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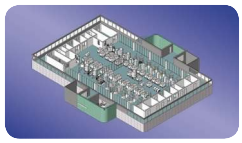

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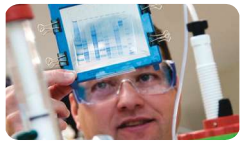

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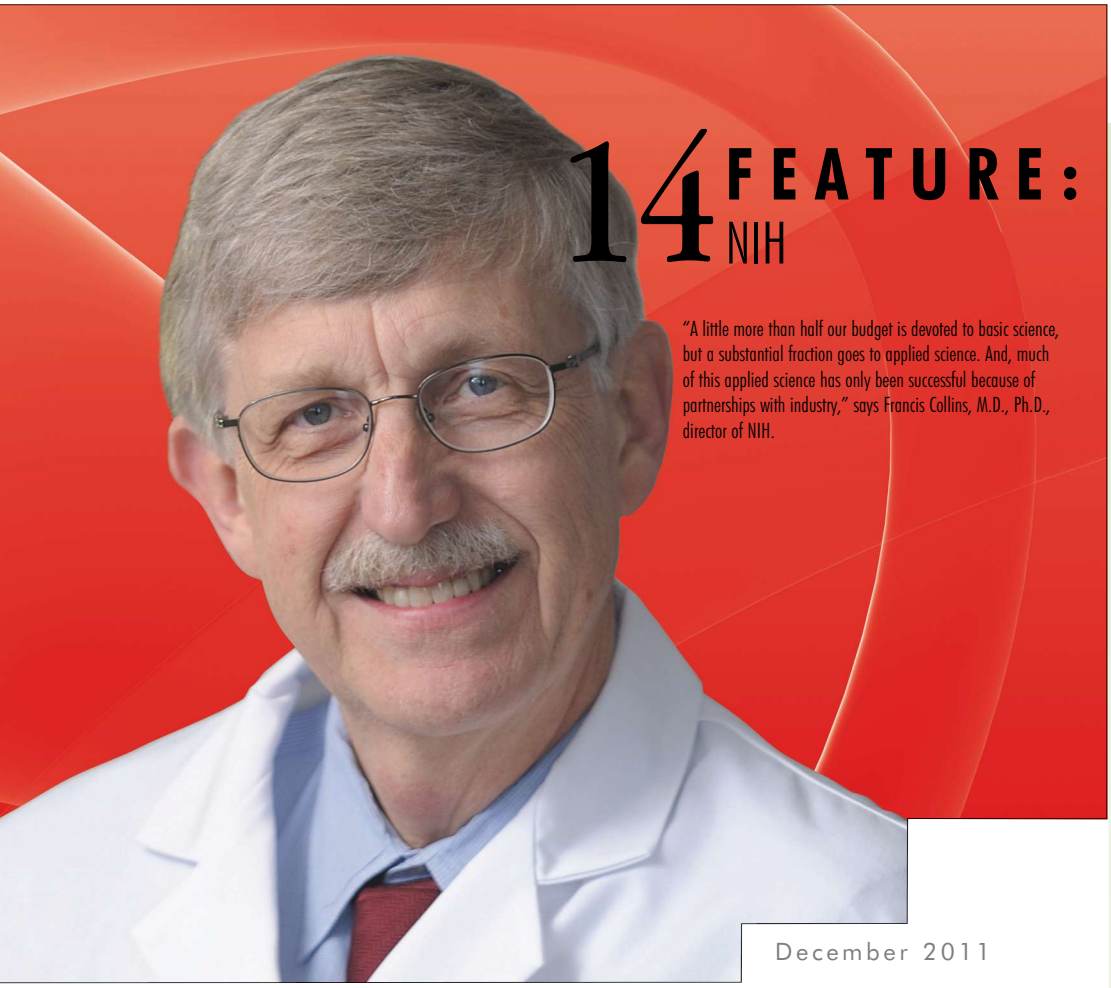

14 FEATURE: NIH

"A little more than half our budget is devoted to basic science, but a substantial fraction goes to applied science. And, much of this applied science has only been successful because of partnerships with industry," says Francis Collins, M.D., Ph.D., director of NIH.

December 2011

Welcome to *Life Science Leader*

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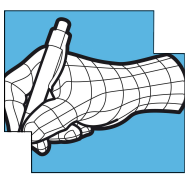

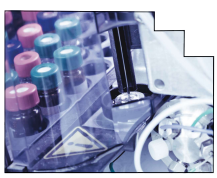

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DECEMBER 2011

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LIFE SCIENCE LEADER (ISSN: 21610800) Vol. 3, No. 12 is published monthly by VertMarkets at Knowledge Park, 5340 Fryling Road, Suite 300, Erie, PA 16510-4672. Phone (814) 897-9000, Fax (814) 899-5580. Periodical postage paid at Erie, PA 16510 and additional mailing offices.
SUBSCRIPTION RATES for qualified readers in the US $0. For non-qualified readers in the US and all other countries $97 for one year. If your mailing address is outside the US or Canada, you can receive the magazine digitally if you provide a valid email address. POSTMASTER: Send address corrections (Form 3579) to Life Science Leader, Knowledge Park, 5340 Fryling Road, Suite 300, Erie, PA 16510-4672.

EDITOR'S NOTE

Cherish The Mavericks

This month's cover feature story is an interview with Dr. Francis Collins, director of the National Institutes of Health, by Sara Gambrill (p. 14). I am excited about this interview because this year Collins created the National Center for Advancing Translational Sciences (NCATS) in an effort to spur drug discovery and development, as well as to help biotech and pharma companies rescue and repurpose compounds. But, there is another reason I am excited about this article — it's another example of how *LSL* has some of the most influential and controversial scientists on our covers. For instance, in March we featured John Craig Venter as a cover feature story. Venter, who worked at the NIH prior to leaving to start his own company, was passionate about using genomics and shotgun sequencing as a means to accelerate the gathering of useful data in the Human Genome Project (HGP). He left the agency out of frustration — viewing the progress of the government as being too slow. Venter founded Celera Genomics with a goal to sequence the entire human genome more quickly while using less money than the government-run HGP.

As Venter spearheaded commercial efforts, Collins represented the federally funded side of the equation, serving as the director of the National Human Genome Research Institute. The race between the public and commercial sector as to which would be the first to successfully map the human genome became center stage, with bickering between the two sides becoming downright nasty. Pressure was applied to Venter and Collins to resolve their differences by a variety of sources including U.S. President Bill Clinton and British Prime Minister Tony Blair. According to the article, "The Race Is Over," *Time* magazine, July 3, 2000, the two sat down to begin solving their differences on May 7 over pizza and beer. Thus began the successful collaboration between the public and private sector on the HGP — resulting in its successful completion, three years ahead of schedule and $400 million under budget.

There are several key learnings from these events. One, two heads are better than one. Two, the public and private sectors can successfully collaborate. Finally, there is nothing which can't be solved with a few beers and good pizza. The highly controversial Venter with his private-sector initiatives did push the government into action. Today the shoe is on the other foot. Collins is leading efforts to push drug discovery and development of the private sector from his government position.

One thing is certain — both Collins and Venter are mavericks and should be cherished. *Life Science Leader* is considered to be somewhat of a maverick. At recent conferences and tradeshows, readers have told me they like the magazine because "We do things differently." Those who deserve the credit are you, our readers, who take the time to call and write us with your recommendations and suggestions. At *Life Science Leader* — like Venter and Collins — we like doing things differently. We have some new things in the works for 2012 — so stay tuned.

Rob Wright
rob.wright@lifescienceconnect.com
@RFWrightLSL

WAYNE KOBERSTEIN

Wayne is the former editor in chief of *Pharmaceutical Executive* magazine and was the founding editor in chief of *BioExecutive International magazine*. He is a 25-year veteran of the publishing industry, with extensive experience in publishing, communications, and business development. During his business journalism career, mainly focused on the pharmaceutical and biotechnology industries, he interviewed and profiled more than 200 top executives in pharmaceutical companies, as well as major regulatory and healthcare leaders around the world.

KARL SCHMIEDER, M.S., M.F.A.

Karl is an award-winning writer and marketing strategist with nearly two decades experience helping life sciences companies market their products and attract customers and investors. An advisor to numerous start-ups, Karl is the founder of MessagingLab, a branding firm focused on emerging life sciences companies, and cofounder of Bridge 6, a digital agency helping life sciences companies reach healthcare providers.

CLIFF MINTZ, Ph.D.

Cliff Mintz, Ph.D., is a regular contributor to *LSL*. He has degrees in microbiology and bacteriology and 15 years of experience as a life sciences freelance writer with a focus on topics such as regulatory affairs, bioscience career development, and social media.

SARA GAMBRILL

Sara Gambrill is an independent communications consultant to the clinical research industry. She was senior editor for nine years at CenterWatch. She writes about clinical research conduct in the United States, Europe, and emerging markets.

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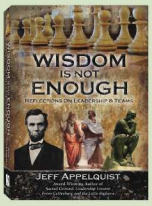


Ask the Board wants to hear from you. Have a question that you would like to pose to our editorial advisory board of experts? Send it to atb@lifescienceconnect.com.

If we select your question for publication, we will provide you with a complimentary copy of a business book, such as Jeff Appelquist's *Wisdom Is Not Enough: Reflections on Leadership and Teams.* Appelquist is the founder and president of Blue Knight History Seminars, LLC, which provides leadership and team development training at famous historic landmarks. He is a former U.S. Marine Corps infantry officer, practicing attorney, and corporate executive.

ASK THE BOARD

Have a response to our experts' answers? Send us an email to atb@lifescienceconnect.com.

Q: What is the biggest challenge presently facing our industry in the area of R&D, and what should be done to overcome?

The key to success in pharmaceutical R&D is having a robust discovery group. Specifically, there needs to be a tremendous focus on the difficult task of identifying good targets and finding compounds that modulate that target safely and specifically. This work, predominantly done by chemists and biologists, is time-consuming – there are no shortcuts.

Disruptions to these groups can be debilitating. Reorganizations, shifting of work to different sites, and most concerning, major mergers are killers to the focus and flow of the productivity of these groups. It can take years to recover the momentum that was once generated in these groups.

Discovery groups should be coddled. They must have stretch goals and strict timelines for productivity. But, to deliver for the corporation, they need to be resourced and nurtured. The biggest challenge, therefore, is maintaining focus on discovery at a time of industry upheaval.

John LaMattina, Ph.D.
Dr. John L. LaMattina is the former senior VP at Pfizer Inc. and president, Pfizer Global Research and Development. In this role, he oversaw the drug discovery and development efforts of over 12,000 colleagues in the United States, Europe, and Asia.

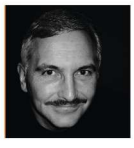
Q: What are the key steps to creating and implementing culture change within a large, established organization?

Change must come from the top, and those leading the organization need to clearly articulate the vision of the new culture. The leaders must truly believe in the culture and be willing to "walk the walk." Everyone will know if the vision is just another poster statement on the wall. Leaders should allow different groups within the organization to set their own goals and plan for how their individual groups will implement this cultural change. As the new culture begins to take shape, celebrate these small wins, so that others in the organization can see it happening and be encouraged to change as well. Talk with those who may ultimately refuse to adopt the new culture or who undermine the progress being made, to help them determine if the new organizational culture is a fit for them. They may find that they can't or don't want to change, so another organization may be a better fit for them.

Lynn Johnson Langer
Lynn Johnson Langer, Ph.D., MBA, is president emeritus of Women In Bio and the director of enterprise and regulatory affairs programs in the Center for Biotechnology Education at Johns Hopkins University.

Q: What can an executive quickly do to improve their effectiveness as a leader?

While leadership begins with you, it clearly does not end with you. Leadership is not the sole responsibility of one person, but rather a shared responsibility among members of a collective group. As much as some in leadership may not want to hear this, a leader belongs to a group, and each member has responsibilities to fulfill. An individual leader can accomplish much, but a culture of leadership can accomplish more. Formal leadership positions are merely added responsibilities aside from their obligations as members of the team. Effective leadership requires members to do their share of work. Starting as a mere group of individuals, members and leaders work towards the formation of an effective team. In this light, social interaction plays a major role in leadership. Learning how to work together requires a great deal of trust between and among leaders, as well as members of an emerging team. Trust is built upon actions and not merely on words.



Mike Myatt
Myatt is a noted leadership expert, author, and widely regarded top CEO coach in America. As a thought leader and columnist on topics of leadership and innovation, his theories and practices have been taught at many of the nation's top business schools.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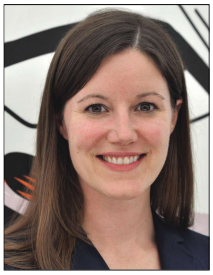


OUTSOURCING INSIGHTS

Why Sponsors Should Regularly Reevaluate Their Preferred Vendor List Of CROs And CMOs

By Kate Hammeke, research manager, Nice Insight

If one word could sum up the key focus of an industry, that word, in the case of drug development, would be innovation. Unlike a decade or two ago, when incremental changes through invention or renovation were enough for shareholders to feel confident in earnings and security in the pipeline, current pressures for profitability present the need for substantial improvement in terms of streamlining processes, improving technologies, and manufacturing more effective products. With many pharmaceutical companies having scaled back and refocused their own business and internal staff already, they are looking to external partners for help with innovation.

Success in the search for an external partner that augments competitive advantage takes time. The process of reviewing staff resources and compatibility, operating procedure documentation, equipment, and costs for even a small number of providers takes anywhere from months to years to complete. This time and resource-intensive process is a short-term obstacle to innovation. This has led to a popular practice of establishing preferred vendor lists comprising partners that have already undergone a thorough review process, which reduces the time spent identifying best-suited CROs and CMOs for specific projects or long-term outsourcing relationships. Then, when new projects arise, partners are selected from the preferred vendor list.

Businesses with preferred provider lists should have an internal system to gather feedback throughout the course of the project and after its completion. However, internal feedback shouldn't be relied on as the only basis for evaluation of companies on the preferred vendor list. Outside factors can influence how a contract business operates, ranging from the exit or promotion of a key staff member (someone influential in the specifics of the project relationship and process) to a significant change in operations or personnel due to a merger or acquisition.

NEW ACQUISITIONS

Six of the businesses included in Nice Insight's quarterly industry survey on pharmaceutical and biotech CMOs and CROs were acquired by other contract pharmaceutical companies and subsequently presented new branding / identities in the third quarter of 2011. Of these six, three were CROs and three were CMOs. The CROs were INC Research (formerly Kendle), Aptiv Solutions (formerly Fulcrum Pharma), and Agilent Technologies (formerly Biocius). The CMOs were Aptalis (previously known as Eurand), Fujifilm Diosynth (formerly Avecia), and Monument Chemical (formerly Johann Haltermann).

Productivity is a key outsourcing driver with respect to innovation, as it contributes to the sponsor's ability to help speed the product to market. If an acquisition results in a decline in customer perception for productivity, which is a metric continuously monitored by Nice Insight, this indicates that the business should be reevaluated to mitigate issues relating to the change in perception. CROs were not as successful as CMOs in maintaining their productivity scores post-integration. All three CROs recorded lower productivity after the acquisition, relative to quarterly data gathered prior to the integration. Inc. Research showed the largest drop in the category (down nine percentage points) relative to Kendle's score in the previous quarter. Conversely, CMOs were able to maintain or improve their postintegration perception in productivity. Aptalis' productivity score was already strong and remained steady at 78% through the transition. And, both Fujifilm Diosynth and Monument Chemical received higher productivity scores with 10 and 11 percentage point increases respectively.

