eurofins | BioPharma Product Testing

Bio/Pharmaceutical NEWS

Fall 2019

In this Issue

Eurofins Lancaster Sustainability Team preserved 6 acres of wetlands and wildlife, created a 1/2 mile walking trail, and planted 1,000 trees on its 50 acre campus.

Making our world healthier and safer

Neal Salerno, President, Eurofins Lancaster Laboratories

As businesses grow and expand their footprint, it's essential to do so in a socially responsible manner. Embracing corporate sustainability benefits people, our planet, and even the bottom line.

This year, Eurofins Lancaster Laboratories celebrates its Sustainability Program's 10th anniversary. What began as a grass-roots employee-volunteer Green Team, blossomed into a team of full-time sustainability staff and hundreds of employees pitching in to find ways to reduce company waste, water, and energy usage. The program also encourages and organizes on-campus and local volunteerism initiatives vital to our community's health and well-being.

In terms of the environment, we have made significant strides towards finding ways to decrease our environmental impact as well as have a positive effect in the community. For example, we remain a sponsor for the Lancaster County Conservancy's annual Water Week event, which promotes the importance of clean water and natural habitats through kayak paddles, guided hiking trips, tree plantings, and river clean-ups. We've helped organize a Conestoga River clean-up for the past several years where our employees helped collect 5.5 tons of trash in just 2.5 hours at seven sites around Lancaster County.

In 2018, we were recognized in the "Best Workplaces for Commuters" program because of the various benefits we provide our employees who choose to carpool or take alternative modes of transportation such as walking, biking, or taking public transit. And we continually are in the process of researching greener on-site transportation services (electric shuttles, bike service stations, carpool/vanpool program enhancements) which strengthen our business by improving employee morale and retention, achieving cost-savings through environmentally responsible processes, and allowing us to continue offering world-class services to our ever-growing community-minded client base.

We are fortunate to have on our 50 acre campus approximately six acres of open space comprised of wetland and grassland cover. We have partnered with The Lancaster County Conservancy and The Alliance for the Chesapeake Bay to plant a riparian buffer and other native vegetation as part of a formal land management plan for responsible maintenance of this green space. Through this partnership, we received a grant to plant 1,000 native trees

Nearly 100 employees and their friends and families signed up to plant 1,000 trees on the Lancaster campus preserved green space.

and shrubs, and nearly 100 employees volunteered during a weekend to plant them all. Around the wetlands we have installed a half-mile walking path used by employees for exercise and a nice respite from the challenges of the day. This area is already home to a wide variety of plant and animal species. To this, the Sustainability Team also conducted a BioBlitz on the walking trail to identify both native and invasive species of plants, insects, mammals, birds, amphibians, and reptiles to create an even better habitat for more species. And on another part of our campus our Garden Club annually plants/maintains a 1,400 ft^2 garden, which consists of vegetables, herbs, fruits, as well as a native pollinator plants. This year, over 1,000 plant saplings were planted. We are recognized by the National Wildlife Federation (NWF) as a Certified Wildlife Habitat for providing food, water, shelter and places to raise young wildlife and qualify as a business partner with iConservePA to show a commitment to promoting conservation in Pennsylvania.

Stepping inside our facility, our Green recycling and conservation design initiatives were strategically infused in our newest building expansion that opened in 2019 as well as significant green improvements to renovated lab and office spaces to reduce our energy usage. (For more details see article in Spring issue of this newsletter at EurofinsLancasterLabs.com) As a member of the US Green Building Council (USGBC), we are committed to creating a sustainable environment for our employees and community by creating a healthy and efficient workplace. For example, we reduced our carbon footprint by over 25,000 pounds of CO_2 annually, implemented campus-wide recycling program, purchase new ENERGY STAR® rated equipment where possible, and are reducing water consumption through water monitoring programs and converting to LED lighting and installing motion sensors. And as part of our new 168,000 ft^2 expansion, we opened an onsite Wellness Center to benefit all employees at the Lancaster site by providing fitness classes and wellness resources for employees.

Beyond our campus, we have also had great accomplishments in our community involvement and student educational programs. For the past few summers, we presented our Chemistry Magic Show to the School District of Lancaster/Lancaster YMCA Power Scholars Academy and Camp Exploration to support STEM education. Participating children of the camps were able to learn about chemistry in a safe and fun way. We continue to sponsor several STEM organizations and programs, including The North Museum's STEM Sisters and Science and Technology Fair, The Community Action Partnership (CAP), the Lancaster Science Factory, and Junior Achievement STEM Summit to name a few. Further, we helped break ground on a new STEM learning facility at Millersville University in coordination with CAP. We also joined forces with the Lancaster County STEM Alliance to host a three-day educational Externship opportunity for 50 Lancaster County teachers, helping them better prepare students for the workforce. And we offer shadowing experiences to high school and college students as well as internships to support our growing workforce.

