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Lancaster Laboratories, Inc.

for exceptional
performance in quality, speed,
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as support to Eli Lilly and Company's
strategic objectives.

April 29, 2009

**Pharmaceutical
NEWS**

Spring 2009

Emerging stronger than ever



by Timothy Oostdyk, Ph.D., executive vice president and COO

In every corner of the world, there is unprecedented financial turmoil felt by nearly every business segment. All industries today, including the laboratory business, are taking stock of their strengths and weaknesses with the goal of emerging from this recession—for themselves and their customers—stronger than ever.

At Lancaster Laboratories we have a long history of growing our business through both good and bad economic times. Founded in 1961, and with a leadership team that averages more than twenty years with the business, we've seen our share of tough economic times. While every economic recession presents its own unique challenges, we believe the formula for success includes a number of consistently steadfast in our approach over the years. Specifically, key cornerstones for success are:

Financial stability

Stable workforce

Broad portfolio of customers

Diversified and innovative service offering

Investment in the future

So what does this mean for our customers?

Financial stability – Now more than ever customers need to be concerned with

the financial stability of their outsourcing partners. Lancaster Laboratories is fortunate to be part of one of the strongest companies in the world today, Thermo Fisher Scientific, the world leader in serving science.

Stable workforce – We believe strongly that if you take good care of your employees, they will take good care of your customers, and business success will follow. In good times or bad, we work to take care of our employees, which means the same people serve you year after year.

Broad portfolio of customers – At Lancaster Laboratories we provide scientific services for a diverse group of approximately 2,000 active customers. This means we have a tremendous understanding of the challenges you face, and a broad perspective from which to share best practices.

Diversified and innovative service offering – Our service offering is the most innovative and comprehensive available in the laboratory industry today. This means that all your laboratory needs, from a single test, to a major program, to onsite scientific staff, are all available from one trusted source.

Investment in the future – To be an industry leader, investment in the future is critical in both good times and bad. We've just expanded our Lancaster operation with the completion of a new 45,000-square-foot state-of-the-art building addition. We hope you'll set aside some time to visit during our Open House in September.

The bottom line is that our success is directly attributable to doing the right things for our customers at the right time. We understand that the pressures on you to do more with less are greater now than ever. And so our solutions for you are more comprehensive and more flexible than ever before.

Thank you for your business and for the trust you have placed in us. Our business continues to grow because of it, and I want to assure you that we never take it for granted. I wish you and your business all the success in the future, and by working together, may we all emerge stronger than ever.

Lancaster Labs earns Lilly Global Supplier Award

Lancaster Laboratories has been awarded the 2009 Eli Lilly Global Supplier Award. Lancaster Laboratories was one of a few companies selected among Lilly's 6,500 global suppliers.

Lancaster Laboratories earned the distinguished honor as an elite supplier for having a measurable impact on the company's objectives and priorities. Items of particular interest to be nominated for the Lilly Supplier Award were delivery of exemplary quality, service, speed, total cost reduction and other value adds.

"Since our founding in 1961, a key strength of ours has been our ability to form partnerships and collaborate effectively with our customers for their success and ours," says Dr. Wilson Hershey, Lancaster Laboratories president. "We are delighted our customer service and scientific expertise have served Lilly well."

Open House slated for new Biopharm Building

Lancaster Laboratories will host an open house of its new state-of-the-art pharmaceutical and biopharmaceutical building the week of September 14.

The 45,000-square-foot addition will accommodate growth in all scientific service areas as well as house 100 new employees.

We look forward to showing you our expanding capabilities and hearing how we can help you with your outsourcing needs.

Rapid Growth of Full Time Equivalent Staffing Programs

by Travis Emig, director, and Nathan Wisniewski, manager, pharmaceutical chemistry

With the global economy in a recession, a vast majority of pharmaceutical companies are being forced to cut costs and control spending. For most companies this means a reduction in workforce and tighter outsourcing budgets. Companies are left with the same amount of required laboratory testing, but with fewer employees to perform the work in-house. Clients are left searching for value-added programs that will allow them to project all of their outsourcing costs for an entire year in order to lock in on set annual costs. As a result, Lancaster Laboratories is seeing an increased interest in its Full Time Equivalent (FTE) staffing programs.

