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# Janssen

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# Janssen Biotech: Efficiency Through Consolidation p. 16

Janssen Biotech President Rob Bazemore and Sue Dillon, global therapeutic area head, immunology, Janssen Research & Development

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## 16 FEATURE: JANSSEN BIOTECH

"The recent major changes in our company are largely related to our structure and what we look like, and less about our vision and our mission," says Janssen Biotech President Rob Bazemore.

March 2012

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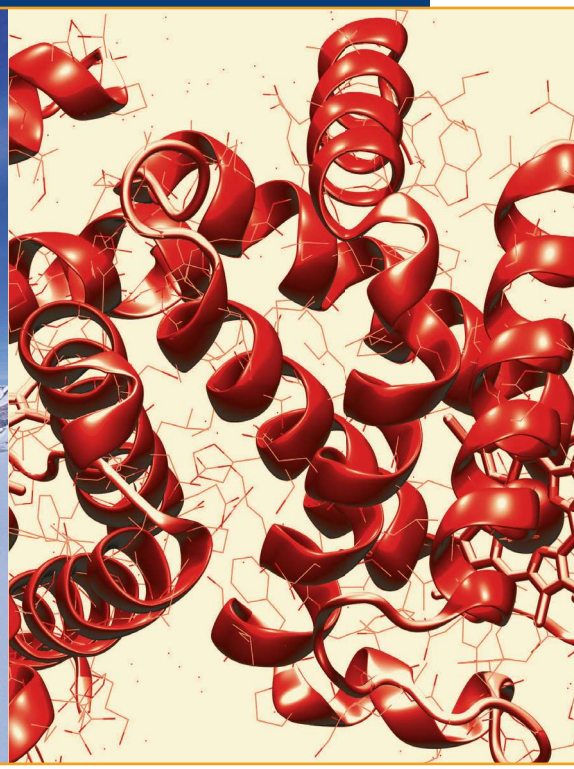
## Value through Innovation



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LIFE SCIENCE LEADER (ISSN: 21610800) Vol. 4, No. 3 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

## We're Still New And Still Growing

**February marked the three-year anniversary of the first issue of *Life Science Leader*. So what, you say? Well,** to the rest of the team and me, it's a big deal. I doubt a lot of people in the industry thought we would last this long. After all, we launched during one of the worst recessions in history. During that time, we have seen other well-known companies and dozens of magazines — prestigious magazines — close their doors. Somehow, we managed to crank out 33 regular issues (that doesn't include special supplements or guides), every one of which I am quite proud.

Don't get me wrong; I know we're still considered the new kid on the block in terms of pharma/bio industry publications. This fact was evident during a recent conference call we held with seven members of our contributing editor team. The majority of them told us that many of the industry executives they interview for our articles have limited knowledge of the magazine. My experience has been mixed in this regard. For example, when I asked the chief medical officer from Pfizer, Dr. Freda Lewis-Hall, for her opinion of the magazine, she not only gave us a rave review, but also made specific comments about a recent article she had read. On the flipside, I recently had a conversation with an executive who had been given a copy of the magazine by one of his colleagues. He told me after reading it that he was somewhat embarrassed for not having heard of it sooner. Given the amount of information available and our stage of evolution, it is understandable if some people are just finding out about us. But, all indications point to an improvement in our name recognition. We attend and exhibit at a lot of the top industry trade shows each year, and that's also increasing. People are talking about our first CMO Leadership Awards (www.cmoleadershipawards.com), and they'll soon be talking about our upcoming CRO Leadership Awards. We're definitely moving in the right direction.

I'm especially happy about the ongoing improvements we've made to *Life Science Leader*'s content. During the past few years, we've learned a lot about what you want to read. We are adapting with each issue — our own quality by design (QbD) if you will. Of course, much of the credit for those changes lies with our editorial board as well as feedback from readers like you.

We still may be considered new, but that's not always a bad thing. Sometimes new can mean better, and we hope that's the impression you have of us as we embark upon our fourth year — and beyond. So, keep those suggestions coming, and FYI — if you get an email from me asking in the subject line for feedback — the answer to your question is yes, I sent it, personally. I really do want to know what you have to say.

**Rob Wright**
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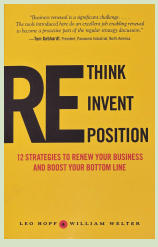


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If we select your question for publication, we will provide you with a complimentary copy of a business book, such as *Rethink, Reinvent, Reposition: 12 Strategies to Renew Your Business and Boost Your Bottom Line* by Leo Hopf.

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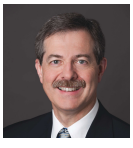
## ASK THE BOARD

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

### Q: How do you reestablish confidence and trust with your team or organization when this trust has been broken by prior leadership?

I've had to manage through this type of challenge, and it requires two key things. First, you need complete openness and honesty regarding what happened in the past, and acknowledgment of what went wrong. This needs to be done without disparaging the prior leadership, which can be a challenge. Second, you need to lead by example and know everything you say and do will be watched very closely. Be patient, since it will take time to rebuild the trust of your team and organization. Moreover, the recovery and subsequent rebuilding of trust can even be stronger.



**John Hubbard, Ph.D.**
Dr. Hubbard is senior VP and worldwide head of development operations for Pfizer. In this position, he is responsible for global clinical trial management from Phase 1 to 4, which includes more than 700 clinical projects. He has been leading pharma R&D activity for more than 25 years in various companies.

### Q: How does the biologics pharma industry create a workplace culture (at the manufacturing and management levels) of good corporate ethics?

Management must first live up to the patients-first approach to business. "Patients before profits" and "patients before KPIs (key performance indicators)" are phrases which cannot be overemphasized and which can drive a high level of ethics. This leads to a culture of no fear, where employees are actually rewarded for pointing out deficiencies rather than being punished. Management also must actually get down to the manufacturing floor and talk to people. The workers on the floor are often the best ones to spot deviations from a quality procedure. Having a direct link to an ethical management empowers and encourages all employees to operate at the highest level. The sum of these actions drives ethical behavior both top-down and bottom-up, which goes a long way toward ensuring a high set of ethical standards throughout the company.

**Mark Snyder, Ph.D.**
Dr. Mark Snyder is manager of the Process R&D Applications Group in the Process Chromatography Division of Bio-Rad Laboratories. He has a bachelor's degree in biology from MIT and a Ph.D. in biochemistry from the University of California, Berkeley. He previously worked for Scios and XOMA.

### Q: How do you foster an exciting learning environment throughout your organization?

Our training platform focuses on offering multiple forums for educational opportunities, maintaining compliance, enriching the employee educational experience, and focusing on the training needs/interests. Some of our training initiatives included:

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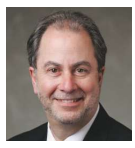
- interviewing each department and asked functional heads and staff to assess their needs/interests
- conducting an increased number of live training sessions (vs. read-and-understand method)
- using new approaches and technologies in a classroom setting (interactive games, break-out sessions)
- offering webinar sessions as an alternate to external conference and seminar training
- procuring more than 80 Kaplan Eduneering learning courses to make accessible to the organization.



**Mitchell Katz, Ph.D.**
Dr. Mitchell Katz has 26 years' experience in the pharmaceutical and biotechnology industries, including preclinical research, pharmaceutical operations, and regulatory affairs. In his position at Purdue Pharma L.P., he is the executive director of medical research operations.

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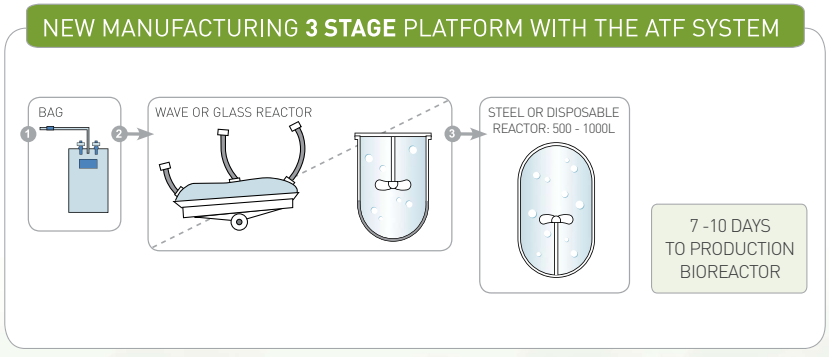


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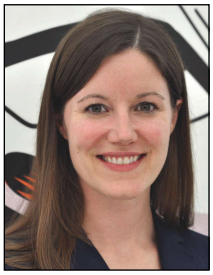

# OUTSOURCING INSIGHTS

## The Evolving Dynamic Of The Sponsor-CRO Relationship

*By Kate Hammeke, research manager, Nice Insight*

Seasoned industry professionals will remember a time not too long ago when the dynamic between the sponsor and CRO was purely that of a client/vendor. CROs were engaged to reduce the fixed labor costs on the sponsor side for work that varied in demand. At the time, the focus was controlling capacity fluctuations that impacted overall profitability. The work assigned to contractors was commoditized and not directly involved with the generation of intellectual property, and the majority of contracts went to businesses in the United States and EU. Ultimately, the opportunity for savings didn't pan out as desired because hiring out mass production of unspecialized products didn't provide any advantage when the subcontractors' expenses were comparable to internal rates.

The true opportunity for savings through outsourcing started to take shape in the early part of the 21st century. Developing countries with strong education systems relaxed their trade borders to Western businesses around the same time that China and India started to strengthen their patent laws. While some pharma companies opted to open their own research facilities overseas, others sought CROs in these emerging markets. Within a few years, the amount of work and the complexity of the projects increased. The tipping point in the shift of the dynamic between sponsor and CRO from a client/vendor relationship to a partnership occurred when some CROs started to expand their service offering to include discovery programs.

### OUTSOURCING THE DISCOVERY PHASE

Big Pharma was the first sponsor segment to risk outsourcing discovery phase work — a leap of faith where a level of uncertainty still persists — with the hopes of ensuring a strong drug pipeline alongside considerable savings over maintaining an internal research staff. This practice only continues to increase in popularity. The results from Nice Insight's Pharmaceutical and Biotechnology Outsourcing survey indicate that for the year ahead 50% of survey respondents specified the company they work for will engage outsourcing services for discovery phase work. As a matter of fact, after preclinical (53%), discovery is the second most popular phase during which sponsors engage outsourcing services. The likelihood of engaging outsourcing services decreases somewhat through the subsequent phases, from 48% during Phase 1, 39% for Phase 2, 33% for Phase 3, and 31% for Phase 4/postlaunch studies.

### EMERGING PHARMA SEEKS MORE OUTSOURCING SERVICES

Among the different sponsor segments, there was some variation in the frequency of outsourcing services for discovery phase work. Interestingly, emerging pharma companies are the most likely to outsource discovery, with 58% of respondents indicating their company would engage services for this stage. Biotech and Big Pharma followed, with 53% and 52%. Just under half of emerging biotech companies (46%) outsource discovery; however, only 1/3 of specialty pharma companies engage outsourcing services during this phase of the drug cycle. Of all discovery-phase outsourcing, 2/3 is sourced by pharmaceutical companies: 30% by Big Pharma, 25% by emerging/niche/start-up pharma companies, and 11% by specialty pharma. Biotech companies source 1/4 of discovery-phase projects, and emerging bio comprises 6% of that total.

Of respondents whose companies outsource discovery phase projects, 60% also engage outsourcing services during the preclinical phase. Just under half (46%) will also outsource Phase 1, approximately 1/3 (36%) will also outsource Phase 2, and 30% will outsource Phase 3 services, in addition to discovery. One quarter of companies that engage outsourcing services during the discovery phase also engage outsourcing partners for Phase 4/postlaunch studies.

It may be too soon to tell how successful engaging CROs at the discovery phase will be when it comes to bringing better, less expensive drugs to market. However, the process of lead optimization has drastically improved and NME (new molecular entities) approvals are on the rise again. Perhaps most importantly, the change in how sponsors and contract research organizations work together — sharing in risk and reward and establishing transparent strategies based on mutual trust — will continue to positively impact the future of drug development.

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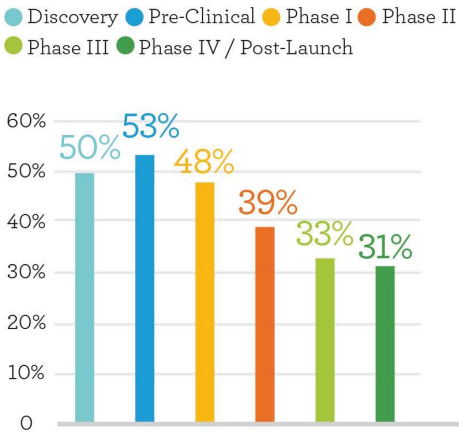
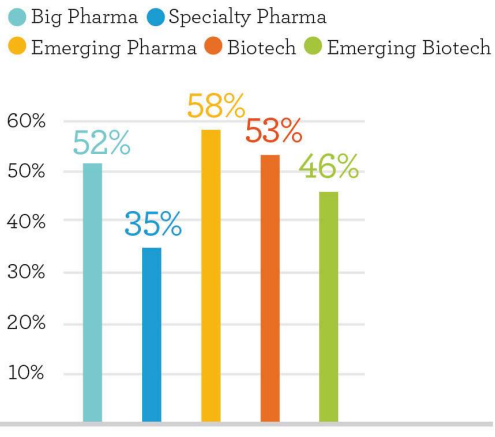
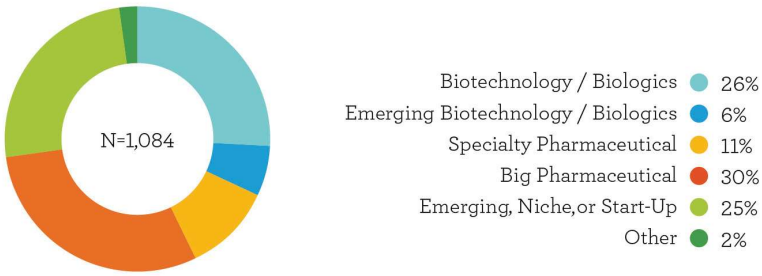
## Percentage of Respondents Who Engage Outsourcing Services at Each Phase, Overall




## Percentage of Respondents Who Engage Outsourcing Partners During the Discovery Phase, by Business Type




## Profile Breakdown of Respondents Who Engage Outsourcing Services during the Discovery Phase sourcing Services at Each Phase




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 [Q4 2011 sample size 2,619]. The survey is comprised of 1000+ questions and randomly presents ~30 questions to each respondent in order to collect baseline information with respect to customer awareness and customer perceptions on 300 companies that service the drug development cycle. More than 1,200 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.