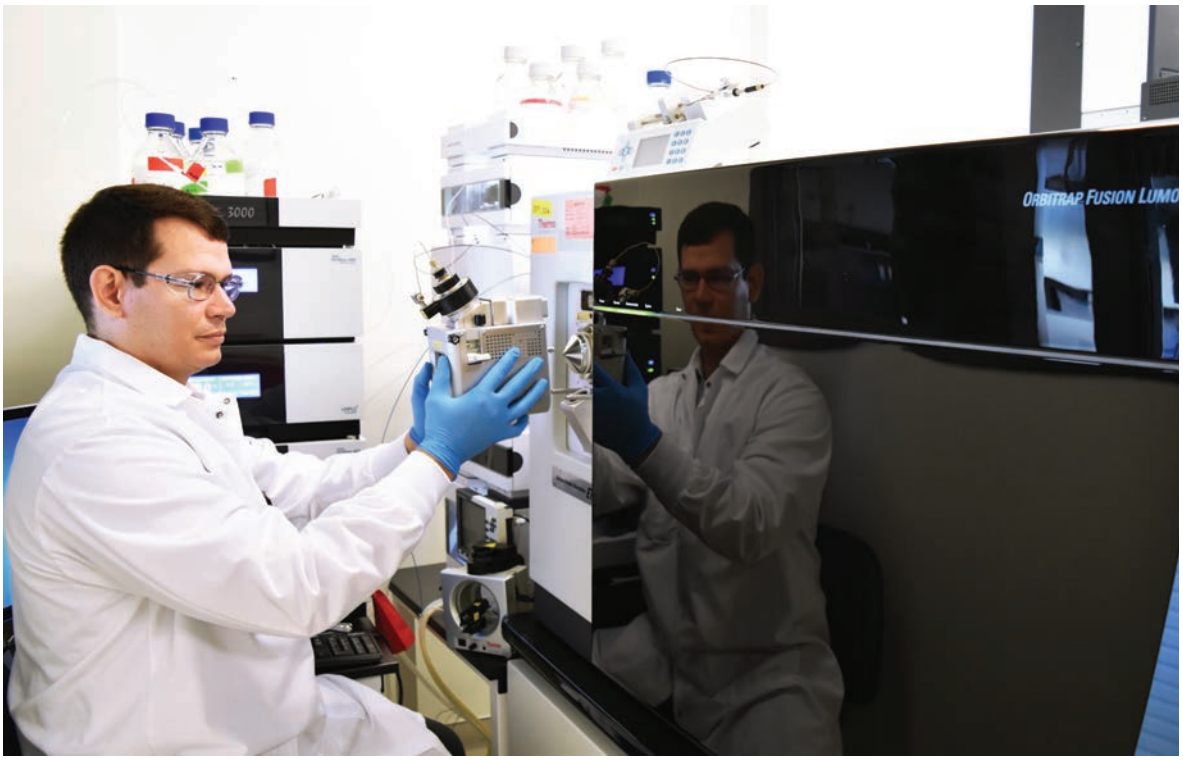
We have also continued our Community Heroes Program, where we organized several donation drives and service projects during the year to benefit organizations throughout the community. We have grown our contribution to the United Way and qualified for the Circle of Honor.

At Eurofins Lancaster Laboratories, we implement conscious choices throughout our organization in an effort to reduce our impact on the environment we all share and do our best to make the world healthier and safer.

Considerations for Selecting your Partner for Biologics Characterization

Berangere Tissot, PhD, Director, Biochem Method Establishment & Biologics Characterization

Throughout the course of product development, Biopharma companies need to consider multiple outsourcing plans, ranging from very early discovery support to late phase stability and release programs. When selecting a vendor for their Biologics characterization needs, companies often consider the following criteria: reputation, expertise, state-of-the-art instrumentation, ability to consult and provide support for the data interpretation. At this stage of the product development, compliance generally ranks low on the priority list; however, this criterion should be carefully reconsidered.



Even if companies first encounter the need for characterization at an early stage of their product development, in the pre-IND space, the application of these complex techniques is certainly not limited to pre-clinical/R&D phases.

Characterization methods are an integral part of the qualification or requalification of Reference Standards (RS) throughout the entire development cycle. These methods are included in RS management programs, including post-approval ones. The results generated using these complex methods may be reported in the Supportive Data Section. Since they are part of the application, data integrity requirements apply to any of the information provided to the agency for review and sustaining the use of a new RS lot.

