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Bio/Pharmaceutical
NEWS

Winter 2014

Globally Harmonized Brand, Systems and Services



by Timothy S. Oostdyk, Ph.D., President, Eurofins Lancaster Laboratories, Sr. Vice President, Eurofins BioPharma Product Testing Group

One of the key factors to providing a compelling, high-quality service offering to a diverse global audience such as the bio/pharmaceutical industry, is harmonization. When working with a global laboratory group like ours, clients must be confident that they will receive the same level of expertise, quality, best practices and overall service from any one of our laboratories, no matter where they are in the world.

Eurofins Lancaster Laboratories adopted this philosophy of harmonization when we acquired our Ireland facility in 2007, and clients tell us that this has been very valuable to them. Most recently, we've had the opportunity to lead the efforts to further harmonize Eurofins global bio/pharmaceutical product testing laboratories, including driving the harmonization of the brand, systems and services.

Harmonized Brand



I am very pleased to announce that we have a new brand for our group, Eurofins BioPharma Product Testing. Our network of 13 GMP product testing laboratories had previously operated under a number of different brands. In order to

align these laboratories and present one cohesive global unit, we have developed this single brand for the overall group.

With service offerings that are fully comprehensive for both small and large molecule products, Eurofins BioPharma Product Testing is the largest network of harmonized, GMP bio/pharmaceutical product testing labs worldwide.

Harmonized Systems

While a global presence is very valuable, what is really important to international clients is the ability for all laboratories to operate under the same policies, procedures and guidelines. This kind of consistency requires a significant investment of resources and technology, which we at Eurofins are making in order to achieve full harmonization.

Today, all 1,700 employees of Eurofins BioPharma Product Testing operate under the same Global Quality Policy Manual and utilize the same CAPA/ Exceptions Management System and Document Management System.

Starting in the first quarter of 2014, clients working with any of our laboratories will also be able to review project data and reports 24 hours a day, 7 days a week with our global online portal, LabAccess.com. Whether a client is working with our laboratory in Lancaster, Munich or Paris—or all three for various projects—project information such as reports, test results, status of samples and project information for any project within the Eurofins BioPharma Product Testing network will be available through this single, online portal.

Harmonized Services

It is also very important that our laboratories operate with a consistent level of scientific expertise, and offer a consistent, market leading product to our customers. Therefore we routinely and deliberately drive collaboration on services, regulations and new technology across our network. Most recently, our Eurofins Lancaster Laboratories scientists in Lancaster have been actively working with our team in Munich to launch our European Viral Safety and Clearance services, an exciting addition

to our rapidly growing service offerings in the EU.

Active collaboration is also continuing between Lancaster and Copenhagen to set-up harmonized service offerings in trace metals testing to address the emerging requirements in this area, including newly designed labs and protocols. We have also harmonized our rapid sterility methods in the US and Ireland, and we collaborate regularly with our Ireland lab to support products being released in both the US and EU. These types of active collaborations drive consistency and excellence in our science and services.

Importantly we have also harmonized our service models to offer all global clients the same flexible service models with the ability to tailor programs to maximize cost effectiveness and meet project needs. This includes our traditional fee-for-service model, our managed hours program, full time equivalent (FTE) program, and our award-winning Professional Scientific StaffingSM program, which has grown to include more than 30 locations in 7 countries.

At Eurofins Lancaster Laboratories, and throughout the Eurofins BioPharma Product Testing Group, we are working extremely hard every day to deliver to you the most harmonized and comprehensive GMP service offering available in the industry. Our commitment and passion is to deliver the same high levels of quality, technology and scientific expertise throughout the world. Thank you for your business, and we look forward to serving you.