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# BIO DATA POINTS

## Biopharmas Increasingly Satisfied With Vendors Of Single-Use Products

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

Biopharma manufacturers are increasingly satisfied with their suppliers of single-use devices, but that satisfaction is sometimes misplaced on less-critical attributes. Data from our study, 9th Annual Report and Survey of Biopharmaceutical Manufacturers, indicates that 68.5% of end users of single-use devices are "satisfied" or "very satisfied" with the quality of their vendors' products. Among the 13 attributes we evaluated, product quality again this year topped the satisfaction list.

In addition, we found that 31% of end users report being happy with their vendor regarding product costs. For the first time since 2008, "cost of product" did not appear at the bottom of our list. Both this year and in 2011, availability of a full line of products was near the top of the list. This year, we found that 59.7% were "satisfied" or "very satisfied" with availability. In addition, a majority of respondents reported satisfaction with their vendors for providing useful quality data, while nearly half were "satisfied" or "very satisfied" with "custom design of systems and assemblies."

Lowest on the totem pole was "vendor recycling programs," a new factor we measured this year, with just 8.7% of end users reporting a level of satisfaction with their vendors in this regard. On the other hand, more than 30% of decision makers consider vendor recycling an "important" factor. As more single-use devices are used at greater numbers of facilities, we expect this factor will increase in importance. If vendors are not ready to improve their single-digit satisfaction rating for this attribute, they may miss an opportunity to differentiate themselves.

Similarly, "standardization of devices" rates near the bottom of the satisfaction scale, but in terms of importance, there is a big gap, as 62% of the industry considers this to be an "important" selection attribute.

### IMPORTANCE FACTORS WHEN SELECTING A VENDOR

Product quality rated at the top of the vendor attributes list this year; factors such as "deliver on schedule" were close behind. An important area where vendors have limited control is in avoiding raw materials changes that require QA documentation. Nearly 40% of the industry indicates this to be a critical decision factor, yet being able to document and communicate changes in raw materials from their many dozens of raw materials, chemicals, parts and plastics suppliers is a daunting challenge. However, in a regulated environment, the ability to provide accurate raw materials data is critical to the quality of the high-value drug products.

### TRENDS EMERGE

When comparing this year's data to 2011 and years prior, we find that satisfaction with product costs ticked up even if it did remain low on the list. "Availability of a full line of products" jumped from 32.1% of respondents in 2011 reporting being "satisfied" or "very satisfied" to 59.7% this year. This factor rose rapidly to second place this year, which could signal that vendors are responding to demand and are rapidly developing new products.

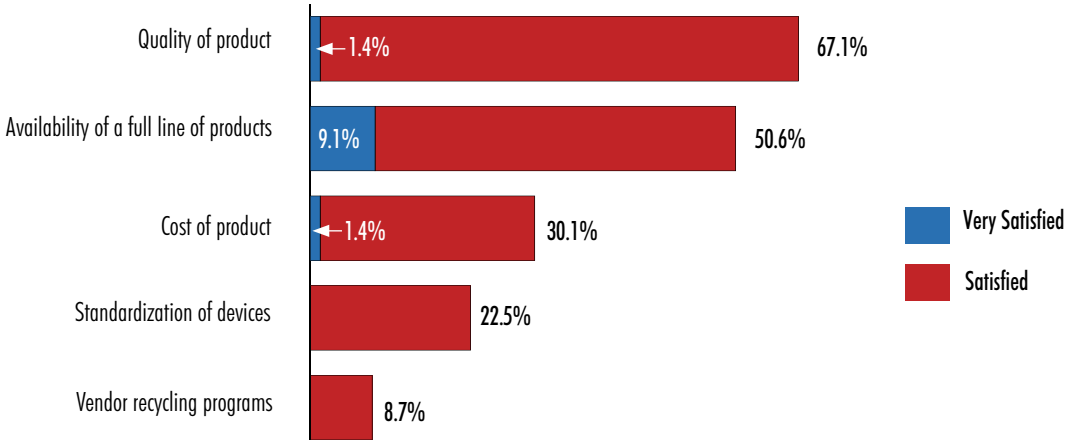
"Custom design of systems and assemblies" has continued its steady growth begun in 2009, suggesting that the design services at vendors are beginning to meet demand or expectations of the clients. Satisfaction with vendors' ability to "deliver on schedule" has continued to hover at around 50% over the past three years.

The data on vendor satisfaction within the biopharma industry paints a mixed picture. This is partly the result of the current financial situation. Decision makers have become more critical of their suppliers' value, the quality being offered, and how vendors' products and services fit end users' needs for improved productivity. This maturation process was stimulated by the tightening of budgets a few years ago. And, even as budgets have loosened, according to our study, over the last two years, buyers of these products, instruments, raw materials, and services have continued to scrutinize how each purchase will affect the overall productivity.

Vendors are acutely aware of this shift and appear to not only be developing more and different product lines and offering greater quality, but also to be beginning to focus on how their solutions improve overall industry productivity. For example, on the one hand, vendors are improving their satisfaction levels with factors such as "cost of product" and "availability of a full line of products." These are positive developments and likely stem from end users' demands for better value and improved efficiencies. In fact, the cost of products may not have actually gone down, but rather the actual (and probably the perceived) value of vendors' products and services has likely gone up. On the other hand, if vendors are to continue to differentiate themselves in this increasingly competitive market, they will need to address emerging factors like recycling and standardization.

# Selected Single-Use Vendors' Satisfaction

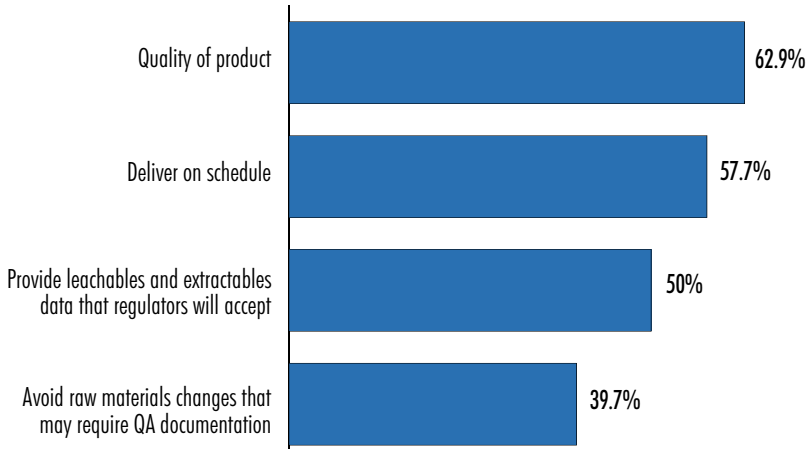
% Indicating satisfied or very satisfied, 2012




*Source: 9th Annual Report and Survey of Biopharmaceutical Manufacturing, Preliminary Data, Release Date April 2012, BioPlan Associates, Inc. www.bioplanassociates.com*

# Importance Of Single-Use Attributes In Vendor Selection

% Indicating very important




*Source: 9th Annual Report and Survey of Biopharmaceutical Manufacturing, Preliminary Data, Release Date April, 2012, BioPlan Associates, Inc. www.bioplanassociates.com*

**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.

Janssen Biotech President Rob Bazemore and Sue Dillon, global therapeutic area head, immunology, Janssen Research & Development

# Unity In More Than Name

## How Janssen Biotech And The Company's Global R&D Group Make Restructuring And Collaboration Look Easy

By Wayne Koberstein, contributing editor

In the beginning, there was Paul Janssen — a veritable god of pharmaceutical innovation in his time and founder of the company that bears his name. In the present, the eponymous company has evolved into the family of Johnson & Johnson (J&J) businesses called Janssen Pharmaceutical Companies, including the newly named Janssen Biotech (JB) and a global R&D organization responsible for all Janssen discovery and development.

Janssen Biotech brings the combined heritage of J&J's biotech businesses into the Janssen family fold, capping the past half-decade of reorganization and change. To examine the company's recent history and transformation — as well as how it interacts with the global R&D group — I spoke with JB's President Rob Bazemore and Sue Dillon, global therapeutic area head, immunology, Janssen Research & Development. We discussed the pathway that led to JB's new identity and structure, the advantages and challenges it inherited from its predecessors, and its unfolding contribution to the kind of innovation the company's namesake championed.

## FROM MANY TO ONE

On the surface, the shift to Janssen Biotech may appear as little more than a logo change — from Centocor, its predecessor as leader of the J&J biotech pack, to the new name. But the larger significance of bestowing the Janssen name upon its biotech division seems unavoidable, as do the related organizational changes, largely beyond public view. (See "What's in a Name?")

Only six years ago, Centocor was center stage. J&J had always been a relatively opaque organization, with the operations, results, and even the management of individual units hidden behind the corporate face. But in 2005, to spotlight its biotech side, J&J decided to make the Centocor brand more visible and transparent to investors and the public. At the same time, it separated the commercial entity of Centocor, R&D, and manufacturing into three business units to serve what were then multiple biotech companies within the corporation.

Centocor absorbed Ortho Biotech in 2008, however, combining their respective areas of immunology and oncology. In June 2011, formally joining the Janssen pharma group, Centocor and the other J&J biotechs such as Scios, Alza, and Tibotec came together under the new entity Janssen Biotech.

"The recent major changes in our company are largely related to our structure and what we look like, and less about our vision and our mission," says Bazemore. "J&J has always been a company that operates with small independent operating companies; that internal structure works well for us, and it hasn't changed. But, what has changed is our face to the customer," Bazemore explains.

Having so many commercial entities, from pharmaceuticals to devices to consumer products, complicates relationships with payers, managed care plans, and other customers, he says. "So we decided to unify our presence to our customers worldwide into one pharmaceutical business called Janssen." The Janssen group now contains Janssen Biotech, Janssen Therapeutics, and Janssen Pharmaceuticals with its separate CNS (central nervous system) and internal medicine business units.

Within the commercial entity now called Janssen Biotech, Bazemore runs a board that includes all of the "cross-functional partners" who head areas such as manufacturing and supply chain. Dillon also sits on the board. Further, she has an R&D board to run the immunology R&D organization, and that board includes one of Bazemore's commercial vice presidents.

"With the dual-board structure, we can ensure good commercial input into clinical trial design, selection of products for development, and so on," Bazemore says. "But we also make sure we are staying close to what's happening within the R&D organization as we make commercial decisions, and that affects how we think about our longer-term commercial strategy in a therapeutic area like immunology."

Bazemore also sits with other Janssen-company presidents on a North America leadership team, where "we talk a lot more about how best to optimize the value of a compound that might apply across businesses." He cites JB's star immunology product Remicade (infliximab). "Because the internal medicine business calls on gastroenterologists and other specialists who use Remicade, they copromoted the product for us. Vice versa, our internal medicine unit sells Nucynta [tapentadol] as part of its pain franchise, but we also sell Nucynta to the oncologists as a pain option for cancer patients. So being a part of a larger

## THE TROUBLE WITH DOXIL

One of Janssen Biotech's key oncology products is Doxil (doxorubicin HCl liposome injection), which made headlines in 2011 when Boehringer Ingelheim's (BI) Ben Venue Laboratories (BVL) unit, the CMO with sole responsibility for making the product, suddenly announced it could no longer do so. President Rob Bazemore speaks about his company's response to the crisis, its support for affected patients, and the lessons learned.

**Bazemore:** Like most companies, we will always rely on strategic partnerships with CMOs, because some of these products that we make are extremely complex and difficult to make. For 10 years now, we've had the partnership with BVL without a single issue of quality or missing shipments or any other problem. Here are some lessons I have learned about what to do when a crisis occurs:

- Communicate quickly and frequently with the FDA, physicians, and patients to make sure they understand the issue and its potential impact. Seek out the FDA to help you create solutions.

- Provide whatever resources you can, even if it means sending your own company people to the contract manufacturer to help resolve the issue as quickly as possible.

- Probably the most important lesson is to be ready to do some extraordinary things, as we've done with Doxil. We put together a program which helped us quickly identify patients who were on the drug and who should be prioritized for receiving the drug when we had it. It prevented product hoarding and price gouging. If we had just put the available drug in the market on a monthly basis, there was no certainty that the patients who got the drug one month would be the same patients who got the drug the next month.

