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BioPharma Services News

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Genetic stability testing ensures product integrity

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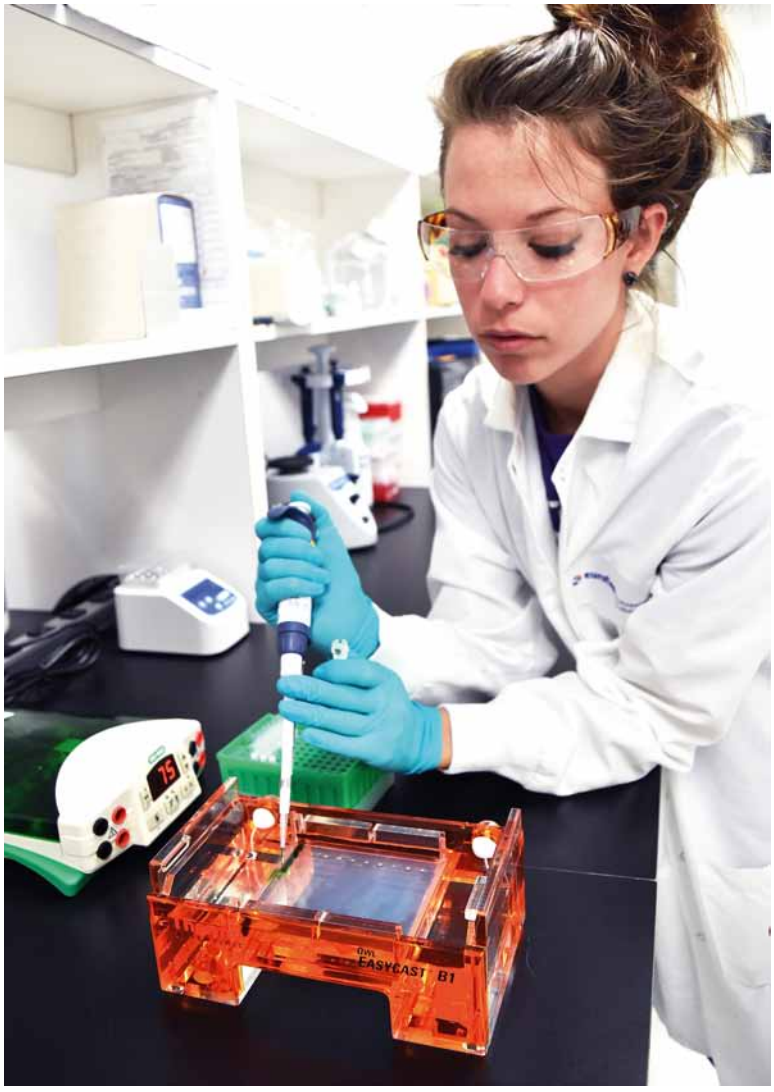
Genetic stability testing is a key component of GMP production cell bank characterisation and a regulatory requirement. Typical mammalian production cell lines are created by stable transfection of the expression vector into the host cell line. During subsequent cell culture, genomic events such as deletions, rearrangements and point mutations may occur and result in an altered cell phenotype and/or gene expression profile. The instability of the cell line is of great concern as it may negatively impact product integrity, posing a risk to patients. Even when product integrity is not immediately impacted, the possible reduction of productivity and the elevated risk of future events still raise concerns from an operational perspective.

Genetic stability testing includes an array of assays that are typically performed on a manufacturer's master cell banks (MCB) and representative lot(s) of end of production cells (EOPC). Genetic stability testing of the working cell banks (WCB) may also be performed at a manufacturer's discretion. Typical assays include, but are not limited to, those intended to confirm the integrity of the product transcript (mRNA/cDNA sequencing and Northern analysis), the genomic structure at the integration site (restriction digestion map via Southern analysis), and the ratio of insert gene copy number relative to host genome (via qPCR). Testing results from the EOPC and WCB are compared to those of the MCB to allow the detection of any changes that may be indicative of cell line instability.