Characterization methods will also be required for any comparability study at each of the phases where critical changes are made. Platform methods and head-to-head comparisons could be acceptable for an early phase minor change, but this strategy will not be sufficient for a more critical change or a later stage change. The guidelines enforce fit-for-purpose demonstration for these complex assays as they are now utilized outside of their typical "one-off characterization" context. The later the changes are made within the product development life cycle, the more stringent are the requirements around the "qualification" of the characterization assays. For example, if the major changes happen to be made after pivotal clinical trials or after commercial approval, the characterization methods will be part of a critical data set to be provided for regulators to review. At this stage, the regulatory bodies are all in agreement: not only are the characterization assays an essential part of the comparability exercise, but they now need to be demonstrated fit-for-purpose at a level equivalent to what is in essence an R&D validation. The concepts applied to this demonstration of fitness are equivalent to the elements of a validation, including specificity, sensitivity and repeatability.

Even though the regulatory agencies are not going to expect full cGMP compliance for these complex methods, it is also clear that performing these R&D assays cannot be performed by documenting them on the back of a napkin either - far from it.

Over the past decades, the FDA and other regulatory agencies around the world have extended their overview of the product development lifecycle to the early phases, leading to a more thorough evaluation of R&D laboratories. Indeed, the FDA would expect early phase and characterization results to sustain their scrutiny, should the need for this data to be used or reviewed by regulatory bodies at a later stage during the product's approval process.

Biopharma organizations might therefore be prudent to consider items such as data integrity, documentation management and instrument performance management when choosing an outsourcing partner, which will guarantee that the investment they make in the very early stages of their product's development is a robust and fruitful one. Thanks to their long history of providing a high level of regulatory compliance, including for complex assays, Eurofins Biopharm Services can be a trusted partner in biologics characterization outsourcing.

Cell and Gene Therapies show promise to enhance treatment of diseases

Katherine Bergmann, Ph.D., Manager of Viral Safety & Viral Clearance

The development of Advanced Therapy Medicinal Products (ATMPs), such as gene and cell therapy products, has made significant progress in the treatment of many diseases, including cancer, genetic, and autoimmune disorders. Regulatory agencies have seen a large increase in the number of submissions over the last two years, and further increases are expected to continue for years to come. With the promise to enhance treatment, greatly reduce side effects, and potentially cure many types of diseases and disorders, these therapies are in high demand, and biopharma companies are in a race to the clinic.

However, these technologies are very complex in nature and are vastly different than traditional biopharmaceutical products, especially when it comes to the use of these products for personalized medicine. The complexities span the development pipeline, creating challenges for manufacturing, testing requirements, regulatory approval, and commercialization.

In gene therapies, a defective gene is replaced with a functional one using a transmission system called a vector. This may occur by injecting the vector into the patient, or cells may be removed from the patient, exposed to the vector, and then returned to the patient.

In some cases a single therapy may be used for many patients with the same condition. In other cases, there may be a custom treatment for each patient (known as personalized medicine).

Gene therapies provide the ability to treat genetic diseases such as hemophilia by a single gene therapy treatment, in contrast to repeated treatments needed with conventional therapies. In addition to enhanced treatments, other potential benefits include reduced side effects, and the potential to cure, rather than just treat, many types of diseases and disorders.

With cell therapies, human or animal cells are administered to "repair, replace, regenerate, or augment a recipient's cells, tissue, or organs that are diseased, dysfunctional, or injured" (USP <1046>). The cells may be used without alteration, or they may be engineered to add a specific function (for example, using CRISPR or CAR-T technologies). Cell therapies may be used for disorders such as knee cartilage defects or organ failure, where cells can be implanted that will replace the damaged tissue.

Eurofins BioPharma Product Testing supports the development of ATMPs both for traditional use as well as for use in personalized medicine.

Eurofins provides comprehensive GMP-compliant CMC testing support to ensure the identity, potency, purity, and safety of starting materials, cell and virus banks, intermediate products, vectors, and final drug products, as well as support for manufacturing process development and validation.

Our staff is your staff with FTE

Nathan Whitford, Site Director, Eurofins Lancaster Laboratories Portage

Full Time Equivalent (FTE) Programs have proven to be an excellent flexible service model for management of projects and programs within Eurofins Lancaster Laboratories. When and why to evaluate an FTE team is a question that I often field from our clients.

These programs need collaborative involvement from both the client and Eurofins Lancaster Laboratories to be successful. Building the right FTE team to meet individual customer needs is obviously critical to the process as well.

