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BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

BioPharma Services News

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Detecting more pathogens for more patients, through Target Enriched Multiplex Polymerase Chain Reaction (TEM-PCR™)

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Eurofins expanded its footprint in specialty clinical diagnostics with the acquisition of Diatherix Laboratories, Inc., a highly-specialised laboratory based in Huntsville, Alabama (USA), that provides cutting-edge molecular diagnostic testing services to hospitals and physicians using its proprietary TEM-PCR technology. TEM-PCR is a unique, multiplex amplification platform that delivers increased sensitivity and specificity and simultaneously identifies bacteria, viruses, parasites, Candida and antibiotic resistance genes from a single sample, with one day results (typically within eight hours of specimen receipt).

Given Diatherix's synergies with Viracor-IBT Laboratories—another member of the Eurofins Scientific Group known for its expertise in infectious disease testing with fast turnaround time—the companies have partnered to be able to provide testing services utilising TEM-PCR technology to even more hospitals and patients.

Viracor-IBT recently launched its first panel utilising TEM-PCR technology: the Respiratory Pathogen Panel (RPP) TEM-PCR, which gives hospitals the ability to detect 26 common and important bacterial and viral pathogens from one specimen in one day, to improve patient outcomes and reduce healthcare costs. RPP TEM-PCR also allows physicians to detect co-infections, withhold antibiotics in patients with viral detection, administer appropriate antibiotic and/or antiviral therapy and incorporate evidence-based medicine to enhance the quality and cost-effectiveness of patient care.

Current TEM-PCR panels available through Diatherix include multiple types of respiratory panels (such as Upper Respiratory, Pediatric Respiratory and Atypical Pneumonia, to name a few), as well as Gastrointestinal, Urogenital and General Infection panels. Both companies will continue to offer more TEM-PCR testing panels and options in 2016 to help physicians and patients get accurate results faster, when it matters most.

For more information, please visit *www.viracoribt.com* and *www.diatherix.com*

Evaluation of cytokine storm risk during drug development

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Induction of cytokines, termed cytokine storm, is a common consequence of the administration of therapeutic antibodies. The most publicised occurrence was in 2006 when the administration of TGN1412 to subjects in a Phase I trial resulted in unprecedentedly high levels of cytokine release, leading to hospitalisation of the subjects with systemic organ failure. The subsequent focus on additional safety testing to prevent such tragic events has led the development of *ex vivo* assays capable of indicating whether a novel therapeutic antibody would present a significant risk for cytokine release. Such assays are critical safety evaluation tools in early stage drug candidate screening and are integral to the drug development process.

Eurofins has developed pre-qualified Cytokine Release Assays that encompass several of the key variables required for the cytokine release testing, including a modular choice of positive and negative controls (pavilizumab, trastuzumab, alemtuzumab, OKT3 and YTH12.5, as well as user-defined controls), and also solution, wet and dry coating presentations of compounds. Typical cytokines and chemokines tested are IFN-γ, IL-2, TNF-α, IL-10, IL-1β, IL-8 and IL-12p70. Additional markers can be added upon request.

The assays use heparinised whole blood, plasma depleted whole blood or isolated PBMC samples which are incubated with the investigational drug as well as with positive and negative controls. Plasma fractions are generated and then subjected to analysis on a choice of Luminex or Meso Scale Discovery platforms. Additionally, the treated blood samples can be subjected to analysis by flow cytometry for intracellular/surface marker analysis. For very early stage safety evaluations, Eurofins also offers cytokine release assays using specific cell lines.

The Cytokine Release Assays from Eurofins provide drug developers with rapid access to early drug safety data, and as core assays are pre-qualified, development costs and time are eliminated.

For more information, visit:
www.eurofins.com/bioanalyticalservices

Chemical characterisation of medical devices: from theory to real applications

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Chemical characterisation is becoming increasingly more important in the world of medical devices at various stages throughout a product's life cycle. The extension and depth of biological investigations are normally directly linked to the level of risk associated with the device, and this is true for chemical characterisation as well. Innovative devices are becoming more complex, and it is therefore imperative that the manufacturer has an extensive knowledge of the device.

At the initial phase of a new device development process, information gained by performing chemical characterisation provides the manufacturer with valuable knowledge to progress towards the final prototype.

Once the device design is completed and it is time for the crucial safety assessment phase, the data obtained from chemical characterisation provides important information to be evaluated together with toxicological data to fulfill international regulations. This characterisation takes the form of an extractable study, whose data is critical to determining device safety for patients. The extractable study data is evaluated by following the approach dictated in the ISO-10993-17:2002 standard ("Biological evaluation of medical devices -- Part 17: Establishment of allowable limits for leachable substances").

