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Bio/Pharmaceutical NEWS

Spring 2021

Celebrating 60 years & 10 with Eurofins

Neal Salerno, President, Eurofins Lancaster Laboratories Inc., a Eurofins BioPharma Product Testing Company

In 1961, Lancaster Laboratories began its iconic success story in a 2,500 ft^2 building on farmland owned by the family of company founders Dr. Earl and Anita Hess. Lancaster Labs' seeds of success were firmly planted in the founding principle that providing personal quality testing services in an ethical manner would not only delight clients, but also ensure continued record growth and longevity. Six decades of a strong work ethic, unrivaled data integrity, and unparalleled customer service turned a small dream into 1/2 million ft^2 state-of-the-art laboratory testing campus, employing more than 2,000 and serving clients across the globe.

This year we also celebrate 10 years as part of Eurofins Scientific. In 2011 when we joined Eurofins, we couldn't have imagined a better parent company which held the same standards in ethics and customer service. With the help of Eurofins, our global growth trajectory sky-rocketed. Eurofins Lancaster Laboratories became part of Eurofins BioPharma Product Testing, the largest network of harmonized biopharmaceutical GMP product testing labs in the world with 36 facilities in 19 countries. Fueled by strong and steady business growth the group continued to hire talented staff and make strategic investments in capacity and offerings. In 2017 Eurofins Lancaster Laboratories grew 200 times its original size and constructed its 13th and largest building expansion. In addition, the team created a Medical Device testing business at the site and became part of the Eurofins Medical Device Testing network which consists of over 20 laboratories worldwide. The company also realized outstanding growth and development for its unique client-site laboratory management service model, PSS Insourcing Solutions, which has grown to 85 sites in 20 countries with more than 2,000 employees since its inception in 2002.

Biopharmaceutical service offerings have grown exponentially over the last several decades as the world's largest drug developers and manufacturers continue to trust our renowned reputation for regulatory compliance, technical expertise, and impeccable data integrity. Successfully delivering innovative, timely and cost effective scientific solutions to help customers better manage their testing challenges and advance drug development have been the catalyst for our sustained success. We take a lot of pride in what we do and enjoy working with each other.

Decade after decade, with growth comes exciting new technology and instrumentation to deliver the most comprehensive service offering in the industry. Partnering with our clients' to meet their ever-expanding needs allows us to be at the forefront of the industry. Just this past year, we've enhanced capabilities for mRNA COVID-19 vaccine support, rapid mycoplasma testing, rapid sterility, and surgical mask testing. We have added instrumentation like ddPCR, AUC, and MALS for GMP product testing. We continue to invest in equipment like new sterility isolators and invest in our infrastructure like new lab expansions for Virus Safety, Cell Based Assay, Stability, Product Testing, Category 5, Portage Microbiology Lab, BSL2 labs in San Diego and Columbia, and a Sterile Fill/Finish lab in San Diego. Finally, we also have created a state-of-the-art LIMs system and improved LabAccess functionality. We've done all this to ensure that we may continue to service our customers for the foreseeable future.

Behind the science, equipment and facilities are our scientists who are the most important element in our chemistry and the reason for our satisfied clients and historic success. We are humbled by the hard work and dedication of each member of our team. Our profound gratitude goes to our clients for choosing us to be part of their groundbreaking solutions that help make the world healthier and safer. Please join us in celebrating 60 years of remarkable partnerships and accomplishments.

New Sterility Isolator delivers greater efficiency, increased throughput, and individual customizations

Suzanne Williams, Manager, Bio/Pharmaceutical Microbiology

Experienced and high quality sterility testing is in demand, and Eurofins BioPharma Product Testing's Microbiology Team responded to growing client needs by adding a new isolator, a Bioquell Qube to its comprehensive laboratory suite of isolators. The Qube is an aseptic processing workstation with an integrated Hydrogen Peroxide Vapor (HPV) decontamination system.

Performing sterility testing using soft-walled isolators since 1997, the Micro Team chose the Qube because it enables greater efficiency, productivity and increased throughput. The team plans to purchase an additional Qube System in 2021.

The Qube is a modular system that is configurable and allows for individual customization as it can be purchased as a 2-, 4- or 6-glove unit. The system at Lancaster is made up of the following main modules: two Qube Extension Modules (QEXT), two Qube Material Transfer Devices (QMTD) and one Qube Hydrogen Peroxide Vapor Module (QHPV). The external surfaces of client samples and media containers as well as supplies are decontaminated with HPV in the QHPV module prior to transfer into the QEXT modules for testing. Samples and supplies are then moved into the QMTD prior to being placed into incubation.