During the past two years, the number of pharmaceutical clients requesting information about Lancaster Labs' FTE model has increased significantly, and the company has positioned its global operation in a way to fully support the increased demands. Lancaster Labs is also seeing a trend toward an increase in the overall size of FTE programs already in-place, indicating current customer allegiance to its FTE programs. Approximately 20 percent of Lancaster Labs' pharmaceutical staff members are FTE employees, supporting customers around the world. Forecasts for 2009 indicate continued expansion of the current teams as well as the establishment of additional teams.

How is the FTE program cost-effective for the client? An FTE program consists of a team of dedicated full-time employees, working at a Lancaster Labs' site, using Lancaster Labs' instruments and resources. Project priorities and deadlines are set by the client. This model works successfully for clients who need to outsource a consistent amount of work that is sufficient to fully utilize a dedicated team for an extended period of time. There are set monthly fees for each member of the team with specific rates corresponding to various staff levels. Clients pay one billing each month. Utilization reports are generated to disclose exact hours and activities performed by all team members. Most testing, review and consumables are covered in the set rates with certain highly

technical activities such as Mass Spec analysis and high-cost consumables like specialized columns available at increased rates. These items will typically be covered as pass-through costs in a program and may be defined at project initiation. The duration of any FTE is typically contracted for a minimum of six months, while many contracts are multi-year agreements.

There can be numerous cost savings that are passed onto the client with an FTE program. Using a team of dedicated individuals, instruments and physical resources, the client does not need to be concerned about long-term costs incurred with hiring employees or costs for additional instruments and physical space. All testing is performed at Lancaster Labs, using validated equipment and trained analysts in a complete GMP environment.

Lancaster Labs' programs are highly effective since the same level of quality, performance and productivity expectations for its fee-for-service offerings are used to manage the FTE staff. This results in highly motivated and productive teams that are both results and service focused. The way in which these teams are managed, the technical and regulatory security the Lancaster Labs organization is known for and the ability to provide extensive and useful detail in utilization reporting, differentiates Lancaster Labs from other contract laboratories offering an FTE type program.

Clients have found the FTE programs reduce time for new project initiation. This is easily accomplished through the program as there are no individual quotes needed and limited purchase order requisitions. Other external factors that could be perceived as rate limiting steps have been incorporated into the FTE model as well, including protocol establishment, harmonization assessments for raw material programs and customized reporting requirements. Establishment of test methodology can be streamlined by having the ability to utilize the dedicated staff effectively. Often, Lancaster Labs integrates with clients to provide results and data directly into

clients' LIMS systems. Additionally, when testing needs to be expedited, there are no rush surcharges incurred when expedited results are needed.

FTE teams have shown to be efficient and effective in delivering clients results. This is accomplished by the diversity of technical experience that each member of the team brings to the table. The specific skill set for each member of the team is determined during initial planning meetings with the client, so all technical needs for a program are covered. Staff members on FTE programs work very closely together to

share expertise and strengthen the analytical capability within the group. This "team-based" approach to testing has been shown to increase the efficiency of the team and shorten turnaround times for the client. In conjunction with LabAccess, where clients have 24/7 access to all their lab reports and raw data, Lancaster Labs provides transparency while meeting all client targets.

Communication channels are another advantage to an FTE program. The client always has the direct communication link with the technical team leader. All teams have a routine meeting schedule with the client, where updates, planning and action plans are established. This open communication policy allows the client to have immediate feedback on timelines and utilization of the FTE team. Since the client sets the priority, resources can be shifted to focus on the projects that take precedence.