Chemical characterisation can prove to be very useful when it comes to change management. Complex devices are often impacted by changes, from production process to cleaning procedures, from materials suppliers to the sterilisation phase. In many cases a thorough chemical characterisation may help in decreasing the amount of biocompatibility testing to be performed. For example, if the comparison of extractable profiles between an "old" and "new" device shows no relevant differences or are toxicologically equivalent (bridging concept), then you may be able to limit the requirements to the execution of a reduced set of biocompatibility tests.

This area is evolving quickly, and the availability of extended and comprehensive guidelines is limited. Eurofins experts are ready to support medical device companies in identifying the proper solutions and best testing options for their medical devices. Please contact *medical-device@eurofins.com* for any query or need you may have.

To read a previous article pertaining to this topic, visit (*http://www.eurofins.com/pharma-services/media-centre/pharma-newsletters/eurofins-pharma-services-newsletter-12-october-2015/revisions-of-iso-10993-medical-device-standards.aspx*)

Microbiological potency testing of antibiotics: facing USP and EP requirements

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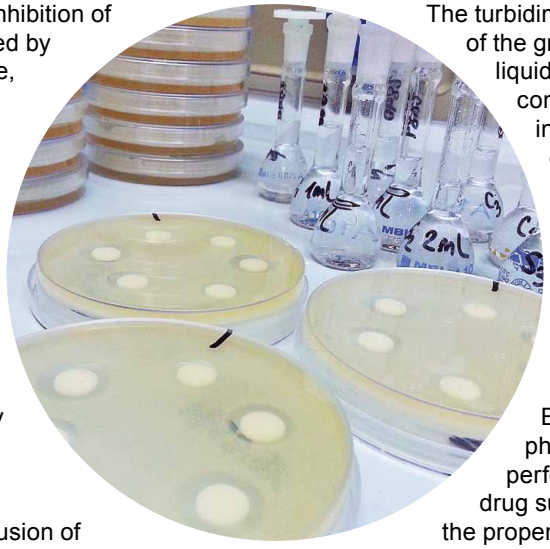
For several antibiotics, the European Pharmacopoeia 2.7.2 and USP <81> specifications about the product potency require testing through microbiological assays. The activity of the antibiotic is estimated by comparing the inhibition of the growth of susceptible strains, produced by different concentrations of the test sample, compared to the one coming from a reference preparation.

The advantages of microbiological methodology (diffusion or turbidimetric methods), as opposed to chemical assays, are represented by the possibility to measure the activity directly on a specific microorganism, taking into account the actual availability of the active substance as well as the ability to determine the activity of a substance without the information of the exact qualitative composition.



The diffusion method is based on the diffusion of the antibiotic in the solid culture media. The test sample and the reference standard are placed on the surface of a solid medium inoculated with a microorganism suspension; the growth of the microorganism into the culture medium will be visibly inhibited after the incubation.

The turbidimetric method is based on the inhibition of the growth of a sensitive microorganism in liquid culture exposed to different concentrations of the antibiotic. The inhibition is measured by the different degree of turbidity of the suspension, which is proportional to the different level of microbial growth.

EP and USP mainly differ on the design of the assay itself and the choice of mathematical models used to determine the potency.

Eurofins is able to support pharmaceutical companies needing to perform GMP testing on antibiotic-based drug substances or drug products in selecting the proper test system based on regulatory requirements and running the actual testing according to either USP or EP test methods. For more information, visit *www.eurofins.com/pharma-services/biopharma-product-testing*

Biomarker analysis by flow cytometry–a powerful technique in clinical trials

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The past decade has witnessed a remarkable increase in small and large molecules, especially therapeutic antibodies – a trend, which is predicted to continue. Cellular biomarkers are necessary in defining disease pathology, toxicological assessment and efficacy. Flow cytometry is a powerful cellular analysis technique, which has proved to be valuable in research and clinical trial environments to further drug development.

Eurofins is well positioned to assist clients with specialised flow cytometry assay development, validation, and sample analysis needs. Eurofins has developed five modular core assays that drug developers can use as they are or can modify with additional markers to meet the needs of the specific clinical investigation, including:

- TBNK assay (T-cell, B-cell, NK-cell)
- Leukocyte activation panel
- FceRI / IgE basophil assay
- T-Helper cell panel
- Monocyte, dendritic cell panel

The rapid-access of the “off the shelf” qualified panels provide: reduced cost, quick development time and flexibility to be validated according to the levels required by the study.