Installation and Operational Qualification has been performed on the system. In addition, decontamination cycles for the entire empty system as well as the loaded middle module or QHPV have been qualified using biological indicators. Aeration data was acquired to confirm VHP levels inside the isolator were acceptable. Studies were performed to ensure there is no ingress of hydrogen peroxide into representative sample containers at a level that could lead to false negative sterility tests.

Features of The Qube:

- Provides a GradeA/ISO 5 environment
- Uses 35% hydrogen peroxide to produce Vaporized Hydrogen Peroxide (VHP) for surface decontamination
- Construction allows for quick installation
- Maintains a cascading positive pressure from the test to the transfer modules and then to the ambient environment
- Utilizes a touchscreen display user interface
- HPV technology allows for shorter decontamination cycles which provides the ability to turn around the system in a timely manner and to execute more decontamination cycles daily
- Integrated Steritest Symbio System to perform membrane filtration sterility testing
- Glove Leak Tester which integrates with the system to ensure glove integrity
- Ability to purchase software to operate and control environmental monitoring of the system

The improved efficiency obtained from using the Qube System will allow the Micro Team to perform and report sterility test data to clients within their expected timeframe.

For information about sterility testing or the Qube System, please contact your Project Manager.

ddPCR in GMP product testing quantifies without calibration curve & determines absolute DNA concentration

Weihong Wang, Manager, BioPharma Biologics

In recent years, the number of biopharmaceutical products incorporating nucleic acids has been steadily increasing in the drug development pipeline. Some of these have made it to the market in a very visible manner such as COVID vaccines that deliver messenger RNA to encode for spike protein and gene therapies for the unmet needs of those with rare genetic disorders. Characterization of the purity, efficacy and safety of these products is highly dependent on a technique known as Polymerase Chain Reaction (PCR). A relatively new technique for the detection and quantification of nucleic acid is digital droplet Polymerase Chain Reaction (ddPCR). In this technique, the PCR mix containing the test sample is partitioned into a large number of water-oil emulsion droplets, and PCR amplification of the target DNA sequence occurs in each individual droplet. Following PCR amplification, each droplet is assessed to determine the fraction of positive droplets in the sample. These data are analyzed using Poisson statistics to determine the target DNA template concentration in the original sample.

Compared to quantitative real-time PCR (qPCR), which has become a standard methodology in most molecular biology laboratories, ddPCR has several advantages, especially in a GMP QC testing environment. First and foremost, samples can be quantified without the need for a calibration curve. In qPCR methods, a calibration curve is typically prepared from a DNA reference standard, and used to interpolate sample results. Therefore, the quality and concentration assignment of this reference standard can greatly influence the accuracy and even the validity of the reported sample results. ddPCR however, determines absolute DNA concentration through the power of statistics, thanks to the creation of tens of thousands of droplets that allow the generation of large numbers of data points from each sample. This is particularly welcomed when a well characterized reference standard truly representative of the test sample is not possible, such as in the case of viral vector genome copy determination. Another advantage of ddPCR is that it is generally considered less susceptible than qPCR to PCR inhibitors that may be present in samples. This feature is especially important in the context of residuals testing, where assay sensitivity is of great importance. The better tolerance of ddPCR to inhibitors allows testing of samples without extraction, therefore greatly reducing the necessary volume of the drug substance and/or drug product allotted for testing. In the case of viral vector product testing, this can result in better preservation of products that are often produced in much smaller batch sizes compared to traditional biologics.

With the advantages discussed above, ddPCR has gained rapid momentum in QC testing laboratories. Eurofins in Lancaster has installed and validated the BioRad QX-200 ddPCR system within our molecular biology laboratories. We have successfully performed method development, transfer and validation projects, and a majority of them supporting viral gene therapy products. In addition to customized methods for individual clients, we are also developing generic ddPCR methods targeting consensus sequences within various viral vector backbones, to support testing, including viral genome and infectious titer determination. Our in-house method validation, in conjunction with a product specific qualification, will allow quick implementation of GMP testing of many sample types.

