.

Comparative table for the most common RA and their applications on APC&MS

European set up at Asian price levels: what do you need more ?

By Dr. Emilie Vaquer, Eurofins ADME BIOANALYSES, France, emilievaquer@eurofins.com

Quality, timelines and costs are of the highest importance for the market of generic drugs. Eurofins ADME BIOANALYSES has adapted its services to clients' needs and offers an attractive and full package to complete successfully bioequivalence studies.

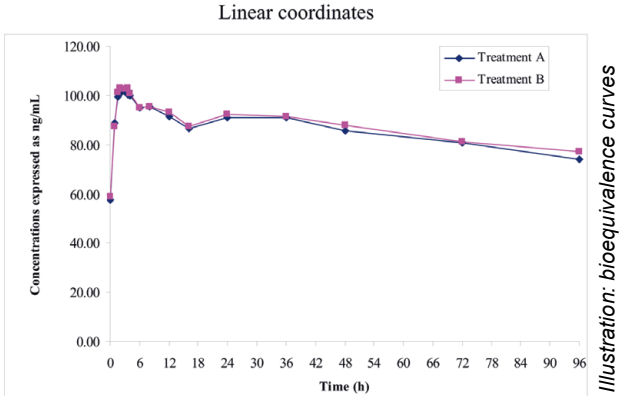


Illustration: bioequivalence curves

Today, Eurofins has strong partnerships with several global clinical centers: in France with Eurofins Optimed, in Europe and worldwide. Clinical trials are performed in close collaboration with these trustworthy and successful experienced clinical units, which are recognised by International authorities, such as FDA, Afssaps, WHO, MHRA.

All clinical trials comply with applicable Good Clinical Practices (GCP) and safety measures. These units are managed by efficient and experienced teams of clinical research professionals who give advice on the most relevant study design in line with the latest regulation and propose full clinical services, including study document writing and submission as well as medical support.

These clinical units have a large pool of healthy volunteers and specific populations (diabetic, dyslipidemic, overweight, high blood pressure subjects). The largest unit has a capacity of 130 beds.

The samples collected during clinical trials are analysed and pharmacokinetics parameters are calculated by Eurofins, using fully validated Software.With this new full package, Eurofins ensures high quality and cost effective opportunities for drug development.

Contact: *bioanalysis@eurofins.com*

eurofins

Pharma Services

COMING EVENTS

EVENT	DATE & PLACE	MORE INFO	CONTACT
EBF Focus Meeting	12.-13.06.2012, Brussels, Belgium	*Attend only*	*bioanalysis@eurofins.com*
PCMG	13.-15.06.2012, Albufeira, Portugal	*Attend only*	*clinicaltrials@eurofins.com*
Central Labs USA	19.-21.09.2012, Boston, MA, USA	*Attend only*	*clinicaltrials@eurofins.com*
ICAAC	9.-12.09.2012, San Francisco, CA, USA	*Booth N°901*	*clinicaltrials@eurofins.com*
Land '0 Lakes Conference	8.-10.08.2012, Merrimac, WI, USA	*Contact us*	*GMP_US@eurofins.com*
Contract Pharma	20.09.2012, New Brunswick, NJ, USA	*Contact us*	*GMP_US@eurofins.com*
BioProcess International	8.-12.10.2012, Providence, RI, USA	*Booth N°225*	*GMP_US@eurofins.com*
AAPS Annual Meeting	14.-18.10.2012, Chicago, IL, USA	*Booth N°3030*	*GMP_US@eurofins.com*
PDA on Pharm Microbiology	22.-23.10.2012, Bethesda, MD, USA	*Booth N°30*	*GMP_US@eurofins.com*
Well Characterized Biologicals	30.10.-01.11.2012, Bethesa, MD, USA	*Booth N°2*	*GMP_US@eurofins.com*

General contact
pharma@eurofins.com

Phase I, phase II, late phases, food trials, clinical enquiries, vaccine studies
clinicaltrials@eurofins.com

Bioanalytics, pharmacokinetics, metabolism
bioanalysis@eurofins.com

Global Central Laboratory
clinicaltrials@eurofins.com

Pharma Products Testing USA
GMP_US@eurofins.com

Pharma Products Testing Europe
GMP_EU@eurofins.com

For further information & contacts in other countries please refer to our website *www.pharma.eurofins.com.*