By having a team of dedicated employees working for one client, the relationship between the lab and the client grows into a collaborative partnership as each party learns to understand each others' needs and operations. The ultimate goal for most of Lancaster Labs' clients is to have their contract research organization become an extension of their own in-house lab. The value Lancaster Labs is able to provide with its FTE services is clearly why there is an escalating demand for this model of service. For FTE queries, contact Pharmaceutical Business Development at 717-656-2300.

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Residual Solvents: Alternate Validated Methods

by Nathan T. Whitford, senior chemist/
group leader in Method Development and
Validation

Since the USP General Chapter <467> on Residual Solvents became effective on July 1, 2008, Lancaster Laboratories has seen a multitude of requests for many different solvent and sample matrix combinations. The new General Chapter applies to both monographed and non-monographed items, including all drug substances, excipients, and products "subject to relevant controls." So a number of manufacturers have turned to Lancaster Laboratories for assistance. The methodology provided in the General Chapter can be utilized for many of these requests (Class 1 and Class 2, Mix A and B compounds). However, the Class 2, Mix C compounds, all of the Class 3 compounds, and any other unlisted solvents used in manufacturing, cannot be tested by the General Chapter's GC method. In these cases, an alternate method may need to be developed and validated.



Wes Atkins, senior method validation chemist, performs residual solvent analysis by headspace GC.

One approach Lancaster Laboratories analysts have been utilizing is a technique referred to as a self-validating method. This particular approach is a possible alternative to the traditional method development and validation project. The self-validating method parallels the USP General Chapter <467>

methodology but takes it a step further by using a minimum of a three point calibration curve rather than the single point method of additions indicated by the General Chapter.

Prior to performing the self-validating method, feasibility would be performed to determine an appropriate solvent that provides acceptable sample solubility. Chromatographic conditions would also be evaluated and optimized for the compounds being analyzed. Once this evaluation has been performed, a Lancaster Laboratories analyst would test the sample matrix (unfortified) along with direct fortification of the sample matrix at a minimum of three levels. These three levels will bracket the limit concentration and would typically be made at a tenth of the limit, the limit and two times the limit concentration.

In addition, system suitability injections are made to ensure the system is precise and accurate by performing multiple injections of a standard prepared at the limit concentration along with evaluating the recovery of a second working standard preparation. Linear regression analysis of the curve that is generated from the fortified sample preparations yields the compounds concentration and may be considered a quantitative result provided the determined coefficient of determination is acceptable ($r^2 = 0.99$) and the value falls within the range evaluated. Due to the method of additions approach utilized with the self-validating method, many of the tests performed in a traditional method validation are evaluated with each analysis. Linearity is directly determined at the actual time of analysis by evaluating the linear

regression data available from the different fortification levels. Specificity can be determined by evaluation of a blank injection and the unfortified sample injections made during the analysis. If significant interference is observed, an alternate approach would be attempted. Accuracy, range, and

precision are determined by evaluating the agreement of data from the different fortification levels in the presence of sample matrix. Quantitation will not be performed if the

result is below the lowest fortification level, and the results will be reported as less than lowest level. The result is only reported as an estimate if the result exceeds the highest fortification level. Finally, the self-validating method evaluates a practical working limit of quantitation based on the concentration of the lowest fortification level. Although the actual LOQ may be significantly lower, this is beyond the scope of interest for quantitative evaluation of residual solvents around a much higher limit concentration.

The benefits to this self-validating method approach include a faster timeline when compared to the traditional method development and validation project. This approach is more cost effective than the traditional approach for clients having a short term or infrequent need for testing. Additionally, the approach parallels the USP General Chapter <467>, while taking it a step further by utilizing multiple fortification levels. For samples that contain multiple solvents (five or more) or for samples in which testing will be performed frequently, the traditional method development and validation approach may prove to be a more cost effective analysis. Clients are encouraged to consult their internal SOPs regarding validation requirements since the self-validating method does not perform validation in the traditional sense.

For more information on residual solvent testing and the self-validating method approach, contact Pharmaceutical Business Development at 717-656-2300.