To this day, although we could have done some things better, our response has stood the test of time, and I believe it will be a best practice example of how to handle situations like this when you can't completely supply the market with drug.

company helps us leverage the assets across all four of the businesses."

For similar synergistic reasons, it was a logical step to consolidate J&J's biotech units into one commercial entity. Not only did the units' customers overlap, so did their science and technology. Immunology and oncology are increasingly interrelated, and immunology itself links to other therapeutic areas and new technologies.

Thus, JB markets products that extend beyond dermatology, gastroenterology, nephrology, and rheumatology to areas such as virology and surgery. Procrit, for example, is indicated for HIV-related anemia (virology) and for reduction of allogeneic red blood cell transfusions in nonvascular surgery. In some cases, "pure" biotechnology gives way to small molecules as the best tool for the job.

But, according to Bazemore, the foci of JB's R&D and commercial strategies are not just targets chosen for their market potential; they are the natural result of the company's leadership and innovation in those areas. Immunology products Remicade, with indications in dermatology, rheumatology, and gastroenterology; Stelara (ustekinumab) in dermatology; and Simponi (golimumab) in rheumatology have all broken new ground. In oncology, Procrit for chemo-induced anemia with indications in several other areas, and most recently the small-molecule drug Zytiga, approved for metastatic castration resistant prostate cancer, are also breakthroughs.

JB's challenge was to transfer the "visibility and equity" of the Centocor brand to the newly named entity. "It was all about communication," says Bazemore. "We had to be very clear with our customers why and how we were making the change and that it didn't involve any changes in our company structure, leadership, products, or anything else they relied upon. Everything essentially works just as it did before the integration under Janssen. From a customer's point of view, the change has gone smoothly."

## MATRIX DEVELOPMENT

Internally, the view is more complex. First, says Bazemore, the company rationalized support services for the formerly separate businesses. "We took away a lot of duplication. By consolidating services such as market research, you can make your organization just work more efficiently. And now we can share best practices and talent across brands or therapeutic areas."

Meanwhile, the company's R&D organization went through a substantial structural transformation, as Dillon describes. "We had all the components of discovery and development holistically within the Centocor group, but we were really only focused on the two disease areas, immunology and oncology," she says.

"Now with the unification of all R&D groups and the

> "We have several instances of collaboration between different groups to bring compounds forward that we know from the outset will be applicable beyond immunology."
>
> Sue Dillon, global therapeutic area head, immunology, Janssen Research & Development

formation of the new organization that consists of the Centocor legacy groups and the legacy groups of J&J Pharmaceutical Research and Development, we're focused on more therapeutic areas. In the immunology space, my group has responsibility for all of the research and development — whether biologics or small molecules or regardless of location around the world, it all rolls up into one end-to-end organization."

Dillon explains that some of the functional groups that supported discovery and development are now matrix groups that support immunology and the other therapeutic areas. For example, the groups involved in creating small-molecule therapeutics in the discovery stage are now global organizations that support all the different therapeutic areas and their global regulatory organizations, global development organizations, and so on.

So what happens when the same compound overlaps multiple therapeutic areas? Which group takes the lead? Dillon answers that no hard rule applies.

"It depends on the stage of development," she says. "For example, we have compounds already in development in immunology, and we recognize there is also an interest in developing the drug in cancer. So we coordinate through a global compound-development team, which then becomes responsible for moving the compound toward all of the potential indications. Of course, some teams specialize in specific diseases, but often there is tremendous common ground around the science, regulatory approach, safety, clinical-development strategies, and other areas, so it becomes a joint effort."

Dillon says her group also has opportunities at the discovery stage to discuss drug targets that may have application in different diseases. "In fact, we have several instances of collaboration between different groups to bring compounds forward that we know from the outset will be applicable beyond immunology."

Dillon says immunology most often interacts with oncology, but the company has an emerging interest in immunological approaches to neurological, pulmonary, and inflammatory diseases. In a May 2011 presentation, Chairman Duato, noting that JB leads the U.S. and Chinese markets with its immunology franchise, put a high priority on expanding the franchise worldwide. Oncology, likely working often in tandem with immunology, is set to expand in parallel.

Another level of collaboration takes place inside the company — the marriage of therapeutics and diagnostics. In immunology and oncology, for example, the therapeutic side looks for biomarkers of disease progression or response to certain drugs in development. And it cooperates with a recently created group, the Co-Diagnostic Center of Excellence, charged with developing diagnostic tests that could be commercialized along with specific drugs.

"You could think of it as a parallel to the paradigm of drug discovery and development," observes Dillon. "There's also diagnostic discovery and diagnostic development, and the expertise is somewhat different and specialized. We have set up these groups so that we can work together and ultimately bring drugs and companion diagnostics to the marketplace."

Bazemore points to a supporting example in oncology: In 2011, J&J integrated Veridex (www.veridex.com), its developer of diagnostic tests, into Janssen R&D. "One of the tests measures circulating tumor cells. The decision was made to break that organization out of the J&J devices unit and move it under our

## WHAT'S IN A NAME?

What is the significance of applying the Janssen name to its now consolidated biotech business, replacing its former Centocor brand?

Paul Janssen's own research steered clear of biotechnology; he was the master of small-molecule invention, a blend of shrewd science, pure logic, and uncanny intuition. But no doubt he would be proud of the innovation already produced by the formerly separate businesses now under the Janssen Biotech banner — which, as it turns out, also includes a stable of small molecules.

His surname evokes the man's unique but productive philosophy: He focused on conditions he believed he had a chance to cure, not on diseases as huge potential "markets." Still, when the cures came, the markets followed. For instance, his antifungals, once denigrated as only "third-world" treatments, eventually found wide application in human medicine and agriculture worldwide.

Similarly, Janssen Biotech has focused on developing products for diseases with relatively small markets such as Remicade for Crohn's disease. But as those products emerged out of the company's two leading research groups, immunology and oncology, many of them have found additional uses in conditions with much larger patient populations — as Remicade did in rheumatology and dermatology.

pharmaceuticals R&D, specifically so that it can be a part of how we approach R&D investment in the oncology stage."

## PARTNER APPROACHES

Knowing JB's development goals and plans can be generally useful to other, often smaller companies that seek corporate partnerships. But Bazemore and Dillon also give some insights into how their company evaluates and selects its research partners.

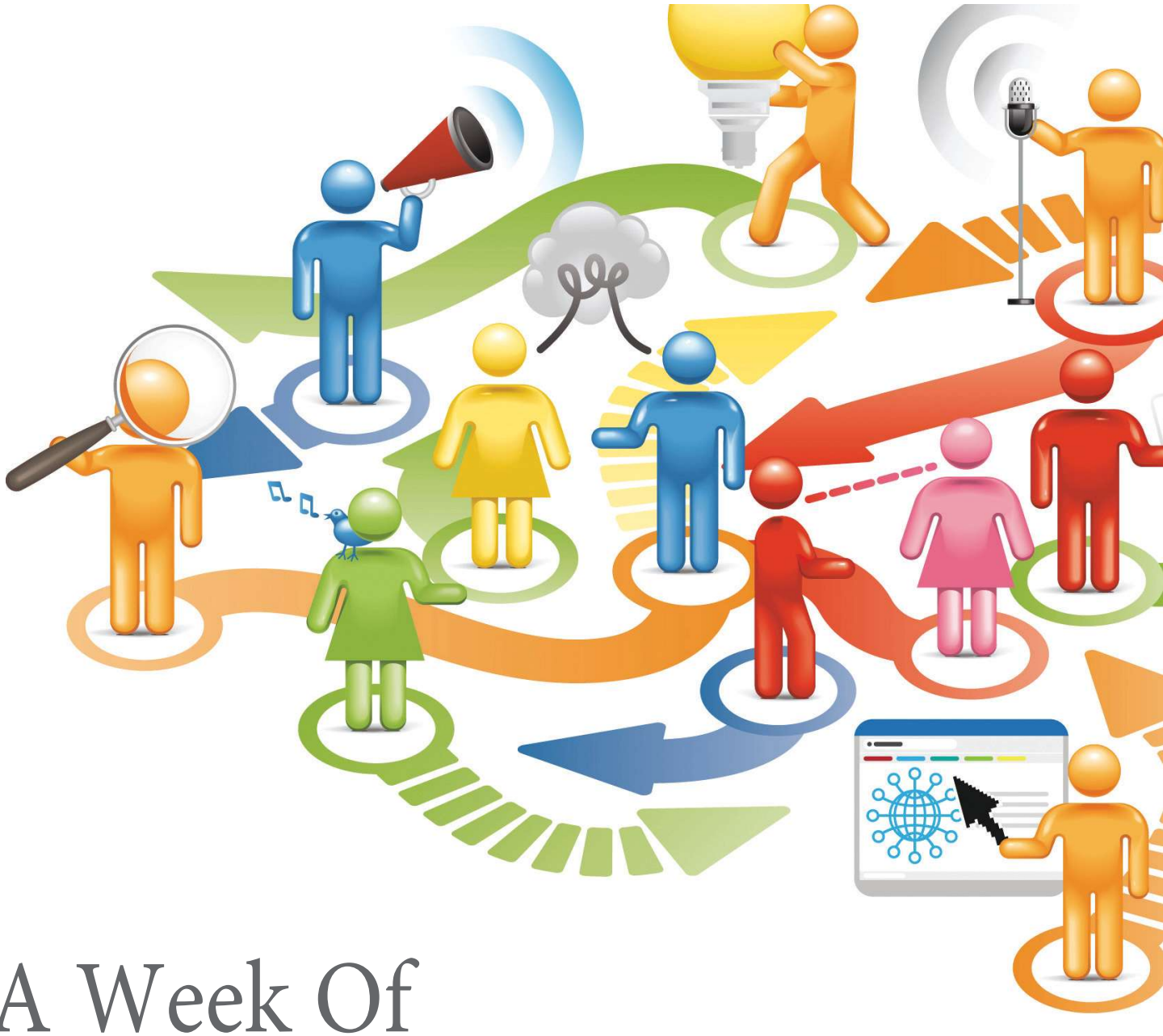
An outside company developing an immunological approach to cancer might contact JB at one of several levels, according to the state of development, explains Dillon. "We have a scientific licensing group and business development groups within immunology, and they work along with us to talk to biotech companies and academic groups about early-stage compounds or new platforms and technologies that align with our strategies." Ones that already target a given disease might then be diverted to the appropriate TA group, she says, but if the approach focuses on a basic target in an inflammatory pathway, her group would evaluate it.

For a compound in late-stage development, Dillon says the evaluation is coordinated between the R&D group and Bazemore's team, along with the other global commercial teams, to decide whether to establish a partnership around the asset. From the earliest to the latest stages, she says, Chairman Stoffels (Dr. Paul Stoffels is worldwide chairman, Janssen Pharmaceutical Companies of Johnson & Johnson) "keeps a good view across what's happening in all of the different areas. But again, there is always close contact between all of the areas."

Beyond evaluating the incoming approaches from potential partners, the company's R&D groups work to stay in touch with the various consortia, academic centers, and even patient groups that often identify, fund, and advocate for innovative technology. Typically, says Bazemore, the patient groups become more involved in later-stage developments.

Late-stage clinical trials are also where the company places most of its R&D investment, according to Bazemore. Besides the more stringent regulator demands every company faces, JB has also been aggressive in generating cost-effectiveness and comparative-effectiveness data, as with its hallmark head-to-head psoriasis trial of Stelara versus the then market-leader, Enbrel (etanercept).

By such boldly intended moves, Janssen Biotech may hope to share Paul Janssen's inventive spirit, follow his example, and build new markets in biotechnology, one step at a time. "We believe in the paradigm by which you can ultimately build to a blockbuster even if each separate disease, though an important unmet medical need, may not be a very large commercial opportunity," says Bazemore. "That paradigm of success will carry us into the future."



# A Week Of Pharma/Biotech Dealmaking

## Insights From The JP Morgan Healthcare Conference And The EBD Group's Biotech Showcase

By Wayne Koberstein, contributing editor


In the new year's early wake, the JP Morgan Healthcare Conference (JPM HC) spreads over San Francisco's central downtown blocks, sparking private meetings and satellite seminars in hotels and eateries all around the event site at the St. Francis. Inside the site, perhaps several thousand people at any time fill the lobbies and shuffle between sessions and company presentations in a half-dozen parallel tracks. Over four days, the JPM HC attracts more than 7,000 invitation-only registrants, growing in number most years.

Add to that the simultaneous events scheduled close by — a phenomenon that has also grown in recent years — and you have a larger congregation that I call, collectively, "JPM Week." Besides JPM HC, one of the more prominent events this year was the EBD Group's Biotech Showcase, whose more intimate format encouraged even more small-company presence and large-company interaction.

But, the main action in this concentrated space and time is outside the conference rooms and often off-site — one-on-one meetings between life sciences companies, investors, customers, and suppliers. Frequently more than mere introduction, the meetings may serve many purposes, from indispensable human contact to significant deals, and every level of business exchange in between.

And, the conference-related networking also spreads beyond the four days in the city. Returning home, most if not all participants spend days to months catching up, following through, and generally dealing with the harvest of opportunities and commitments cultivated at the gathering.