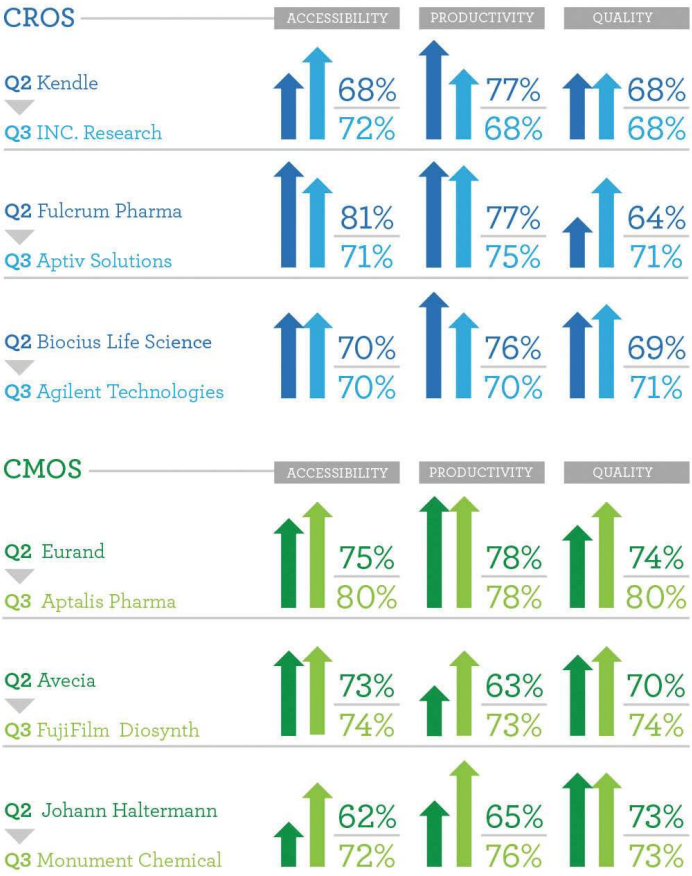
Reliability and accessibility categories are reflections of how a contract organization satisfies the sponsor's needs. Shifts in these scores also warrant investigation, as the ability to meet project milestones (reliability) directly impacts the sponsors' ability to deliver. While accessibility has less of a direct impact on the end product, it is equally important for personnel to be able to respond to sponsor needs and present potential issues before they develop into problems. Once again, CMOs proved more likely to maintain reliability and accessibility scores postmerger or acquisition than CROs. This finding suggests that when a CRO on a preferred vendor list is acquired by another company—even if it is another company on the preferred vendor list—the sponsor's procurement staff should reevaluate the new entity to ensure it still meets the criteria of a preferred vendor.

Our data indicates that each of these businesses maintained or improved their quality score postintegration. Among the CROs, Fulcrum Pharma realized the largest increase in its quality score (seven percentage points) after the merging of Fulcrum Pharma, Averion International, and ClinResearch formed Aptiv Solutions. Among the CMOs,

Axcan's acquisition of Eurand and subsequent name change to Aptalis stood out with the greatest increase in quality customer perception score, at six percentage points.

While each of the businesses referenced was able to maintain a solid customer-perceived quality score, fluctuations among other key outsourcing measures support the importance of continually evaluating preferred vendor lists. Monitoring the partners on the list to see if they have undergone significant changes in structure or staff is a good first line of assessment. Next, the opinions of sponsor company colleagues are also obviously valid, but a review how the business is rated among industry peers—measuring pre- and postchange—provides fundamental ongoing due diligence.

Tracking Customer Perception Before And After M&A



Survey Methodology: The Nice Insight Pharmaceutical and Biotechnology Survey is deployed to 40,000 outsourcing-facing pharmaceutical and biotechnology executives on a quarterly basis/four times per year [Q3 2011 sample size 3,021]. The survey is composed of 1,200+ questions and randomly presents ~30 questions to each respondent in order to collect baseline information with respect to customer awareness and customer perceptions on 406 companies that service the drug development cycle. Over 1,600 marketing communications, including branding, websites, print advertisements, corporate literature, and trade show booths, are reviewed by our panel of respondents. Five levels of awareness from "I've never heard of them" to "I've worked with them" factor into the overall customer awareness score. The customer perception score is based on six drivers in outsourcing: Quality, Accessibility, Regulatory Compliance, Pricing, Productivity, and Reliability, which are ranked by our respondents to determine the weighting applied to the overall score.

If you want to learn more about the report or how to participate, please contact Victor Coker, director of business intelligence, at Nice Insight by sending an email to niceinsight.survey@thatsnice.com.

BIO DATA POINTS

Biopharma Vendor Satisfaction: Are Suppliers Doing What's Best For The Industry?

By Eric Langer, president and managing partner, BioPlan Associates, Inc.

Biopharmaceutical manufacturers are demanding more from their vendors' R&D teams. This year, we found in our annual study that end users are more aggressively asking their suppliers for solutions to their biomanufacturing problems. In our 8th Annual Report and Survey of Biomanufacturers, we asked end users to indicate the top five new product and service areas they want their suppliers to develop. Our objective was to identify "problems in need of solutions." We then compared this to the areas that vendors are actively investing in with R&D resources.

The largest portion of end users used one of their five "wish list" choices to cite better disposable purification products (37.9%), followed by disposable probes, sensors, etc. (37%) and disposable products such as bags and connectors (36.5%). In services areas, "process development downstream" made the top again in 2011. Stainless equipment remains at the bottom of the list, with only 6% of vendors indicating they'd like new products developed in this area.

Additional areas of interest among buyers, both this year and last, included:

- online monitoring and control
- improved quality and consistency of materials
- energy efficiency
- quality control and consistency
- reliability/robustness of analytical equipment.

"Disposable products: purification" was not unexpected and is due to improved upstream performance, such as with better cell lines and expression systems. In contrast, downstream purification processes have changed little and are increasingly the major limiting factor in commercial-scale biopharmaceutical manufacture.

ON THE VENDOR SIDE

Vendors recognize the gaps in what is needed and are starting to invest heavily into the technical solutions that biomanufacturers demand. In addition to surveying biopharmaceutical manufacturers, we also surveyed 186 suppliers to the industry on issues associated with business growth, budgets, new product development, training, and what biomanufacturers expect from their suppliers.

From our study, the largest number of vendors to this industry indicated they are working on new disposable, single-use bioreactors, bags, and consumables. The same percentage noted that "bioprocess development services" are the next New Product Development area (indicated by 40.5% of vendors). Disposable chromatography is the third largest area, with 34.2%.

Other new product development activities by vendors:

- services, technology transfer
- services, process validation
- continuous processing
- upstream process — transfection in synthetic media
- single-use connection technologies
- sterilizing filtration validation services, filtration process training
- open facility designs
- services, extractables & leachables testing.

Given the increasing use of disposable products in biomanufacturing, it is not surprising that the development of new disposable products is among the top R&D products/services now being developed by vendors.

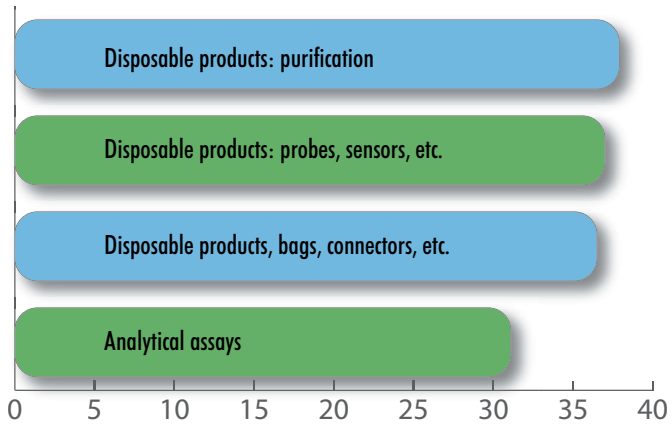
This year's study indicates that, in general, the biggest problems being faced by the industry are also being addressed by suppliers. Success in these areas will help ensure individual vendors maintain a technical advantage. Vendors face a dilemma, however; they need to discuss their R&D efforts with their customers, yet not overpromise. In fact, biomanufacturers report in the study that one of their biggest problems with vendors is that they make promises they cannot keep. Managing customer expectations is particularly important. Communication with the customer stakeholders is critical and is recognized by vendors.

Other results in the study reported by vendors indicate a sense of optimism about the market. Revenues and budgets have increased, along with the demand for new biopharmaceutical approvals and improvements in the economy. This has led to budget increases and focus on new product/service development in response to the acceptance of innovative products such as single-use disposable products.

Top Areas Suppliers Want Their Vendors To Focus Development Efforts

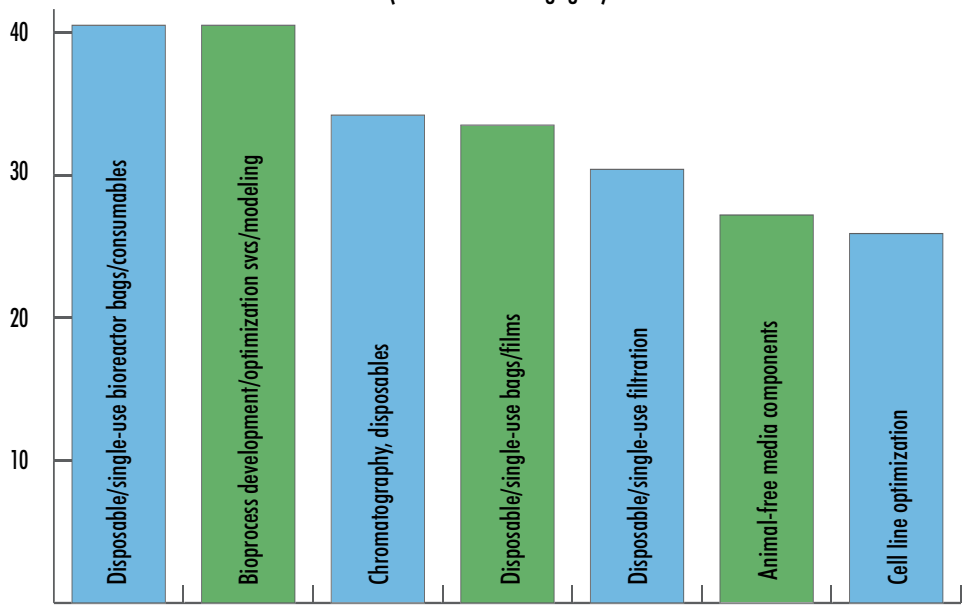
(percentages of respondents)

(As indicated in BioPlan Associates' 2011 Eighth Annual Report and Survey of Biopharmaceutical Manufacturing, April 2011)



New Product Development Areas Vendors Are Working On Today

(% of vendors engaged)



Survey Methodology: This eighth in the series of annual evaluations by BioPlan Associates, Inc., yields a composite view and trend analysis from 352 individuals at biopharmaceutical manufacturers and CMOs from 31 countries. The methodology also encompassed an additional 186 direct suppliers (vendors) of materials, services, and equipment to this industry. This year's survey covers such issues as current capacity, future capacity constraints, expansions, use of disposables, trends and budgets in disposables, trends in downstream purification, quality management and control, hiring, employment, and training. The quantitative trend analysis provides details and comparisons by both biotherapeutic developers and CMOs. It also evaluates trends over time and assesses differences in the world's major markets.

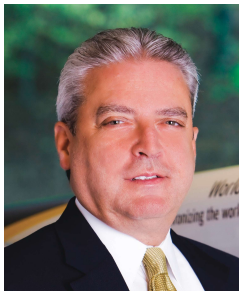
If you want to learn more about the report, please go to bioplanassociates.com.

Francis Collins, M.D., Ph.D., director of NIH

NIH, Industry, And The Translational Science Revolution

By Sara Gambrill, contributing editor

The National Institutes of Health's (NIH's) reputation has been built, in large part, on discoveries made during basic science research — original insights about pathways, receptors, and targets for drugs. These discoveries have led to a significant percentage of new drug approvals in most of the major classes of drugs. However, Francis Collins, M.D., Ph.D., director of NIH, wants to make clear, "NIH doesn't only do basic science. A little more than half our budget is devoted to basic science, but a substantial fraction goes to applied science. And, much of this applied science has only been successful because of partnerships with industry." NIH wants its relationship with industry to be even more productive.



Mark Davis
HEALTHCARE LOGISTICS
PRODUCT MANAGER
UPS

The Benefit Of A Logistics Provider With A Healthcare Focus

Because of the sensitive nature of healthcare products and the industry's complex business and logistical needs, UPS developed a focus specifically designed to address the needs of this industry. Mark Davis, healthcare logistics product manager for UPS, shares his insights on the challenges and solutions related to shipping and distributing time-and-temperature-sensitive products.

What are the biggest challenges or gaps for healthcare manufacturers when it comes to protecting temperature-sensitive products?
Controlled room temperature (CRT) product remains a constant challenge because it has no universal definition. From a Parenteral Drug Association (PDA) perspective, CRT is 20-25 degrees Celsius. Yet, many manufacturers may still consider CRT to be ambient or room-temperature and therefore may not believe their CRT products need any special packaging. These manufacturers need to be aware of how the potency and stability of these products can be affected in the supply chain.

I don't think the industry has been focusing on that particular product line in terms of packaging protection. There is very little regulatory guidance for CRT in the supply chain, but this is clearly a space in which more and more manufacturers will need to pay closer attention. It's an area that UPS is prepared to help manufacturers handle.

How is UPS's global network and broad range of capabilities in transportation, distribution and logistics an advantage for healthcare manufacturers who need to manage temperature-sensitive products?
One of our biggest strengths is having 30 dedicated healthcare-compliant facilities around the world. They are fully cGMP-compliant and include capabilities for frozen, refrigerated and controlled-room-temperature storage. This allows us the flexibility to move products into our multi-client facilities and not only maintain and control the temperature, but also feed into our integrated transportation network for fewer hand-offs.

More than just physical space, UPS has experts who understand temperature-controlled logistics and can help companies with evolving regulations and putting the right solutions in place. For example, we can help with technology for better shipment visibility and build in risk-mitigation strategies to protect products while in-transit to ensure supply. UPS manages more than 800 licenses in the United States alone to ensure compliance and help healthcare companies plan ahead to avoid surprises in the supply chain.

At UPS, we find building partnerships with our clients brings about the most success. This way, we not only understand their product, its temperature requirements and the best packaging to do the job appropriately, but we have an understanding of their larger business objectives and the needs of their customers.

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A TURNING POINT FOR NIH AND THE BIOPHARMACEUTICAL INDUSTRY

It could be argued that passage of the Bayh-Dole and Stevenson-Wydler acts into law was a watershed moment for NIH's relationship with industry and therapeutics development. Prior to their passage in 1980, the federal government owned the IP resulting from research it funded. But, it was not efficient at transferring its technologies, licensing fewer than 5% of its patents. The Bayh-Dole Act stimulated technology transfer by NIH-funded organizations, allowing private institutions and public institutions, such as teaching hospitals, universities, and nonprofit research institutes, to have ownership of the inventions resulting from research funded by the federal government. And, if they chose to, these institutions could transfer the inventions through patent license agreements to the private sector for commercialization and public use. The Stevenson-Wydler Technology Innovation Act and the subsequent Federal Technology Transfer Act of 1986 granted new authorities to federal laboratories, such as the NIH intramural research program, to engage in technology transfer and partner with industry.

In 1982, the federal government established the Small Business Innovation Research (SBIR) program and, in 1992, the Small Business Technology Transfer (STTR) program, to which various government agencies devote funds. Fully 2.5% and 0.3%, respectively, of NIH's extramural research and development budget ($24 billion), or $682 million in Fiscal Year 2011, is invested in these programs, which award grants to small businesses of fewer than 500 employees for the exploration of the technical merit or feasibility of an idea or technology (Phase 1) and, subsequent to that, for the full research and development of the technology toward commercialization (Phase 2).

NEW NIH PROGRAM TO BENEFIT START-UPS

In October 2011, NIH launched a program that marks the most recent milestone in its relationship with industry. This program makes it much easier for start-up companies — or companies that are less than five years old, have fewer than 50 employees, and have received investment of less than $5 million — to license inventions made by intramural scientists at NIH and the FDA.

Ten percent of NIH's budget, or $3 billion, is dedicated to its intramural program, comprising NIH investigators who are federal employees and conduct research with an aim toward clinical applications. According to Collins, this research has led to "a substantial number of IP discoveries." By reducing paperwork and costs, obtaining licenses to commercialize these inventions has been made easier for start-up companies. Now these companies can apply for any of the pending or issued patents for drugs, vaccines, or therapeutics in the NIH/FDA portfolio by submitting a business plan for how they propose to develop them. A start-up evaluation license costs $2,000 and can be converted into an exclusive Start-up Commercial License Agreement within a year. NIH is willing to share some of the risk with the companies such that royalty payments under the licenses are deferred for three years or until the company gets a cash investment. Royalty payments on product sales are limited to 1.5% of sales. The low financial bar for start-ups should help increase technology transfer.

But, as Collins puts it, "All of that's good, but I wouldn't say it's sufficient, particularly because the science has moved along in such gratifying ways. We are trying to identify ways NIH can make an even larger contribution to therapeutic development. That's the motivation for NCATS [National Center for Advancing Translational Sciences]."