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EPA test methods support Pharmaceutical Operations

As one of the largest contract laboratories in the country, Lancaster Laboratories provides comprehensive testing services in the environmental, pharmaceutical and biopharmaceutical sciences. While the clients for the two latter categories are almost exclusively Pharmaceutical and related firms, the testing performed in the Environmental Sciences Division supports a wide variety of industries, from local municipalities to world

Pharmaceutical Effluent Guidelines (PEG), found in 40 CFR Part 439 include nontraditional analytes and analytical methods specific to the industry. The monitoring requirements are based on the type of operations at the facility, and Lancaster Labs is capable of testing for all of the contaminants listed in the regulation. The contaminant list and more information about the regulations are available at www.lancasterlabs.com/environmental/9043_02.pdf.

Assurance Unit has procedures in place to provide the extra oversight required in the GLP regulations. Because projects requiring strict GLP compliance involve more up front planning than typical projects, communication with the laboratory about the project requirements is paramount to a successful outcome.

For more information, contact Barb Weyandt at 717-656-2300, Ext. 1576.



Environmental chemist Lindsey Lafferty analyzes water samples for contaminants.

wide petrochemicals companies. Not surprisingly, there is some crossover between the client lists for the three divisions.

Pharmaceutical clients typically require testing to meet USFDA requirements, but there are some applications for USEPA methods to support their development and manufacturing operations. Monitoring of plant effluent for contaminants specifically related to pharmaceutical manufacturing operations is one example where Lancaster Labs' Environmental Sciences laboratories can help pharmaceutical clients meet government regulations. The

ensure that contaminants known to be capable of interfering with the study are not present in significant levels. Since Lancaster labs is certified to perform drinking water analysis, firms with animal facilities can request testing in support of GLP projects with the assurance that they are using a firm with experience and expertise in the test methods. In addition, the standard operating procedures for documentation, instruments and personnel used in the Environmental Sciences laboratories include the requirements of the GLP regulations, and if strict GLP compliance is requested, Lancaster Labs' Quality

Verifying the purity of plant influent and drinking water used for toxicology testing is another niche that Lancaster Labs can fill for pharmaceutical clients. USFDA Good Laboratory Practice (GLP) regulations require that water supplied to animals used in testing within the scope of GLPs must be analyzed periodically to

Certificates of Analysis available electronically

This spring Lancaster Laboratories made a significant improvement in the way we deliver our product. Our Quality Assurance Team is now electronically signing and releasing our Certificates of Analysis reports so that the signed report is available electronically the second it is released. This new system eliminates the waste of printing hard copy reports, hand signing them, and sending the hard copies via FedEx.

Clients are now receiving the signed copy via e-mail as soon as it's released by QA. In addition, the report notification e-mail now contains a hyperlink to the corresponding sample information on LabAccess. Initial response from our clients has been very favorable.

Contact us

For information on services, literature requests, or address changes, please contact:

Pharmaceutical Business Development
717-656-2300
pha@lancasterlabs.com

Gene sequencing added to microbial identification options

The use of genotypic tests to identify the source of microbial contamination is changing the pharmaceutical microbiology laboratory in much the same way that DNA testing has changed the forensic laboratory. Globally, many regulatory agencies now consider DNA-based techniques to be more accurate than phenotypic methods. Lancaster Laboratories is expanding identification options by offering gene sequencing through its European facility. In addition, the recent installation of software upgrades for ribotyping and fatty acid analysis (FAME) augments their existing identification capabilities.

Lancaster Laboratories Europe, located in Dungarvan, Ireland, is currently using the MicroSEQ® Microbial Identification System manufactured by Applied Biosystems to perform gene sequencing. For this analysis, DNA is extracted from the cell culture, amplified by Polymerase Chain Reaction (PCR) and then sequenced. The resulting genome is compared to a database to identify the DNA. The bacterial library contains over 1800 species, and the system is also capable of analyzing yeasts and molds by comparison with a library of fungal species. This automated technique is more accurate and reproducible than traditional manual methods, which are highly dependent on analyst skill and consistency. In order to offer this testing to US based clients, Lancaster Laboratories will use a validated process for preparing cultures and shipping the resulting DNA to their Europe location for gene sequencing.