Eurofins’ Immunoanalytics Department operates multiple flow cytometry Canto II systems. Due to special needs for human material of clinical trials, the team has developed a method to ensure equal results of one sample measured on two machines. This represents a perfect back-up system. Sample analysis is performed in compliance with G(C)LP.

As a leading innovator in flow cytometry supporting long-term clinical trials, Eurofins uses molecules of equivalent soluble fluorochrome beads to enable the standardisation of fluorescence intensity units irrespective of instrument and day of measurement. Eurofins is highly experienced in supporting worldwide clinical trials and handling various samples from numerous clinical centres. Training of clinical sites by flow cytometry experts ensures high quality samples.
For more information on our services, visit:
http://www.eurofins.com/pharma-services/immunoanalytics

Window on the world of samples

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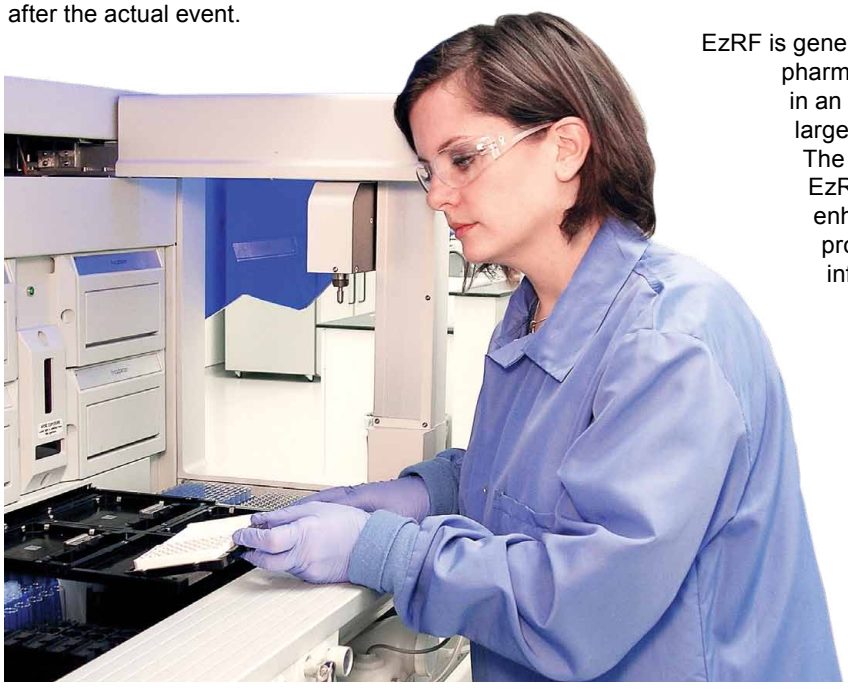
One third of the cost of a clinical trial is typically devoted to laboratory testing. A submission to a regulatory authority is at least 60-70% data generated by testing samples, the rest being clinical observations of patients.

With so much depending upon the specimen element of a clinical trial, it is not unexpected that much of a client's focus is not necessarily on the laboratory testing but on the support functions that track and trace samples throughout their entire life cycle.

A lot of effort is expended to track and trace samples whilst at the laboratory, quickly locating aliquots, for testing. It is rare that a laboratory will have complete oversight of samples from patient to the laboratory. Sites are required to complete handwritten request forms, which by their nature create many discrepancies in the records which need reconciliation and digitisation, usually many months after the actual event.



Eurofins Central Lab (ECL) has developed a web based tool, EzRF, which allows the Clinical Sites to directly enter sample details into the ECL systems, thereby bypassing the need for paper-based request forms. EzRF is able to immediately detect discrepancies and captures a resolution in real time—anything from an incorrect date of birth to wrong samples being collected. EzRF will also maintain a record of samples that are being temporarily stored in the physicians' offices for a later shipment, allowing the project manager visibility to the location of their samples.

In global clinical trials supported by ECL, samples may be transported around the globe. Utilising a tool such as EzRF enables the PM and/or the client to know where samples are at any time and facilitates effective sample management. Many problems are detected in real-time, saving a significant amount of time in reconciliation, which of course ultimately saves time and money.

EzRF is generating a great deal of interest within the pharmaceutical sector, proving truly innovative in an aspect of the industry that has remained largely unchanged for almost two decades. The development of the next iteration of EzRF has already begun and will further enhance the suite of tools available to project managers and clients. For more information, visit *www.eurofinscentrallab.com*

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