THE NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

Dependent upon an appropriation in the Fiscal Year 2012 budget, Collins is preparing to establish the NCATS. He remains opti-

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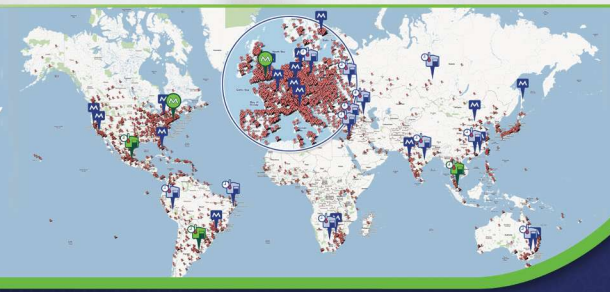

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mistic that there will be an appropriation for NCATS, due to the President's and the Senate's strong endorsement of it. "NCATS is the newest concept to add greater energy and strength to NIH's relationship with industry," Collins says. "The goal of NCATS is to identify bottlenecks in the process of going from a great idea to an actual, approved therapeutic, diagnostic, or device. We will look at the development pipeline itself as a scientific problem in the way that an engineer would — take it apart, look at the various steps, and identify those that are particularly vulnerable to failure. We will try to identify new approaches that might result in a shortened timetable, a higher chance of success, or failure earlier in the development process before a lot of money has been spent. After many conversations over many months with biotech and pharma, these areas have been identified as ones very much in need of attention." Collins stresses that the goal of NCATS is not to become a drug development company, nor is it to compete with industry, but rather to work more closely together.

In 2009, Dr. Collins (center) performed live in Washington with Aerosmith's Joe Perry at the The Rock Stars of Science briefing. The Rock Stars of Science initiative focuses on recognizing the brilliant and dedicated men and women leading research today who have made significant contributions to health research.

The proposed center will be formed by integrating translational research programs from the National Human Genome Research Institute, the National Center for Research Resources, the NIH Director's Common Fund, the Office of the Director, and the Cures Acceleration Network, a program enacted as part of healthcare reform legislation to give the NIH director substantial authority to identify and direct funding to "high need cures" using flexible research authority. In addition, the network of 60 clinical research centers across the country that have received Clinical and Translational Science Awards (CTSAs) will also come under the direction of NCATS. These CTSA centers are located at many of the major medical centers in the United States and represent $500 million of NIH investments. They also represent what Collins refers to as "a strong clinical research engine for NCATS."

Recognizing that translational sciences' endeavors increasingly involve industry, government, academia, and other sectors working together, the central role of NCATS will be to work with these stakeholders to provide integrated, systematic approaches to link basic discovery research with therapeutics development and clinical care. To support these undertakings, NIH already has announced initiatives that will be centrally supported by NCATS. "Seeing appropriations for NCATS as a strong possibility, we wouldn't want to have spent the last few months waiting around for ideas that might feed into it. So, there's been a lot of activity to try to prepare for NCATS' arrival," Collins says.

The new center will not have a top-down approach, but rather ideas and proposals for projects will come from various stakeholders in the therapeutics development enterprise. Discussions with stakeholders have already identified components of translational science that could benefit from NCATS' scientific approach. They include: therapeutic target validation, chemistry, virtual drug design, preclinical toxicology, biomarkers, efficacy testing, Phase 0 clinical trials, rescuing and repurposing compounds, clinical trial design, and postmarketing research.

During my discussion with Collins, he spoke about two of NCATS' major initial activities in depth. The first of them involves a collaboration with the Defense Advanced Research Projects Agency (DARPA), the principal agency within the Department of Defense for development and demonstration of new technologies and systems that serve the country's defense. DARPA's better-known successes include the Internet and global positioning system (GPS).

NIH, DARPA, FDA TO WORK ON CHIP TO PREDICT DRUG SAFETY

In September, NIH announced its collaboration with DARPA and the FDA to develop a chip to screen for safe and effective drugs faster and more efficiently than current methods allow. The way drug manufacturers currently assess whether a drug is going to be safe in humans hasn't changed much during the past decades. The current method of testing a compound in a few cell models, then small animals and large animals doesn't always give an accurate assessment of a compound's safety for, or toxicity in, humans. This sometimes results in compounds that might have been safe in humans being discarded early on or finding unanticipated toxicity in humans from compounds shown to be safe in animals.

The purpose of the joint initiative is to create a system that is a more reliable indicator of whether a compound is going to be harmful to human cells, without having to test it on human subjects. DARPA and NIH plan to create a collection of human cell types representative of human tissues — including the liver, heart, muscles, and kidneys — on a chip. Recent developments would allow NIH and DARPA to generate such cell types by using stem cell biology, and new tissue engineering methods would allow them to generate cells growing in three-dimensional form, closer to what happens *in vivo*.

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"We will try to identify new approaches that might result in a shortened timetable, a higher chance of success, or failure earlier in the development process before a lot of money has been spent." Francis Collins, M.D., Ph.D., director of NIH

"DARPA is excited about taking this to a very bold level where you would have as many as 10 different human tissues represented on this chip. NIH is excited about the science that would be built into the chip to give readouts showing how cells react when you hit them with a new, potentially perturbing influence like a drug. It's fairly unprecedented for these two government research agencies to work as closely together as we will on this," Collins says. "I have encountered a lot of excitement from people in industry about the potential of this chip for providing rapid and reliable information about whether particular compounds are going to be safe and, presumably, allow them to get this information about many more drug candidates than they can now through animal testing. This chip could allow very high throughput." For the five-year effort, NIH plans to allocate $70 million, and DARPA will commit a comparable amount.

The FDA's partnership in this initiative is key, as the agency will need to have access to the data generated to make decisions about changes to the regulatory process. The FDA also will provide an advisory role, making scientific input throughout to ensure the regulatory requirements and process are considered. "We want to create methods and technologies that get translated into a regulatory science change. We don't want to create a chip that is just one more requirement, on top of many others. Our hope is that, after some proof of principle, the chip could substitute for the animal testing currently required before entering Phase 1 clinical trials in humans. This is where having a center at NIH that serves as a hub for a focus on translation would be extremely useful," Collins says.

Collins envisions the new chips becoming a commodity for researchers; all biotechs, pharma companies, and academics with an interest in using the technology would be able to gain access to it. "This is a great example of how NIH can participate in an effort that insists upon open access to the information and, ultimately, to the technology. We're big on that."

RESCUING AND REPURPOSING COMPOUNDS

Another initiative that would be organized through NCATS is the rescuing and repurposing of compounds. NIH held a meeting about this initiative in April, participating in detailed and specific discussions with industry about finding new uses for compounds that were found to be safe but failed in clinical trials due to lack of efficacy, the most common cause of failure in a Phase 2 trial.

Through this initiative, NIH would like to help the industry find new uses for its compounds. Collectively, biopharmaceutical companies have tested thousands of compounds in human subjects, with information attached to them about what pathways or targets they hit — but many of those failed to show efficacy for the disease being studied and so were abandoned. At the same time, NIH has an enormous amount of new information about the molecular basis of diseases, both rare and common.

"There is a lot of opportunity here when you look at the inventory of compounds not being used and the inventory of targets that haven't been hit. NIH could serve a very useful role as honest broker/matchmaker to put those projects together," Collins says.

Collins envisions biopharmaceutical companies making what compounds they have available, including information about their known targets, their appropriate dosing, and, ideally, the compounds' structures. NIH could match investigators looking for new therapeutic options for a disease that has had its molecular basis identified with the inventory of available compounds that target those molecular changes and offer assistance in how to handle IP. Collins says that representatives of the pharmaceutical industry have already reviewed the model agreement that would be used in these cases and that it's close to being finalized.

Because these compounds have already gone through all the steps in preclinical assessment, made it through an FDA IND (investigational new drug), and been tested in humans, investigators could go straight to a clinical trial for a new application. If the trial were successful, they could get approval for the drug in perhaps three or four years, according to Collins — a much shorter timeline than is usual.

"The initiative will be most successful if you have the largest collection of compounds and the largest network of ideas about uses. So, it will benefit from a community-oriented effort, which NIH is well positioned to organize through NCATS," Collins says.

LOOKING AHEAD

Though Collins is clear about the fact that NCATS does not formally exist yet, he was just as clear in his enthusiasm for the opportunities the new center would offer various stakeholders in revolutionizing the science of translation in a comprehensive, systematic, and creative way, ultimately improving human health. It's up to Congress now, but it looks as though the odds are good.

What's R&D Got To Do With It?

A candid conversation with pharma veteran John LaMattina, Ph.D.

By Cliff Mintz, Ph.D., contributing editor

Over the last five years or so, many big pharmaceutical companies concluded that their internal R&D activities were no longer delivering the ROI they had grown to expect. This resulted in the elimination of hundreds of thousands of jobs and the outsourcing of many R&D activities. While most executives and industry insiders believe that downsizing and outsourcing R&D is a sound idea, John LaMattina, Ph.D., former senior VP at Pfizer and president of Pfizer Global R&D, who spent 30 years in R&D after joining the company in 1977, is not so sure.

During his tenure at Pfizer, Dr. LaMattina oversaw the development of new treatments for cancer, smoking cessation, rheumatoid arthritis, and AIDS. After retiring in December 2007, he decided to write a book to dispel some of the myths and misconceptions about the pharmaceutical industry and its products. *Drug Truths: Dispelling the Myths about R&D* was published in 2008. In 2011, he decided to start a blog called *Drug Truths* (after an appearance on the Dr. Oz Show) to better inform the public about the drug development and commercialization process. In addition to his literary pursuits, Dr. LaMattina is a senior partner with the VC firm PureTech Ventures and serves on the board of directors of Human Genome Sciences and Ligand Pharmaceuticals. He also serves on the board of trustees of Boston College and is active in the Terri Brodeur Breast Cancer Foundation.

During his conversation with me, Dr. LaMattina shared his views on the dramatic changes taking place in pharmaceutical R&D and the effects that they may have on the future health of the industry.

AS A SCIENTIST WHO SPENT HIS ENTIRE CAREER IN R&D, DO YOU THINK THE ERA OF THE "BLOCKBUSTER DRUG" IS REALLY OVER?

From my perspective it depends on the context of the use of the word "blockbuster." I believe it is still possible to develop drugs for certain indications that could yield sales of $1 billion per year or more. Analysts have coined the term "niche blockbusters" for these molecules, and it is not unreasonable to include drugs to treat certain cancer indications or genetically inherited diseases in this group. Interestingly, one of the major factors that will allow these new drugs to reach blockbuster status is the high prices that historically have been associated with them. I think the niche blockbuster business model will be the one embraced by most pharma executives going forward.

While others have suggested that the advent of personalized medicine may be a death knell for blockbuster drugs, I believe that personalized medicine may actually generate more blockbusters. This will certainly be the case if payors, physicians, and patients can be guaranteed that a disease-specific, personalized treatment is better and safer than other treatment options out there. This will allow drugmakers to obtain reasonable pricing and generate significant sales of these drugs. We are clearly in the early days of personalized medicine, but I think that reasonably priced, highly safe, and efficacious medicines will be the business model going forward. However, from a more traditional perspective, there is no doubt that companies that are able to develop drugs to treat Alzheimer's disease will have a blockbuster on their hands, mainly because the incidence of Alzheimer's disease continues to skyrocket as baby boomers age. Similarly, because of growing patient populations, development of a safe and effective (based on long-term clinical outcome and safety studies) treatment for obesity or diabetes could easily achieve blockbuster status.

I think the current interest in biotechnology drugs and biologics is largely based on the current prices commanded by these products.

John LaMattina

Practically speaking, however, it is difficult to predict whether or not a new molecular entity will achieve blockbuster status. Obviously, that depends on the overall performance of a drug in Phase 3 studies and, ultimately, the label you can get from the FDA. However, I can tell you after spending 90% of my career in discovery, that at the beginning of every new development program we were asked by upper management to assess a compound's commercial potential. Because we were discovery scientists, we really had very little idea about potential commercial success of a drug candidate. That said, spending valuable time and resources on compounds with only minor commercial potential was frowned upon. Nevertheless, I believe that if drug discovery is driven by the desire to develop treatments that address unmet medical needs, then the compounds that make it through will enjoy commercial success.

WHAT FACTORS DO YOU THINK CONTRIBUTE TO THE CURRENT HIGH ATTRITION RATE FOR NEW MOLECULAR ENTITIES?

First, over the past decade, the FDA has clearly raised the bar for approval of new molecular entities (NMEs). This is because the FDA learned that drugs cannot solely be approved using biomarkers or surrogate clinical markers. Consequently, the agency insisted that long-term outcome studies to demonstrate safety and efficacy would be required for drug approvals. This caused clinical trials to take longer and become more expensive, costing literally hundreds of millions of dollars, than in the past.

Second, at about the same time, payers (government agencies in Europe and insurance and health management companies in the United States) began playing a more prominent role in the drug approval and commercialization process for NMEs. That is, payors are less inclined to pay higher prices for new medications unless drugmakers clearly demonstrated improved clinical outcomes for the patients who were treated with them. Put simply, why spend more on reimbursement costs for a prescription drug if it did not offer any clinical benefits or improvements as compared with a less costly generic version of the medication?

Both factors not only increased the time and cost of running late-stage clinical trials but also increased the failure rates of many NMEs. Historically, you could be reasonably assured that 90% of NMEs would ultimately be approved if your Phase 2 data looked good. This is no longer the case. These days, the results from Phase 3 clinical trials can make or break a compound — or a company for that matter. Put simply, late-stage clinical development became riskier and more costly. And, not surprisingly, the approval rate of drugs coming out of Phase 3 clinical trials has consistently dropped for the past five years or longer.

Is this a bad thing for patients or society in general? No! But, at the same time, higher regulatory requirements and standards have caused major problems for drugmakers. Many

"While others have suggested that the advent of personalized medicine may be a death knell for blockbuster drugs, I believe that personalized medicine may actually generate more blockbusters."

John LaMattina

big pharma companies are still grappling with them and trying to adjust. Like it or not, I don't think that these new, more stringent regulatory requirements are going to change anytime soon. To that end, if you are able to clear the high bar set by regulatory agencies and garner approval for an NME, then it is likely you will have a winner on your hands.

WHAT ARE YOUR THOUGHTS ON OUTSOURCING?

I think that there are two distinct types of outsourcing, and, unfortunately, they are frequently lumped together. One type that I embraced while I was running R&D was to use it to maximize my budgetary reach. For example, when my IT head came to me and suggested that we could reduce our IT costs by 90% by outsourcing those functions to India, then I considered it. This is because it gave me an opportunity to shift and divert funds originally allocated for IT to a key clinical trial that I wanted to run.

The second type of outsourcing involves determining how much to invest in external R&D to either complement or supplant your internal efforts. I believe it is critically important to invest in outside ideas, and an R&D budget must have monies allocated specifically for it. This is because no matter how big an internal R&D organization is, it will never be large enough to explore all of the possible ideas out there for new drug development. However, I don't think it's prudent to overly rely on external R&D to drive drug development. To be successful in this business, it is critically important to have a strong, internal scientific organization to help evaluate NMEs and ultimately decide on what to invest in the outside. Further, while I am not an economist, I think that relying on in-licensed compounds is ultimately less profitable for a company, mainly because of up-front costs, milestone fees, and downstream royalty payments. According to my formula, 1/3 of a company's pipeline ought to come from external sources and the remainder from internal R&D efforts.

WHAT EFFECTS HAVE MERGERS AND ACQUISITIONS HAD ON THE LIFE SCIENCES INDUSTRY?

Consolidation in the industry has resulted in massive downsizing and outsourcing of many R&D functions. This turmoil has placed an enormous stress on R&D personnel, many of whom wonder on a day-by-day basis whether or not they will have a job tomorrow. Not surprisingly, this has resulted in a loss of concentration and lack of R&D focus among pharmaceutical employees, which, in turn, has resulted in thinning pipelines at most big pharma companies.

While some companies have embraced a downsizing strategy, others have not. Lilly's CEO John Lechleiter has publicly asserted that he will not downsize R&D operations and continues to invest heavily in R&D. Unfortunately, Lechleiter is being punished by Wall Street analysts for his decision. In marked contrast, Wall Street has tended to reward CEOs like Pfizer's Ian Reed, who is downsizing R&D operations to precariously low levels.

I believe that if downsizing of R&D operations continues at its current rate, the uptick in R&D productivity that occurred over the past few years will be lost. And, it will be a very long time — at least 5 to 10 years — before the delicate equilibrium is restored between drug discovery and commercialization. Based on my experience running R&D, the discovery pipeline needs to be regularly filled and replenished to remain robust; this is simply not happening at most big pharma companies today.

HAS BIG PHARMA REALLY SHIFTED ITS FOCUS FROM SMALL MOLECULES TO PROTEIN-BASED DRUGS?