While each program begins differently, we have often found that successful programs start with the Fee for Service model of work and transition into FTE through growth and increasing demand on the project team. With these programs, a group leader or technical leader is already familiar with the workflow and client needs and can transition into the FTE Team Leader role toward building a dedicated staff with expertise on the program for future success.

The FTE programs often spark interest due to higher program needs with shorter and shorter project turnaround time requirements. When inquiring about a client's due date for a new project, the most frequent response I receive is that it needs to be done as soon as possible. Due to project based backlogs, timing becomes a critical factor in the overall success of a new program coming in.

The FTE model essentially allows for a fast pass beyond the typical backlog of work since there is a dedicated team set aside to perform work for client projects only. Clients that have a mix of method development, validation, registration stability, Phase II/III submissions as well as routine release, and stability studies can take advantage of this model when project work can be forecasted in the future. This forecasted work helps to assign the right number of scientists on a staff to build the team to meet each client's individual needs.

Have dedicated staff at our site poised to perform your testing whenever you need them when you choose the FTE service model.

Whether a team of four or a team of 80, having that dedicated Team Leader and dedicated staff allows for us to understand client expectations to consistently deliver the quality results expected. The team can also build LEAN processes into the workflow through their knowledge of the individual assays and dedication to lab space used for the program work.

Most importantly, the client can drive the prioritization of the project work without facing backlogs from other client work so that overall timelines can be met within their company goals. Outside of the technical and quality aspects provided by these FTE models, they also add advantages of eliminating rush fees, investigation fees, and simply the budgeting process for work to be performed.

While the FTE program will not work for every client, the implementation of these programs has been extremely successful to meet a variety of our clients' needs. These programs often lead to long lasting partnerships and successful programs for many years.

Are you ready for the new USP Chapter <60> B. cepacia guidelines?

Randy Wolford, Microbiology Group Leader

Burkholderia cepacia is a gram-negative aerobic bacteria commonly found in soil and water. It is an opportunistic pathogen that has the ability to remain viable under harsh conditions as it is resistant to certain preservatives and antimicrobial agents. Pharmaceutical water systems are especially susceptible to contamination by these organisms. The prevalence of this organism in the manufacturing environment leads to the increased risk that finished drug products will be contaminated with B. cepacia.

In 2017, the FDA issued an advisory to drug manufacturers concerning the risk of contamination of non-sterile water based drug products with microorganisms from the Burkholderia cepacia complex (Bcc). This advisory was in response to drug product recalls regarding their contamination with B. cepacia. The FDA advised drug product manufacturers to establish scientifically sound and appropriate test procedures for detection of Bcc for both drug product components and finished drug products. There was no method for the detection of B. cepacia complex published in the compendia during this time.

In September 2018, the USP Pharm Forum 44(5) published a new proposed chapter titled, "USP <60> Microbiological Examination of Nonsterile Products - Tests for Burkholderia cepacia Complex." The chapter provided methodology and testing parameters for the detection of organisms in the B. cepacia complex. In June 2019, USP <60> was published in its final form with an effective date of December 1, 2019. Eurofins Lancaster Laboratories actively participated in the comment portion of this chapter and has established a new internal method to meet the requirements of USP <60>.

Contamination of finished drug products by B. cepacia complex will continue to be an area of increased scrutiny by the regulators. Eurofins Lancaster Laboratories is currently offering Bcc testing that is compliant with the USP. For additional information refer to the Eurofins Lancaster Laboratories Webinar "Bcc Testing for Water-based Drug Products is Coming–Get Ahead of the Game."

Eurofins' E&L Event draws distinguished industry presenters and attendees

Eurofins hosted its 3rd annual Extractables and Leachables Symposium for Drugs and Devices on September 19 in Cambridge, MA. Attended by more than 50 industry professionals, the full-day seminar was filled with informative sessions on regulatory expectations, best practices for E&L testing and study design, toxicological assessments, risk mitigation, and more.

We would like to thank our presenters from the United States Pharmacopeia, Biogen, Bristol-Myers Squibb, SafeBridge Consultants, Regeneron Pharmaceuticals and C&M Technical Consulting for contributing to our successful event. We are already planning for the fourth annual E&L Symposium to be held in Fall 2020. Stay tuned for more details to be released next year!

People Are our Chemistry

At Eurofins Bio-Pharma 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.

Greta and Dave Bender

While in very different roles at Eurofins Lancaster Labs, Greta and Dave Bender agree that the best part about their jobs is hearing clients say how Eurofins' work has a major impact on patients getting the timely drugs they need.