The Molecular Biology Testing Team at Eurofins Lancaster Laboratories has established generic methods of cDNA sequencing, restriction digestion mapping via Southern analysis, and gene copy number determination via qPCR. A generic method for transcript size determination via Northern analysis is currently under development and is expected to be available soon. These generic methods for genetic stability testing can be adapted quickly to each client's unique cell line/cell bank. Product specific method validation can also be performed per client request to support CMC filings for later phase clinical trials and/or commercialisation.

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

Extractable and Leachables Team continues to expand in both capacity and capabilities

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Eurofins Lancaster Laboratories, Inc. continues to increase its Extractables and Leachables testing capacity and capabilities with the addition of accurate-mass quadrupole time-of-flight mass spectrometry (QTOF) capabilities, and the establishment of a testing regimen that meets the requirements of the BioPhorum Operations Group (BPOG), an industry-formed working group.

QTOF provides a third accurate mass liquid chromatography mass spectrometer dedicated to extractables and leachables testing. QTOF, coupled with an ultra-high pressure liquid chromatograph, provides high resolution accurate mass data for both parent and daughter ions. When this data is combined with our proprietary database of over 1,300 compounds commonly utilised in the manufacture of plastics and polymers, it provides improved ability to identify unknown compounds observed during an extractables study. The system is equipped with a multi-mode source, allowing for both chemical and electrospray ionisation in a single run.

BPOG has published a guidance document providing a standardised extractables testing protocol focused on single-use systems. The guidance document provides information on appropriate sample preparation, extraction conditions (including extraction time and temperature and extraction solvents) and analytical methods that should be utilised in analysing the resultant extracts. Eurofins Lancaster Laboratories has purchased additional equipment (including incubating platform shakers) to support performing the single-use system extraction as per the BPOG protocol. In addition, previously established

Eurofins Lancaster Laboratories analytical methodologies are in line with the methodology recommended in the guidance document.

Eurofins has sites in the US and the EU that can assist with E&L needs. All sites combined performed over 300 controlled extraction studies last year and can design an extractables study to meet clients' project needs. Whether the study will be performed on a container closure system, single-use system, or medical device, Eurofins has experience in designing and performing studies based on guidance from the Product Quality Research Institute (PQRI), the Bio-Process Systems Alliance (BPSA) or BPOG.
For more information, please visit *www.eurofins.com/biopharma*

Eurofins Kit Packing and Distribution Services – anything, anywhere

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In clinical trials, it is of pivotal importance that any clinical trial sample taken from volunteers and patients is analysed and reported to meet the objectives and purpose of the clinical study protocol. To ensure specimen integrity with the current increasing complexity in study protocols and geographic areas used, Eurofins Central Laboratory has used its 20+ years of experience in kit packing and logistics services to ignite a new business model for its Global Kit Packing and Distribution Services.

Building on the expertise of supplying Clinical Trial Investigator Sites with customised specimen collection and transportation kits, Eurofins Central Laboratory refreshed its layout to become a turnkey provider which deploys globally standardised processes, enabling high quality GMP and FDA compliant kits to be distributed worldwide.

Its Kit Packing and Distribution Services are not only offered in conjunction with a clinical trial protocol, but are now also available as a clinical and non-clinical stand-alone service to BioPharmaceutical customers and Eurofins affiliates alike.

For the past three years, Eurofins Central Laboratory has used a green field approach for its wholly owned and managed Kit Packing Facility in the Netherlands. This has translated into a clear design of the work floor based on the kit packing workflow, colour-based zoning to support the processes and an optimised layout of warehousing. The design of the facility is based on the lean principles that create value, efficient flow, and continuous improvement to better meet customer needs.

The layout of this Kit Packing Facility was recently copied to the Eurofins Genomics multi-functional hub in Louisville, KY, to create a US based counterpart. With hundreds of thousands of kits distributed in 2015, Eurofins supplies optimally-designed, easy to use, intuitive visit-specific specimen collection and transportation kits that incorporate all relevant materials and forms for handling and shipping to Eurofins Global Central Laboratory or other Eurofins laboratories for analysis.