While many big pharma execs are talking up the promise of biotechnology drugs and biologics, I believe that small molecules will continue to play a vital role in treating certain indications, especially those in oncology and chronic diseases like rheumatoid arthritis.

From a patient perspective, it is easier and much more convenient to take a pill rather than receive a weekly or monthly intravenous infusion of a protein-based drug. Nevertheless, there is currently general agreement in the industry that effective treatments for certain indications, most notably oncology, will require a poly-pharmacy approach. By that, I mean a combination of compounds (both small and large molecules) will be required to contain or control those diseases. That said, both small and large molecule capabilities are required for companies to remain competitive in today's market.

Finally, I think the current interest in biotechnology drugs and biologics is largely based on the current prices commanded by these products. I don't think that 15 to 20 years ago anybody would have believed that the current pricing for biologics would have been sustainable over time. This has been an eye-opener for many pharmaceutical executives and may be responsible for their changing attitudes about large molecule drugs.

WHAT ARE THE GREATEST CHALLENGES FACING BIG PHARMA TODAY?

I think my answer may surprise you. I believe the loss of public

trust in the pharmaceutical industry is the greatest challenge we face today. Unfortunately, this loss of trust has been largely self-generated. Not a month goes by without new reports about improper detailing or marketing of drugs or legal settlements for inappropriate business activities. Moreover, I believe the industry still suffers from a lack of transparency. Admittedly, however, clinical trial data is more readily available today than it has ever been in the past.

Finally, there is a misconception among many people — maybe 80% to 85% — that drugs are discovered by the U.S. government or academic institutions, repackaged by pharmaceutical companies, and then sold for outrageous sums of money. The pharmaceutical industry needs to better educate the public on the drug development process and more clearly enunciate the benefit/risk ratio for all drugs.

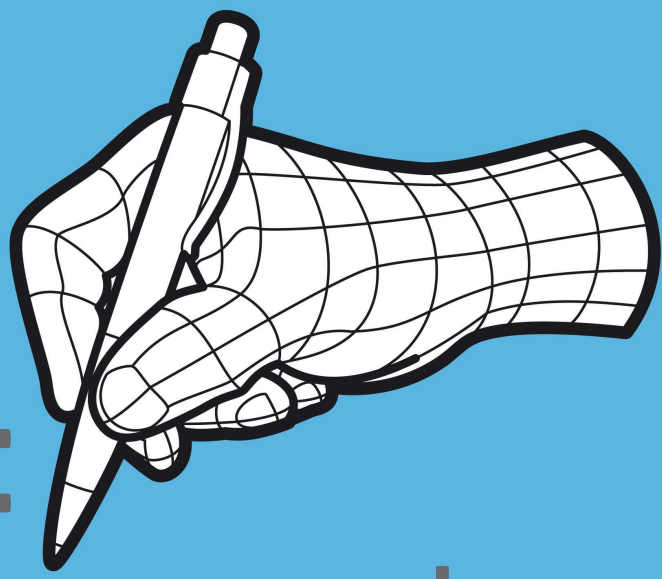
Until big pharma companies figure out how to regain the public trust, the path forward will be an extremely difficult one for them.

WHAT IS THE MOST IMPORTANT THING THAT YOU LEARNED DURING YOUR 30 YEARS WITH PFIZER?

The single most important thing that I learned is that it takes hundreds, perhaps thousands, of people to discover, develop, and successfully commercialize a new drug. No one person is solely responsible, and contributions made by all team members can never be underestimated. I have a great story that illustrates this point.

Nurses who were running Phase 1 clinical trials in England for a compound that was being developed to treat congestive heart failure noticed that men who were to have blood drawn for analysis were consistently lying on their stomachs during these examinations. A nurse finally realized that these men were lying on their stomachs to hide erections induced by the compound. This led to development of the compound which is now called Viagra. In hindsight, the erectogenic properties of the drug were not surprising because it is meant to be a vasodilator; it was simply working on a different organ than originally envisioned!

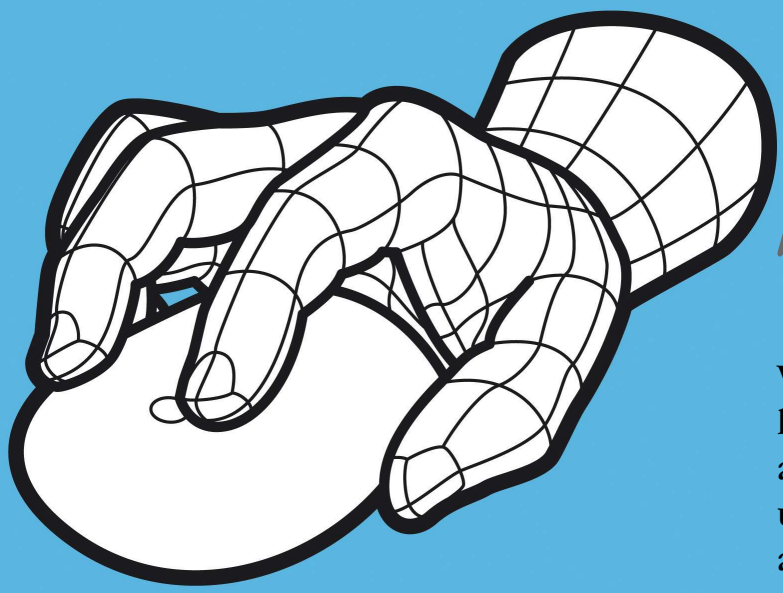
Looking back over my career, I realize it was a great job to run R&D. I had the privilege of working on a daily basis with thousands of very smart and talented people who were committed to developing drugs that could possibly benefit millions of people around the world. What greater thrill can you have as a scientist?



Email Shenanigans: Who *Really* Requested That Clinical Trial Info?

A Digital Identity And Digital Signature Roundtable

By Rob Wright



Thanks to the creation of the personal computer and the Internet's coming of age via the World Wide Web in the early 1990s, the digital revolution has forever changed how we live and conduct business. Transactions which used to require paper documentation and a handwritten signature can now be conducted more economically via digital identity and digital signature technologies.

However, in addition to the benefits reaped from the digital revolution, it has also resulted in new forms of theft. Cybercrimes, such as identity theft, have resulted in boons to digital authentication and verification technologies, which have posed a significant challenge for the pharmaceutical and biopharma industries to manage.

A variety of organizations have developed solutions to assist life sciences organizations in the effort to be compliant with good practice quality (GxP) audits, Health Insurance Portability and Accountability Act (HIPAA), Sarbanes-Oxley (SOX), ISO, and FDA regulations, such as the 21 CFR part 11, which requires organizations to guarantee the authenticity, confidentiality, and integrity of electronic records. To gain a better understanding of the digital identity and digital signature conundrum, *Life Science Leader* contacted the following experts: Peter Loupos, VP, scientific information systems, Sanofi-Aventis; Gary Secrest, recently retired as director, worldwide information security, Johnson & Johnson; and Mollie Shields-Uehling, president and CEO, SAFE-BioPharma Association. They discussed their opinions on digital identities, digital signatures, the need for them to be interoperable, and future trends for these technologies applicable to the life sciences industries.

WHY SHOULD THE INDUSTRY BE INTERESTED IN USING DIGITAL IDENTITIES?

Peter Loupos of Sanofi-Aventis: Advancements in pharmaceutical R&D and enhanced quality of healthcare are predicated on an efficient flow of information amongst all stakeholders. A universally accepted trusted information infrastructure to allow this free flow does not currently exist. This has negative consequences in the timely approval of promising new treatments and costly consequences regarding healthcare delivery.

Gary Secrest, retired from Johnson & Johnson: As the entire healthcare space continues to move to electronic records for enhanced patient care and greater efficiency, the availability of a trusted digital identity to assure proper authentication before granting access to sensitive healthcare information is critical.

Mollie Shields-Uehling of SAFE-BioPharma Association: There are numerous factors that make it essential to know and trust the identities of people on the other side of the screen. The biopharmaceutical industry works with confidential information. It conducts business in a regulated and legally enforceable environment. And, it relies on global collaboration for research, development, sourcing, manufacturing, and other functions.

> *"CROs already are testing digital identities and digital signatures and recognize their inherent efficiencies and cost savings."*
>
> Mollie Shields-Uehling, SAFE-BioPharma Association

WHAT IS THE SIGNIFICANCE OF A DIGITAL IDENTITY BEING INTEROPERABLE?

Loupos: In a perfect world, free flow of information between patients, healthcare providers, payers, researchers, and regulators would result in rapid access to promising new treatments for unmet needs and more efficient and higher quality healthcare. However, information sharing of personal information is a highly sensitive topic. Trusted interoperable digital identities would enable access of information for the benefit of all stakeholders.

Secrest: There will always be many application vendors and associated systems. To meet the goals of better care and efficiency, standardization is critical. It is simply too onerous on users to have multiple credentials with multiple levels of trust in the credential. A single, interoperable, trusted credential provides a way for an authorized user to work across a variety of systems in a seamless manner.

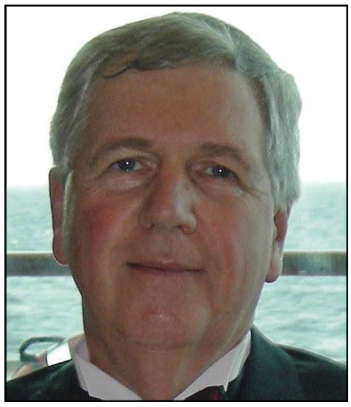
Shields-Uehling: There is a growing system of identity trust hubs across the globe, each containing many identities that can be trusted within its own hub. Interoperability means that an identity asserted by one hub will be trusted within another hub. That process occurs when trust hubs agree to follow a standard set of rules. For example, SAFE-BioPharma Association is a trust hub for the biopharmaceutical and healthcare sectors and follows the rules of the Federal Bridge, the identity trust hub serving U.S. federal agencies. Thus, all U.S. agencies which utilize Federal Bridge identity credentials have agreed to trust the digital signatures as being authentic.

WHAT MAKES A DIGITAL SIGNATURE DIFFERENT FROM OTHER ELECTRONIC SIGNATURES, AND WHAT MAKES THE DIFFERENCES SIGNIFICANT FOR THE LIFE SCIENCES?

Loupos: Many transactions in the life sciences have either legal or regulatory implications. Most existing processes, even with some level of

technology support, are still paper-based. This can be error-prone and introduces expensive delays as well as significant material costs. The identity of an electronic signature cannot be ensured. Digital signatures, legally defensible and nonreputable, hold the promise of quality and efficiency improvements through total electronic interoperable processes.

Secrest: There are two major differences — first, a digital signature cryptographically guarantees the integrity (i.e. it has not been violated) of the information which has been signed; what was signed has not been altered in any way, and if it has been altered, it is readily apparent. The second difference is in regard to the standardization of the digital signature. A digital signature made in one application can be verified in another application as long as the digital signature standard was followed.



Shields-Uehling: Digital signatures are more secure and legally binding than simple electronic signatures. Each signature is tightly bound to the individual's proven identity, and the integrity of the entire document to which the signature is applied is cryptographically guaranteed. Digital signatures are legally enforceable, nonrepudiable (its use cannot be denied by the person who applied the signature), and are instantly auditable. Additionally, any change to a signed document invalidates the signature and graphically shows it is no longer valid. This level of protection is extremely important for the life sciences because it helps prevent fraud and shows the document is compliant with regulatory requirements.

> *"A single, interoperable, trusted credential provides a way for an authorized user to work across a variety of systems in a seamless manner."*
>
> Gary Secrest, retired from J&J

HOW ARE DIGITAL IDENTITIES AND DIGITAL SIGNATURES CURRENTLY BEING USED IN THE LIFE SCIENCES?

Loupos: Digital identities are used wherever there is a desire to replace inefficient paper processes where legal and regulatory requirements must be met. Specific examples include electronic laboratory notebooks (which could be implicated in patent protection), regulatory filings, and contracts.

Secrest: Trusted digital identities enable strong user authentication processes in addition to enabling the use of digital signatures. These are imperative factors in a highly regulated environment such as life sciences. The integrity of data is a critical element for regulators as provided by a digital signature. So, we see data such as that from electronic lab notebooks or documents such as SOPs being digitally signed by individuals, authorized, and strongly authenticated using the same trusted credential. And, it's becoming more common to use digital signtatures for signing contracts, clinical protocols, and drug prescriptions — including controlled substance prescriptions.

Shields-Uehling: For several years, digital identities and digital signatures based on agreed-upon standards have been used to sign virtually every form of eDocument, including forms used from discovery through all phases of clinical development (e.g. electronic laboratory notebooks, government forms, electronic submissions, approvals, contracts). Importantly, they also are used to authenticate the digital identities of internal and external collaborators (e.g. CROs, clinicians). Soon we will see clinicians use them to access clinical portals and to sign ePrescriptions. We also will see them used extensively in conjunction with cloud collaboration. Interoperable digital identities will allow a variety of disparate collaborators to access documents and data from the cloud, apply digital signatures to them, and return them to the cloud. The time and cost savings over the current approaches will be enormous. We're at the threshold of this new era in the use of digital identities and digital signatures. An early indicator of this is the ongoing pilot between industry researchers and their counterparts at the National Cancer Institute, where clinical trials are initiated using interoperable digital identities and signatures.

HOW DO YOU EXPECT DIGITAL SIGNATURES TO BE USED IN THE FUTURE?

Loupos: The opportunity exists for digital signatures to be used to replace any process where efficiencies can be realized by evolving from paper to electronic while meeting all legal or regulatory requirements. It can be envisioned that academic researchers, pharma companies, healthcare providers, payers, and regulators would all work together to share data to gain greater insights into diseases, patient needs, and healthcare practices to the benefit of

> *"Trusted interoperable digital identities would enable access of information for the benefit of all stakeholders."*
>
> Peter Loupos, Sanofi-Aventis

patients everywhere.

Secrest: Strong digital credentials are a key enabler for the continuing drive for paperless systems. Over the past several years it has become clear that simple passwords do not provide strong identification or authentication which is required for sensitive healthcare-related systems. We will see a continuing push to improve processes via electronic systems across the entire space from biopharmaceutical companies developing and selling drugs to doctors in hospitals providing patient care. A single, trusted digital credential will allow disparate users such as providers, payers, and researchers to share information via access to electronic systems instead of paper.

Shields-Uehling: The next big area of use will be expansion in clinical development. CROs already are testing digital identities and digital signatures and recognize their inherent efficiencies and cost savings. In the not too distant future, manufacturing will turn to digital identities and digital signatures as a way to manage and track the supply chain. The old ways of doing things are rapidly changing. Digital identities and digital signatures are in wide use today. We anticipate that over the next few years their use will expand significantly.

WHAT ARE YOUR THOUGHTS ON THE USE OF INTEROPERABLE DIGITAL IDENTITIES WITHIN HEALTHCARE?

Loupos: Very simply, this is a requirement to contribute to fundamental change in the way healthcare is delivered. Until the free flow of healthcare information can occur amongst all shareholders, R&D and healthcare delivery will not reach its full potential.

Secrest: Simply put, interoperable digital identities are a vital enabler to improved healthcare at lower costs. Interoperable systems which provide for the free flow of healthcare-related information are the future.

Shields-Uehling: It is inevitable. Digital identities are needed to control access to patient records. Interoperability will allow for managed access to records across the firewalls of separate health systems. Physicians will use them to sign electronic prescriptions, including those for controlled substances. Healthcare is just crossing the threshold into electronic communications. It is just a matter of time before healthcare enters the era of secure and trusted communication based on interoperable digital identities.

The 7 Laws Of Identity

The seven laws of identity were developed by Kim Cameron, chief identity and access architect at Microsoft, and then refined in the blogosphere through his identity weblog at www.identityblog.com. The laws have been compiled and enhanced during an ongoing conversation among numerous people and represent the best available advice for developing and implementing an identity solution at your company.

1. Technical identity systems must only reveal information identifying a user with the user's consent.
2. The solution that discloses the least amount of identifying information and best limits its use is the most stable long-term solution.
3. Digital identity systems must be designed so the disclosure of identifying information is limited to parties having a necessary and justifiable place in a given identity relationship.
4. A universal identity system must support both "omnidirectional" identifiers for use by public entities and "unidirectional" identifiers for use by private entities, thus facilitating discovery while preventing unnecessary release of correlation handles.
5. A universal identity system must channel and enable the interworking of multiple identity technologies run by multiple identity providers.
6. The universal identity metasystem must define the human user to be a component of the distributed system integrated through unambiguous human/machine communication mechanisms, offering protection against identity attacks.
7. The unifying identity metasystem must guarantee its users a simple, consistent experience while enabling separation of contexts through multiple operators and technologies.

