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BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

BioPharma Services News

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Eurofins BioPharma Product Testing expands global ID Footprint

By Mark Kaiser, Eurofins Lancaster Laboratories Senior Director, MarkKaiser@eurofinsUS.com

Eurofins Biopharma Product Testing group has enhanced its identification capabilities with the acquisition of IDmyk, a laboratory specialised in identification and molecular typing of microorganisms. Integration of the IDmyk databases for sequence analysis into the Eurofins Biopharma Product Testing laboratory network, including the laboratory in Lancaster, PA, USA, provides a global platform for clients using multiple Eurofins locations.

IDmyk, located in Lyon, France, offers the largest proprietary databases for sequence-based identification of organisms. The databases contain 8,450 type strains of organisms relevant to the bio/pharmaceutical industry and are updated regularly with new organisms through a validated process. The use of long sequencing for bacteria as a standard approach improves the accuracy of the identification when compared with partial sequencing commonly used in the bio/pharmaceutical industry. Multilocus Sequence Analysis (MLSA) is available and uses sequencing of housekeeping genes and extended databases of reference sequences to further discriminate organisms at the species level.

IDmyk also offers molecular typing to differentiate strains of the same species to support contamination investigations. Services include MultiLocus Sequence Typing (MLST), Arbitrary Primed PCR (APPCR), Variable Number of Tandem Repeats (VNTR), Pulse Field Gel Electrophoresis (CHEF) and MicroSatellite Analysis (MSAT).

In addition, Eurofins Lancaster Laboratories (ELLI) has added the capability to identify bacteria using MALDI-TOF which provides phenotypic identification using organisms' protein patterns. ELLI uses the Bruker platform and its validated database of 4,600 organisms. The MALDI-TOF service provides clients with cost-effective identification in short timeframes, including same-day service and is ideal for identification of isolates from environmental monitoring.

The addition of MALDI-TOF, the largest libraries of organisms worldwide for sequencing and molecular typing through IDmyk, provides clients with comprehensive services and the option to choose the appropriate level of identification to fit their needs.

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

Eurofins Lancaster Laboratories expands cell banking capabilities, meeting stringent grade A/Grade B EU requirements

By Jeri Ann Boose, Ph.D., Senior Biopharmaceutical Director, Eurofins Lancaster Laboratories, JeriAnnBoose@eurofinsUS.com

Enabling global clients to bring products to the market under both US and EU regulatory environments, Eurofins Lancaster Laboratories (ELLI) is enhancing its current cell banking capabilities. ELLI is doubling the number of cell banking clean-room suites from two to four, adding long-term cell banking storage for both production and non-production cell banks, and increasing the maximum bank size from 400 to >1000 vials.

For many years, ELLI's Cell Banking Group has prepared a wide variety of mammalian cell banks in support of GMP production, GMP non-production (e.g., banks for bioassay), and R&D needs. Currently, the two suites used for the preparation of GMP production banks are designed to meet ISO5/ISO7 FDA clean-room requirements. The two new suites have been designed to meet the more stringent Grade A/Grade B EU requirements, therefore enabling global clients to prepare their production master and working cell banks in an environment that without question will be acceptable to EU Regulatory Authorities.

ELLI also provides extensive support to clients needing non-production master and working cell banks. These banks are typically used in cell based potency assays that are part of the lot release testing panel for a given product. In response to increasingly frequent requests for large banks of ready-to-use cells to support these assays, ELLI is currently validating the fill of banks exceeding 1000 vials at the cell concentration specified by the client. This service will be offered concurrently with the opening of our Grade A/Grade B suites.

Offering long-term storage solutions, cell banking clients may now elect to store part or all of their banks at the Lancaster, PA, facility.

The combination of these facility expansions and service offerings, high level of technical expertise in cell banking and characterisation, and extensive project management tools have been designed to provide clients with a single source solution for all cell line needs.

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

Cleaning validation: health based exposure limits in shared facilities

By Paolo Pescio, Eurofins BioPharma Product Testing Italy, PaoloPescio@eurofins.com

In shared facilities, the possible cross contamination between different active substances is an issue of concern. An active substance could contaminate the next product manufactured in the same facility; therefore, its presence should be restricted to a level that can be considered safe for all populations.

During cleaning validation some practical and arbitrary criteria are in place:

- a relative limit considering a contamination lower than 1/1000th of the lowest clinical dose of any product in the maximum daily dose of the next product, or
- an absolute limit of 10 ppm of the previous active substance in the next product manufactured.

