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Pharma Services News

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Isotopic fingerprinting of goods–providing evidence for counterfeit pharmaceuticals

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Ensuring the safety and efficacy of pharmaceuticals in an increasingly complex global supply chain is a major concern for government agencies worldwide. The most common fraudulent practice involves a medicine that contains the wrong or no active ingredient, or even the right active ingredient but at the wrong dose. There are however other more sophisticated practices such as the deliberate copying of existing patents for processes or formulations or the relabelling of stolen drugs or of their provenance to circumvent anti-dumping measures or to benefit from a “clear status” of a producing country.

Given the wide range of products and practices that come under the “counterfeit” umbrella, no single method is available for the identification and prevention of counterfeit medicines. Amongst the anti-counterfeiting technologies that have been developed are those based on stable isotope analyses in which the unique chemical properties of a substance provides forensic evidence of its manufacturing process or the raw materials used.

The two most commonly used methods for measuring stable isotope ratios are IRMS (Isotope Ratio Mass Spectrometry), which measures isotope ratios of several nuclei (C, H, N, O, S), and SNIF-NMR (Site specific Natural Isotope Fractionation studied by Nuclear Magnetic Resonance spectroscopy), which provides information on different molecular sites simultaneously. Recent technological developments have made it possible to measure site-specific 13C/12C ratios directly using quantitative 13C NMR, in addition to the better-known 2H SNIF-NMR. The combined information from multi-element IRMS measurements and from 2H and 13C SNIF-NMR creates a unique isotopic fingerprint of a compound. This “isotopomic” approach has been applied to the authentication of commonly used generic pharmaceuticals, such as ibuprofen and naproxen, demonstrating its potential to provide evidence in cases of patent infringement or to help track a product along its supply chain.

As Eurofins Scientific was founded 25 years ago based on their patented SNIF-NMR technology, the Group has the scientific experience and expertise to support clients’ most challenging testing projects. For more information contact: *asmnantesauthenticity@eurofins.com*

References

[1] 16.E. Deconinck, A.M. van Nederkassel, I. Stanimirova, M. Daszykowski, F. Bensaid, M. Lees, G.J. Martin, J.R. Desmurs, J. Smeyers-Verbeke, Y. Vander Heyden, Isotopic ratios to detect infringements of patents or proprietary processes of pharmaceuticals: two case studies, J. Pharm. Biomed. Anal. 48 (2008) 27-41.

[2] U. Bussy, C. Thibaudeau, F. Thomas, J.R. Desmurs, E. Jamin, G.S. Remaud, V. Silvestre, S. Akoka, Isotopic fingerprinting of active pharmaceutical ingredients by 13C NMR and polarization transfer techniques as a tool to fight against counterfeiting, Talanta 85 (2011) 1909-1914.

[3] G. S. Remaud, U. Bussy, M. Lees, F. Thomas, J.R. Desmurs, E. Jamin, V. Silvestrea and S. Akoka, NMR spectrometry isotopic fingerprinting: a tool for the manufacturer for tracking Active Pharmaceutical Ingredients from starting materials to final medicines. European Journal of Pharmaceutical Sciences 48 (2013) 464–473.

Rapid evaluation of disinfectant activity: a semiautomated bioluminescent ATP assay

by Pilar Visa, Eurofins Biolab S.L.U., Spain, PilarVisa@eurofins.com

Culture-based microbiological methods currently used for the evaluation of disinfectant activity under simulated practical conditions of use are labourious and lengthy. These tests, generally known as suspension and carrier tests, include several manual steps, and their execution requires a lot of time and material. Therefore, they allow only a few sets of conditions to be tested for a given product in a single run.

Eurofins Biolab now offers a new in-house developed semi-automated rapid method for the evaluation of the bactericidal and yeasticidal activity of disinfectants. The new test's approach consists in scaling-down to 96 micro-well plates of the EN standard suspension and carrier tests procedures. After the contact time with the disinfectant, the quantity of viable microbial cells is calculated within a few minutes by ATP quantification with a luminometer, through luminescence measurement.