According to Joshua Trupin, executive editor of *MSDN* and *TechNet* magazines, these seven laws are important because digital identities play a key role in today's information infrastructure. "If users and companies do not see identification as safe, private, and secure, the lack of trust will end up undermining any products and technologies that are built upon it," says Trupin.

The Virtual Pharmaceutical Manufacturing Company:

Building Effective Commercial And Government Contracting Operations

by Chris Cobourn and Dean Erhardt

Unlike large pharmaceutical manufacturers that handle the majority of operations in-house, many small and emerging pharmaceutical and biotechnology companies are now adopting a "virtual model" to support their day-to-day commercial operations. Due to the expense, infrastructure requirements, and increasing regulatory risk of building commercial and government compliance programs from the ground up, these companies rely on third-party vendors to support their commercialization, contracting, government program operations, and compliance functions, to name a few. Specialized, best-in-class vendors have emerged to provide the "three legs to the stool," which consist of logistics (distribution), reimbursement (market access), and back office support, allowing pharma and biotech companies to focus their resources on developing and marketing new products.

According to a large database provider, there are 6,700 pharmaceutical and biotech companies in the United States, and 60% of these organizations have fewer than 25 employees. With the virtual model, the manufacturer gets the best of both worlds: staff augmentation with experienced staff offering expertise, relationships, and insights in commercial and government operations, and systems and automations, without the staffing and systems footprint of the traditional software model.

Manufacturers have several pressing commercialization needs, including the need to gain market access, while also developing a robust corporate compliance program. In addition, they must maintain compliance with applicable government programs, including Medicare, Medicaid, Veterans Affairs (VA), and the Public Health Service (PHS) or the 340B program, while also meeting federal and state reporting requirements. In the past, many small companies had the feeling that they were under the government's radar; however, this is no longer the case. In today's regulatory environment, a solid compliance program is critical to the long-term sustainability of an organization.

In the past few years, vendors that provide service-based approaches to commercialization and compliance have worked together so often that the virtual model can be considered seamless and integrated. Where coordinating interactions with multiple vendors used to increase a manufacturer's risk, there is now a familiar, organized approach. Manufacturers like to know there are experts in each key area of commercialization to lead them through the process. By utilizing a virtual model that includes the "three legs to the stool," manufacturers have experienced resources to help plan and orchestrate their commercialization.

Commercialization processes, specifically related to ensuring the ability to distribute product, collect cash, and get product reimbursed, are as diverse as there are types of product in the market. Hiring the right expertise across 3PL (third-party logistics), distribution (e.g. wholesale, specialty pharmacy, oncology), and payer access (commercial and public payers) is expensive and time-consuming. The ability for a small manufacturer to have the right experts to guide the development of necessary infrastructure and to understand the timing of key events can drive commercial acceptance from the various trading partners and save the manufacturer significant expense of time and manpower. Having experts who can expeditiously accomplish major commercial setup is crucial during the early commercialization stage where conserving cash flow is paramount. Many aspects of commercial structure go unnoticed until there is a problem. Issues like 3PL setup, state licensing, wholesaler agreement, and payer acceptance are crucial in the overall success of any product, but perhaps even more important for virtual organizations.

"I was tasked with building a commercial organization from scratch and needed flexible options based on

financial execution and timing," said Michael Adatto, senior VP, sales and managed care at Horizon Pharma, Inc. "The virtual model allowed me to focus on hiring best-in-breed vendors and not worry about creating overhead in places where the services were needed to ramp up activities and taper off as we are in marketplace. Through this model, I can help make sure that Horizon gains the insight into changing government regulations and best practices to successfully develop and maintain a compliance program."

The key components of a virtual model are summarized in the following categories:

STRATEGY AND COMMERCIAL RELATIONSHIPS

The first component in developing a commercialization model is to understand the requirements of the product and to develop the strategy relative to the distribution model. The right strategy will ensure the manufacturer has the product in the right place at the right time and will enable the manufacturer to minimize future issues such as out-of-stock problems or higher-than-anticipated returns.

When starting to evaluate the distribution model and understand the channel requirements, start with the end user in mind. In this case, the end user needs to encompass both how a patient will access the product as well as how (and whom) will reimburse for the product.

- Where will the patient access the drug (retail, hospital, clinic/office, mail order, specialty pharmacy, specialty distributor, etc.)?
- What will be the route of administration?
- Who will pay for the drug (physician, patient, third party, government)?
- What type of education materials are needed and for whom?
- Reimbursement support required?
- Injection/infusion training required?
- Patient mobility issues?

LOGISTICS AND DISTRIBUTION

Many emerging pharmaceutical companies rely on 3PL companies to function as their customer service and shipping. The 3PL is effectively the face of the manufacturer to the manufacturer's

trading partners. In addition, manufacturers continue to look for efficiencies in the supply chain. Smaller population products typically will not need open access models. Limited and exclusive distribution models have gained increasing acceptance, particularly when also having REMS requirements. Alternative regionalized distribution solutions have also become more popular. When looking at various distribution options, the manufacturer must understand that different distribution models will have a direct impact on key issues, such as state licensing requirements and potential reimbursement issues. Understanding the impact of these decisions and how to select the right partners that can provide the right services under the auspices of Fair Market Value contract pricing is imperative to the success of a virtual manufacturer.

BACK OFFICE SUPPORT AND GOVERNMENT PROGRAM PARTICIPATION

Once the product is on the market, the manufacturer must have the operational support for contract operations, group purchasing organization (GPO) contract management, chargeback processing, class-of-trade management, and managed care rebate processing. They also must have the support for their government contracting operations, which primarily includes their statutory pricing calculators under the Medicaid, VA, Medicare Part B (ASP), and public health service programs, and the complexities of claims management for Medicaid, Tricare, and the Medicare Part D Coverage Gap.

INFRASTRUCTURE TIMELINE

One area where virtual manufacturers sometimes struggle is in understanding the timelines required to appropriately set up the required infrastructure. Manufacturers should have a distribution channel and third-party payer or benefits provider strategy "gut check" starting approximately 24 months prior to anticipated approval. This timeline ensures that manufacturers have adequate time to account for issues like 3PL, state licensing, wholesaler contracting, and retail stocking models. As some commercial activities are sequential, getting in front of timelines is crucial to commercial readiness.

As previously mentioned, government program compliance and commercial compliance are critical factors in successful commercialization. The government market can, and should, be viewed in two ways. First, VA and CDC reports show it to be an ever-growing market segment with nearly 40% of Americans accessing pharmaceutical benefits through a government-funded program. Second, the compliance requirements and risks for pharmaceutical manufacturers who participate in Medicaid, VA, PHS (Public Health Service), Medicare, and Tricare are high, regardless of the size or company type. As government programs grow and as federal and state budgets supporting the programs grow, scrutiny on the programs also grows. With a continued fiscal crisis at the federal and state level, enforcement agencies place increased focus on program integrity and using audit and investigative activity to recoup monies from pharmaceutical manufacturers under the False Claims Act. According to Office of Inspector General (OIG) semiannual reports, the OIG recouped over $7 billion from pharmaceutical manufacturers over the past five years. Under the Deficit Reduction Act of 2005, the OIG was given the mandate and the budget to perform proactive audits. Additionally, the OIG published guidance in 2003 outlining their commercial compliance oversight requirements for pharmaceutical manufacturers. Multiple states have incorporated these requirements into their state transparency reporting requirements. In addition, under the Patient Protection and Affordable Care Act (PPACA), the federal government is instituting aggregate spend and transparency reporting requirements.

Start-up and emerging pharmaceutical manufacturers have embraced the virtual model as an efficient and cost-effective way to develop and commercialize products, focusing on product development and leveraging various service providers to support commercialization through sales and marketing, logistics, reimbursement, and back office support. Various best-of-breed vendors have worked collaboratively over the past five years to successfully integrate services into a seamless model. This provides value to the manufacturer, as they know that the model has been fine-tuned over time and that service providers can develop a clear and specific timeline of activities, integrate their services, and provide excellence in service delivery with contractual relationships, customer service, and operational support, while also ensuring that the manufacturers maintain a high level of compliance with government requirements.

About the Authors

Chris Cobourn is senior VP of Commercial Compliance, Compliance Implementation Services. Cobourn works closely with pharmaceutical manufacturers in areas related to government programs management, including policy review, methodology development, policy documentation, and systems implementation.

Dean Erhardt is principal of strategic distribution and product support initiatives for D2 Pharma Consulting. Dean offers more than 20 years of strategic marketing and management experience with expertise in development of pharmaceutical support programs, pharmaceutical and consumer product distribution, and specialty pharmaceutical product management.

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[1] Survey Details: *Q4 2011 figure is an estimate based on previous quarters.

[Q1 n=2,402]
[Q2 n=2,614]
[Q3 n=3,021]
[Q4*n=3,200]

800,000 SURVEYS

4,800 QUESTIONS

6,400 SAMPLES OF MARKETING

4 MILLION DATA POINTS

5 AWARENESS LEVELS

6 OUTSOURCING DRIVERS

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How To Maximize Returns And Minimize Damage When Closing A Manufacturing Plant

By Karl Schmieder, contributing editor

In the past 18 months, a number of large pharma companies have announced downsizings and plant closings. Behind the headlines stand billions of dollars in real estate, and laboratory, manufacturing, and packaging equipment that had to be decommissioned, redeployed, or sold. The manager tasked with closing a facility faces a daunting task: Maximize the value of assets and minimize potential risks while juggling hundreds of details and minding a clock that is ticking nonstop toward a deadline.

Closing a facility is typically a once-a-career event. To give you a high-level overview of the process, we developed this guide.

BE PROACTIVE

A plant closing is often a race to the finish. As soon as it is announced, you will need to do three things: Form a closing team, develop a plan and budget, and inventory the facility.

Your team will typically include the staff members most familiar with the facility and its contents: security, environmental, facilities, and plant maintenance managers. It also can include an accounting and property team. In some cases, you'll want to hire external resources to help you inventory your plant, appraise your equipment, and sell, liquidate, or move it from one place to another. In total, your logistics team will involve six or seven different groups of people. The team should have a clear communications plan and regular meetings.

At the same time, you'll need to put together a budget for the removal or disposal of assets and their marketing and a plan that answers the following: Are you shutting down the facility completely? Do you have assets you can redeploy in other plants? Do you plan to sell your assets and leave the facility move-in ready? And, perhaps most importantly, when must you vacate the facility?

"Don't be the victim of a short timeline," says Matt Smith, a VP at EquipNet, a provider of asset management services and solutions. "When closing a facility, most people tend to focus on the people, the transfer of operations, and the real estate. They leave equipment and logistics for the last minute. They forget that they'll have to host potential buyers and manage removal. A short timeline is the number-one mistake you can make when shutting down a facility."

An anonymous source who recently shut down a 20,000-square-foot wet lab added, "To be successful, it may take four to six months to get organized, inventory, decontaminate, and sell your equipment. Moving the equipment and clearing the facility may take as little as two weeks."

HOW LONG DO YOU NEED TO CLOSE YOUR FACILITY?

A 1-million-square-foot processing plant can be successfully closed in 6 to 12 months if you have the right buyer or buyers in place. A laboratory requires a minimum of three to six months, especially if you can redeploy assets.

Timelines can be impacted by your building's rules and local regulations. For example, your building may have strict policies around when you can move and use the elevators or loading docks. Your community may have environmental regulations that govern how you dispose of consumables, scrap materials, or equipment, and permits may be required for construction activities. Check locally.

If you absolutely must, you can shut down a plant in 30 to 60 days, but if you do, don't expect to receive the maximum value for your assets. Regardless, plan on keeping the coffee pots full.

KNOW WHAT YOU OWN

The second biggest mistake a company can make when shuttering a facility is not understanding the plant's content, what it's worth, and how to maximize price. A small laboratory can contain balances and scales, centrifuges, refrigerators and freezers, mass spectrometers, and hundreds of small pieces of equipment. A large facility can include bioreactors, blenders, granulators, packaging equipment, scrubbers, and dozens of other large pieces of equipment.

"Unfortunately, many companies don't

inventory their facilities on a regular basis," says Randy Small, VP of operations, North America, GoIndustry DoveBid, a provider of asset management services. "Companies that regularly conduct a physical inventory every three to five years will know where they've deployed 85% to 95% of their assets. They will have the documentation that shows when the equipment was last validated or calibrated."

Once your inventory is complete, you'll need to figure out what it is worth. You can add hundreds of thousands and even millions of dollars to your bottom line by selling the equipment. But, not all equipment is created equal. Commodity items such as benchtop equipment and labware are low risk and easy to sell. As equipment goes up in value, it becomes a bigger risk, and buyers will insist on a thorough due diligence process. This will be the case for items such as a high-performance liquid chromatography unit, a mass spectrometer, or any type of processing or manufacturing equipment.

"There is no Blue Book for used equipment, and most people don't understand the value of what they own. That makes it difficult to value used process and packaging equipment," says Matt Hicks, COO, Federal Equipment, a supplier of used process and packaging equipment. "Online marketplaces that try to empower sellers and help them succeed in maximizing the value of their assets are often confusing. For this reason, it is important to work with someone who understands the value of equipment and can help determine the ways to get the best returns."

Hicks continues, "On the other hand, online marketplaces for laboratory equipment can be very effective because many systems are used interchangeably throughout pharmaceutical facilities, and there is a steady demand for laboratory equipment."

The best place to get the highest dollar for equipment is on the secondary market. Auctioning your equipment will get you less because dealers will buy high-value items in auctions at prices that are a fraction of what the equipment is worth. If you're in a liquidation or demolition scenario, disposing of your equipment may end up costing you money.

Unfortunately, by the time you get around to closing the facility, most plants are running on a skeleton crew. For this reason, many companies hire an outside firm to inventory the equipment, appraise its value, help find the most appropriate sales channels, and move the equipment out. Even a desk appraisal can be a very valuable piece of information. If you do go the outsourced route, you will want a vendor that will provide project management, communicate regularly throughout the process, and take you all the way to the end. Our anonymous source continues, "Effective communications between teams is essential. Make sure everyone has the same inventory lists and facility maps. Cross reference and index those on a daily basis. Meet with your team every shift so everyone understands what is going out the door, when it will be picked up, and who will be picking it up."

AVOID CARELESS REDEPLOYMENT

When you've been asked to close a facility, the idea of redeploying equipment may seem like a good one. The equipment has been in your facility, your team has maintained and validated it, and moving the equipment from one facility to another can save you the hassle of finding a buyer. To do so correctly, you need to give yourself and your company sufficient time to take advantage of redeployment. In most cases, that requires 60 to 90 days of internal marketing.

On the downside, redeploying assets means you will incur the cost of crating and shipping the equipment. For example, crating a high-performance liquid chromatography or nuclear magnetic resonance unit can cost between $5,000 and $15,000. Removing equipment that has been engineered into a plant can easily run into the six figures.

According to GoIndustry DoveBid's Small, "We recommend that equipment already be on a requisition list 90 days before it is redeployed and suggest coming up with criteria for redeployment. That way you don't have divisions jostling for assets because they are suddenly available."

MINIMIZE DEVASTATING ERRORS

Imagine you've closed down your facility, leaving it "broom swept," and ready for the next occupants. You move on to your next job. A few months go by, then a major news program runs an investigative report about children recycling e-waste in India. Items featured in that story are labeled with your company's name. Welcome to a public relations nightmare that could have been avoided.

Companies often run afoul of Hazardous Materials Regulations when employees unfamiliar with these regulations start selling equipment or start transporting materials from one facility to another. Your facility closing plan must include a process for decontamination and decommissioning to prevent devastating errors. The plan must include validation and documentation that shows the equipment and facilities have been decontaminated according to local and federal guidelines. That information needs to accompany the equipment and remain on file.