These limits do not take account of the available pharmacological/ toxicological data and possible duration of exposure and may be too restrictive or not restrictive enough.

Threshold value (permitted daily exposure - PDE) or threshold of toxicological concern (TTC) should be used as actual limits for cleaning validation.

Determination of a PDE involves:

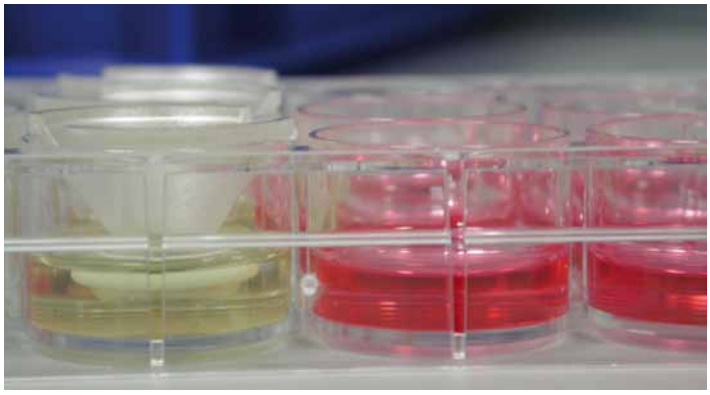
- hazard identification by reviewing all relevant data
- identification of "critical effects"
- determination of the No-Observed-Effect Level (NOEL) of the findings that are considered to be critical effects (if no NOEL is obtained, the Lowest-Observed-Effect Level or the benchmark dose could be considered)
- use of several adjustment factors to account for various uncertainties (also referred to as safety, uncertainty, assessment or modifying factors) to account for various uncertainties and to allow extrapolation to a reliable and robust no-effect level in the human or target animal population).

Eurofins can perform PDE and TTC evaluation on the basis of available pharmacological and toxicological data, including both non-clinical and clinical data as required by **EMA guideline, "Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities."**

For more information on how Eurofins can help you with cleaning validation, visit *www.eurofins.com*.

Step into the Future: Trendsetting role of BSL BIOSERVICE in animal-free medical device testing

By Helge Gehrke, BSL BIOSERVICE GmbH, (a Eurofins partner laboratory), Germany



Acute irritation is a local, reversible inflammatory response of normal living skin to direct injury caused by the application of an irritant substance. The potential to induce skin irritation is an important consideration and is, beside cytotoxicity and sensitisation, one of three biocompatibility testing recommended for all medical devices (MD).

Up to now, current guidelines (ISO 10993-10) refer to the *in vivo* Draize Test that has been widely used to screen MD for skin irritancy. In order to replace *in vivo* testing, the ISO Technical Committee 194 published a revised version 10993-1:2009, in which the use of alternative animal free methods is specifically encouraged. Based on validation studies under the auspices of ECVAM, reconstructed human epidermis (RhE) models showed evidence of being reliable and relevant replacement tests for *in vivo* skin irritation. RhE models consist of normal human epidermal keratinocytes and therefore represent *in vitro* the target organ of the species of interest and closely mimic the biochemical and physiological properties of the upper parts of the human skin. The determined endpoint (cytotoxicity) is reliable and well known and can be combined with inflammatory markers, for further confirmation of obtained results.

So far, being an established standard for chemical testing, the method can be adapted for medical devices. Therefore, these models can be a suitable alternative for the *in vivo* rabbit skin irritation test to evaluate MD biocompatibility and can be a step into a free animal testing future. The reduction of animals in biocompatibility tests by encouragement of the development and validation of effective *in vitro* alternative methods is one of the outmost concerns at BSL BIOSERVICE (a Eurofins partner laboratory).

Being convinced that *in vitro* alternative methods represent the future, BSL BIOSERVICE takes a leading role and already offers different RhE models (EPISKIN™/EpiDerm™) for testing the irritating potential of medical devices.