Generally, the most common patterns are well known:

- Small-company leaders may wait years just to earn an invitation to the main show, JPM HC, meanwhile meeting privately with contacts off-site or working the alternative venues. After the first JPM invitation, they typically wait a few more years before becoming presenters (competition for the 300 or so slots is fierce), but caution is also abundant among small young companies until they grow to a certain critical mass.
- Large-company executives run their own marathons in selecting among the huge number of companies in town that they want to meet and, of course, in conducting meetings literally nonstop all week. Often the meetings are fateful for both sides, leading to partnerships that succeed or fail, false hopes foregone, or true opportunities found or lost.
- Investment bankers and analysts, lawyers, academics, healthcare managers, researchers, and journalists all take part in the mix, with people sharing and exploring every angle, from the smallest details to the largest issues that affect healthcare investment.

## THE SELLING SIDE

Other patterns emerge only from personal experience of the event and surrounding confabulation, a word that describes the collective discussion as well as the hyperbole that inevitably accompanies it. For, selling — selling one's company, technology, partnering skills, and other expertise, resources, and services — lies at the heart and soul of the diverse congregation.

The sellers labor under the supposedly cold, calculating gaze of investors and Big Pharma. But passion on both sides plays at least as big a role as reason. With the next generation of medicine and healthcare at stake, it is difficult for any player to be dispassionate.

The biggest players get most of the attention, of course. Big Pharma presentations are always overattended, mass reported, and followed thereafter, often in the mass media. Yet, for all their dominance, the big companies seem relatively passive, sorting through all the entities that offer the most potential for innovation and business growth: the typically small, frequently young companies that assume most of the risk and must constantly prowl for funding to develop new technologies and products.

That is why I spent most of my time meeting with such companies — more than a dozen, representing a range of technologies, therapeutic areas, and funding models. A closer look at these companies yields important lessons, benchmarks, and cautions, not only for their peers, but also for the players of all sorts represented at JPM Week. For balance, I also spoke with several large and midrange companies, as well as venture capital and angel investors, analysts, and others at the event.

## OCCUPYING SPACES

Pitching a truly novel technology may be one of the loneliest of all pursuits. But, so is seeking attention as one of many players in a hot new area. Every company dedicated to developing new life sciences technology faces its own mix of challenges unique to its entry point, position, and circumstances in the space targeted by its business plan. Theoretical models are thus limited, but parallel experiences among companies often yield useful lessons. Beyond this report, I will continue to follow these companies and hope to spotlight their post-JPM progress in future months.

I spoke with companies competing in a variety of areas, from small-molecule and biotech therapeutics, to vaccines and immunotherapies, diagnostics, and specialty pharma. Some struggles they hold in common; others are specific to each company. Likewise, the competitive spaces they occupy vary greatly, from lonely for the most novel technologies, to crowded for the latest and hottest.

Novadigm Therapeutics typifies the novel extreme with its vaccine engineered to generate a single antigen against both a fungal and a bacterial infection: candida and staph aureus – the first cross-kingdom vaccine. A team of infectious disease specialists led by company founders at UCLA conducted 3-D homology to find the surface protein common to the fungus and sepsis-causing bacteria.

Staph and candida are two of the worst pathogens in the ICU, and thus Novadigm is already positioning it for the hospital-infection market, but with a much larger potential market in infection-prone patients that are immune-compromised, on antibiotics, or who have hard-to-treat conditions like recurrent vulvovaginal candidiasis. A typical Phase 1 vaccine study showed a four-fold increase in antibody levels and a steep rise in immune response in all 40 patients, but the company faces a long haul in proving its concept, gaining sufficient clinical adoption (at least in recruiting investigators), and eventually gaining regulatory approval.

Novadigm is still early in its funding race, having started in 2008 with an $18 million Series A round from Domain Associates, followed by $17 million in government grant funding, including $12 million from the DoD. The company has licensed its technology from research partner LA BioMed and has a network of service providers, but is putting off major partnerships until its vaccine clears Phase 2 proof-of-concept. Already, though, its executive team echoes a unanimous theme among all those interviewed: Fundraising and the search for partners never stops, nearly constant travel is required, and perseverance pays.

Other companies developing especially novel approaches include Scynexis, Ligocyte, and Epizyme — although in speaking with them, I saw how different their development challenges, corporate models, and investment strategies were. Scynexis is pioneering a new anti-infective MoA (mechanism of action), cyclophilin inhibition, specifically in a compound to fight hepatitis C, while also selling its R&D services for "shared-risk" projects. Ligocyte is in Phases 1 to 2 with a vaccine for novovirus, along with other "virus-like-particle" (VLP) vaccines and has depended mainly on DoD and NIH grants and a Series A round.

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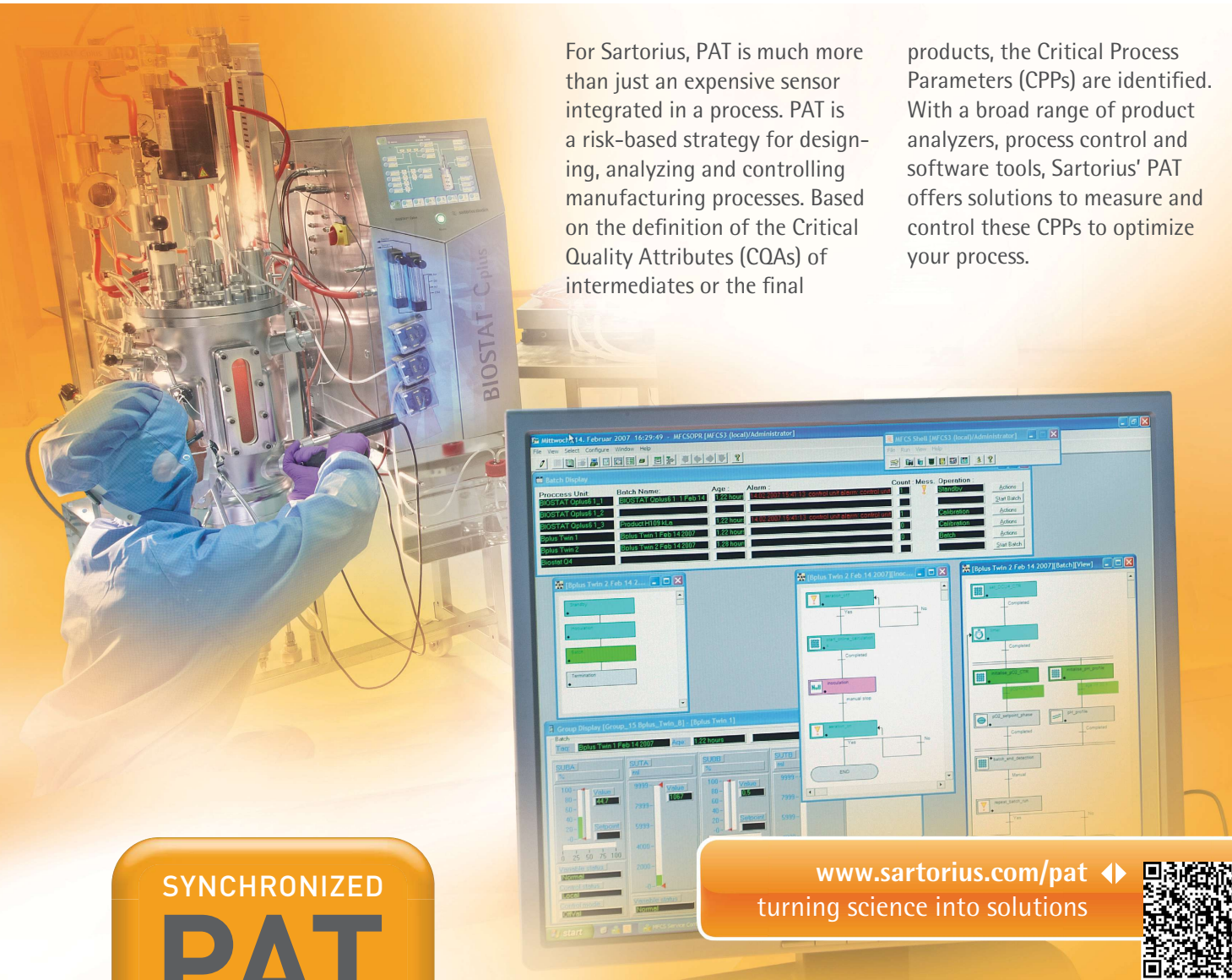


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Epizyme may appear to be yet another targeted-therapy company, but actually its small molecule histone methyltransferase (HMT) inhibitors and screening technology may have wide cancer and noncancer applications. It has drawn on two venture rounds, with participation by Amgen and Astellas and research funding from GSK and Eisai.

Comparable novelty exists in the diagnostics companies, but it is safe to say that diagnostics face much less severe entry barriers than do therapeutics, thus somewhat easing their development. All three diagnostics companies I spoke with drew a distinction between the regulatory and clinical-adoption pathways in their business.

These days, every new diagnostic tool stems from unique assumptions about key biomarkers and disease mechanisms. T2 Biosystems has what amounts to a minute MRI to measure the activity of oxygen molecules as a key to molecular diagnostic tests, immunodiagnostic tests such as protein and molecule detection, and platelet function and coagulation capabilities. SuperNova Diagnostics is developing a tiny liquid-crystal chip for in-office tests based on "direct detection" of DNA. And BioBehavioral Diagnostics develops computer-based units for diagnosing and dosing medications in ADHD and other neurological disorders. To ensure wide use in the clinic, the companies must achieve something approaching consensus among physicians, opinion leaders, and payers.

On the other end of the scale, some companies are wading into waters frothing with potential competitors, all vying for opportunities in the latest, hottest technology space. Probably no other area fits that description better than molecular targeting in oncology. I spoke with Idera Pharmaceuticals, which is developing drugs aimed at Toll-like Receptors (TLRs) for cancer, autoimmune, vaccine adjuvants (with Merck & Co.), and gene-silencing oligonucleotide (GSO) technology. Idera is a public company and was founded as Hybridon in 1989.

Outside of oncology, another popular target market is Age-related Macular Degeneration (AMD). Using new insights from Dr. George Chiou, the same researcher responsible for the glaucoma drug timolol and AMD breakthrough Macugen (pegaptanib), MacuCLEAR is hoping to defeat market-leader Lucentis (ranibizumab) with a new treatment to arrest progression of "dry" AMD to the more serious "wet" AMD. On the other hand, it is quite early in its program and has had only limited private-placement and grant funding since 2007.

So-called specialty pharma companies were also among those I interviewed. NuPathe is in Phase 3 development with a "smart" transdermal patch for migraine treatment. Coincidentally, MAP Pharmaceuticals has filed an NDA for a migraine therapy improvement: an inhaled aerosol form of dihydroergotamine (Levadex). Both companies are fascinating in how they have combined older, reliable drugs with new technology designed to improve patient treatment, as well as their status and experience as public companies.

## REFLECTING VIEWS

All of the perspectives voiced by the small companies have echoes in the large-company views of AstraZeneca's head of partnering, Shaun Grady. Neither his company nor others its size can hope to cover the entire universe of start-ups and new-technology developers seeking Big Pharma partnerships. In one sense, the big players hold all the chips in the partnering game and could theoretically dictate deal terms that essentially transferred all risk to the smaller ones. But AZ, at least, has decided to play nice, reaching out to potential partners in actively interested and sympathetic ways, but with one caveat: Show us something we can get to patients in the shortest possible time.

By the end of JPM Week, I sensed a consensus among participants that the meeting's liveliness belied a mixture of hope, desperation, and practicality amidst the general and continuing economic recession. Perhaps one tangible change was that the economy hardly entered people's discussion. Instead, everyone's focus was on what companies could do with the opportunities available to them, however modest. The obvious intimacy and interaction at the EBD Biotech Showcase, where many of the companies I interviewed presented, reinforced the overall vitality of the greater gathering catalyzed by JP Morgan in San Francisco this year — and its rippling effects beyond.

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P11-3519A-Jan., 12

# Clinical Trial Approval Process In Brazil — Clearing The Roadblocks To International Studies

By John Andrews and Eduardo Pizolato

The regulation of clinical research in Brazil started at the national level in 1996 with the publication of Resolution 196 from the National Health Council (CNS, which is a Portuguese acronym). The CNS provides statutory regulation of all research involving human beings, including ethical evaluation, which is performed by Local Ethics Committees (CEPs) and, in certain cases, by the National Ethics Committee (CONEP). Further regulatory assessment is the responsibility of the National Health Surveillance Agency (ANVISA) and is required for trials with drugs and medical devices aimed at future marketing applications.

Brazil's health statutes have grown over the years since inception and now include approximately 20 regulations at the national level, from the Brazilian Ministry of Health and the National Ethics Committee, as well as the international requirements included in the International Conference on Harmonization (ICH), principles of Good Clinical Practice (GCP), and the Helsinki Declaration.

The complexity of the Brazilian human health regulatory environment originated from the country's concern for the safety of its people as potential participants in international studies. The socioeconomic disparity in certain regions of Brazil relative to the countries of origin of the pharmaceutical sponsors of clinical trials was seen as a potential enticement for study participation that may disguise the risk.

As a result, the regulation of clinical research in Brazil ensures a high ethical standard comparable to internationally accepted benchmarks, yet has resulted in a lengthy process, slow to reach its conclusion due to the requirement for several independent and somewhat redundant reviews and approvals.

## THE PROCESS

"From 2005 until today, there was a 4% decline in the number of recruiting patients for new studies in Brazil," says Fabio Thiers, founder of ViS Research Institute, whose information is derived from work performed in conjunction with the Massachusetts Institute of Technology and the National Bureau of Economic Research, which evaluates the growth and decline of this economic segment.