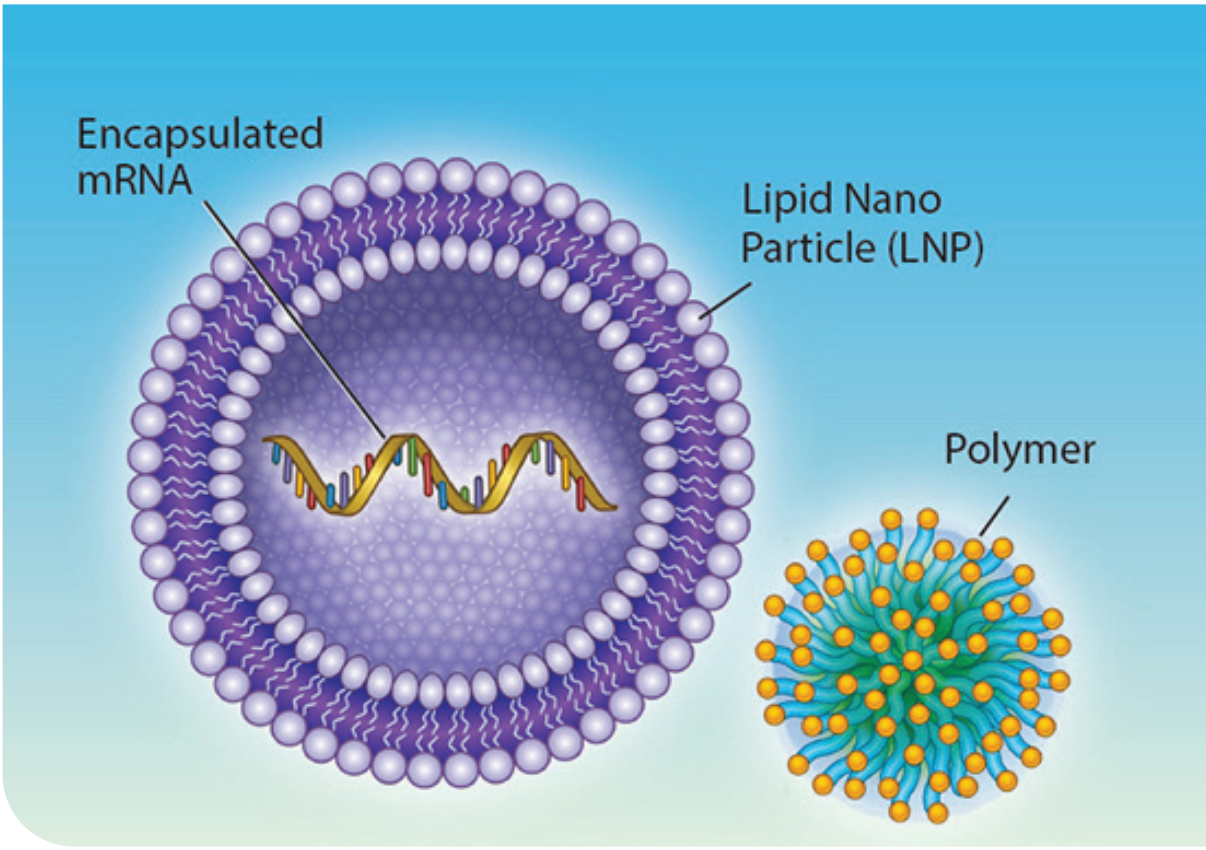
Check out EBPT's latest LinkedIn posts

Visit our LinkedIn page, which focuses on all four of the US Eurofins BioPharma Product Testing locations, including Lancaster, PA; Portage, MI; Columbia, MO; and San Diego, CA.

We invite you to follow this new page and engage with meaningful content to help gain awareness of our capabilities. See the latest news here: *www.linkedin.com/company/eurofins-biopharma-product-testing-usa*

Eurofins BioPharma Product Testing brings a wealth of cGMP experience testing RNA based drugs

Jon Kauffman, Ph.D., Vice President Biologics; Michael J. McDowell, Executive Vice President, Eurofins BioPharma Product Testing



In December 2020, the Food and Drug Administration granted emergency authorization to the Pfizer/BioNTech and Moderna coronavirus vaccines. This historic research sprint has reduced the typical seven-year vaccine development process to an unprecedented 10 months. As the initial winners in the coronavirus vaccine development race, the Pfizer and Moderna vaccines have one thing in common, they are both mRNA based, resulting in a new focus on RNA drug development technology.