Contact: *hgehrke@bioservice.com*

Taking fingerprints of medical devices – Chemical characterisation according to ISO 10993-18

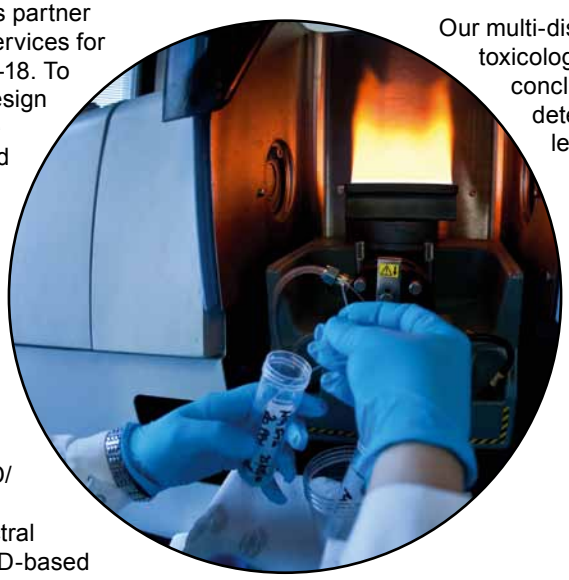
By Dr. Enrico Franzoni, Eurofins BioPharma Product Testing, Italy, and Dr. Christoph Höppner, BSL Bioservice GmbH, Germany

As part of the biological evaluation of medical devices as described in the ISO 10993 series, Eurofins BioPharma Product Testing and BSL BIOSERVICE (a Eurofins partner laboratory) joined forces to offer testing services for medical devices as outlined in ISO 10993-18. To compare medical device products after design and material change, we have created the "GC/HPLC/ICP fingerprint," a standardised service for chemical characterisation of MDs.

Even for complex geometry, materials and consistency, we offer solutions to prepare, extract and analyse in full compliance with ISO 10993-18. High accuracy and sensitivity are guaranteed by fully validated analytical methods.

BSL BIOSERVICE is specialised in performing GC-fingerprint using a GC-FID/MS setup, which provides both high identification rates within NIST mass spectral library and excellent linear range of the FID-based quantification method.

Eurofins BioPharma Product Testing is able to perform screening of more than 35 inorganic elements by ICP technique and is equipped with two kinds of LC-MS for organic non-volatile compounds: Ionic Trap and Q-TOF with an internal database of more than 100 known compounds that is constantly updated.



Our multi-disciplinary team of analysts and toxicologist is proficient in researching and concluding expert statements about the detected chemical substances and will leave no question unanswered.

Contact: *EnricoFranzoni@eurofins.com*; *choeppner@bioservice.com*

Eurofins selected to be a partner of Cosmetics Europe Task Force Skin Bioavailability and Metabolism Project

By Céline Bonati, Eurofins ADME Bioanalyses, CelineBonati@eurofins.com

The Eurofins DMPK centre located in Vergeze, France, has expertise in pharmacokinetics and immunogenicity and has developed over several years the specific skills to perform dermal distribution and permeation studies. Since 1987, Eurofins has successfully provided these services to its clients and strengthened its presence in this market. This selection to the task force acknowledges the recognition from the pharmaceutical and cosmetic world of Eurofins' expertise in this field. As part of the proposal request initiated by Cosmetics Europe, the task force will study a wide range of molecules, commonly found in cosmetic formulations that have various chemical properties.

Thanks to Eurofins' expertise in this field, Cosmetics Europe has awarded Eurofins-Vergeze to be their dedicated partner for dermal distribution and permeation studies. This leadership position brings Eurofins to the forefront of dermal product assessment.

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

COMING EVENTS

EVENT	DATE & PLACE	MORE INFO	CONTACT
BioEurope	03-05.10.2014, Frankfurt, Germany	*Contact us*	*CamillePicq@eurofins.com*
CPHI	07-09.10.2014, Paris, France	*Booth 39-41*	*CelineBonati@eurofins.com*
BioProduction	08-09.10.2014, Barcelona, Spain	*Contact us*	*GMP_US@eurofins.com*
PDA Global Pharm Micro Conference	20-22.10.2014, Bethesda, MD	*Contact us*	*GMP_US@eurofins.com*
BioProcess International	20-23.10.2014, Boston, MA	*Contact us*	*GMP_US@eurofins.com*
GMP *(Groupement metabolisme et pharmacocinétique)*	22-24.10.2014, Paris, France	*Contact us*	*CelineBonati@eurofins.com*
ISBioTech	27-29.10.2014, Rosslyn, VA	*Contact us*	*GMP_US@eurofins.com*
IFSCC *(International Fed. of Societies of Cosmetic Chemists)*	27-30.10.2014, Paris, France	*Contact us*	*CelineBonati@eurofins.com*
AAPS	02-06.11.2014, San Diego, CA	*Contact us*	*GMP_US@eurofins.com*
EBF *(European Bioanalytical forum)*	19-21.11.2014, Barcelona, Spain	*Contact us*	*CelineBonati@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

Pharma Discovery Services
discoveryservices@eurofins.com

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