Furthermore, considering just clinical trials of new pharmaceutical products conducted in BRIC (the acronym for the four largest emerging markets: Brazil, Russia, India, China), the number of trials performed has decreased in all nations, but the decrease in Brazil was greater than in any of the other three countries. A total of about 50 trials of new chemical entities was performed in Brazil compared to about 75, 100, and 150 studies performed in India, Russia, and China, respectively.

The origin and disparity in the number of clinical trials performed in Brazil are largely due to the period required for the approval of clinical studies by the National Research Ethics Committee, the CONEP. A survey by the University of São Paulo showed that the national average just for ethics approval of a study by the Local Ethics Committee followed by approval by CONEP may be as long as 100 to 150 days. According to the Association of Pharmaceutical Research, the national average for the overall approval of a new clinical trial from the time the documents are first submitted by the sponsor to ANVISA and by the investigator to the Ethics Committees, until the full review and approval by all agencies involved is complete and the drug has been imported into Brazil and accepted by Customs, may be as long as 10 to 14 months. In contrast, the United States, Canada, Russia, and most other countries around the world range from 3 to 6 months, with China being the only other country with an approval time of at least a year.

It is widely recognized that a major bottleneck in clinical trials in Brazil

is the long time line for study approval in relation to other countries, resulting in the loss of the country's competiveness in the case of international multicenter trials.

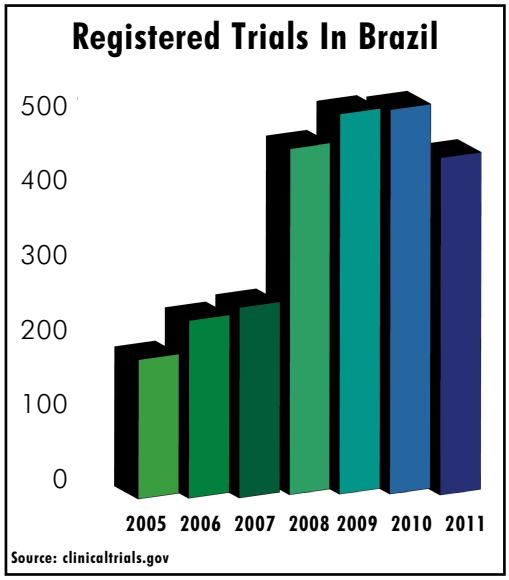
## THE CAUSE

The president of CONEP, Gyselle Tannous, has stated publicly that the delay in clinical trial approval derives from the arduous national policies that are in place to ensure conformity to the international requirements governing the use of humans in experimental trials. For example, the standard template required for national approval of any study requiring the patient to give informed consent consists of 30 pages. "Hardly any patient will read it all. We have to make changes," said Tannous. Another bottleneck in the arduous process is the need to provide each study subject free access to treatment for the disease under study until the new drug is commercially available. "Clinical research is a field of conflicts of interest. We are rigorous in the defense of the rights of research subjects," she stated.

The Ministry of Health recognizes this issue and is implementing changes quickly in order to shorten the study-approval time line to international standards. In the last six years, according to estimates by ABRACRO — Brazilian Association of Clinical Research Organizations — Brazil missed realizing investments of more than $200 billion (USD), although Brazil has more than 300,000 active physicians/investigators and more than 600 local ethics committees installed. If this matter can be successfully addressed, capturing this missed revenue, the impact on the national economy, the viability of Brazil as a participant in international drug development, and the resulting improved healthcare that can be offered to its citizens will be substantial.

These issues have been discussed in meetings between investigators, ethicists, the pharmaceutical industry, and the Brazil Ministry of Health. The investigators agree with the importance of the Local Ethics Committee authority over

participating institutions and the coordinated review and approval process through CONEP, which manages and administers the work. The proposal for revision of the process is to create and release five regional CONEPs and require just one ethics review in which the approval process is monitored and time lines are standardized as much as possible.




## FACILITATING THE CLINICAL TRIAL APPROVAL PROCESS IN BRAZIL

By 2015, the Brazilian Ministry of Health plans to invest $1.5 billion (USD) in research of new drugs, treatments, vaccines, and devices. The value is almost four times greater than the investment portfolio accumulated in the last four years, about $400 million (USD).

The regulatory agencies in Brazil are addressing changes in the review and approval process in order to speed up the actual time lines for study start-up. Implementation of the improvements began in 2005 with the publication of Resolution 346. This new regulation facilitates the process of the multicenter research protocol review by the National Ethics Committee, requiring the dossier to be submitted only once by a single Local Ethics Committee, unlike the previous process in which each Ethics Committee from each participating research center was required to submit the same dossier for individual review and approval.

In 2008, the ANVISA published new regulations for clinical trials in Brazil, Resolution 39. The major importance of this resolution was the establishment of parallel procedures for both regulatory and ethical review, as well, under certain circumstances, importation of investigational products even before the ethics approvals of the study.

Until recently, the ethics approval process was performed using hard paper copies and the national postal system, without taking advantage of the efficiencies of modern communications technologies. According to Reinaldo Guimarães, Secretary of Science and Technology of the Ministry of Health, "In part, industry and investigators are right; the first step will be to put in place a system that will allow the online tracking of protocol assessment." Consequently, in November 2011 the minister of health launched the Platform Brazil and Brazilian Registry of Clinical Trials (REBEC), programs that will unify data from research involving human subjects. With this platform, researchers can follow the project review via the internet. With REBEC, the first database for registration of clinical trials, the researcher will not have to resort to foreign databases to record the trial and track its progress. The REBEC is endorsed by the WHO.

With the unification of data, the expectation is that time for authorization of research in Brazil will be decreased by many months, solving one of the main frustrations of the scientific community, research institutes, and laboratories. The National Ethics Committee posted a letter on its website stating, "We advise that after the usual vacation of CONEP, from Dec. 15, 2011 to Jan. 15, 2012, all studies must only be submitted to ethics review by electronic system named Plataforma Brasil."

We hope that Platform Brazil will help speed up the ethics time lines in Brazil. The expected total new ethics time line — EC and CONEP — is now eight weeks.

Platform Brazil is a national and unified electronic database of clinical trial records that allows for the submission of study-related documents in digital form. It allows studies to be followed through their different stages — from submission to final approval by the EC and CONEP, and, when necessary, also allows monitoring of the study progress through approval phases, including the submission of interim and final reports.


### About the Authors

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# Are Your Foreign Manufacturing Sites FDA-Ready?

By James Prutow, Frances Palomar, and Vignesh Ramesh


FDA inspections of overseas plants manufacturing pharmaceuticals and medical devices sold in the U.S. market are on the rise. The inspection frequency for a foreign manufacturing plant was once in nine years, as compared to once in 30 months for plants based in the United States, according to a 2010 GAO Report. While the FDA has long focused its time and resources to inspecting plants inside the United States, there is now a strong trend indicating a shift in this approach, driven by two major factors:

**Slowing U.S. Growth/Strong Overseas Demand:** Due to sluggish growth within the United States, it has become imperative for companies to drive down costs in order to remain profitable. The FDA realizes that more than 50% of pharmaceuticals and medical devices sold in the United States are supplied by factories overseas. As U.S. companies are expanding to meet growing demand from the global market, they are also trying to maintain a low-cost global supply chain.

**Major Quality Nonconformances From Market Leaders:** Another driver to the FDA's shift has been the recent wave of well-publicized quality mishaps from market leaders with a global manufacturing footprint. For example, quality issues at an Asian API supplier of a large pharmaceutical company resulted in multiple allergic responses and deaths in the United States. In another case, a global drug manufacturer suffered multiple international recalls in the past year. Finally, another large pharmaceutical company headquartered in Asia suffered a number of problems with its API supply resulting in extended quality holds and recalls in the United States. The agency is under intense pressure to ensure that the quality of drugs and medical devices sold in the United States meets required standards.

## THE FDA'S RESPONSE

In response, the FDA is stepping up its enforcement activities through warning letters, 483s, consent decrees, and other enforcement activities related to good manufacturing practices (GMPs). For instance, GMPs have doubled between 2008 and 2011. Additionally, the FDA's budget has nearly doubled since 2008, from $2.1B to $4.1B in FY2011.

In particular, the agency increased the 2011 budget for manufacturing plant inspections (domestic and international) to $135M — a jump of more than 30% from the previous year, according to a PwC (PricewaterhouseCoopers) analysis.

This increase in budget is equipping the FDA to pay increasing attention to overseas plants, among other high priority initiatives. To reinforce its presence abroad, the agency has added staff and/or opened international offices in every major continent and country in the past three years. In 2010, 10% of inspections were outside the United States; this percentage is expected to increase substantially with the addition of these offices.

## INSPECTIONS OF GENERIC MANUFACTURERS

In addition to the overall increase in resources, the agency is poised to receive a significant boost in international inspection funding over the next few years. Congressional leaders will deliberate on the proposed legislation in 2012, which will launch user fees for generics manufacturers. These fees are similar to what branded pharmaceutical companies have paid in the past and would fund the significant expansion required to inspect generic manufacturing plants overseas. These inspections would include the manufacturers of APIs as well as those of finished doses. Many of these manufacturing plants are also part of the global supply chain of brand pharmaceuticals sold in the United States.

The end goal is to bridge the large compliance gap between domestic and foreign inspections over the next several years. Therefore, life science executives should be prepared to face scrutiny of


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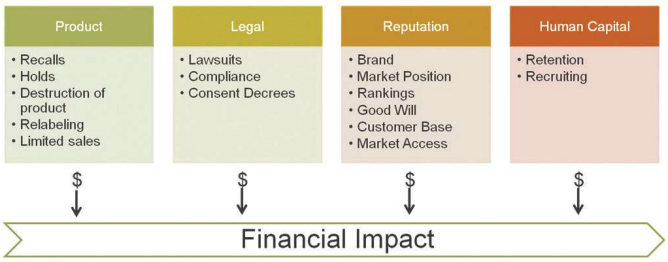
Figure 1: Impact Of Enforcement Actions From FDA




their overseas supply chain by the FDA.

## WHY SHOULD CEOs CARE?

Failed GMP inspections have an enormous impact on revenue and the brand of the company. Besides the obvious loss in direct product revenue from recalls, quality holds, import bans, and consent decrees, the brand of the company suffers. As illustrated in Figure 1, the impact of quality issues spans all business functions.

A poor report from the FDA could even damage partnerships with overseas suppliers. Governments and companies in developing countries are sensitive to quality problems, especially if the company is requesting permission to conduct clinical trials in that country. If a multinational drug or device company has a record of failed inspections, it might lose out to rivals in establishing or renewing relationships in those countries.

Conversely, successful FDA inspections could give a well-prepared company a competitive advantage. A company with a robust quality system is less likely to suffer disruptions from recalls, quality holds, or import bans. These companies can gain a reputation for reliability during a time of uncertainty and distrust within the global market.

To gain that advantage, executives should identify sites within their manufacturing network that might be a soft target internationally. At a minimum, foreign sites should be compliant with the quality system regulations (QSRs): 21 Code of Federal Regulations (CFR) 210-211 for pharmaceuticals and biotech and 21 CFR 820 for medical devices.

## HOW TO PROCEED

Managing compliance in the overseas supply chain can be an enormous challenge. It is important to set priorities and to prepare for a multistage process.

**Step 1 – Assess:** The first step is to assess the quality levels of all facilities, whether owned or contracted. Identify processes which are directly impacting product quality. Which sites need the most attention, because of their systemic issues or their importance in serving the U.S. market?

**Step 2 – Address Systemic Quality Gaps:** Next, systemic gaps in processes must be addressed with the approach of sustaining quality (vs. the band-aid approach). The goal is not just to get the paperwork in order but to invest in a culture of quality that can be preserved over time.

**Step 3 – Reassess:** Sustainability is key to success. Once the changes have settled in, companies need to reassess quality levels and capabilities — even multiple times. Managing quality is an ongoing effort, not just a one-time program. Figure 2 breaks these steps down in more detail.

The FDA's compliance list provides a good reference point for pharmaceutical and life science executives charged with assessing their company's quality systems. Through an empirical analysis of observations cited by the agency, PwC identified "hot items" to be aware of on the FDA's compliance list. While plants outside the United States may have different dynamics, the results indicate the FDA's leading concerns. For example, the most common failing had to do with the plant not following through on a corrective and preventive action

Figure 2: What CEOs Should Do


(CAPA) process in response to external complaints. The next most common observation involved inadequate or poor design controls. Poor training of personnel was also common. Lastly, inadequate risk management for both products and processes was a major shortfall. Compliance in all of these areas is required while building a discipline around quality. There is no quick fix.

## FORWARD-LOOKING EXECUTIVES WILL BENEFIT

The FDA is poised to ramp up foreign inspections in the near future. While some pharmaceutical and life science leaders may be tempted to put off quality measures overseas until clear regulatory oversight is established, forward-looking executives will make the most of the lead time to meet the new compliance challenge in a careful, sustainable way. They will address systemic issues by lowering cost, streamlining quality operations, and promoting a culture of quality. This investment will equip the company to remain competitive in this stringent regulatory era and position it for long-term advantages over the next decade.