Messenger RNA (mRNA) is a type of oligonucleotide that is critical to the translation of genetic sequence information of DNA into proteins manufactured in the cell. In the case of these new vaccines, this protein is the signature spike protein of the coronavirus. These mRNA products are considered to be their own unique modality. Distinct from traditional small molecule drugs and biologics such as monoclonal antibodies, they have their own unique analytical challenges. At Eurofins BioPharma Product Testing, supporting RNA based drug development candidates is nothing new. Eurofins' laboratories in Lancaster, PA; San Diego, CA; and Dungarvan, IRE, have supported both mRNA and RNAi development candidates from leading innovators with their broad cGMP testing service portfolio for close to a decade. Some of the methods employed include:

- **Characterisation of Exons (5' Cap) and Poly (A) Tails (3'End) by Orthoginal Mass Spec**
- **Purity/Impurity of Starting Materials by LC/MS**
- **Purity/Impurity by Ion Exchange RP-HPLC and CE**
- **Identity by Reverse Transcription (RT) Sanger Sequencing**
- **Total RNA by Spectroscopy**
- **Potency - Cell Based Bioassays**
- **Residual Solvents and Metals by GC and ICP**
- **Residual plasmid DNA by PCR**

The approved vaccines are carried into the body by lipid nanoparticles with polyethylene glycol (PEG), adding to their complexity. Therefore, additional analytical methodologies are employed to characterize the lipid and drug product, including, % RNA encapsulation by Ribogreen, Lipids by HPLC-CAD, Particle Size and Dispersity by Light Scattering.

As with any biopharmaceutical product, various other characteristics are typically required to support stability and release testing as described in USP/EP, including pH, osmolality, appearance, particulate matter, sterility, bacterial endotoxin, and bioburden.

Finally, drug developers are constantly employing novel delivery systems and formulations to increase the efficacy of their products, so additional assays may be required to provide information to cover these aspects of the final product. Contact us to learn more: *www.eurofins.com/BPT-Contact-Us.*

Eurofins Medical Device Testing helps ensure Sterile Barrier System integrity for patient safety

Sunny J. Modi, Ph.D., Director of Package Testing, Eurofins Medical Device Testing

Medical device and pharmaceutical companies across the globe are keenly focused on developing their product and often miss the critical requirements for creating a safe packaging system that will protect the product during manufacturing, transport, and storage. One of the areas that should be evaluated is how the sterile barrier is maintained to protect the patient and prevent the transmission of diseases from the manufacturing line to the surgical suite. The regulatory agencies across the globe recognize the critical nature of a Sterile Barrier System (SBS) by considering it a component of a medical device or pharmaceutical product. One key function of an SBS is to maintain the safety of terminally sterilized products until the point of use in a healthcare setting. The sterile integrity of the final packaging design can be evaluated through a series of seal integrity and seal strength testing outlined in ISO 11607 - Packaging for Terminally Sterilized Medical Devices.

Seal integrity testing identifies any leaks for the area around the perimeter of your packaging system. Some of the commonly used standards for seal integrity are ASTMs F1886, F2096, F1929, and others. Seal integrity testing is followed by seal strength testing to evaluate the mechanical strength of your packaging system and the force needed to separate and open the seal. ASTMs F88 and F1140 are commonly used standards to measure strength of the seal. A high force numerical value could indicate challenges in opening your packaging system by hand. A low force numerical value could indicate poor bonding of materials, which would result in a breach of sterile integrity. As Medical device and pharmaceutical companies continue to innovate across the globe, the Sterile Barrier System (SBS) should be evaluated not only at final design stage but also during the continuous manufacturing of the product. For more information visit: *www.Eurofins.com/Medical-Device*

Regulators enforce ISO 18562

Andrew Blakinger, Manager, Extractables & Leachables Testing, Eurofins Medical Device Testing

All medical devices must be assessed for biocompatibility. Medical devices containing breathing gas pathways (e.g., ventilators, breathing tubes, and anesthesia equipment) have traditionally been evaluated as external communicating devices according to the ISO 10993 series of international standards. Unfortunately, this approach leads to testing that provides questionable benefits and may result in hazards being missed. Therefore, a new set of standards – ISO 18562 – was released in March 2017 and is now starting to be enforced by regulators. This four-part series is specifically geared towards the biocompatibility evaluation of breathing gas pathways in healthcare applications. ISO 18562-1 outlines the overall risk management process for the biocompatibility evaluation, while parts two through four each address a specific type of hazard.