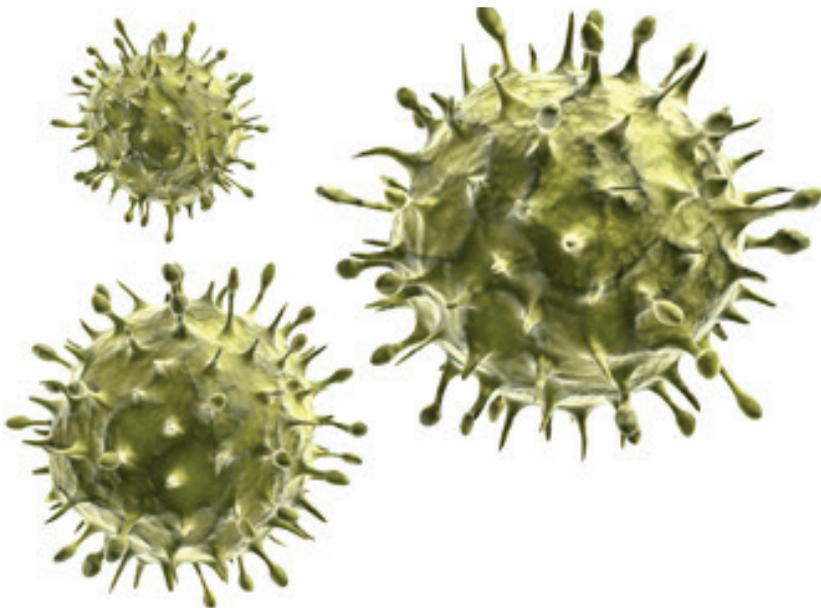
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For information on services, literature requests or address changes, please contact: Bio/Pharmaceutical Business Development, 717-656-2300 or pha@lancasterlabs.com

See how our Flexible Service Models can meet your project needs at: LancasterLabsPharm.com.

UV-C Inactivation: A New Viral Inactivation Method for Biopharmaceuticals

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Viral clearance studies are performed for biopharmaceutical products to ensure that any virus that might be present in the starting material is removed and/or inactivated during purification. The majority of industry contamination events have historically been due to non-enveloped viruses (viruses that have no lipid envelope). Since these viruses can be difficult to inactivate, there is a need for an inactivation step that is effective on such viruses.

In collaboration with Sartorius-Stedim Biotech, Inc, Eurofins Lancaster Laboratories, Inc. scientists have been evaluating the effectiveness of UV-C treatment for inactivation of viruses. UV-C treatment at 254 nm targets primarily nucleic acids rather than proteins, so it should inactivate viruses while sparing the product.

UV-C treatment is most effective against parvoviruses such as Murine Minute Virus (MMV). This is important, as MMV is very difficult to inactivate and has been found in bioreactors a number of times over the last 20 years. Other virus families show lower inactivation that varies from

family to family. The inactivation is consistent over a variety of conditions. UV-C treatment does cause product aggregation; however, typically the

aggregates can be removed by subsequent purification steps.

This technology is simple to integrate into a purification process, as it operates in flow-through mode and has a very limited

number of critical process parameters. We see several ways in which this new technology can be useful in assuring that viruses are not present in the final product:

- Raw materials can be treated by UV-C before they enter the bioreactor. The materials are not generally affected by UV-C, so the dose applied can be high.
- UV-C treatment can be a useful addition to a purification process for “difficult” products where it is challenging to achieve sufficient viral clearance.
- UV-C treatment can be used to replace a more complicated purification step (such as chromatography). This may allow simplification of the purification process and save costs as well as time.

For more information, please contact us to discuss how this technology can help you to achieve your viral clearance goals or visit: www.Lancaster-LabsPharm.com.

Biologics Expanding Space, Services and Staffing

To meet the increasing demands of biopharmaceutical customer needs, Eurofins Lancaster Laboratories continues its significant investment in growing the biologics side of the business. With the completion of its new 80,000 square foot building addition this year, the Viral Safety & Clearance and Molecular & Cell Biology teams are expanding capacity, capabilities and expertise. In addition to our well-established programs housed in nearly 50,000 square feet, we’re adding:

Capacity

- Four Viral Clearance Suites, totaling six suites
- Triple Expanded Viral Testing Laboratories
- State-of-the-art BSL3 Laboratory
- Two A/B GMP Cell Bank Production Suites in addition to an ISO5/7 Suite for GMP non-production banks
- Additional 7,500 sq. ft. of Biochemistry Space

Capabilities

- Four Viral Clearance Service Models
- New Viral Stocks and Assays for Viral Clearance Studies
- New Viral Stock Purification Methods
- New Viral Assays for Lot Release Testing

Expertise--Given our impressive successful growth rate and industry reputation for quality data and client service, we receive literally hundreds of resumes weekly from experienced BioPharm scientists wanting to be part of our success story. Here are a few new industry pros who will be serving your biologic needs.