For more information visit: *www.eurofinscentrallab.com*

Eurofins BioPharma Product Testing introduces new cGMP NMR testing and R&D capabilities

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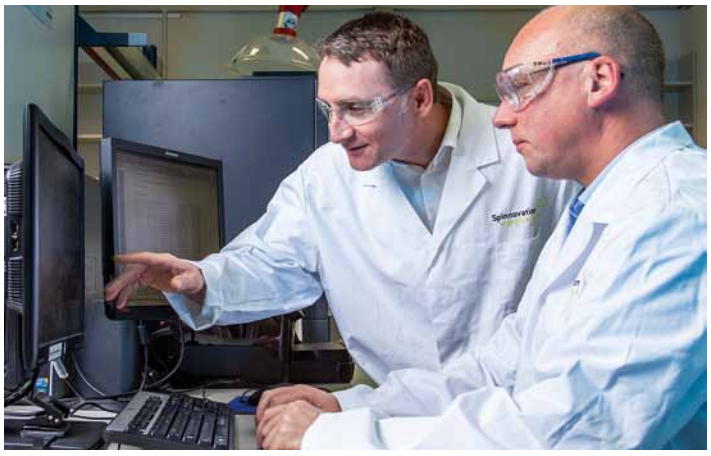
Through Eurofins' acquisition of Sinensis Life Sciences, Eurofins BioPharma Product Testing has added new and unique capabilities to its existing portfolio of services and solutions to support clients' needs for FDA/EU-GMP compliant NMR QC testing, as well as for accessing the proprietary SPEDIA-NMR method for faster upstream process development of biologics. As one of five Sinensis labs, Spinnovation Analytical specialises in high-end analytical R&D and QC testing. Spinnovation Analytical, located in the Pivot Park in Oss, Netherlands, manages an advanced technology platform, including solution-state and solid-state NMRs dedicated to support the BioPharma industry. The platform operates under an EU-GMP certificate (Dutch Health Authorities) and has been successfully inspected by the US FDA.

Solutions--Spinnovation offers a differentiated set of NMR solutions to respond to a broad range of clients' needs. First, a (400MHz) Open-Shop NMR service is made available to accommodate local clients' demand for rapid identity and in-process control testing to support MedChem activities. Second, Spinnovation delivers cGMP compliant NMR Quality Control Testing (solution- and solid-state) for raw material and drug product release. This concerns pharmacopeia and/or internal methods related to products like heparin, poloxamers and many other polymers, and also includes identity verification and quantification of reference compounds (qNMR for %w/w). Finally, Spinnovation offers innovative and unique solutions for BioPharma companies dedicated to Biologics Upstream Process Development with its Spedia-NMR™ service for profiling cell cultures, and Spedia-Predict™ to address bioprocess performance variabilities.

Technology--The NMR platform encompasses three solution-state NMR Avance III Bruker spectrometers (1 x 400 MHz, 2 x 500 MHz) fitted with SampleJet accessories for rapid throughput, and cryoprobe technology for high sensitivity (at 500 MHz). It also houses a solid-state 400 MHz spectrometer fitted with a 19F-NMR MAS accessory and sample changer, which is rather uncommon to find operational under cGMP. In addition, Spinnovation runs an XRPD from Empyrean Panalytical, an ICP-OES 7100 from Agilent as well as different HPLC/UPLC-(Q) TOF systems.

All these capabilities and expertise are gathered in Eurofins' new European Centre of Excellence for NMR and XRPD in the Netherlands. For more information visit: *www.sinensislifesciences.com ; www.spinnovation-analytical.com*



Eurofins Genomics and Agilent Technologies collaborate to expand the SureVector Cloning System, offering full flexibility in Vector creation

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Eurofins Genomics, a leading provider of DNA sequencing and genotyping services, has teamed with Agilent Technologies, a leading provider of molecular biology tools, to offer custom components and an assembled plasmid service for Agilent's SureVector next-generation cloning kits. Users gain versatile options to design their individual vector for any gene. With Agilent's Sure Vector system they can make use of the most convenient way to broaden their vector portfolio. Agilent will also offer a set of catalogue components for its leading-edge SureVector cloning kits, enabling the creation of over 1 million different cloning vectors.