To support our clients, we now offer the full spectrum of testing required by the ISO 18562 series of standards to assess these three hazards. The first hazard is the emission of particulate matter. To evaluate this hazard, a particle counter is used to detect any particles in gas passing through the device.

ISO 18562-3 addresses the second hazard, that of volatile organic compounds (VOCs) emitted from the gas pathway. As air passes through the device, the VOCs are collected on a thermal desorption tube. These VOCs are then analyzed by gas chromatography mass spectrometry (GC/MS) to identify and quantify them.

Leachables in condensate are the final hazard. During usage, water condenses inside the gas pathway. Compounds may then leach from the medical device into the condensate. Per ISO 18562-4, an aqueous extraction is first performed. Inductively coupled plasma optical emission spectroscopy (ICP-OES), direct injection GC/MS, and liquid chromatography mass spectrometry (LC/MS) are used to identify the leachables. Identification of these compounds is needed for a toxicologist to provide an accurate safety assessment. To identify the leachables, our scientists use the Eurofins Extractables Index, our proprietary database of over 1500 compounds, in conjunction with the Wiley/NIST databases.

Complete understanding of the requirements of ISO-18562 – including regulatory expectations – is important in order to save valuable resources when working to get a medical device to market. Having successfully performed ISO 18562 for over a dozen medical devices, many of which have already received regulatory approval, the analytical scientists and toxicologists here at Eurofins are in a unique position to help medical device companies meet this testing requirement.

People Are our Chemistry

At Eurofins BioPharma Product Testing, we believe that our people provide our strength. Their dedication to quality, professional competence and hard work are the key elements in the company's success. In this regular feature, we introduce you to some of the people who have helped make Eurofins an industry leader.

Michelle and her son, Zach, hike on the horseshoe trail behind their house.

As a Research Fellow for Eurofins' Extractables & Leachables Team, Michelle Kolodziejski brings 36 years of analytical expertise to safeguarding clients' biopharmaceutical products from potentially harmful impurities and unknown compounds migrating from pharmaceutical container closure systems, medical and delivery devices, and manufacturing components.

To remain compliant, deliver best-in-class service to clients, and ensure patients receive safe pharmaceuticals, Michelle continually investigates new techniques for ever-changing ISO regulations. "My team is awesome," says Michelle. "There's great collaboration when it's time to solve a problem and help a client identify and quantify product adulteration."

When Michelle isn't uncovering potential toxins in drugs or biological products, she and her husband love to go camping, hiking and canoeing near their home in the PA State gamelands. Read more about Michelle:

What does your current job entail?

As a Research Fellow in the Extractables/Leachables Group, my job includes leachables method development and validations, peak identification investigations, and routine extractables testing. New techniques, such as ISO 18562 Part 4 gas pathways process development are also part of my role.

What is the scope of your group?

The extractables/leachables group performs testing to evaluate potential contaminants that may be introduced into pharmaceutical products from direct or indirect contact with polymeric materials during storage or production. Medical device testing for potential extractable or leachable compounds is also performed. This includes mass spectrometry analyses for volatile, semi-volatile, non-volatile compounds, and ICP analysis for multiple elements.

What process improvements does your group initiate to serve clients better?

We are always striving to provide lower detection limits, widen our scope of testing, and develop our analysts to improve skills in interpretation.

Why should clients trust us with their projects?

Eurofins E/L team has been performing extractables/leachables testing for nearly two decades. Our team includes highly skilled analysts.

You've been here for many years and seen countless changes. Is there anything that hasn't changed during your tenure?

In the 26 years at Eurofins BioPharma Product Testing in Lancaster, PA, the constant has been the focus on quality and ethics.

How does your group's work impact/benefit society?

Our work contributes to the safety of pharmaceutical products and medical devices. Everything from over-the-counter medications to vaccines are evaluated to ensure that they are safe.

And when you're not working?

When I am not working, I enjoy audiobooks, Celtic music, hiking, canoeing, and travel. My favorite trips have been to Scotland and Iceland. Next year, my husband and I are planning a cross Canada trip to Alaska, assuming it is open.

Contact us

For information on services, literature requests or address changes, please contact: Bio/Pharmaceutical Business Development, 717-656-2300, pha@eurofinsus.com, or visit *www.eurofinsus.com/bpt*

Bio/Pharmaceutical NEWS is published for clients, employees and associates of Eurofins BioPharma Product Testing US. Editor: Lisa Bamford, LisaBamford@EurofinsUS.com

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