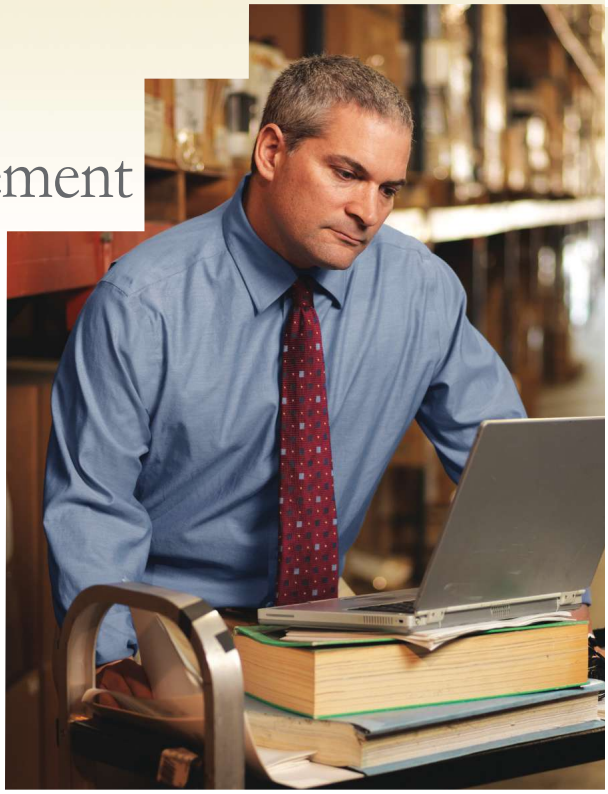
"Decommissioning and decontaminating laboratory equipment involves conforming to all regulatory requirements," says EquipNet's Smith. "You want a robust audit trail to prove you've been compliant when it comes to decontamination and you've disposed of items in an environmentally responsible way. If you don't, you could face prosecution or substantial fines." In addition, you'll need to include the proper disclaimers to avoid exposure to lawsuits if the equipment buyer suffers an injury while using machines you have sold.

MAXIMIZE RETURNS

The used equipment industry is booming, and market pricing is strong. Laboratory and analytical equipment, in particular, is one of the fastest-growing categories of preowned equipment. There has been an increase in B2B asset purchases with the largest pharma companies buying each other's assets. One reason is they know the equipment comes certified and validated. If you're a start-up, buying preowned equipment may make it easier to reach profitability faster.

Save Time, Money, And Improve Supply Chain Management With E-Procurement

By Karl Schmieder, contributing editor



If your staff is using a manual, paper-based procurement system, they probably search through stacks of catalogs and visit multiple websites for the products they need. They likely fill out paper requisition forms, submit requests for approvals, and wait for procurement to process their order. The entire ordering process can require countless people and drag on for weeks.

In the age of e-commerce websites like Amazon.com and Zappos.com, we've gotten used to features like shopping carts, favorites, recommendations, one-click ordering, and overnight shipping. As a result, using a traditional process to order critical supplies is not only less than satisfying, it slows down the discovery process and wastes valuable dollars. In addition, traditional ordering processes give your procurement staff no insight into supply chain weaknesses — you might have surplus inventory or be overpaying preferred vendors without even knowing it.

E-procurement strategies and solutions can accelerate the purchasing process, eliminate supply chain issues, and help you and your employees spend more time creating value for your company.

WHAT IS E-PROCUREMENT?

At its most basic, e-procurement allows buyers and sellers to connect electronically via the Internet and information networking systems such as electronic data interchange (EDI). E-procurement systems are available on-demand or as Software as a Service (SaaS) and can be used in every stage of the buying process, allowing you to direct spending via purchase orders to preferred suppliers, manage catalogs from multiple vendors, and contract prices quickly and accurately with a seamless user experience.

Features of e-procurement systems can include purchase orders, purchase order template management for easy reordering, purchase order confirmations with tracking links, advanced ship notices, and comprehensive order management, along with user access across your company.

BENEFITS OF E-PROCUREMENT CAN BE SIGNIFICANT

For research-intensive companies, there are strategic, opportunity, and operational benefits associated with using an e-procurement solution. Strategically, e-procurement can help consolidate purchasing practices that lead to greater discounts and better service from suppliers, accelerate the flow of important information, and reduce the administrative time necessary for ordering. From an opportunity point of view, e-procurement can help enhance and improve important corporate-to-corporate relationships, improve buyer/seller relationships, and increase the accuracy of orders because orders are less likely to be delayed or the wrong goods delivered because there are fewer transaction errors.

Operationally, e-procurement can improve financial controls, making it easier to match orders, eliminate paperwork that results in greater savings, improve auditing and better security by enabling staff and auditors to more easily verify and track orders. It also can reduce inventory levels and the costs associated with inventory, shorten delivery times by cutting the time associated with waiting for documents in the mail, and eliminate time zone obstacles since e-procurement is 24/7.

"We realized we needed a system that would be more compliant when industry regulations changed," said Vicki Blankenship, manager, procurement services, e-procurement, Allergan. "Previously, we'd used a keycard or purchasing card system that wasn't sufficient to meet new industry standards and exposed the company to risk. With an e-procurement system, we were able to meet the compliance standards, and we sent a message to suppliers and partners that we were looking to take some of the risk out of procurement."

PROCUREMENT VS. THE ENTERPRISE

Procurement is a largely data-driven function, and the procurement staff benefits from real-time visibility into where dollars

are being spent and what supplies are being ordered from which vendors. If procurement is being handled retroactively or on-the-fly, it can be difficult to forecast future spending.

Researchers, on the other hand, prefer to order supplies from their own chosen vendors. They seek systems that are easy to learn and easy to use. In some e-procurement systems, for example, researchers can flag products as favorites, which facilitates reordering, or draw out the chemical structure of a compound instead of having to type its long name.

To help procurement and research staffs meet their individual goals, an organization about to deploy an e-procurement system would do well to introduce the solution gradually, starting perhaps with a meeting between key researchers and procurement staff. "Show researchers that the system being proposed works the way they already work. Let them adopt the tool, embrace it, then advocate it to their peers," said Max Leisten, market director, SciQuest. "That way, you don't risk alienating anyone and can accelerate adoption because once the word gets out, other researchers will want to use the system because it gets them back to the bench faster."

At Allergan, the company first deployed its e-procurement solution at its Irvine, CA, headquarters, initially with the information systems (IS) staff. Corporate managers were introduced to the system next, followed by commercial operations, research and development, and finally manufacturing. Then, the company introduced the solution globally across its 40 commercial locations, 4 research and development facilities, and 6 manufacturing plants.

Today, when an Allergan staffer orders, their shopping cart is converted into a requisition that is routed through the company's existing SAP supplier relationship management (SRM) system. That system hosts more than 40 catalogs across a broad range of categories including information technology, office supplies, lab materials, and other areas.

CHANGE IS THE ONLY CONSTANT

When deploying an e-procurement system, it is essential that staff throughout your organization understand the benefits of moving from their old method of ordering, whether paper- or purchasing card-based, to the new solution that requires purchase orders and up-front approvals. In general, individuals focus on what affects them directly and need to be told how the company will benefit once the e-procurement solution is deployed. Helping staff understand the new system and its benefits to the company and to them individually, in terms of decreasing ordering times, will go a long way to accelerate adoption.

WHAT GETS MEASURED GETS MANAGED

Cost-saving with an e-procurement system comes not only from ordering from preferred vendors but also from increased spend visibility. Insight into spending can be very powerful when it comes to negotiating or renegotiating terms and conditions with suppliers.

According to Blankenship, during an eight-month period in 2010, Allergan saved approximately $2 million by directing its spending through its e-procurement system. "Integrating all suppliers into an e-procurement solution allows us to manage our suppliers more strategically, reduce our reliance on vendor-managed inventory, and meet corporate compliance goals," said Blankenship. "In addition, the solution allows Allergan to be more proactive about its indirect spending, and our staff can make smarter buying decisions."

SciQuest's Leisten adds, "Sadly, most procurement people have no idea what is being purchased across the enterprise. Many times, they rely on their suppliers to give them information retroactively. Without a clear picture of spending, they can't negotiate discounts for their organizations."

Research-intensive companies that streamline their purchasing processes across the enterprise often realize savings in areas outside of research and development spending, including, for example, in administrative, clerical, and even executive management. Administrative time required for purchasing can be significant, but e-procurement accelerates purchasing and decreases time spent on purchasing tasks, which in turn increases the time employees spend creating value for the company. A better understanding of procurement can lead to an understanding of weaknesses and areas for improving efficiencies in supply chain management.

BEYOND PROCUREMENT: IMPROVING SUPPLY CHAINS AND MITIGATING RISK

Over the past two years, supply chains have been disrupted by natural disasters, product contamination in regulated industries, political instability, the continued threat of terrorism, and social unrest in certain countries as a result of economic uncertainty and a loss of jobs. The potential for major supplier failures across many industries has become a real possibility.

Structurally, supply chains are changing, and strategies must be able to flex in the face of weaknesses, uncertainty, and increased risk. Supply chains that once focused on supporting product movement from a lowest-cost manufacturing location to regional distribution hubs based on product availability are giving way to strategies designed with the customer and demand in mind. These innovative strategies synchronize supply-to-demand activities using business processes, technology, and geographic footprints.

Companies that examine their supply chains may find ways to balance risks while increasing efficiencies. To determine the optimal supply-to-demand strategy requires evaluating suppliers, costs, product life cycle, forecast accuracy, logistics, and customer requirements. A high degree of collaboration and an understanding of technology tools will help drive these efforts forward. To create the most cost-efficient and risk-balanced supply chain requires redoubling efforts, collaboration, and hands-on, tech-savvy management.

Sponsor And CRO Relationships: Time To Grow Up?

By Graham Bunn

Traditionally, the biopharmaceutical industry has relied heavily on outsourcing R&D trial tasks to CROs that help manage clinical trials. Large pharmaceutical companies tend to use CROs for overflow study volume or large, global trials. Small and medium pharmaceutical/biotechnology organizations typically outsource complete R&D functions they cannot or wish not to develop in-house.

Current data shows this outsourcing trend is only set to continue, and a steady rise in future outsourcing is predicted. It is vital that pharmaceutical companies of all sizes get this process right to remain competitive and drive toward more efficient yet higher quality operations.

TACTICAL ENGAGEMENT

To date, a large volume of studies outsourced by the industry have been tactical engagements in which a sponsor outsources either individual tasks or perhaps the entire management of a single clinical trial. A biopharmaceutical study team, assisted by their outsourcing group, will issue a study-specific RFP, receive responses from a variety of (or list of preferred) CROs, and assess each response based on the CRO's ability to deliver on their requirements. The emphasis is for the sponsor to hold each service provider to metrics around individual study delivery — typically timeliness, cost, and quality. It is not that different from a teacher giving a child a homework assignment and then grading it (paying, in the CRO's case) according to the results. For their part, service providers measure their own success by their ability to profitably meet the sponsors' delivery criteria. In tactical engagements, the CRO is generally allowed to choose how they work to ensure they do not have a process or technology excuse for failing to deliver. In working with a variety of CROs in this model, sponsors must continually adapt to the CROs' different work processes, SOPs, and technologies. This results in an inefficient way for the sponsor and associated site staff to work, and change is clearly needed.

SPONSORS GO STRATEGIC

Sponsors have moved more toward strategic outsourcing to solve the inefficiencies in tactical CRO outsourcing that are particularly obvious in selection, contracting, process and technology change, reporting, and data delivery. Recent examples of strategic outsourcing relationships include GSK with PAREXEL and PPD, BMS with PAREXEL and Icon, and Sanofi with Covance. Typically, CROs selected as strategic partners are awarded a two-to-five-year contract. This eliminates the need for multiple rounds of RFPs, vendor selection, and contract negotiation. Moreover, the outsourcing organizations work according to the sponsors' SOPs, rather than dictating their own, following agreed-upon standards and formats for reporting and data delivery. The sponsor benefits from a reduction in the overhead associated with contracting with multiple outsourcers as well as a more efficient approach to reporting and data management. Moreover, the CROs are usually able to offer lower rates given the longer-term guarantee of a volume of business.

Another benefit of this model to sponsors is that they can take typical tactical outsourcing performance metrics — timeliness, quality, and cost — and add metrics associated with multiple studies. For example, the service partner is expected to drive long-term increases in efficiency, time, and/or quality over the duration of the contract — such as a 10% reduction in study costs along with a 15% improvement in quality and 5% reduction in study timelines over the duration of a three-year contract. From this perspective, strategic outsourcing is a win-win for both pharmaceutical company and CRO. In the classroom analogy, the sponsor is now giving the outsourcer more autonomy, akin to a high school teacher assigning their pupil many pieces of homework with the confidence that the work will be completed to a high quality and standard. The teacher also has the expectation that the ambitious pupil's work over time will get even better as the pupil prepares to depart for a university or the outside world and needs to learn to work more independently.

LOST OPPORTUNITY

Despite all of the benefits, the current trend towards more strategic outsourc-

ing represents a huge missed opportunity to change the way the industry works with CROs. Moving to two to three preferred partners is a tiny first step in outsourcing maturity that only simplifies the process and gains some efficiency over time through increased elements of trust. To achieve much greater efficiencies, there is a need to adopt a more university research-centric approach. In that environment, it is common for professors and research students to openly collaborate on the same topic. While the professor's name may well be the one that ends up on the published scientific paper, there is knowledge that the research students often contribute as much, if not more, to the original work through a cooperative, creative environment.

For this approach to work in an outsourced clinical trial environment, it is necessary to standardize both the outsourcing and clinical trial process. That requires a framework of shared technology and a process of technology and outsourcing governance. In the past, clinical trials technology was largely client/server-based, and both sponsors and CROs preferred to keep the infrastructure (and access to it) behind firewalls. The beginning of the century brought change when Web-based Software-as-a-Service (SaaS) solutions for electronic data capture (EDC) started becoming popular. Suddenly, sponsor, CRO, and site could easily share access to the same application, see the same data, run the same reports, and work as a team to ensure optimal trial conduct. If problems were identified, such as slow recruitment or monitoring bottlenecks, the sponsor, outsourcer, and if necessary, the site could meet and discuss the issues and agree to the best solution to the problem, all armed with the same information.

The industry has rapidly caught on to the benefits of SaaS technology, and many SaaS-based solutions are now available. They exist not only to support data gathering through EDC but for a range of clinical activities including protocol design, document management, clinical trial management, trial master file, site budgeting and contracting, randomization and trial supply management, and patient reported outcome (ePRO). Each individual SaaS solution brings advantages to site, CRO, and sponsor, but through the rapidly maturing portfolio, it is now possible to conduct an entire clinical trial using only SaaS technologies — from protocol design and creation, study budgeting, and contract negotiation to study conduct, document management, and finally, data analysis and submission.

While the focus to date has been on the advantages of individual applications — typically faster deployment and productivity, streamlined use and management, increased flexibility and scalability, and better reliability and performance — little has been made of the fact that SaaS applications provide a secure mechanism for multiple organizations around the world to share access to common data and information. This offers tremendous potential within the strategic global outsourcing business if a few guidelines are followed:

Do care about technology choice. Traditionally, the pharmaceutical industry has left technology choice to its outsourcing organizations. Whether tactical or strategic, if each of the outsourcing organizations is using different technologies, opportunities for efficiency gains will be missed. For best results, the pharmaceutical organization should standardize on SaaS applications that best support their outsourced activities.

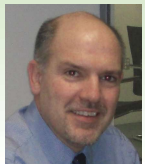
Do not think it is just about technology. Technology choice needs to be supported by a SaaS outsourcing deployment framework (governance) before deploying to multiple CROs. Using a common technology is no guarantee of common processes, standards, or workflow. Thinking about global library standards, common elements of look and feel, workflow processes, and data standards can impact the efficiencies of those using the application — sites, clinical monitors, data managers, and statisticians, as well as managers reporting on progress.

Do think about an integrated approach to clinical trials. Do not look at the individual SaaS technologies as point solutions. Significant efficiency and quality gains are available by taking a holistic approach to integrating solutions and processes across different technology suppliers or by integrating SaaS technologies with key in-house solutions. Standard integrations using open Clinical Data Interchange Standards Consortium (CDISC) and Web services standards are essential. Once data is entered in SaaS technology, it should not need to be reentered in another system.

Do not use the SaaS tools to micromanage. Use the tools to work together and create increased bandwidth to deliver high-quality, faster, and safer clinical trials. All organizations need to fail if any one organization fails to encourage this process, so joint risk-sharing is an important element in outsourcing strategy.

Do think outside of the box when deploying SaaS solutions rather than following the pack. In tactical outsourcing, the sponsor will design the protocol, the CRO will negotiate the site budgets, control the site contracts, build the electronic client report form (eCRF), etc. SaaS solutions enable workflow within a task across different and remote people and organizations. This mix of workflow and expertise across organizations can dramatically help to reduce study costs, avoid high dropout rates/nonevaluable patients, increase patient safety, and hence improve the opportunities for a rapid and successful final study submission.

About the Author



Graham Bunn, Ph.D., is the VP of partnerships & alliances at Medidata. He has more than 20 years of experience in the pharmaceutical industry, coordinating and managing relationships with various CRO and systems integrator partners in the sales and delivery of Medidata products and services.