An expert in developing and validating PCR and nucleic acids sequencing assays for more than a decade, Klaudia Shick, Ph.D., will lead the QPCR assay development team.

With extensive experience in cell banking and virology, Lana Mogilyanskiy, MBA, M.S., will oversee the new cell banking facilities as well as manage the production of all non-production cell banks.

Honing expertise for the past 15 years, Mary David has developed and optimized cell based assays for MOA of novel oncology drugs, DNA extraction of patient samples, and PCR & QPCR assays and sequencing.

With more than a decade of experience performing viral safety and viral clearance testing, as well as preparation and purification of viral stocks, Svetlana Sherbaty will focus on optimizing virus stocks using a variety of purification techniques.

For all stages throughout the development, manufacturing and release of your biological product, Eurofins Lancaster Laboratories offers the most comprehensive, fully cGMP-compliant testing services.

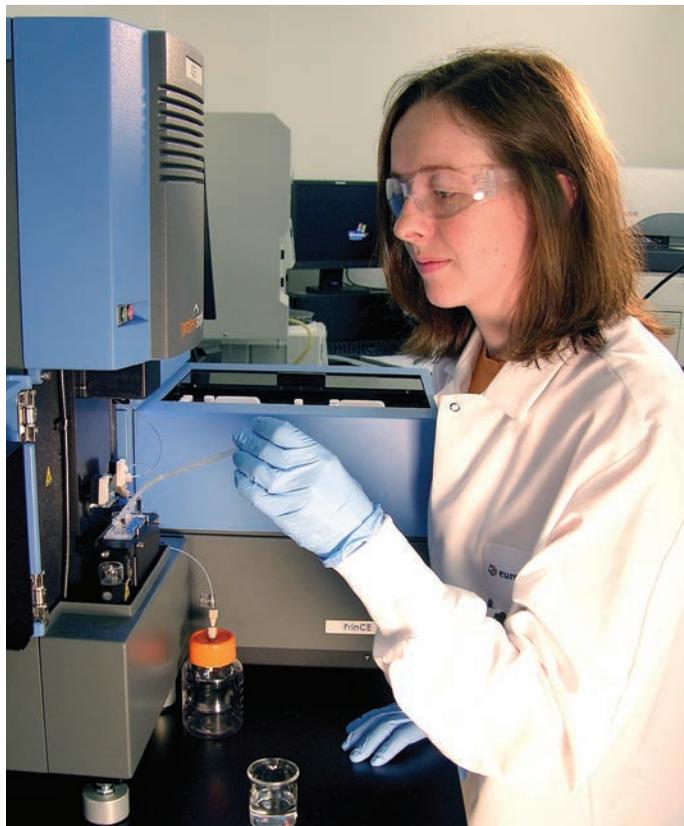
Biosimilars: An evolution in the biopharmaceutical industry

Michael J. McDowell, Eurofins Lancaster Laboratories, mmcdowell@lancasterlabs.com

Patents for 12 blockbuster biologic compounds, generating a combined \$67 billion in annual sales, will expire by 2020. In February 2012, the FDA released its long-awaited draft guidance on biosimilars, providing a regulatory framework for the approval of a biologic demonstrated to be similar to an already marketed product. The confluence of these two events has

clinical studies, thus moving testing to the front of the development process.

For the past several years, Eurofins Lancaster Laboratories has won many significant biosimilar testing programs from new and existing clients due to its unique and compelling value proposition. Eurofins Lancaster Laboratories offers the extensive capacity, breadth of capabilities, innovator product expertise and global coverage to execute effectively on these very complex programs. Clients have been pleased



to find experts in Eurofins' Lancaster and Munich facilities to establish the often challenging cell based potency assays critical to these products. Clients have found state-of-the-art equipment, including CE, iCE, CD, LC-MS/MS, LC-TOF, MALDI-TOF, Q-TOF, TOF/TOF, and Orbitrap MS for orthogonal characterization, including intact mass, peptide mapping, charge isoforms, carbohydrate sequencing, post translational modifications, and higher order structure.

Our experience working with various clients on biosimilars

resulted in an evolution in the biopharmaceutical industry involving most players, but none more dramatically than a biopharmaceutical product testing laboratory.