The validation study, performed by comparison to the EN standard tests, showed that the new assay evaluates the activity of biocides as well as the EN standards, but it allows a larger number of test conditions to be efficiently analysed, with a very high reproducibility as it is a semi-automated procedure.

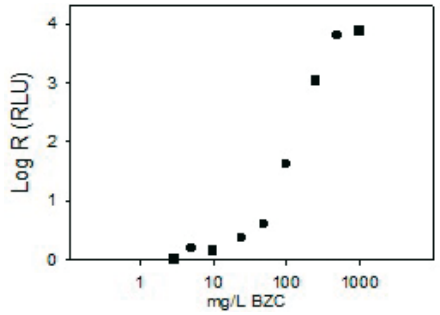


Figure 1. Inactivation curve for Staphylococcus aureus with increasing concentrations of a benzalkonium chloride at contact time of 5 minutes

The new assay can be used to accurately assess the lowest active concentration of a disinfectant and to compare the microorganisms' susceptibility via inactivation curves.

Since this procedure allows testing in the same run many conditions for the same microorganism, temperature and contact time, it is a very useful screening tool.

Eurofins' rapid assay scientific advancements with a full description of this new assay and the results of the validation study were published in April 2012 by the Journal of Applied Microbiology. To find out how Eurofins can assist your testing needs, contact: GMP_EU@eurofins.com

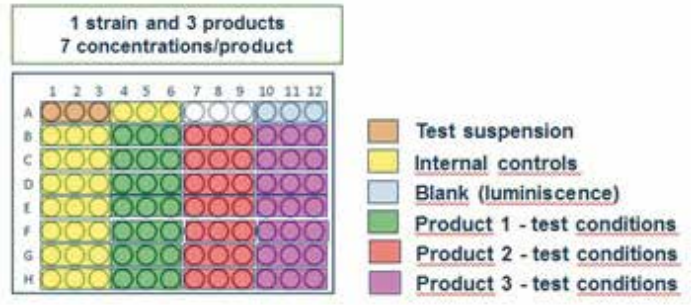


Figure 2. Example of design of experiments

Reference

Aragonès, L., C. Escudé, P. Visa, L. Salvi and L. Mocé-Llivina. "New insights for rapid evaluation of bactericidal activity: a semi-automated bioluminescent ATP assay". Journal of Applied Microbiology. 2012

Innovation for pharmaceutical and cosmetic product delivery

By Christelle Gélis, Eurofins ADME Bioanalyses, France, ChristelleGelis@eurofins.com

After 11 July 2013, all performance of cosmetics will have to be clearly documented. Due to the cost of development of a new ingredient (REACh: Registration, Evaluation and Authorisation of Chemicals), most of the companies would prefer to use an approved ingredient. Therefore, most of the cosmetic research is directed toward the use of new local delivery devices, for example:

- Different types of patches

- Textile prints with an embedded active ingredient such as caffeine to improve lipolysis

- Pre-treatment of the skin to improve dermal absorption

To validate these different techniques, the availability of the active ingredient at the site of action has to be confirmed. In vitro testing, using human skin mounted on Franz cells, allows for the measurement of the active ingredient present in the different skin layers.

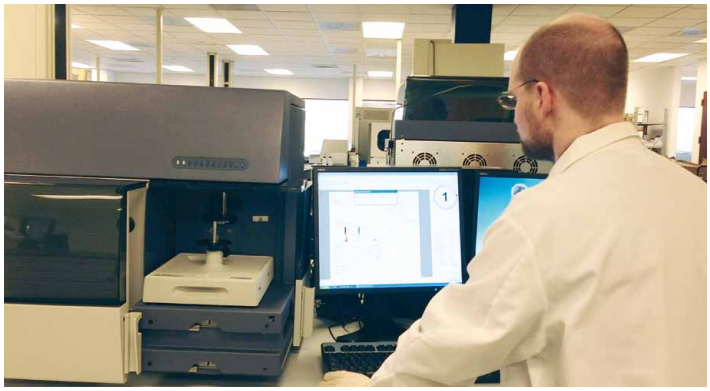
Internal dermal absorption data generated by Eurofins' dedicated team show that these innovative technologies can significantly improve the absorption of active ingredients through human skin. They also demonstrate the importance of testing active ingredients and formulations utilising Franz cell technology. To discover how Eurofins can meet your pharmaceutical and cosmetic testing challenges, contact: skin@eurofins.com