As Manager of Cell & Molecular Biology, Dave shares the profound gravity in hearing real life outcomes of their work: "Running samples with various challenges and timely deadlines can sometimes be stressful, but when a client comes back and says this is what the drug is being used for and how well it's doing in clinical trials, you get a big-picture moment, realizing we are a cog in this magnificent machine that is treating diseases and improving the quality of lives–this job is not just a job." And as a Group Leader in BioPharmaceutical Project Management, Greta reiterates how rewarding it is to have a hand in helping improve people's lives.

Married for 12 years, the couple is the perfect match. Though they attended the same college, overlapping three years with mutual friends, they didn't meet until they were introduced on Match.com. Now they've got two kids, one dog, great long-term careers, and a lot of talent and dedication to offer clients, and ultimately, patients. Here's a slice of their lives:

Greta:

What does your current job entail? I am a project manager, so lots of client contact since I act as a liaison between my clients and the lab. I run conference calls, schedule visits and attend business review meetings. I am also a Group Leader so I make sure my direct reports are getting what they need, whether it be answers to questions, advice, support, etc…

Why should clients trust us with their projects? One word…quality. Eurofins has a reputation for producing excellent quality data, and I think clients value that. Even if they have to pay a little more for the work, clients can count on us getting the job done right.

And when you're not working? When I'm not working I spend time with the kids. I help coach my daughter's softball team, and I also run her to all of her sporting events (practices, games, swim meets, etc.) We also just got a new puppy so I spend time training her too!

Dave:

What is the scope of your group? My group (Molecular and Cell Biology Routine Testing) executes testing on a routine basis for established biological based methods in support of drug substance/drug product release testing and stability studies, and "in-process" product characterization. The majority of this testing falls into two categories: determination of product potency/binding and determination of the presence/absence of contaminating residuals from the product production process. Potency/binding is determined by either utilizing an Enzyme Linked Immunosorbant Assay (ELISA) or a cell based bioassay. Presence/absence of contaminating residuals is determined by either utilizing an ELISA assay (targeting mainly host proteins) or by utilizing a real-time quantitative Polymerase Chain Reaction assay (RT-qPCR) for the detection of host DNA. My group also supports a wide range of other testing from polyacrylamide gel electrophoresis (PAGE) for plasmid identification to cytotoxicity testing per USP Chapter 87.

How does your group's work impact/benefit society? Although only a small part of what is needed for the overall characterization of a specific lot of drug substance/drug product, the testing in my group is critical in establishing the quality and function of the sample in question. The data and results that my team delivers to our clients helps them make the decision on whether or not the sample lot in question is cleared to release to the clinic or for commercial use. It guarantees that specific contaminants have been cleared through the production process to a safe level for human exposure and provides critical information in terms of functionality that are used for dosing considerations.

And when you're not working? I enjoy spending time with my family. We have a daughter involved in softball and swimming almost every month out of the year, so we are usually on the go most weeks out of the year. We also have a son who is taking swimming lessons and will be starting baseball and basketball within the next year or two, so that will only add to the excitement. I also like to get out for a round of golf here and there as our schedules permit. We also just got a new puppy so we are spending as much time with her as possible.

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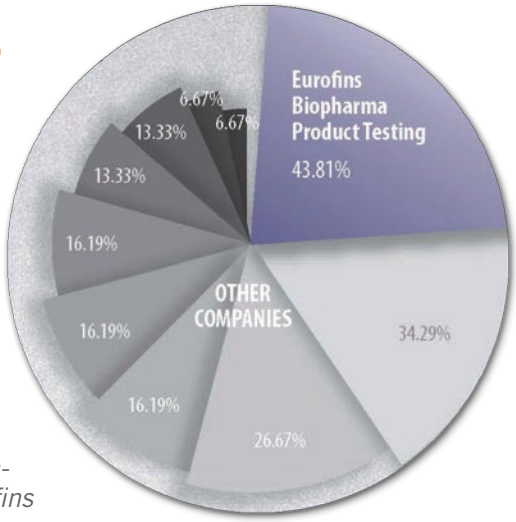
Eurofins ranks #1 Lab of Choice for past 13 years

Eurofins has been ranked #1 in the industry in 3rd party surveys for more than 13 years. In the most recent survey conducted by *American Pharmaceutical Review*, Eurofins BioPharma Product Testing and Eurofins Lancaster Laboratories* together were ranked above the world's leading contract laboratories in **customer service, meeting deadlines, and quality** and were also ranked **#1 laboratory of choice** overall.

When asked which laboratories they prefer to do business with, responders chose us as the #1 laboratory of choice over other leading contract labs.

**Eurofins Lancaster Laboratories is a member of Eurofins BioPharma Product Testing.*



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