Lancaster Laboratories also continues to perform characterization of microorganisms to the strain level using their DuPont Qualicon RiboPrinter®. This genotypic analysis is a powerful analytical tool that creates a genetic snapshot of the organism, which is then compared to the recently expanded database of RiboPrint patterns for accurate identification. Because each organism yields a very specific pattern, the



Mary Kehoe, analyst in the identification laboratory of Lancaster Laboratories' Pharmaceutical Microbiology Department in Ireland, reviews the analytical data obtained following a Microseq run.

Riboprinter® is often the instrument of choice for investigation of positive results for sterility and microbial limits testing. Even patterns that are not identified as a match in the database can be useful to track historical sources of contamination.

Gas chromatographic analysis of fatty acids present in the cell membrane is the basis for a third option for microbial testing. LLI employs two MIDI Microbial Identification Systems to perform this technique, which matches the chromatographic pattern produced by esterified samples to a library of stored patterns. A new software upgrade greatly expanded the number of organisms that can be identified with the MIDI system. Because this technique is fast and cost-effective, it is often used for identifying isolates from environmental monitoring.

"With the addition of DNA sequencing, we essentially offer all of the current technologies that are used for identification, including strain typing. This gives us a broad ability to analyze a range of isolates," explains Mark Kaiser, director of Pharmaceutical Microbiology. For more information on microbial identification, call Pharmaceutical Business Development at 717-656-2300.

Protocol Development and Tech Support services expanded

Based on customers' increasing interest, Lancaster Labs has expanded its services in protocol development and technical support. Customers can rely on the team to assist with CMC FDA filing, regulatory consulting and early-stage partnering to determine project needs and solutions.

Working with customers from project beginning on their regulatory and method development needs, Protocol Development writes technical documents and gives technical support for the pharmaceutical and biopharmaceutical technical departments. Documents include validation/qualification/verification protocols, specification documents, method transfer and other miscellaneous study types of documents performed under GMP and GLP conditions.

Technical support includes help in defining project scope, troubleshooting project challenges and providing background information the technical team may need in order to develop technically sound methods of analysis.

For more information, contact group leader Cindy Eby, 717-656-2300.

At Lancaster Laboratories, we believe that our people provide our strength. Their dedication to quality, professional competence and hard work is the key element in the company's success. In this regular feature, we introduce you to some of the people who have helped make Lancaster Labs an industry leader.

Heather Bridwell has many clients who count on her knowledge on LC instrumentation and theory to assist with solving their chromatographic challenges. A Method Development and Validation principal chemist and group leader, Heather recently won the company's Annual Impact Award, which recognizes employees' superlative services to customers. She was honored for her efforts in meeting customers' deadlines under exceptionally tight timelines.

Heather began her career at Lancaster Labs in 1999. She had to leave for North Carolina the following year to accompany her husband, Erik, who was stationed there as a Marine. During that time, Heather was development/validation chemist for another pharmaceutical lab. She returned to Lancaster Labs in 2003. She also found time to earn a master's degree in analytical chemistry, all while embracing her most important job as mother of two and wife. Here's a slice of Heather's life:

What does your current job entail?

Currently, I am a team leader for an FTE team at Lancaster. My current job has many facets, and my responsibilities include project management and being the main contact for the client; organizing and planning workload; managing seven analysts with varying levels of experience; and

People are the Chemistry



Heather Bridwell with husband, Erik, and sons Mason and Chayton.

at times performing as a bench analyst with responsibilities for working-up data, report writing and investigations. In addition, I am also responsible for communicating with Lancaster Labs in Ireland as we look to transfer a large project's validated methods to them so that they can take over the testing currently being performed at Lancaster Labs and be the primary testing site for the client by mid-2009.