To read Part I of this article, titled, Evaluation of Human Skin Absorption Risk for Pharmaceutical and Cosmetic Products: an In Vitro Approach, please visit: *pharma.eurofins.com*

Figure 1: Franz cell in vitro model

New Flow Cytometry Platform Operational – Eurofins Expands Capabilities in the U.S. and Singapore

By Dr. Christoph S. Eberle, Dr. Charles J. DiComo, Eurofins Global Central Laboratory, ChristophEberle@Eurofins.com, CharlesDiComo@Eurofins.com



Eurofins Global Central Laboratory (EGCL) has broadened its technical and scientific scope with the addition of new flow cytometry (FC) systems in the U.S. and Singapore. Both sites are now equipped with state-of-the-art instrumentation, complementing the existing capabilities in Europe. FC method development and optimisation are being offered for domestic and international clientele. With this expansion, the EGCL can now provide further harmonisation of rapid and sensitive test results being produced in a true global lab setting for clinical and preclinical routines as well as biomarker research.

Since its inception, FC has been used largely as an automated tool for immunophenotyping. Traditionally, this involved limited singled-out particle identification and quantification. However, more of its technological potential has been realised with the design of new antibody-conjugated fluorophores, widening the spectrum of multi-parametric analysis. Testing can be performed using various tissue extracts and body fluids (whole blood, PBMCs, urine, CSF), whilst measuring cells, bacteria, organelles, polymer structures like DNA/RNA, or BRMs.

Many commercially available panels can be customised and assays individually tailored to suit the needs of clients by selecting the panel of pharmacodynamic markers to answer more sophisticated research questions. Recently, FC has been applied to platelet enumeration, antibiotics susceptibility testing, determination of protein phosphorylation, and intracellular cytokine production. Additionally, immunophenotyping techniques are promising for the surveillance of immune cell populations in the CNS or in peripheral blood. Along with image analysis, FC has also been utilised for DNA ploidy and cell cycle determinations. Monitoring cell population total DNA content contributes to a better understanding of tumor proliferation. In breast and prostate carcinomas, such measurements appear to have prognostic value and may well help to improve treatment modalities.

With its new, versatile FC capabilities, the EGCL is well positioned to offer innovative solutions for industrial, clinical, and research partners while maintaining high quality control standards.

For more information: *centrallab.eurofins.com*

Development and optimisation of (bio) analytic procedures for difficult matrices

By Sabine Thiessen, Susanne Janku and Christoph Höppner, choeppner@bioservice.com

Non-clinical biodistribution or in-vitro skin-penetration studies may be crucial in the development of new pharmaceutical products. These studies require development of robust analytical methods for elucidation of both total concentration and distribution of the substance of interest in its biological matrix. This especially holds true when the work with 14C- or 3H-radiolabelled compounds is not possible for one reason or another. The development of “cold” analytics consists of defining the right combination of preparatory work, extraction procedure and chromatographic technique with the ultimate intention to create a method uniting all favourable characteristics. Ideally, the method should be robust, sensitive, accurate and reproducible. Additionally, it should be quick, simple and inexpensive. While bioanalytics from plasma, serum, urine and other predominantly liquid biological matrices may be challenging at times, there is an escalation. BSL BIOSERVICE (Eurofins partner lab) in Germany has acquired expertise in developing strategies for matrices that combine diverse unfavourable characteristics, e.g. skin and other organ tissues.