The latest in next-generation cloning, SureVector harnesses the power of synthetic biology by allowing the combination of standard DNA components to build a customised vector construct from a set of standard parts. SureVector offers custom components and assembled plasmids as well as a variety of new components for leading-edge cloning kits. To meet the evolving needs and expectations of special vectors, the SureVector service offers a real benefit by delivering stable cell cultures for pharma needs.

Extensively validated, the components are verified to assemble perfectly into functional vectors.

The world's first modular vector kit, SureVector enables biologists to construct customised vectors - small DNA molecules within cells that can replicate independently - from standard components that can be assembled into many of combinations. Customers benefit from individual vectors or the ability to customise any fragment in the SureVector system. Therefore Eurofins Genomics' SureVector service is the perfect cloning service for production cell lines.

Agilent is one of the few companies whose products address the entire workflow for molecular and synthetic biology. For that reason Eurofins Genomics, international provider of genomic services around oligonucleotide and gene synthesis services as well as sequencing, genotyping and gene expression services, is pleased to collaborate with Agilent.

"SureVector is a perfect addition to Eurofins Genomics' gene synthesis and GeneStrands services," said Uwe Koehler, Head of Gene Synthesis and Molecular Biology for Eurofins Genomics. "In this exclusive collaboration, Eurofins Genomics can now offer tailor-made SureVector plasmids, and any component of the SureVector kit can be replaced with customer-specific elements." For more information visit: *http://www.eurofinsgenomics.eu/ http://www.eurofinsgenomics.eu/en/gene-synthesis-molecular-biology/molecular-biology-services/surevector-service.aspx*

Viracor-IBT helps advance drug development through customisable clinical trial testing

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Pharma companies may struggle to find a laboratory that has the experience and expertise required for custom study needs--one that actually delivers outstanding service with the ability to be flexible, while going above and beyond to ensure milestones are met. Viracor-IBT has the ability to perform high-complexity testing on multiple assay platforms and to fully customise this type of testing for clinical trials. Additionally, Viracor-IBT works on the trial sponsor's schedule to support drug development through responsive timelines. As a CAP/CLIA accredited laboratory, Viracor-IBT provides clinical trial testing for phase I-IV trials. Dedicated research, testing and project management teams focused on exceptional delivery and quality make Viracor-IBT Laboratories a leader in the industry.

For example, one pharma company* leveraged Viracor-IBT's expertise to develop an all-encompassing sample testing plan to evaluate viral load, anti-viral resistance and cell-mediated immunity. Another company* contracted Viracor-IBT to perform clinical trial testing to evaluate the study subject's immune response with a combination of IgE testing in conjunction with a custom-designed assay for antigen-specific basophil activation. By combining a number of high-complexity testing methods, these clients were able to gain the full picture of a trial subject's response to the study drug.

"On behalf of the team I wanted to thank Viracor-IBT Laboratories for your many contributions to this trial and your flexibility in working with us on this fast-moving study. Few companies and individuals have the ability to contribute to such an invaluable goal, but even fewer rise to this opportunity. Viracor-IBT Laboratories did, and for this, we, our sites and the patients/their families are incredibly grateful. With warmest regards, MD, VP Clinical Research" *

With 30+ years of specialised experience in vaccine safety and efficacy assessment, molecular infectious disease testing, immune response monitoring, allergy and hypersensitivity testing, Viracor-IBT is an expert in assay design, optimisation, and custom assay transfer and validation programs designed to advance drug development. To learn more visit: *www.viracoribt.com*

**Names withheld for confidentiality.*

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