Given all of your responsibilities, how would you describe a typical workday?

Busy, hectic and sometimes quite stressful. Considering all that, each day is also a welcomed challenge. There are many pieces

to this project, and often we need to focus on different types of testing activities (development/validation, routine testing, stability sample testing...etc) for multiple products concurrently. Everything we are asked to do by the client is a priority and often with aggressive deadlines. Each morning starts with an assessment of data that had been run the previous night, evaluating if the client's priorities have shifted or changed, evaluating what remains to be

completed and then determining if the work schedule needs to be adjusted. Communication has proved to be key, not only with the client, but also within the FTE Team and the other pharmaceutical departments at Lancaster Laboratories to ensure that we have access to the required instrumentation, equipment and the necessary auxiliary support. The days tend to be long and require tremendous effort from all members of the FTE Team. Once you take a step back and look at the volume of work that has been completed

within such tight timeframes, I feel that it is well worth the effort.

And when you're not working?

The majority of my time outside of work is spent with my family. I have a husband and two sons. Erik and I have been married for nine years. It does not feel like it has been that long, which I believe is a sign that it is still a good thing. My eldest son, Mason, is six years old and started kindergarten this year. My second son, Chayton, is two years old and his favorite word is, "no." We tend to spend a lot of time outdoors. This year we are planning to go camping for the first time with the boys. I am a little hesitant, though, as I am not sure how to keep the young one entertained for such long periods of time out in the wilderness. Perhaps we will try out the backyard first before heading out to a real campsite.

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Contract Pharma:

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PDA Annual Global Conference on Pharmaceutical Microbiology:

October 5-8, Bethesda, MD

BioProcessing International:

October 12-16, Raleigh, NC

AAPS Annual Meeting:

November 11-12, Los Angeles, CA

Newsmakers

Dr. Thomas Lehman, manager of method development and validation, published "Lancaster Labs develops extractables database for LC/MS analysis" in *Pharmaceutical Technology*, on-line in May 2009.

Mike Yunginger, manager of non-sterile products and organism identification, published "Harmonized Microbial Limits Methods" in *Contract Pharma*, March 2009.

Dr. Timothy Oostdyk, executive vice president and COO, contributed to the CRO Roundtable in *Life Science Leader*, March 2009. The article is titled, "The Future Of The CRO-Pharma Relationships."

Dr. Shankaramma Shivaprasad, principal scientist, Biopharmaceutical Services; **Dr. Robert J. Duff**, manager, Biopharmaceutical Services; **Dr. Jon S. Kauffman**, director, Biopharmaceutical Services and Analytical Method Development/Validation authored "Protein Sequencing Using High Resolution LC-MS/MS" for WCBP 2009.

Dr. Robert J. Duff, manager, Biopharmaceutical Services, and **Dr. Jon S. Kauffman**, director, Biopharmaceutical Services and Analytical Method Development/Validation Characterization, authored "Synthetic Oligonucleotides by High Resolution LTQ-Orbitrap Mass Spectrometry: Method Development and Qualification" for WCBP 2009.

Dr. Robert J. Duff, manager, Biopharmaceutical Services, and **Dr. Shankaramma Shivaprasad**, principal scientist, Biopharmaceutical Services presented "Characterization of an Oligonucleotide-Derived Conjugate by High Resolution Mass Spectrometry: Method Development and Qualification using LTQ-Orbitrap" at TIDES.

Research advisors **Dr. Neeraj Chopra** (Lancaster Labs), **Dr. David Hollowell** (Eli Lilly) and **Jeff Vincenzi** (Eli Lilly) presented "Analysis of MOE Phosphoramidite Impurities" at TIDES.

Look for Lancaster Labs' cover article on Cleaning Validation in *Pharmaceutical Formulation & Quality's Outsourcing Guide* in the June/July issue.

**Please visit lancasterlabs.com to view the aforementioned presentations and articles.*

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