The strategies for method development can be diverse and labour intensive at times. Ideal results are obtained by wise definition of three key procedures. First, the homogenisation device and protocol best suited for the matrix/analyte combination must be defined. Stability of the analyte in the face of transient heat exposition as a result of violent homogenisation procedures must be taken into account, and alternative methods (e.g. liquid nitrogen deep-freeze followed by mortar pulverisation) may be considered. For extraction of the solvent, dilution factor for the homogenate and time/temperature combination are selected. Time-point for addition of the internal standard must serve the purpose while being practical and technically feasible. Thirdly, the ideal HPLC and MS settings, including choice of column, solvent and run parameters need to be found, often trading off run-time versus sensitivity. Satisfying recovery and accuracy in an analytical method that is fit for analysis of large sample numbers is the goal.

With every new project, the company’s expert advice and customer-oriented efforts are essential to providing clients with the best analytical solutions. For more information, please contact: *info@bioservice.com*

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Pharma Services

in brief

OncoPanel™ High-Content Cell Line Profiling to identify biomarkers of response

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Cancer is one of the most devastating diseases of our time−the second most common cause of death in the United States, exceeded only by cardiovascular diseases. According to the American Cancer Society 1,660,290 new cancer cases are expected to be diagnosed in 2013, and 580,350 Americans are expected to die of cancer, almost 1,600 people per day in just the U.S. alone. Cancer is a set of complex genetic diseases hallmarked by changes in the genome, where a variety of somatic alterations plays a vital role in disease initiation and progression.

Recent years have heralded a marked increase in our understanding of the genetic basis of cancer. Cancer genomics has been impacted profoundly by the application of Next-Generation Sequencing technology, which has tremendously accelerated the pace of cancer drug development. A major focus in cancer drug development is in the identification of genomic biomarkers capable of predicting sensitivity and resistance to new therapies and identifying the patient population who will be responsive for these targeted therapies.

Eurofins Panlabs has developed OncoPanel240, using a High Content Analysis (HCA) platform, to provide multiparametric drug response data, including cell proliferation, apoptosis induction and cell cycle arrest across a large panel of genomically defined cancer cell lines comprising most human cancer subtypes. The Group has developed a genomic data repository composed of internal and public genomics data on all the 240 cell lines to identify significant genomic biomarkers associated with sensitivity or resistance to the tested therapeutic and then to prioritise them based on statistical significance. The most significant biomarkers are further analysed in the context of cancer subtypes. These biomarkers can be utilised in developing diagnostic as well as pharmacodynamics markers.

Eurofins Panlabs' expertise in generating high quality data in screening small molecules, biologics and combination therapies, as well as its unique integration of profiling results with univariate genomics analysis, enables pharmaceutical and biotechnology companies to identify predictive genomic biomarkers of drug response with prognostic relevance for both discovery and clinical development.

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COMING EVENTS

EVENT	DATE & PLACE	MORE INFO	CONTACT
SFSTP Congress	12-13 06 2013 Montpellier, France	*Booth TBA*	*GMP_EU@eurofins.com*
53° Simposio AFI	12-14 06 2013 Rimini, Italy	*Booth 39-41*	*GMP_EU@eurofins.com*
Virus Safety for Biologicals	18-19 06 2013 NH Danube City, Vienna	*Booth TBA*	*GMP_US@eurofins.com*
BioProcess International Conference	16-20 09 2013 Boston, MA	*Booth # 825*	*GMP_US@eurofins.com*
ICAAC	10-13 09 2013 Denver, CO	*Booth# TBA*	*clinicaltrials@eurofins.com*
A3P Congress	15-17 10 2013 Biarritz, France	*Booth TBA*	*GMP_EU@eurofins.com*
Well Characterized Biologicals	21-23 10 2013 Washington, DC	*Booth #3*	*GMP_US@eurofins.com*
PDA Annual Global Conference	21-23 10 2013 Bethesda, MD	*Booth #12*	*GMP_US@eurofins.com*
AAPS Annual Meeting	10-14 11 2013 San Antonio, TX	*Booth #3223*	*GMP_US@eurofins.com*
Partnerships in Clinical Trials	20-21 11 2013 Vienna, AT	*Booth# 447*	*clinicaltrials@eurofins.com*

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