A Global View Of Bio Process And Product Quality

USP meeting advances standards for new biotech and biosimilar drugs.

By Wayne Koberstein, contributing editor

First was the word: Quality. Aside from the conference title — the U.S. Pharmacopeia (USP) Science and Standards Symposium on Biologics & Biotechnology — "quality" was ubiquitous as a theme or term in almost all sessions, whether alone as an ideal goal or together with other terms such as control, monitor, and release. Quality was the key to unlocking the larger meaning of a highly technical program. Second, the people: a diverse, international crowd of mostly scientists and engineers from companies large and small, all united behind the goal of maximizing quality in bioprocessing. Third, the agenda, which addressed in minute detail the technical standards and procedures that underlie strategically important and often controversial issues for the life sciences industry. All three elements made for a fascinating, if at times baffingly arcane, conference over four days in Seattle (Oct. 3-6).

Research, development, commercialization, regulation, and reimbursement are some of the broad areas affected by quality standards for biologics and biotechnology. At the same time, biotechs and biologics cover a wide range of technologies, products, and disease areas that vastly complicate everything from the measurement and control to the setting of quality standards.

The USP has helped lead the setting of standards for natural and small-molecule drugs going back to the 1820s. Now, it is trying to seize the initiative on a global level with "bio" therapies, diagnostics, and assays.

The Seattle meeting was just one example of the USP's global outreach. Convergence of standards is by no means complete, and to an observer it seems that among all parties there is too much redundancy of effort with too little harmony in return. But, the various pharmacopeia and related bodies appeared headed in the right direction in an international session, where the USP's CEO Roger Williams was careful to characterize his group's influence as "collaborative."

Truly, what may appear as redundant efforts by national/regional groups could well be mainly organization building — and perhaps a bit of healthy competition for scientific leadership. But, the conference crowd was obviously focused on building something bigger than any one group could do on its own.

It would be impossible to communicate even one percent of the seminar's technical content in this article because of the highly specialized structure of the related science and technology. Not just layperson trade journalists, but scientists and engineers were challenged by the unique and insular jargon of each other's deep-welled disciplines.

One of the speakers summed it up this way: "I spend every day in my lab speaking a special language with my immediate colleagues. But, if I go to another department — or to a different session in this conference — it is like going to a foreign country. Every area and sub-area of bioprocessing and quality control has its own lingo and knowledge base." Yet, he added, there is also a larger community of interest that unites all the discrete disciplines behind the larger purpose of quality in process and product.

OPENING PATH

Significantly, the first morning session featured a speech by the FDA's Steve Kozlowski, director, Office of Biotechnology Products, on the new regulatory pathway for "biosimilar or interchangeable" products. It was a tacit recognition that the growing demand for biosimilars supplies much of the drive toward new biotech and biologics standards.

The Biologics Price Competition and Innovation Act (BPCI Act) of 2010 included

proteins as "biological products" for the first time and defined a biosimilar as "highly similar" to an FDA-licensed biological product (the reference product), rather than identical. The FDA may depend largely on "analytical studies" rather than new preclinical/clinical data to approve a biosimilar according to the new legal criteria: "no clinically meaningful differences in safety, purity, and potency." Presumably, with no evidence to the contrary, the product will then be "interchangeable" with the original, expected to produce the same result in "any given patient" at no higher risk if substituted.

Biosimilars must employ the same mechanism of action, conditions of use, administration route, dosage form and strength, and manufacturing quality of the original. Future discussion will undoubtedly address thorny questions such as, "What sort of data will satisfy the 'any given patient' criterion?"

The assay transition session panel at the USP meeting (L-R): Rajesh Gupta, FDA; Peter Brugger, Novartis; Jill Crouse-Zeineddini, Amgen; Mehrshid Alai-Safar, Baxter; Timothy Schofield, GSK and USP Statistics Expert Committee.

Kozlowski illustrated the complexity of biotech/biologics standardization with a slide showing a molecular diagram of a monoclonal antibody dwarfing a tiny group of atoms representing aspirin. His next slide diagrammed a protein molecule displaying many of the "attributes and combinatorics" that later sessions would discuss: deamidation, methionine oxidation, glycation, high mannose fucosylation, sialylation, and so on. Each term represents almost endless permutations adding to the complex challenge of characterizing large biomolecules and comparing one to another. The complexity is too great for the simple chemical equivalency tests used with generic small molecule drugs. Just as clinical trials may carry surrogate endpoints, testing and validation of biotech and biologic agents must rely on indirect measures from bioassays and statistical analysis.

As numerous companies shared their experiences, it became apparent that originators must use the same methods in their own bioprocesses. That may explain why they would reveal so much to the larger community — to constantly improve their methods using new science and technology that is only available outside a company's closed system.

Reference standards — product-specific information sets and physical samples — will underlie the analytical studies for biosimilars, relying on suites of bioassays now being revised and augmented. As with small molecule agents, the USP issues broad guidelines called chapters for use of the assays that assess and compare biotech/biologic molecules. Subchapters break down the guidelines and procedures for particular classes such as monoclonals and vaccines. Monographs then characterize the constituents, structures, and other identifying attributes of specific products. Some monographs may refer to general chapters with enforceable guidelines. Monographs also describe product uses, both on and off-label, based on practical experience and literature support. Insurers commonly use the monographs to determine what uses are reimbursable.

CONVERGENT TRACKS

After the opening session, the seminar split into two tracks. Track one began with a review of new USP bioassay chapters now being implemented after years of public feedback and work by a large expert committee. After a final vote by the committee, the chapters will be published in Supplement 1 of USP 35, May 2012, and will become official on Aug. 1, 2012, with another review and update scheduled after two years. Robert Singer, chair of the USP Statistics Expert Committee, and Susan Kirshner of the FDA's therapeutic proteins division discussed the chapters as a new central resource for bioassay analysts and regulators.

For traditional biologics, such as naturally derived hormones, the standard criteria for quality was safety, purity, and potency. Originators could thus make incremental changes in the manufacturing process without new clinical studies. The new chapters reflect the additional criterion for biosimilars in the BPCI Act: interchangeability with the originals based on their effects on individual patients. If interchangeability is to be assessed with nonclinical data, the targeted critical quality attributes (CQAs) and the assays and analyses that measure them must be extremely accurate.

Track two, with the informal tag "Quality by Design" (QbD), logically built upon Track one; it envisioned new production models to measure and control CQAs, using tests and testing procedures at multiple stations along the process flow. Such models, used widely in other industries, could boost output quality, and thus efficiency, in state-of-the-art bioprocessing. Track Two was rich in the details of manufacturers' experiences with applying analytic techniques to entire processing systems.

But, practical lessons and management principles also emerged from the deep technical recesses of the separate but convergent tracks. Simon Szeto of Amgen was especially adept at qualifying his advice on EPO (Erythropoietin) reference standards with comments that accounted for the disparate resources of small and large companies.

In a later conversation, Szeto placed his thoughts in a higher context: "When regulators come to inspect our operations, a primary concern for them is the level of commitment they see in the QA/QC managers. We must show in large and small ways that we passionately believe in quality and take every means possible to ensure it at every step of the process." Those words reflected all the core aims of the USP seminar: quality, collaboration between people, and integrity in setting high standards for the future fruits of the life sciences industry.

China's Pharmacovigilance System: The Hunger For Safety Insights

By Sara Gambrill, contributing editor

China's importance as a pharmaceutical market is well-known. It has the world's largest population of more than 1.3 billion and edged out Japan last year to become the world's second-largest economy as well as Asia's largest. In 2009, IMS Health ranked China as the world's fifth-largest pharmaceutical market, with a market size of about $31.7 billion, and expects it to be ranked the second-largest pharmaceutical market by 2015, usurping Japan's ranking.

Driving the growth of China's pharmaceutical market, in part, is the government's $125-billion healthcare reform initiative, which has resulted in 90% of China's population being covered by health insurance as well as better access to healthcare services and affordable drugs by the country's rural population. In addition, a growing middle class with exposure to Western habits, such as fast food, driving, and smoking, have contributed to an increasing incidence of obesity, various cancers, and diabetes in China.

With nearly 1/5 of the world's population, China's potential contribution to global medical safety is gigantic. Johnson & Johnson — through its pharmaceuticals division, Janssen — is working with regional and national health authorities in China to help support strong pharmacovigilance in China and globally.

"China has a tremendously proactive, forward-looking desire to offer the best safety science. When an opportunity comes to apply a new technique or a new scientific methodology, I've seen openness and an excitement about what this knowledge could do for patients. This is the dynamic I have observed in our interactions with the Chinese health authorities," said Amrit Ray, M.D., MBA, chief safety officer at Janssen.

CHINA'S DRUG SAFETY SURVEILLANCE PROGRAM

China has a relatively short history of drug safety surveillance — compared with the United States, many European countries, and Japan — but, just as its economy is growing at a rapid clip, so, too, is its system for watching over drug safety. The core of China's rapidly developing drug safety surveillance program is its National Center for Adverse Drug Reaction (ADR) Monitoring.

Originally a project initiated with support from China's Ministry of Health in 1988, the National Center was formally established the following year. Ten years after its initiation, the National Center joined the World Health Organization's Collaborating Center for International Drug Monitoring (Uppsala Monitoring Centre). In 1999, the center joined China's competent authority for drug regulation, the State Food and Drug Administration (SFDA), reporting both to it and to the Ministry of Health. The National Center for ADR Monitoring has five divisions and a network of 32 provincial centers for ADR monitoring. These provincial centers are affiliated with local SFDA offices in various provinces, autonomous regions, and municipal governments.

Pharmaceutical companies, hospitals, pharmacies, and drug distributors report ADRs and adverse drug events (ADEs) to regional centers, which then report all new and all serious ADRs and ADEs to the National Center within three days. Other ADR/ADE reports can be sent quarterly. Individuals can file reports with either the regional or National Center. In the National Center's first 11 years, it received only 4,700 reports. But, in 2002 alone, the

number of reports was nearly triple that, and, in 2005, the number of reports grew another tenfold to 173,000. In 2010, the National Center for ADR Monitoring received 692,904 reports of adverse reaction cases, 8.4% more than in the year before, according to SFDA. Of these, 109,991 were reports of new or severe adverse reactions, an increase of 16.2% over 2009. Most ADR cases, 84.7%, were reported by medical institutions; 12.7% were reported by pharma companies; and 2.5% were reported by individuals.

TRAINING FORUM ON INTERNATIONAL PHARMACOVIGILANCE STANDARDS AND PRACTICES

Though the surge in the number of ADR/ADE reports indicate an increased awareness of and participation in reporting, the Chinese health authorities continue to strive to improve pharmacovigilance in the country. For this reason, Janssen has collaborated closely with the Chinese health authorities to develop the "Training Forum on International Pharmacovigilance Standards and Practices," a training workshop held in China every year for the past five years, during which Janssen shares its best practices in pharmacovigilance with Chinese health authorities.

"There's a hunger not only for information on safety but also to go from information to insight. This is what effective safety and pharmacovigilance is all about, making the jump from noise and a plethora of information to insight and meaning that enable effective communication and risk management," said Ray. "We've spent a lot of our time and energy on developing best practices in pharmacovigilance to move patient safety forward globally, including in China. Proactive pharmacovigilance discriminates between noise and signal with a methodology, a process, and an appropriate application of information technology."

One of the recent initiatives that SFDA's office in Beijing has undertaken is an intensive safety monitoring program. The Beijing office of the SFDA has developed a close collaboration with a number of Beijing hospitals, establishing pharmacovigilance centers with trained and certified safety specialists who monitor, collate and report safety data. Collectively, more than 2 million patients are seen at these hospitals every year. With these safety specialists, and associated systems and processes, hospitals can closely monitor adverse events to allow for the early detection of potential safety signals, actively manage high risk medicines, and generate hospital safety surveillance reports submitted on a regular basis to the Beijing office of the SFDA as an integral part of their safety surveillance activities.

This year's workshop in October offered a two-day training session for approximately 200 government and hospital attendees who participated. Also in attendance were safety leaders in China, including representatives from the Beijing office of the SFDA, SFDA's main office, and the National Center for Adverse Drug Reaction Monitoring. Fifteen Janssen colleagues from local and global pharmacovigilance departments also attended.

"In the past several years, Janssen has made significant contributions to China's pharmacovigilance enterprise, supporting safety education and pharmacovigilance knowledge sharing," said Dr. Xiaoxi Du, director, National Center for ADR Monitoring.

The agenda for the workshop is shaped through dialogue between Janssen and the health authorities in China. Both parties work to develop a training that encompasses what will be helpful to Chinese health authorities and also reflects the trends Janssen sees in pharmacovigilance globally. Janssen shared best practices on how a biopharmaceutical company sets up and runs a global pharmacovigilance system, how it codes and categorizes all the data that come from adverse events, the techniques and methodologies it uses to review those events in the process of signal detection, and how it conducts proactive surveillance.

Members of Janssen's local and global pharmacovigilance teams

"The safety specialists are on the ground, near the patient," said Ray. "They need to know what to look for. When the information comes, they need to know how to categorize it, interpret it, and record it in a standardized way from one hospital to another hospital, or from one country to another, to enable cross-analysis. That's why we support international coding standards, which were the focus of this particular training program."

Janssen is well suited to the task of collaborating on a training

workshop for the health authorities in China because its global safety organization has safety officers at the local and national levels in China, as well as the Asia-Pacific regional and global levels, that afford the company insights for proactive pharmacovigilance. The company has a relatively long history in China, as Janssen was the earliest joint-venture pharmaceutical company there — established in 1985 — and its safety officers have a good grasp of the issues and challenges on the ground. These on-the-ground officers worked closely with their Janssen colleagues globally to develop the workshop.

"What is interesting for global pharmaceutical companies is trying to get a perspective on whether there is a safety signal. You have to have an understanding of what are the characteristics in each area of the world and in each patient. You have to know your patient, which can be challenging at a distance, and that is why we are committed to a presence on the ground, with colleagues who speak the language of the patient," Ray said. "Other insights can come when you start looking globally and ask, how does the experience in China compare with the experience in a European country or in the United States and can we learn something for patients from the totality of the experience that we could not learn from partial experience from one country alone? The best science is aimed at trying to take as thoughtful and intelligent a perspective on safety surveillance as possible."

THE FUTURE OF GLOBAL SAFETY IS COLLABORATION

The training workshop exemplifies just one type of collaboration Janssen participates in with China to help support enhanced pharmacovigilance. In addition, a number of Janssen safety scientists have authored academic papers in pharmacovigilance that have been published in the National Center for ADR Monitoring's academic journal, called the *Chinese Journal of Pharmacovigilance*. "This is something we've made a conscious decision to do because we would like our best thinking to be openly available," Ray said. Janssen safety representatives also gave the keynote address at the 2011 Annual China Drug Safety and Public Policy Summit in Shanghai.

> "China has a tremendously proactive, forward-looking desire to offer the best safety science."
>
> Amrit Ray, M.D., M.B.A., chief safety officer, Janssen Pharmaceuticals

China's proliferation of new conferences a few years ago, covering topics related to the biopharmaceutical industry, exemplifies the country's collaborative spirit. These conferences meet annually now and attract key opinion leaders within China from Big Pharma, representatives from the Chinese health authorities, as well as key opinion leaders from the West, both as attendees and presenters. The conferences demonstrate China's great willingness to exchange ideas and information about the industry.

In 2011, an important milestone in global safety involved China's collaboration. The National Center of ADR Monitoring at SFDA and Uppsala Monitoring Centre signed an agreement to enhance data exchange from China's ADR database and Vigibase, WHO's global database of more than 6 million ADR reports. The two-year project is called "Standardization Study and Applications of Adverse Drug Reaction Monitoring Cooperation Agreement." The project consists of various subprojects, including establishment of a data exchange platform, Chinese-English translation standards, and improvement of the Drug Dictionary specifically for China.

"I think there are some very interesting changes that we're seeing in China. There is a recognition that safety is really about collaboration. The goal is to support strong, scientifically robust pharmacovigilance in China. It's ultimately the patient, both in China and globally, who will benefit. We recognize that we have a shared commitment with the health authorities in that we both serve patients," Ray said. "The future of safety is about collaboration, and we are committed to that. No one group can do it alone."

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Clinical development is now entering an era of virtualized research that has the potential to accelerate and bring new levels of cost-efficiency to the drug development and trial process. Health sciences organizations increasingly partner with and rely on a myriad of ad hoc partners from around the globe — spanning academic research centers, private research and development organizations, CROs, public sector agencies, and healthcare organizations — for R&D, as well as clinical trial operations.