### About the Authors

*Jim Prutow is a principal in PwC's Health Industries Advisory Practice, and Frances Palomar and Vignesh Ramesh are senior associates in PwC's Health Industries Advisory Practice.*

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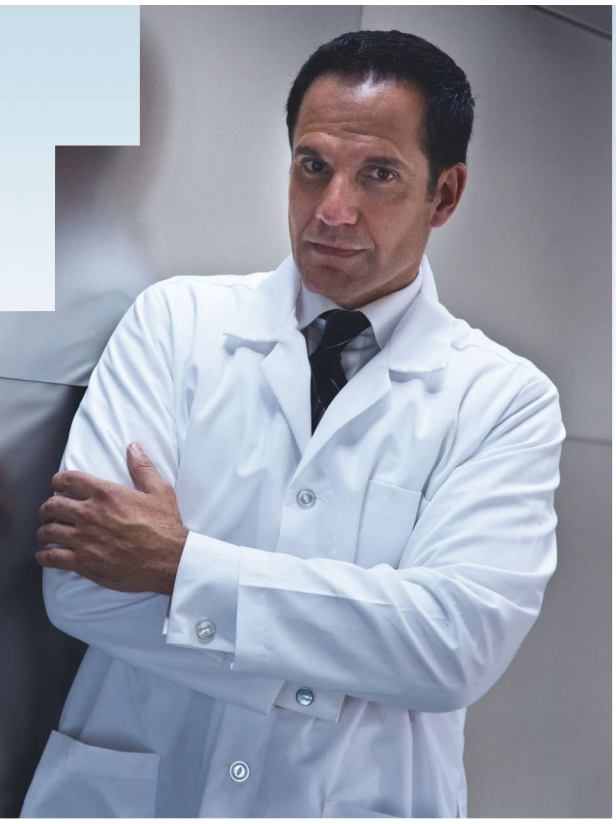



# What's Eating Big Pharma Innovators?

By Matt Gurin

Congratulations! You've been promoted. You're a global leader in the new R&D organization. This is exciting since you've been sweating the outcome of the long-impending transformation for over a year. The good news is that you will lead a global team spanning three continents. The bad news is that your drug development function will be spread across four global centers of excellence, and some of your colleagues will lose their jobs or be transferred.

You begin to formulate an inaugural summit in Singapore to launch the team and determine your priorities. Then the other shoe drops: Travel budgets were slashed as part of reorg, and the new global teams are expected to operate virtually. You take a deep breath. And then you ask yourself, "How can I drive a faster, cheaper, more innovative approach to drug development — asking people to take risks and behave in new ways — if I can't meet with my team to build the relationships and trust?"

This common scenario is just one example of the challenges R&D leaders face as they try to reposition the industry as a beacon of growth. In fact, at the very time that Big Pharma innovation is stagnant, its scientists report record-high levels of demotivation. According to our research, while traditional management approaches are mostly ineffective in motivating bench scientists or driving innovation, a combination of evolving leadership strategies and appropriate incentives is showing promise.

In a recent Hay Group study of more than 800 R&D professionals in Big Pharma, 56% of scientists described their working environment as "demotivating" and another 15% as only "tolerable." These scores are worse than any other function in Big Pharma. In fact, Big Pharma R&D's working environment — what we call organizational climate, or what it's like to work for a specific boss — is lower than the R&D functions of any sector in our database. And this was the case even before the recession. So how can organizations change the tide?

## CHASING BIG, CRAZY IDEAS

According to Naveed Shams, M.D., Ph.D., VP and head of Global Clinical Development and Medical Affairs for ophthalmic pharmaceutical manufacturer Santen, Inc., Big Pharma wants to innovate, but its size and complexity are roadblocks. "Once you are a certain size, with a certain amount of products and revenue, and you have shareholders, you become very territorial," he says. "You spend most of your energy preventing others from invading your territory." In such an environment, companies make sensible investments, such as tweaking a blockbuster drug that's threatened by a generic. But, says Shams, that's not innovation. "You can't make a good case for chasing after a big crazy idea that may pay off," he says. Between the CEO and the bench scientist, there are 13 or 14 layers at a typical Big Pharma company, according to Shams. "If an idea gets stuck in one of these layers, that's the end of it. This is the opposite of an entrepreneurial company."

Another feature of the innovation roadblock, according to Matt Daniels, an HR leader at Merck, is the need for leaders to educate their R&D employees about the new needs of the business. "Given the heightened focus on return on investment for R&D spending and reorganization activities, many leaders have not had the capacity to sufficiently educate their scientists about the changing needs of the business. As the pressure on pharmaceutical R&D organizations continues, it will be very important for leaders and managers to ensure that scientists know how their work aligns with both the scientific and business objectives of the organization."

According to Shams, not enough R&D leaders tie meaningful rewards to innovation. "You say, 'Okay, you are doing routine everyday stuff, but you have a crazy idea.' So, offer a big reward and say, 'Here is a time frame — 5 to 10 years, and here is a clear goal with well-defined criteria.'" That, he says, will encourage entrepreneurship and innovation.

In a 2003 interview in *Strategy & Leadership*, University of Pennsylvania's

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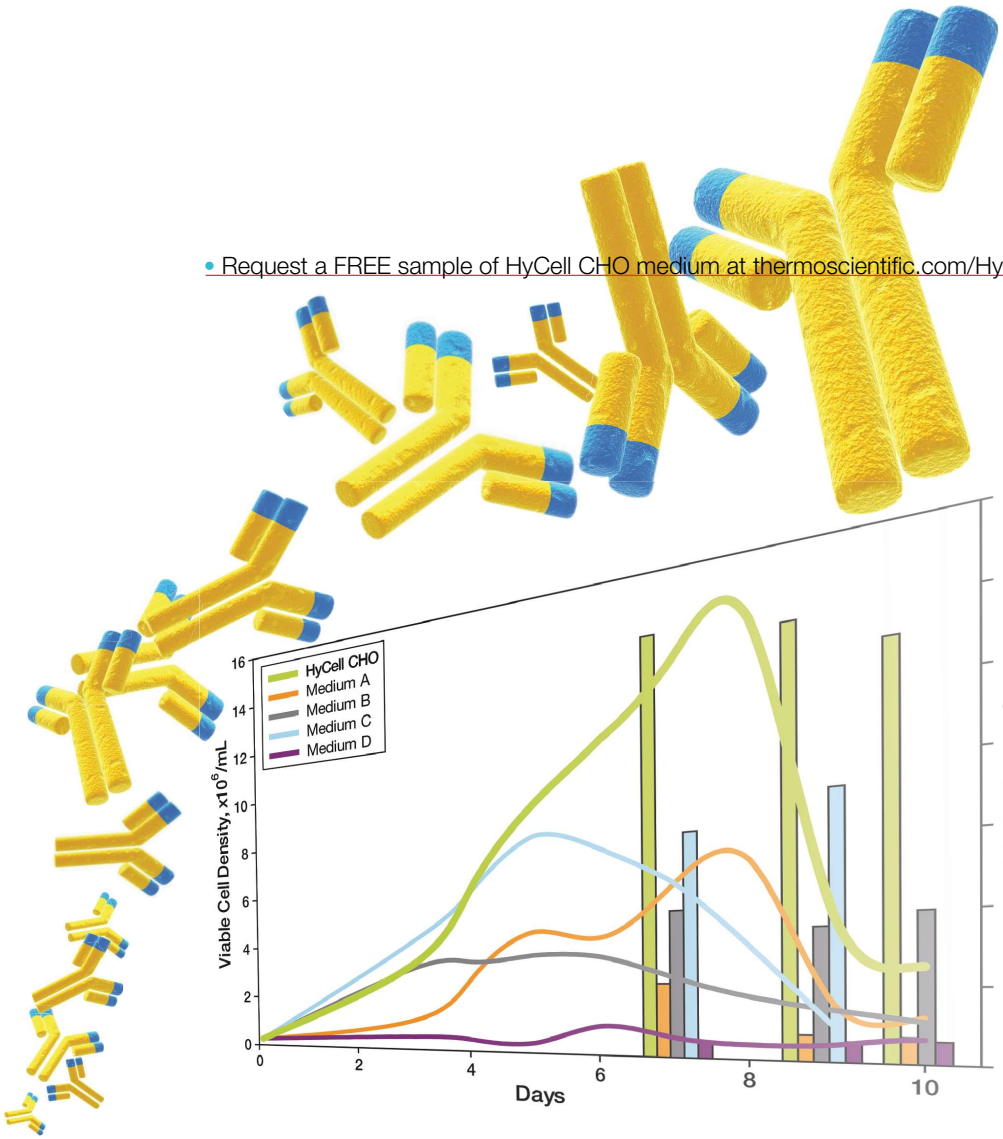


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noted systems thinker Russell Ackoff echoed Shams' thoughts: "Most managers currently manage the actions of their organizations' parts taken separately," he said. "This is based on the false assumption that improving the performance of the parts separately necessarily improves the performance of the whole. That is a false premise. In fact, you can destroy a corporation by improving its individual parts. Try putting a Rolls Royce engine in a Hyundai."

## MAKING A BUSINESS CASE TO SCIENTISTS

Another surprising finding from the Hay Group database: While conventional wisdom suggests that scientists are loners, they describe themselves as professionals who seek collaboration and acceptance from their peers. "Scientists will be more successful if they are able to collaborate well with others — both internally and externally," says Daniels. "The next great idea can come from many different sources, so it is important that scientists have an open mind and leverage learnings from internal peers and external sources."

This resonates with Hay Group research that suggests the most innovative scientists are the ones with the most productive multidisciplinary networks, not necessarily the ones with the greatest ideas. The reality is that scientists are different from most other groups of knowledge workers.

While this may not be popular in the short term, you should start by letting up — just a bit — on efficiency. Sure, it matters, but you also need to invest in enabling relationships and networks. Enable your scientists to share knowledge with external collaborators. This may bring up questions related to intellectual property, and it may require a conversation with the legal department. But, it's worth the time for a pharmaceutical manufacturer looking to unleash innovation. This strategy has worked in other industries and for global leaders such as Procter & Gamble and Intel.

## OPENING UP CAREER PATHS

In Hay Group surveys, fewer than half of the R&D respondents feel their performance is linked either to pay or to career advancement. Nor are they aware of the career paths that are open to them. Further, R&D professionals report issues that actively block innovation. Only 52% believe they are encouraged to take risks to increase effectiveness, despite the fact that risk-taking is a key part of innovation. Slow decision making is another obstacle to innovation. Only 48% of our R&D respondents say that "decisions are made without undue delay."

"I worked for a major biotech company for several years," says Shams. "When I joined, there were 4,000 employees," and he had fairly easy access to the CEO. "When I left, it was up to 12,000, and there were three layers to go through." During that time, he says, decision making slowed down. "The crazy ideas are not floating to the top. I say remove the layers, or create an environment where CEOs have access to the bench scientists. The top has to say, 'I will talk to this small group of mavericks.'" Whether it's an occasional informal get-together or a regular breakfast with scientists, CEOs must empower their scientists, he says.

Again, the leading experts seem to agree with Shams. According to the Harvard Business Essentials *The Innovator's Toolkit*, "Ideas are essential building blocks from which innovation and innovative technologies are made. By one estimate, it takes three thousand of them to produce a single commercial success." So, as former chairman William McNight of noted innovator 3M said, "If you put fences around people you get sheep. Hire good people, and then leave them alone."

Since Big Pharma companies are just that — big — what can one leader do to help foster innovation? We believe R&D leaders must address six key dimensions:

**Clarity:** Is it clear what kind of innovation is expected and how that relates to the big picture? Does my team know how much innovation I would welcome and how it could improve the company?

**Flexibility:** Are new ideas welcome? Do I set an example and a culture of openness to learning? Have we eliminated unnecessary red tape?

**Responsibility:** Do employees have the autonomy and authority to work without interference? Is reasonable risk-taking encouraged? Am I calm and encouraging when the inevitable disappointments occur?

**Team Commitment:** Do people feel they're in it together, working for a larger purpose? Do team members collaborate well? When someone has a partly usable idea, do I encourage the team to help develop it?

**Standards:** Are goals clear and specified? Are our performance standards realistic and "open-ended" enough to encourage innovation?

**Rewards:** Is excellent performance recognized and rewarded? Do I recognize not only my direct reports, but also those who are a level or two lower in the organization? Do I involve my manager in recognizing my group's innovations?

Again, congratulations on your promotion. As you approach new levels of complexity in Big Pharma and address key motivational issues in your R&D group, we're confident that this combination of strategies and incentives can motivate scientists, drive innovation, and deliver some big, crazy ideas.