Foremost in the FDA's approval process is the requirement for extensive testing and characterization of the biosimilar to show that it is highly similar to the reference product. For innovator products, cGMP testing and extensive characterization is loaded toward the back end of the drug development process after years of nonclinical and clinical studies. For biosimilars, the extent of characterization determines the need for additional nonclinical and

targeting many of the blockbuster innovator products has shown these programs to be very method development intensive. The methods that exist for the innovator products are difficult to obtain or lack sufficient detail for a quick method establishment in the laboratory. It is our ability to work through method development challenges early in the project that has allowed us to meet the rigid timelines and manufacturing schedules inherent in biosimilar development programs.

This year, Eurofins Lancaster Laboratories has expanded its facilities, added extensive capital equipment, and attracted some of the brightest

biochemists, cell biologists, and virologists to remain the first choice as a testing partner in this exciting, rapidly growing market. For more information, visit: www.LancasterLabsPharm.com

Capillary Electrophoresis capabilities expand

Jon S. Kauffman, Ph.D., Biopharmaceutical Director, jkauffman@lancasterlabs.com

A thorough understanding of a pharmaceutical product's physicochemical properties is critical to achieving successful outcomes from development, through manufacturing and commercialization. Further, regulatory authorities require demonstration of a thorough knowledge of the protein's structure. This is obtained primarily through extensive characterization studies. Once a knowledge base is established, these characteristics are typically monitored as critical quality attributes during bioprocess development and also used to set specifications for stability and release testing of the final product.

One of the primary techniques employed to analyze proteins is capillary electrophoresis (CE). This technique builds on traditional electrophoresis methods such as SDS-PAGE and Western Blot by utilizing a capillary tube and automating the analysis to transform it into an HPLC-like experiment. Protein species are separated based on their size-to-charge ratio. Critical properties such as the isoelectric point (pI) and charge heterogeneity are measured utilizing cIEF; whereas size and aggregation are studied utilizing cSDS.

Eurofins Lancaster Laboratories recently expanded its CE capacity within the Biochemistry Department due to increased demand from clients. A new lab module is being dedicated and equipped with 4 Beckman Coulter PA800 plus units, a Beckman Coulter PA800, a ProteinSimple iCE280, and a ProteinSimple iCE3. The Biochem Team has extensive experience developing and validating CE methods as well as transferring established methods into its lab to support stability and release testing. And Eurofins Lancaster Laboratories in Dungarvan, Ireland, also has a PA 800 plus and can perform method transfer and/or co-validation of methods developed in Lancaster, US, to support EU release testing of biopharmaceutical products.

Advances in Rapid Microbiology

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For many years the pharmaceutical industry has discussed using new advanced rapid techniques but has been slow to adopt new methods. A number of reasons contribute to this and include the conservative nature of the industry, the lack of viable technologies, and lack of regulatory support for new methods. This has recently changed, and rapid technologies are gaining both industry and regulatory support.

At Eurofins Lancaster Laboratories, we have been monitoring the state of rapid technology in the industry and within the last year have implemented new platforms to support the industry demand.

Rapid Sterility Testing and Bioburden

The compendial method for performing sterility testing has not changed in over 20 years. For sterile products, the 14-day sterility test can be the limiting factor in release and distribution of the product. This lengthy release process increases costs for the pharmaceutical company. More importantly, for products where there is a shortage or high demand, the 14-day delay has the potential to impact public health.

The Microbiology Group in Lancaster has purchased a rapid sterility system from Celsis. The Celsis system uses ATP bioluminescence to detect contaminating organisms. The system can reduce the length of test from 14 days to 4-5 days. The system is operational in both US and Irish facilities, and both sites have initiated validation projects. The system can also be utilized to perform a presence/absence screen of non-sterile products for bioburden. In addition, the Lancaster facility can pro-

vide quantitative bioburden on filterable non-sterile products utilizing the Millipore Quantum system.

Rapid Organism Identification

The Microbiology Group has utilized state-of-the-art technologies for organism identification for many years. A recent identification technology that is emerging is MALDI-TOF, and Eurofins Lancaster Laboratories has acquired a Bruker MALDI-TOF system. All organisms have unique protein patterns, and the MALDI-TOF system uses mass spectrophotometry to determine these patterns for unknown organisms, which are then compared to a data base of patterns for known organisms to determine an identification. Qualification of the system was completed in November, and the service is currently available.