Today, the challenge for many health sciences organizations is finding a way to efficiently manage these virtual environments, which are complex since they are increasingly characterized by:

- a sequential approach to processes and trials as well as compartmentalized stakeholders
- multiple systems/vendors with high integration overhead as integrations are being managed for each initiative/trial
- manual data integration from third-party sources
- a lack of traceability and control

A new generation of best practices and tools can help organizations seamlessly connect with partners and identify and capitalize on pre-existing synergies to realize the full potential of virtualization. These include:

Stick with the standards. An IT infrastructure that supports a virtualized environment must be able to handle the many diverse forms of data that will flow into it from internal as well as external sources. Health sciences organizations and their systems must be able to accept, normalize, and act on this data. As such, standards-based systems are essential. By leveraging external industry data standards, such as CDISC (Clinical Data Interchange Standards Consortium), ICH (International Conference on Harmonization), and HL7 (health level 7), health sciences organizations can greatly simplify the exchange of data between large numbers of diverse partners.

Respect privacy and security concerns. Organizations should ensure that the technology and services they utilize are both CFR Part 11 compliant and HIPAA-certified in order to respect privacy and data protection restrictions.

Identify appropriate data storage resources up front. In a virtualized environment, data volume increases exponentially. Organizations require a robust clinical data warehouse that can centrally aggregate all trial and third-party data for analysis.

Build it once, use it often. Virtualized clinical development environments offer the ability to leverage important data gleaned from an external source throughout the enterprise. An environment with multiple, "stove-piped" systems maintained for separate trials or individual integrations for separate initiatives limits this potential. It also adds unnecessary costs due to multiple and often duplicate integrations. By shifting to a unified, enterprise-wide approach to infrastructure and applications, organizations can facilitate transparency and increase insight, reduce IT management costs, and ease the integration burden as it is "once and done."

Focus on enabling seamless workflows across all key systems — eClinical, safety, clinical data warehousing, and operational planning, tracking, and management. Automated workflow between these core functions will bring new levels of operational efficiency and improve traceability and control. For example, automated workflow can enable seamless data capture, randomization, supplies management, and in-stream coding; streamline adverse events reporting and ongoing pharmacovigilance initiatives; and enable improved data flow. One-off integrations between technology providers can add additional complexity.

Help users direct their focus where it's needed and most productive. Understand there is a growing universe of system users, and ensure your systems are process- and people-centered, versus application focused. It's vital to minimize the complexity of today's clinical development technology to achieve meaningful efficiencies and streamline workflows across technologies, partners, and trials.

A virtualized clinical development environment offers exciting opportunities to advance discovery and contain costs. Organizations embarking on this exciting transformation first need to carefully consider their supporting IT infrastructure. Avoiding complexity by focusing on a standards-based, integrated, and enterprise-wide approach that aligns with organizational data structure and requirements is instrumental in unlocking the full potential of this new approach to clinical development.

Neil de Crescenzo

Neil de Crescenzo is the senior VP and general manager for Oracle Health Sciences, where he supports Oracle's business unit dedicated to producing integrated end-to-end solutions that help health sciences organizations deliver quality products.

Industry Leader

Electronic Signature Technology Saves Time, Reduces Overhead In IT Department

The number of paper contracts crossing the desk of AMAG Pharmaceuticals' IT director had gotten out of hand. The piles of vendor agreements, purchase orders, and other documents in Nathan McBride's inbox represented hours spent printing, completing, scanning, converting, and forwarding files that could be completed far more easily. Thus, McBride started investigating cloud-based contracts and electronic signature technology. By the time he was done, the company had implemented a Software-as-a-Service solution contributing to a 50% reduction in IT overhead without any staff reductions.

"My objective with cloud contracting was two-fold," said McBride. "I wanted to enforce it as the standard in my department and also push adoption to other areas of the company such as legal and finance (essentially the departments that generated many of the documents that my team had to sign). I believe the concept of the data center is archaic in today's companies. SaaS applications can 'consumerize' software, and that benefits everyone in the organization."

AMAG Pharmaceuticals' experience is not unique in its industry. Paper-based workflows introduce inefficiencies and flaws into firms that cannot afford waste or error. For AMAG, which develops a therapeutic iron compound to treat iron deficiency anemia, the paper itself was the problem. The company's IT team felt that all business processes should work on the Web — period. As it turns out, moving contract work online solved the company's original problem and introduced numerous other benefits, including:

- decreasing contract close times from days or weeks to hours
- gaining the ability to track and trace incomplete documents
- automating the process of reminding signers to complete contracts on time
- adopting a technology solution with no hardware investment and virtually no learning curve.

WHEN COMPANIES ADOPT CLOUD-BASED CONTRACTING

The first thing enterprises generally want to know before moving contract work to the cloud is whether doing so introduces risk into their operations. The short answer is, "no." Since the federal Electronic Signatures in Global and National Commerce Act (ESIGN) was signed in 2000, businesses have been able to close contracts electronically while remaining certain that such deals are as legally binding as those signed on paper. Furthermore, electronic documents introduce additional safety measures, since they provide for an easily accessible electronic trail parties can use to confirm transactions.

When firms can move contract work online, they gain efficiencies that support business growth and gain turnaround times that are 10 times faster than those of paper, and this benefits customers as well as drug manufacturers and suppliers. The features embedded within many e-signature services make it easier for parties to do business with companies that rely on cloud-based contracts. For example, automated reminders can forewarn signers of impending deadlines. Such solutions prompt signers to complete all critical fields of a contract, decreasing or eliminating the multiple cycles and inefficiencies that often exist in completing a traditional contract.

E-contracts also enable the collaborative, integrated nature of today's deals. Unlike static paper documents, Web-based agreements allow all parties involved in a deal to negotiate within the contract itself and make edits without opening an application. The result is an on-the-go contract process without dependency on paper, faxing, or shipping of physical documents.

For busy companies, ink-and-paper agreements present a frustrating, expensive, time-consuming barrier to expansion. In an industry where time-to-market is critical for purposes of competition as well as public health, there is little room for outmoded processes. By replacing paper contracting, pharmaceutical companies eradicate inefficiencies and flaws, freeing their organizations to devote more resources toward core business goals.

Jason Lemkin

Jason Lemkin is the vice president of Web services business at Adobe and the former CEO and co-founder of EchoSign. His operational experience spans the business development, sales, legal, human resource, and finance fields, and he is an acknowledged expert in the field of electronic signature and electronic contracting.

Teams Need A Common Purpose

Jeff Appelquist

U.S. Navy pilot Commander James Stockdale was the highest-ranking prisoner of war (POW) during the Vietnam War for his nearly seven years at the infamous Hanoi Hilton camp. He led his fellow POWs throughout their ordeal with imagination and courage, helping many of them survive both physically and psychologically. To do so, he used a variety of leadership techniques, and most importantly, provided the soldiers with a common purpose. "I distilled one all-purpose idea. It is a simple idea, an idea that naturally and spontaneously comes to men under pressure … you are your brother's keeper," he explained.

Unity Over Self

This concept that the well-being of the whole team was more important than the plight of any one individual was described by Stockdale as "Unity Over Self."

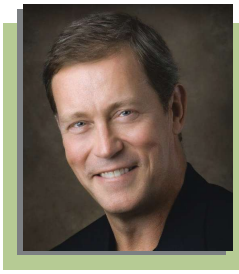
In leading the prisoners, he faced many obstacles. For example, the men were physically separated with no ability to communicate directly. Stockdale developed a wall tap code and other means of secret messaging allowing him to continually lead and encourage his team. The men also faced loneliness, deprivation, and torture on a daily basis. To combat these problems, Stockdale and his fellow captives organized a clandestine society with its own laws, traditions, and customs.

He succeeded in creating a cohesive culture with ironclad and widely known rules, which perpetuated itself and provided motivation and discipline to its members. Of the 591 Hanoi Hilton POWs who returned safely, almost 80% remained in the military, with 24 of them advancing to the rank of general or admiral. A significant number of these POWs became leaders in business, law, government, or politics. Also, 96% of the former prisoners were free of any symptoms of post-traumatic stress disorder.

Relevance To Today's Business Leaders

Why is this amazing story relevant to today's business leaders? Wilson Learning conducted a survey in 2006 of 25,000 workers in finance and high tech who asserted overwhelmingly that they needed a leader who could "convey clearly what the work unit is trying to do." This is an incredibly simple proposition, but many leaders fail the test.

Have you as a leader provided your team with a common purpose? Do team members understand and can they articulate that purpose? What is the central idea that drives your organization forward, through good times and bad? If you are fuzzy on these answers, you can bet your team is confused as well. Now is the time to step up and, with confidence and conviction, "convey clearly what the work unit is trying to do."



Jeff Appelquist is the founder and president of Blue Knight History Seminars, LLC, which provides leadership and team development training at famous historic landmarks. He is a former U.S. Marine Corps infantry officer, practicing attorney, and corporate executive. Jeff is the award-winning author of *Sacred Ground: Leadership Lessons from Gettysburg and the Little Bighorn*, and *Wisdom Is Not Enough: Reflections on Leadership and Teams*. His website is www.blueknightseminars.com and he can be reached at jeff.appelquist@blueknightseminars.com.

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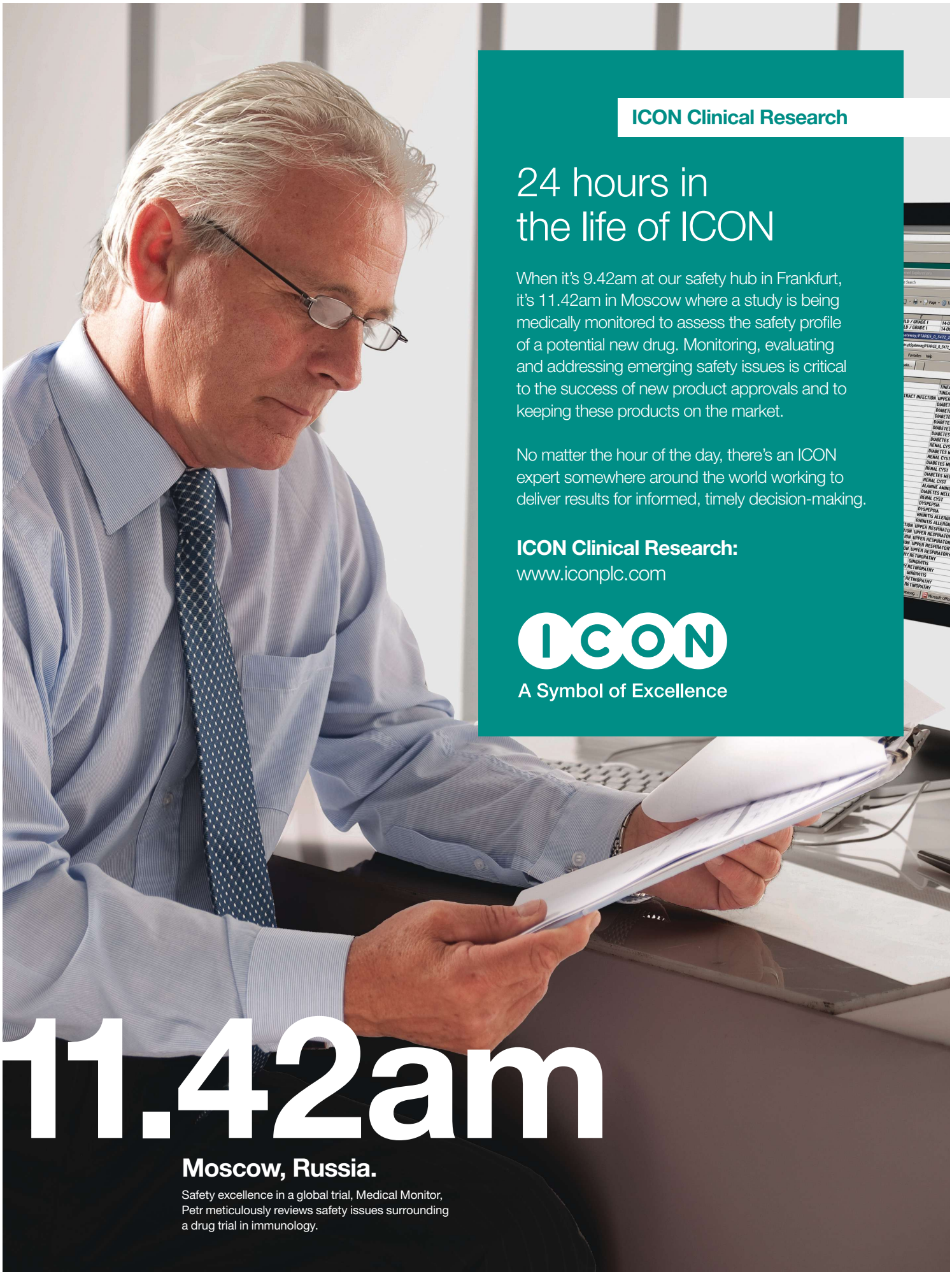

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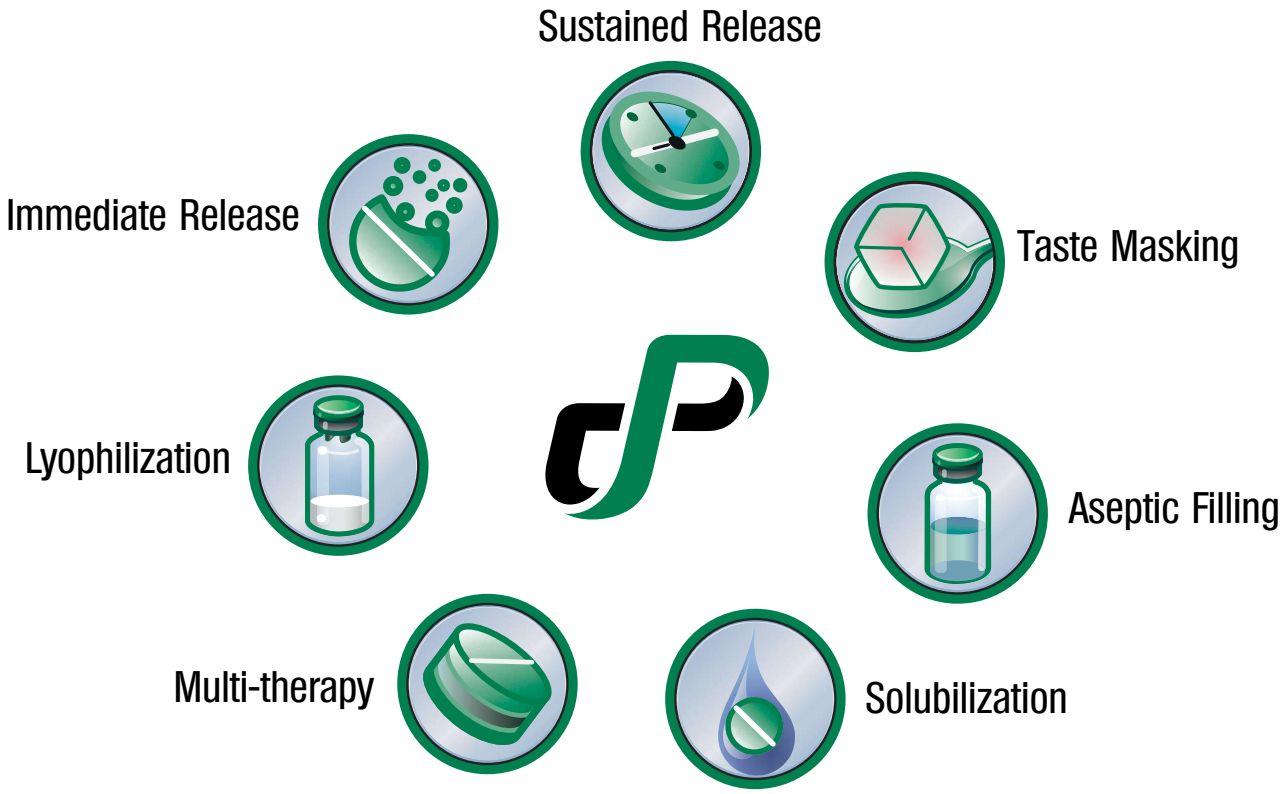

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4721 Emperor Blvd, Suite 200
Durham, NC 27703-8580
USA
P: +1 919 226 3200
F: +1 919 474 2269
www.patheon.com

European Headquarters

Patheon UK Ltd.
Kingfisher Drive
Covingham, Swindon
Wiltshire SN3 5BZ
UK
P: +44 1793 524411
F: +44 1793 487053
www.patheon.com

Published 9/11 PATH0214R0

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