### About the Author

*Matt Gurin is U.S. reward practice leader for life sciences at Hay Group. He works with senior executives and leadership teams to build effective organizations by ensuring strategic alignment of core organizational processes and systems.*

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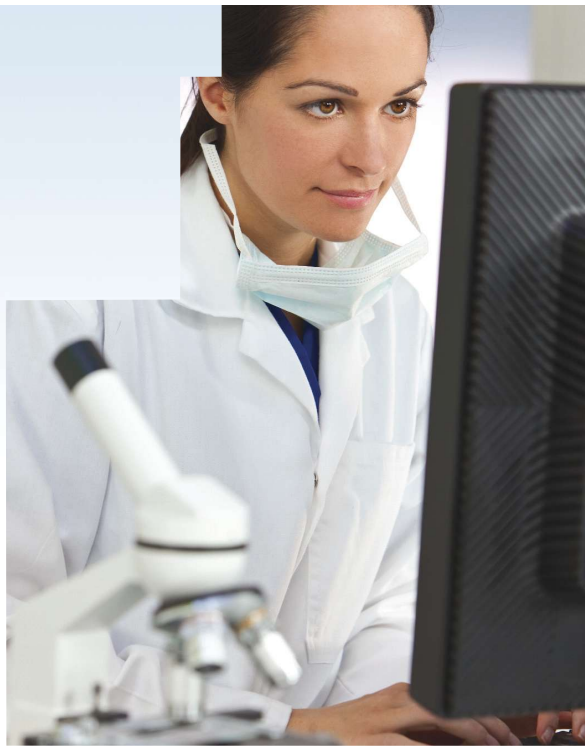

By Alec Fishburne and Malia McFatridge

Since 1989, the Lynn Health Science Institute (LHSI) has been conducting comprehensive medical research. Bringing new drugs to market through its clinical trials program, LHSI has extensive experience in a number of areas, including chronic digestive diseases; cardiovascular diseases and hypertension; disorders such as asthma, lung infections, and cystic fibrosis; women's health; urology; rheumatoid and osteoarthritis; and sleep disorders. LHSI has completed more than 300 clinical trials, working with more than 200 pharmaceutical companies and CROs.

As a busy, growing research organization with multiple site locations, LHSI needed a way to manage the dozens of clinical trials the sites could be conducting at a given time. To produce its reports, LHSI had previously relied on data collected in spreadsheets. However, this method was extremely time consuming. Employees had to manually complete a spreadsheet record of their activities, which required merging various files to complete the reports. And many times, reports contained incomplete or inaccurate data, resulting in delays in getting reports finalized. LHSI was spending at least one week per month collecting data from the spreadsheets, ensuring the data was complete and accurate, and finally generating reports. Seeking a solution, LHSI, which had previously worked with StudyManager and knew that its CTMS (clinical trial management system) product would help improve its workflow, implemented StudyManager Reveal to manage its clinical studies, and is now realizing a variety of business benefits.

## REAL-TIME MONITORING

The ability to measure revenue in real time is critical to any business, as a current revenue position is essential in understanding progress made toward revenue targets. Previously, LHSI had only month-end revenue metrics, with no efficient method to gauge progress prior to month end. In the absence of key benchmarks, identifying efficient, data-driven course corrections to successfully impact month-end financials was a challenge.

"We couldn't monitor benchmarks or look ahead at what we could anticipate in terms of expected patients and appointments," says Christine Ferguson, assistant director of finance, LHSI. "For example, our coordinators have a specific number of patient visits they need to complete to help us meet our business goals. Because our coordinators reported their patient visits to us only at month's end, we had little indication as to whether we would meet our business goals for the month until the month was already over. It would take our coordinators about a week to enter data into spreadsheets. Our department then had to review and analyze this data and recompile the data into revenue reports."

This process is now automated by the Reveal application. Instead of a collection of workbooks and worksheets, all of the studies and data on patients are now in one central system. The company can set its users' permissions so that only their own studies and patients are visible. There is no longer a need to merge various files together in order to create reports because the reports LHSI has built into Reveal provide the company with updated results in one central location.

Ferguson adds that operational and financial planning is also more effective with Reveal. "Throughout the month, we can assess where we are in relation to our goals. It's a much more proactive approach that the after-the-fact, month-end reports don't allow. If it seems we aren't on target for the current month's goals, we can assess upcoming visits since our coordinators also schedule their study patient appointments in Reveal."

## FASTER PAYMENT PROCESSING

At any point in time, LHSI may be involved in dozens of clinical trials, which made generating reports a labor-intensive process. Using Reveal, LHSI has cut reporting times down from a week-long process to just a few hours.

"Our previous method was extremely cumbersome. We needed a better way to streamline data collection and reporting, as well as a more accurate method for tracking coordinator productivity and amounts we owed to our service providers," says Ferguson. "With Reveal, we don't have to spend as much time trying to collect the information we need. Now our coordinators can quickly record the information we require, spending less time on data entry and devoting more time towards making each study a success. As a result of this time savings, our productivity has improved dramatically."

Reveal also has helped LHSI reduce time spent on payables, which are built into Reveal up front. "It used to be a week-long

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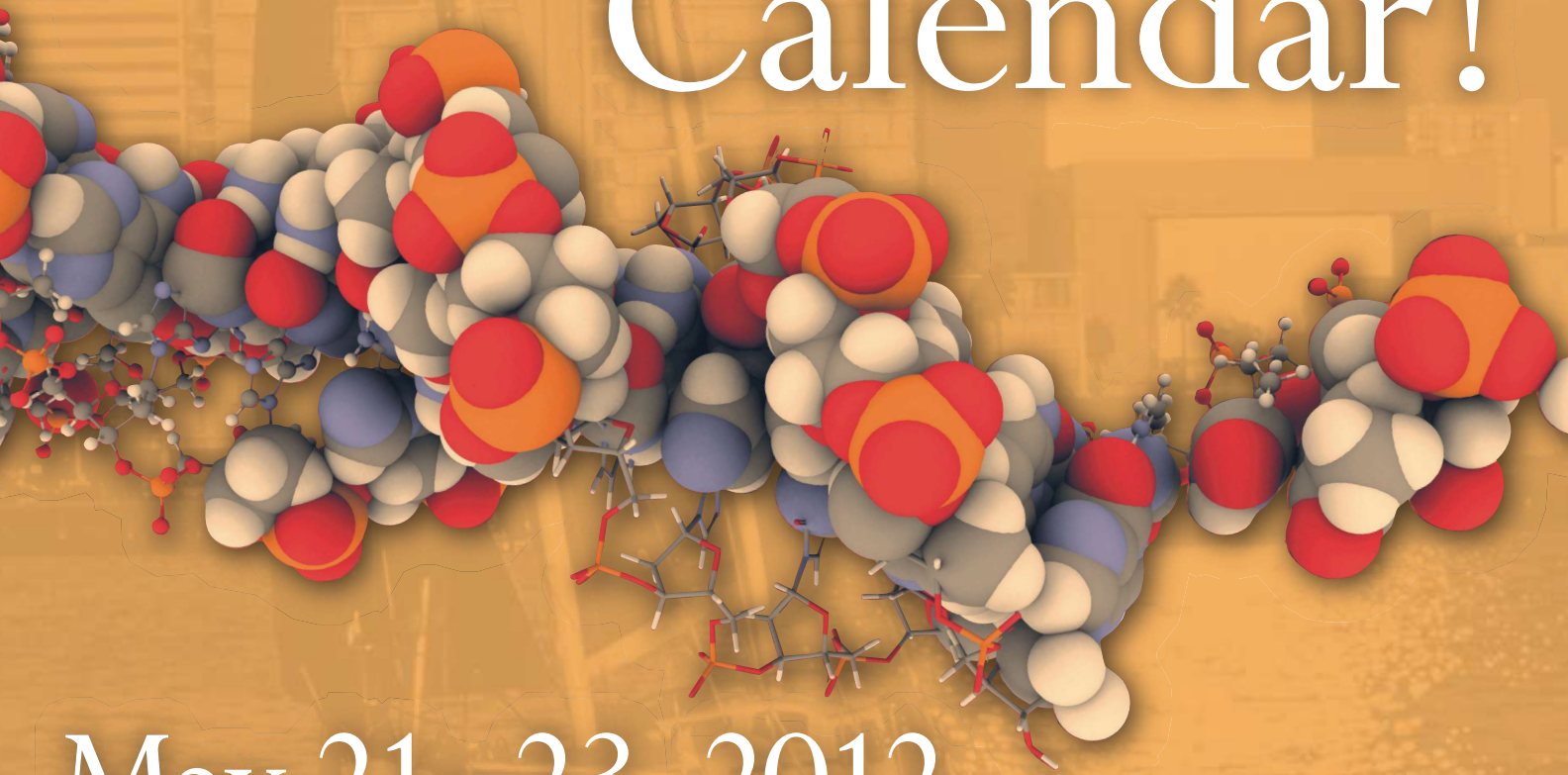

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process to gather spreadsheets, approach each coordinator with reminders to submit any missing or incomplete information, and then consolidate that data in order to cut checks. Now we've reduced the process down to a matter of hours. Our coordinators can log in to Reveal and track their completed visits, and Reveal records the appropriate revenue and payable amounts instantly and simultaneously," Ferguson says.

## REAPING MULTIPLE BENEFITS

Reveal's document tracking feature provides central management of study files, which helps LHSI meet regulatory requirements by ensuring the most recent, approved documents are available to users. "Ensuring use of the correct study documents is much easier now, as we have the ability to upload them to a secure location, accessible from wherever the coordinator is working that day," adds Ferguson.

Another advantage of using Reveal is enhanced business development efforts through LHSI's use of the application's search feature. Since all searches are saved by default, with just a few mouse clicks the company can quickly get the information it needs to fill out site questionnaires for clients, which is the information they need in order to award LHSI with its latest study. After the study is awarded, the company can use the same saved search to identify and reach out to potential participants who are already prequalified. Also, in addition to improved reporting functionality and more efficient data collection, LHSI is realizing greater productivity. One example is the at-a-glance reports, which help monitor patient enrollment to inform or refocus recruitment efforts.

Overall, Reveal has provided multiple benefits to LHSI. Users can log in to one system to schedule their appointments, record completed visits, or download and print study documents. LHSI only has to set up a study once, regardless of how many sites are participating. Reveal even allows each site on the same study to have different budgets.


### About the Authors

*Alec Fishburne is VP of operations at StudyManager and has worked with numerous research organizations as a business process consultant, project manager, and software developer.*

*Malia McFatridge is senior project manager at StudyManager. Previously she worked at a clinical research site in Honolulu for eight years, with experience working in the lab, with regulatory submissions, and as a coordinator.*

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# Optimizing Late Phase PRO Collection With Mobile Technology

In line with recent FDA and EMA guidelines, greater emphasis is being placed on patient reported outcomes (PRO) as a key source of safety and effectiveness data. This emphasis is of particular relevance to late-phase (post-approval) research in which safety evaluation of new products, in addition to the assessment of real-world effectiveness, are two key focuses. Accurate and consistent PRO data is a fundamental part of determining product safety, minimizing risk, and further establishing the clinical and commercial benefit of a treatment. Study design, nature of the intervention, and the target population are all aspects which must be considered when selecting the most appropriate and effective PRO instrument.

The long duration and episodic nature of late-phase studies often results in poor levels of patient engagement and compliance, which can have a negative impact on the accuracy and completeness of PRO data. The smaller budgets associated with late-phase trials, combined with their large scale and long time frame can pose a significant challenge. As a result of this, adoption of technology for the collection of electronic patient reported outcomes (ePRO) data in late-phase research has typically been minimal due to the hardware costs and associated logistics. Additionally, the large population size and resulting patient diversity of late-phase studies means it can be problematic for sponsors to find a PRO model that is flexible and accessible enough to blend unobtrusively into the 'real life' setting of individual participants' lives.

## MOBILE ePRO SOLUTIONS

Technology providers are increasingly recognizing the mobile/cell phone as a simple and effective interface for PRO collection with global reach. The accessible and easy-to-use nature of mobile technology offers a patient-centric approach that is ideal for late-phase studies, enabling patient data capture as close as possible to the point of experience. Cell phone-based ePRO also minimizes many of the logistical problems and cost implications associated with the use of standard ePRO technology for clinical trials, such as the distribution, training, maintenance, and recovery of devices, providing a cost-effective solution to smaller late-phase budgets.

The simplicity and intuitive design of mobile technology removes the problem of patient reporting being too time-consuming or onerous, therefore enhancing compliance rates, regardless of age and demographics. Where specific and targeted data collection is required, patients can complete questionnaires via a series of text messages sent intermittently to their own cell phone. If a response by the patient is not received within a certain time frame, a text message reminder can be automatically sent in order to prompt a response. This is extremely valuable for late-phase trials running over long time frames, ensuring that participants remain motivated and compliant no matter what the length of time between visits or surveys. In addition, the ability to capture patient data in "real-time" means that investigator site staff can be alerted to abnormal patient data and react accordingly to ensure patient safety.


## Judith Teall

Judith Teall joined Exco InTouch in 2010 as director of patient recruitment. Prior to this appointment she headed patient recruitment for GlaxoSmithKline across Europe, Asia Pacific, and Africa. She has more than 20 years of experience in the pharmaceutical clinical research area.


Where more complex patient data or lengthier responses are required, eDiaries can be deployed. Patients receive a simple text message with an embedded link to a secure mobile Internet site that contains the eDiary. On connecting to the mobile internet URL, the patient enters their unique PIN number to access the ePRO questionnaire. This type of technology enables a wide range of questions to be presented and viewed on most cell phones.

As mobile technology continues to be used on a global level for an increasing range of commercial and personal applications, it provides an ideal vehicle to engage with patients and collect real-time and accurate data. Offering a cost-effective technology solution for late-phase studies, mobile ePRO can facilitate enhanced compliance rates, real-time patient progress and compliance monitoring, health tracking, and reporting. In addition to accurate PRO data, the accessibility of mobile technology means that it can be deployed for prospective patient recruitment, observational studies and registries, risk management strategies, disease management, and patient retention programs.

# Congratulations to Carolyn Buck Luce

## 2012 Healthcare Businesswomen's Association Woman of the Year

Ms. Buck Luce's accomplished career includes over 20 years at Ernst & Young, where she is the Global Pharmaceutical Leader for life science clients. The HBA community recognizes Ms. Buck Luce for her decades-long leadership in healthcare and life sciences as well as her tireless efforts for the advancement of women in the industry.