Rapid Mycoplasma

Biopharmaceutical products are required to be tested for mycoplasma as part of the production and release



process. The Cell and Molecular Biology Group has validated a system from Millipore that measures mycoplasma nucleic acids and provides results in 1-2 days. Recently they successfully worked with a client to validate this methodology, who received regulatory approval to use it for release of a cell therapy product (see article at right).

As a contract lab, our goal is to offer our clients multiple rapid microbiology platforms to assist them in reducing turn around time and costs.

Argos Therapeutics earns global regulatory approval with Eurofins Lancaster Labs' rapid mycoplasma MilliPROBE® assay

Argos Therapeutics and Eurofins Lancaster Laboratories have announced regulatory approval from authorities in the US, UK, Canada, Czech Republic and Israel for rapid mycoplasma testing of an autologous cell-based therapy produced by Argos.

Eurofins Lancaster Laboratories validated the use of the EMD Millipore MilliPROBE® system to test samples of the autologous immunotherapy currently in clinical trials for renal cell carcinoma. The assay can deliver same-day preliminary results compared to 28 days required for the standard compendial method, thereby eliminating the need to conditionally release cell-based products that require rapid turnaround time.

The MilliPROBE® system uses Real-Time Transcription-Mediated Amplification (TMA) technology to detect targeted microbial contamination within hours compared to the weeks usually required to generate results using traditional culture-based technology. Faster detection allows biopharmaceutical manufacturers to take corrective action earlier in the production process, which reduces downstream processing risks, optimizes product yields and improves final product quality. The MilliPROBE® assay probe system was designed by sequence analysis to detect Mycoplasma, Spiroplasma and Acholeplasma using a multiplex of conserved rRNA sequences in non-clinical applications. EMD Millipore has validated the non-clinical specificity and sensitivity of the system using 13 key mycoplasma species, which include the eight species specified in EP 2.6.7.

"In addition to accelerating time to results, the MilliPROBE® system validated by Eurofins Lancaster Laboratories offers other important benefits," described Fran Hutson, head of Bio-Monitoring North America sales and marketing, EMD Millipore. "The system can process up to 20 mL of a sample, making it preferable to PCR and RT-PCR methods typically limited to testing sample volumes that are 1-2 mL. The membrane-based sample preparation device effectively removes inhibitory substances that can interfere with nucleic acid amplification technologies."

X-Ray Powder Diffraction: a crystalline fingerprint for identification

Eurofins Lancaster Laboratories offers new technology for material ID & characterization

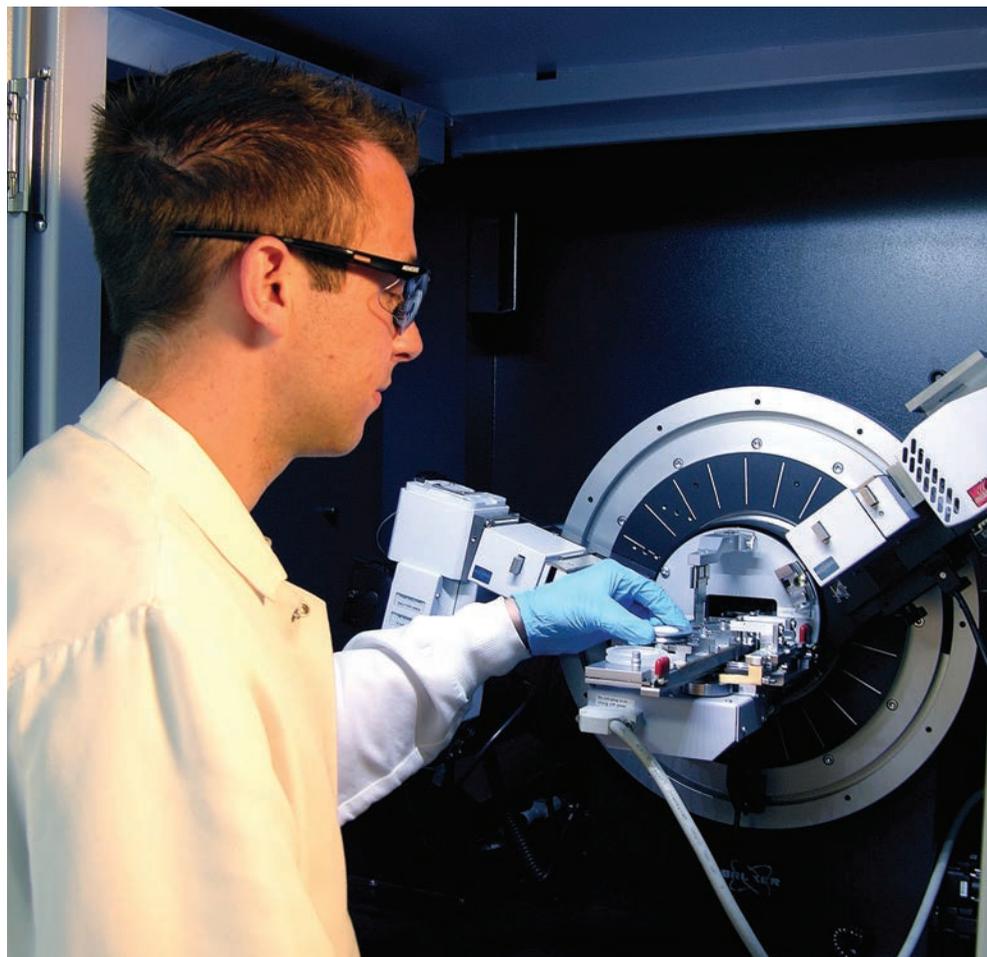
Jon C. Wenger, Principal Chemist, Pharmaceutical Raw Materials