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# How RFID Is Changing The Pharma Cold Chain

Life sciences products have grown more complex, and this complexity often increases product value — and sometimes — temperature sensitivity. Either outcome places a greater burden on cold chain professionals to reduce risk.

Many companies consider wireless technologies to improve temperature monitoring efficiency. RFID is a primary component of this approach. In common usage for the past 20 years, RFID loggers (i.e. tags) store product information in a similar fashion to bar codes. Unlike bar codes, however, they wirelessly transmit data without requiring a clear sightline or close contact with a reader.

Temperature monitoring tags with RFID technology incorporate a sensor that captures the ambient temperature at specific intervals. Sensors are calibrated to detect high and/or low temperatures. Any temperature excursion triggers a visual indication on the tag and also records the temperature, date, and time.

The tough, flexible RFID packaging, about the size and weight of a matchbook, fits well in harsh shipping environments with limited space. In addition to eliminating bulky, sensitive electronic devices, RFID tags speed access to temperature monitoring data.

## THE ADVANTAGES OF RFID

Wireless capabilities allow workers to start, stop, or read the tags without opening boxes. Data from thousands of tags can be captured and reviewed on mobile readers before being downloaded to a PC. Traditional monitoring devices, in contrast, must be unpacked from boxes and taken to a PC for downloading. Report generation often occurs off-site, days later. As a result, RFID tags offer much faster data retrieval.

Another advantage of RFID temperature monitoring involves logistics, with its goal to save time and costs. The benefits of wireless data access, compact packaging, toughness, reusability, and streamlined handling and administration simplify temperature monitoring processes, reducing expense. In addition, RFID tags offer a low cost per use. More important, the logistical benefits favor widespread use of the devices for greater coverage and risk reduction.

Along with simplified logistics, ease of use contributes to the effectiveness of a temperature-monitoring solution. Unskilled shipping workers are less likely to take precautions with sensitive electronic devices, or know how to process or use them. The design of RFID tags encourages interaction. A flashing LED indicates a temperature excursion. Simple directions tell the user to push a button to stop recording. Some versions even embed the logger in a postage-paid postcard for easy processing.

The search for streamlined temperature monitoring represents a growing need for precise monitoring of product quality and care through faster data access. It's especially critical for life sciences products, where temperature excursions may have dire consequences. In pharmaceuticals, for example, shipments worth millions of dollars are at risk. Temperature damage to biologics, medical devices, clinical specimens, and medicines may affect people's health or endanger lives.

## REGULATIONS DRIVE RFID ADOPTION

Regulatory guidelines highlight the primary role RFID will play in the life sciences industry. The FDA's Compliance Policy Guide (Sec. 400-210) "Radio Frequency Identification Feasibility Studies and Pilot Programs for Drugs" states: "We believe that use of RFID technology is critical to ensuring the long-term safety and integrity of the U.S. drug supply."

While the FDA study focuses on counterfeit drugs, the targeted completion date of Dec. 31, 2012 will likely have implications for the overall safety of these products. The guide further explains that RFID tags may include other information, such as storage and handling conditions. Temperatures and expiration dates fall under these categories and will need to be monitored. Whatever the study outcome, the FDA clearly states that the December 2012 date "should provide sufficient time for the industry to gain experience with RFID technology."

It's only a matter of time before smartphones take on a new role in the cold chain of life sciences companies. Smartphone temperature monitoring apps already exist that read RFID tags. They provide immediate insight and instantly upload data to cloud applications for access throughout the organization by authorized users.


## Lee Marts

Lee Marts is the quality assurance and regulatory affairs manager for American Thermal Instruments, Inc. He received a Bachelor of Science degree from South Dakota State University in agriculture and education, and has 30 years experience in education and manufacturing.

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# Renewing Your Business Model

By Leo Hopf

In every business there comes a time when continuous improvement no longer leads to success. This is the inescapable reality of the business lifecycle — all businesses mature and eventually decline. When you are approaching the inevitable decline, it is time to renew your business model.

But how do you make changes to your business model when everyone is busy running the business? And, how do you even begin when there is no one person tasked with renewal, no defined renewal process, and when most organizations are hesitant to take risks?

## The Renewal Process — Rethink, Reinvent, Reposition

The renewal process provides a roadmap to structure the renewal conversation, and provides the milestones and timeline to keep the conversations on track. The renewal process has three phases — rethink, reinvent, and reposition.

The objective of the rethink phase is to identify which pieces of your portfolio need renewal and which do not. Rethink consists of these three parts:

**Scan:** Evaluate your portfolio and develop an initial list of renewal candidates.

**Size:** Estimate the potential value uplift for each renewal candidate. You don't have time to renew parts of your business that do not provide the opportunity for dramatic value gains.

**Select:** Develop your final list of renewal candidates and prioritize them against other ongoing and proposed initiatives competing for management attention and funding.

### Reinvent

The objective of the reinvent phase is to create a powerful renewal strategy. Reinvent consists of three parts: structure, stretch, and screen.

**Structure:** Define who will make the decision and who will do the work. In addition, explicitly state the assumptions you will make to simplify and focus your work.

**Stretch:** Push your team beyond the boundaries of their previous discussions. Almost by definition, everything they have already considered has not been sufficient to renew the business.

**Screen:** Evaluate your renewal alternatives against your organization's key value measures to identify your preferred renewal path.

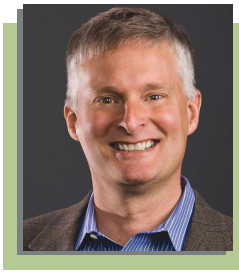
### Reposition

The objective of the reposition phase is to make the transition from the old business model to the new one. Reposition consists of the following three parts:

**Schedule:** Define the discrete projects that will move the organization from the old business model to the new one.

**Secure:** Ensure that sufficient resources are allocated to successfully complete these projects by the deadlines you have set.

**Switch:** Manage the transition in both the marketplace and within your organization. This switch must be managed effectively because you will be redefining who you are and what you do in the eyes of your customers and your employees.



Mr. Hopf works with senior executive teams and boards to bring clarity and alignment to their most pressing strategic issues. He is the author of *Rethink, Reinvent, Reposition: 12 Strategies to Renew Your Business and Boost Your Bottom Line*, which was named the book of the month for July, 2010 by the Institute for Management Studies.

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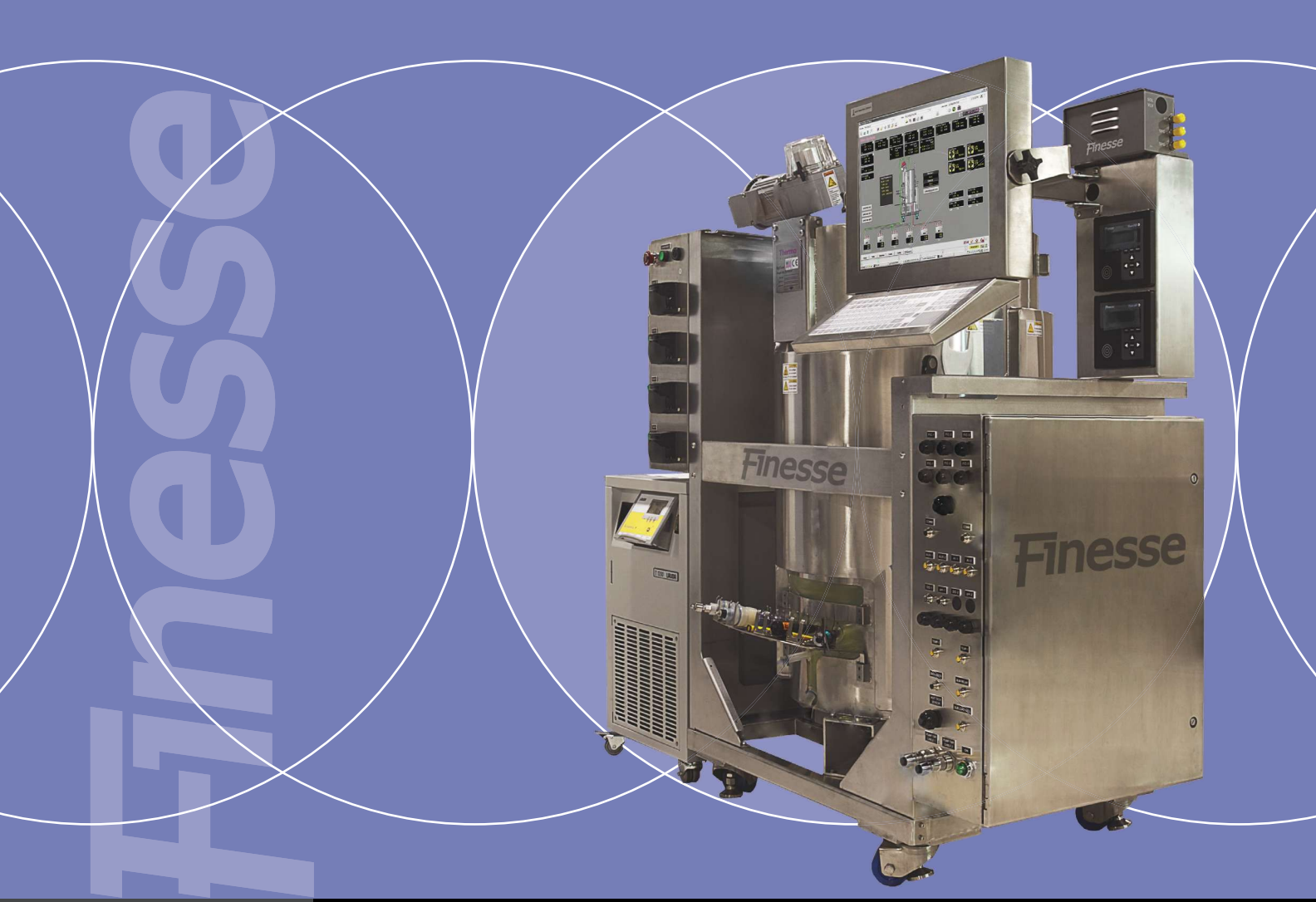


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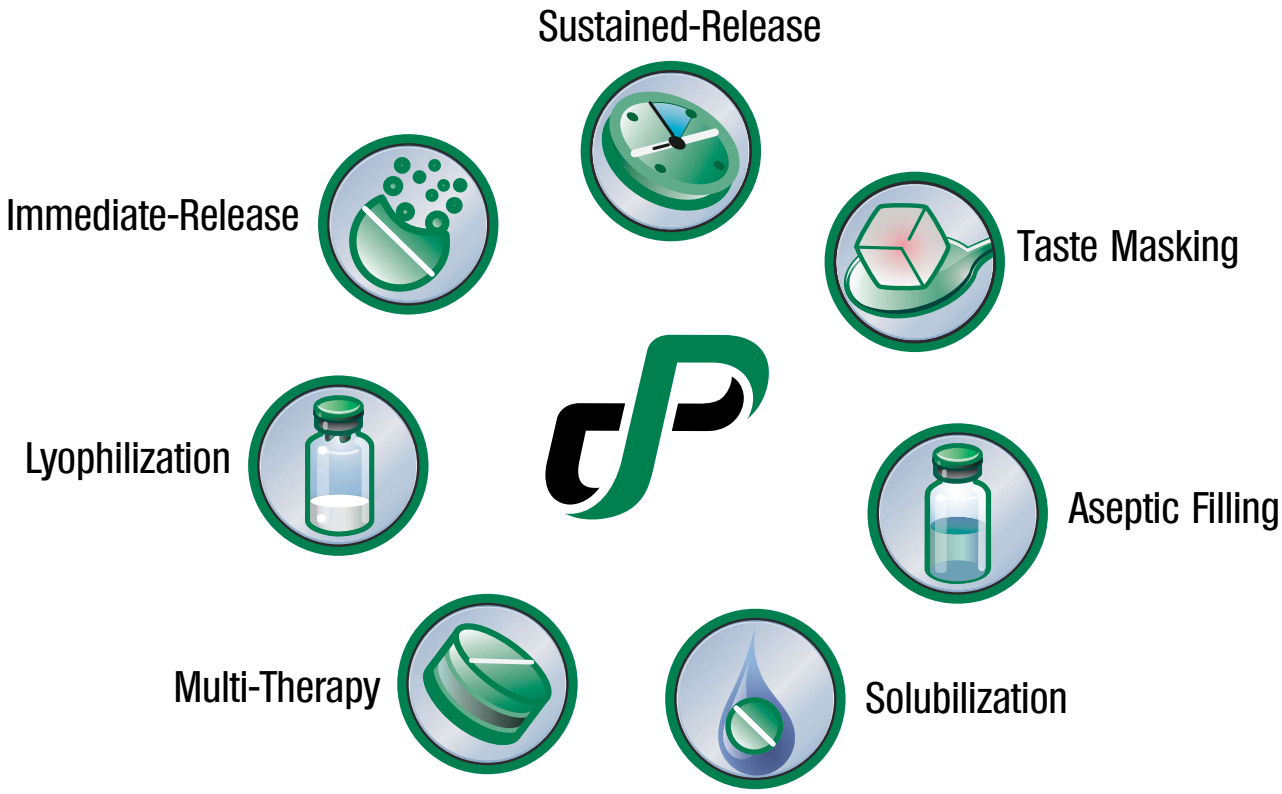


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Published 9/11 PATH0214R0

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