A fingerprint is the residue pattern produced by epidermal ridges of fingertips. Since each person's fingerprint is unique, it is excellent evidence for the identification of one's presence. Crystalline materials, such as APIs, powder formulations, intermediates and excipients, also have unique structural patterns that distinguish one from another. Unlike a fingerprint, this pattern is consistent, repeating throughout the structure. When physically crushed or ground into smaller particles the matrix pattern remains intact in the fragments, yet the human eye cannot discern the structural pattern of the individual cells.

To address identification and characterization challenges of crystalline materials, Eurofins Lancaster Laboratories has turned to an innovative and precise X-Ray technology for identification confirmation as an incorrect or de-natured crystalline structure can affect a drug product's efficacy. Responding to an increasing demand from clients who need this technology as part of characterization testing for API, reference standards, intermediates, as well as a tool for stability monitoring of these materials, Eurofins Lancaster Laboratories has invested in X-Ray Diffraction (XRD) instrumentation.

XRD offers a crystalline fingerprint for material identification and characterization as it studies the pattern produced by the interaction of monochromatic X-radiation precisely directed onto the sample target. This reflected (diffracted) energy is captured by a precisely positioned detector and thus is a critical measurement tool. XRD can also rapidly predict the percentage of crystallinity of a structure.

The basis of this technique is known as Bragg diffraction. X-ray wavelengths are of comparable scale with the inter-atomic distances. As X-radiation is focused on a surface at



an angle Theta (θ) some "waves" will interact with (strike) two atoms specifically located on the atomic lattice but on separate planes – as radiation reflects from these atoms some waves interact. They could be in synchronization producing a constructive signal (a Bragg peak) or out of synchronization and cancel out (no signal). The reflected angle measured from the original beam path is Two Theta (2θ). A full peak profile scan characterizes a material.

For precision ID & characterization, XRD analysis can:

- Fingerprint an unknown crystalline compound
- Confirm material identity
- Detect foreign contamination/other substances present
- Discern material phases
- Estimate percent crystallinity

For maximum testing flexibility and endless adaptability, Eurofins Lancaster Laboratories utilizes the state-of-the-art Bruker D8 ADVANCE with DAVINCI design currently centered in Bragg-Brentano Geometry with a LYNXEYE linear detector to broaden clients' XRD service options, which include ID of excipients and API materials, identity confirmations, stability pull evaluations and method development for characterizing new and previously unknown compounds, transfer of client developed methods for routine testing, phase identification for polymorphic materials as well as maintain a library database for known material XRD scans.

Please contact BioPharm Business Development to discuss how we can solve your ID & characterization challenges at pha@lancasterlabs.com.

At Eurofins Lancaster Laboratories, 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 Lancaster Laboratories an industry leader.

People are the chemistry

As the new Manager of Cell Banking in Lancaster, Svetlana (Lana) Mogilyanskiy brings nearly 20 years of experience in cell banking and virology to the table. She oversees the company's new cell banking facilities as well as manages all non-production cell banks. Lana grew up in the Ukraine and earned a master's in Biochemistry and Molecular Biology from Kharkiv National University. She also holds an M.S. in Microbiology from Thomas Jefferson University and an MBA from Penn State University. Read more about Lana:



What does your current position entail?

With Eurofins Lancaster Laboratories further expanding Cell Banking capabilities, as Manager of Cell Banking my responsibilities involve ensuring clients needs are met, managing the Cell Banking Team, overseeing continuous process improvements, and training additional scientists that will be hired to support expanding services. Most of all, my job is to ensure that we provide the highest quality service in the area of Mammalian and Insect Cell Banking, which means not only producing high quality Cell Banks, but also giving our clients the best customer service in the industry.

What is the scope of your group?

The Cell Banking Team is responsible for Mammalian and Insect Cell Banking (GMP Production, GMP Non-Production, and R&D) and for cell expansion

and preparation of samples for pre-bank testing and for the preparation of samples for the post bank characterization testing.

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

We are in the process of transitioning from the Project Management Group managing Cell Banking communications with clients to a single-point person in the lab liaising with clients, which will be me. For projects of this nature and importance, it is an advantage for clients to have the opportunity to speak immediately and directly to the scientists intimately involved with their product. We see it as a way to improve com-

munications by addressing the issues in a faster pace. To further enhance their service experience, Cell Banking clients will have my cell phone and will be able to call me 24/7 in case they have any questions for my team.

Why should clients trust us with their projects?

Our scientists have significant knowledge and years of experience in the Cell Banking area. I bring to the bench over 15 years of GMP cell banking experience and more than 20 years of general Cell Culture experience. Our goal is to achieve perfection every time we perform a cell bank regardless of its size and/or GMP status. I am and will continue to be in the laboratory to assess the cell growth and morphology, provide guidance to analysts, and personally work with cells at every critical step.

How would you characterize your leadership style?

I have to confess that I am very controlling. I feel personally responsible for clients' projects and everything that is going on in the lab. I feel I need to make sure that things are done perfectly and that clients are well informed about successes and possible challenges as the project progresses. To that, I tend to plan out minute details of every cell banking campaign with the goal of a seamless culture progression, thereby affording clients a timely quality product. Client trust is paramount in this line of work, and I take great pride in nurturing these relationships.

And when you're not working?

When I am not working, I value the time I can spend with my children (ages 10 and 1.5) and my dog 120+lbs Rottweiler. I also enjoy ice skating, cross country skiing (when PA has a snow), and swimming.

Lana Mogilyanskiy

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Can We Talk?

IBC Biopharmaceutical Development & Production:

Kate Bergmann, PhD, will present on *Inactivation of Viruses by UVC Treatment*, March 2014.

View Our Webinar Series

UV-C Treatment—a New Procedure for Viral Inactivation Chemistry and Microbiology Perspectives on Cleaning Validations and Disinfectant Efficacy Studies

Best Practices for Extractables and Leachables Testing

Effective Strategies for Managing Comparator Product Testing

Outsourcing Cell Based Potency Assays: Perspectives from a Sponsor and a Contract Testing Laboratory

Critical Aspects of Antibody-Drug Conjugates: Structural Characterization and Analysis

For registration information for future webinars and access to past webinars, visit LancasterLabsPharm.com.

Look for us at...

WCBP 2014	1/28-30/14	Washington, DC
Biosimilars Congregation	2/26-27/14	London, England
IBC Biopharmaceutical Development & Production	3/24-27/14	San Diego, CA
InterPhex	3/18-20/14	New York, NY
CASSS-Bioassays 2014	3/24-25/14	Silver Spring, MD
PDA Annual Meeting	4/7-9/14	San Antonio, TX
Excipient Fest Americas	4/29-30/14	Raleigh, NC
E&L USA	5/7-9/14	Silver Spring, MD
PR Chemist Convention	7/28-8/3/14	Carolina, PR

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