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July 2012
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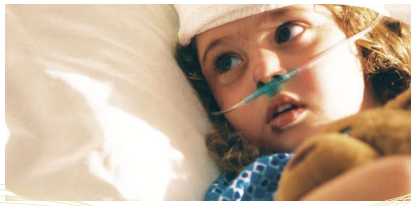

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18 FEATURE: PFIZER

"In the Pfizer of only a few years ago, if we saw something on the outside that we liked, we'd go ahead and buy it. Now we do alliances and limited acquisitions," says Jose-Carlos Gutiérrez-Ramos, Senior VP, BioTherapeutics Research & Development Group, Pfizer.

July 2012

DEPARTMENTS

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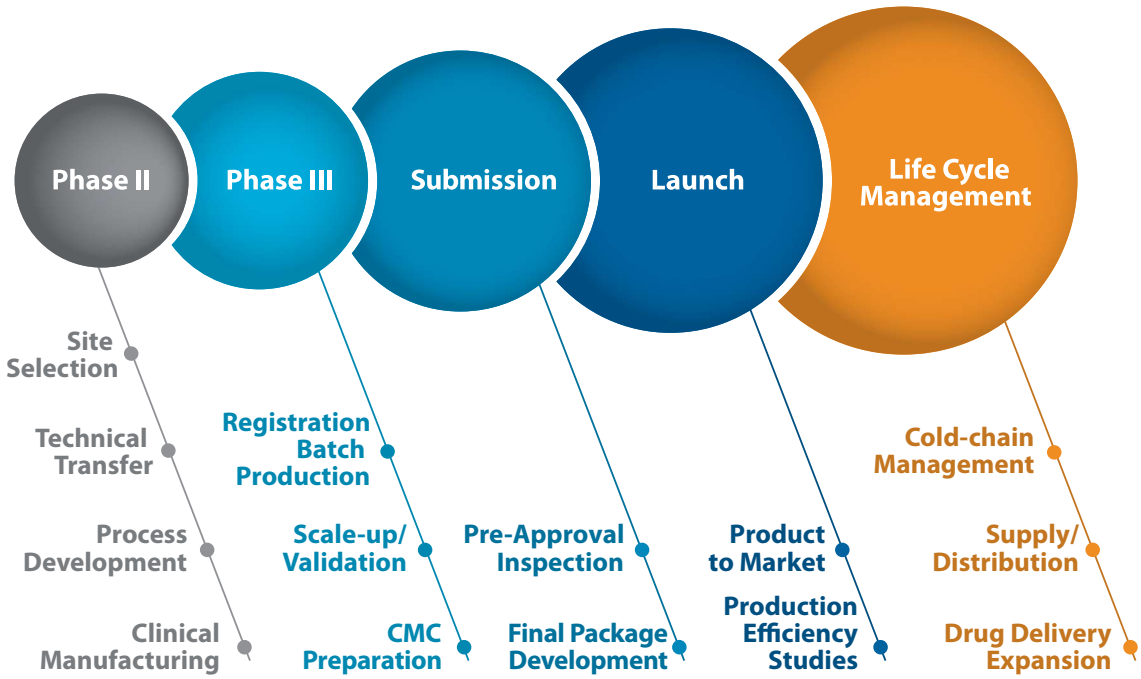

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EDITOR'S NOTE

Part Of The Solution, Not Part Of The Problem

When I worked in the pharmaceutical industry, one of my favorite sayings was, "Be part of the solution, not part of the problem." In the March 2012 issue of *Nature Reviews Drug Discovery*, the authors of "Diagnosing The Decline In Pharmaceutical R&D Efficiency" describe the causes of the pharmaceutical industry's R&D problems. They state their aim as being, "To provoke a more systematic analysis of the causes of the decline in R&D efficiency."

In my opinion, a more systematic analysis is part of the problem and not part of the solution. The reason for the decline in pharmaceutical R&D productivity is simple — companies strayed away from their core ideology. For example, regulators became more cautionary because companies launched unsafe products. In one of the best-selling business books of all time, "*Built To Last: Successful Habits of Visionary Companies*," authors James Collins and Jerry Porras identified 18 companies as visionary and attribute their enduring corporate success to having core values and a core purpose, which remains fixed. Only one pharmaceutical company, Merck, appeared on this list, published in 1994. In 1999, Merck launched the NSAID (nonsteroidal anti-inflammatory drug), Vioxx, which was voluntarily withdrawn from the market for safety reasons in 2004. Documents reveal that the company was aware of the problem as early as March 2000. All of this took place under Mr. Raymond Gilmartin, who served as Merck's CEO from 1994 to 2006. Today, Gilmartin, an adjunct professor at the Harvard Business School and *Harvard Business Review* blog contributor, believes that CEOs of many corporations have relied on a "flawed set of beliefs" which have "influenced them to place way too much emphasis on maximizing shareholder value and not enough on generating value for society." As a former Merck employee and current shareholder, I agree with his assessment and wonder if he wishes he had done things differently during his tenure as CEO.

The solution — get back to the core ideology, which starts with focusing on what is best for the patient. A good place to start is for pharmaceutical companies to embrace charities, foundations, and advocacy groups, for they can provide ready access to a pool of patients interested in participating in clinical trials. Once perceived as a problem to be tolerated, these organizations have evolved into the solution to pharma's R&D woes. Founded out of parent desperation and patient frustration, these groups seek products not profits, are highly focused, and are highly motivated to partner with industry to find treatments and cures. Perhaps, not-for-profits are just what the doctor ordered for stimulating pharma R&D, as well as helping pharma companies to get back to their core ideology — part of the solution, not part of the problem.

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CHIEF EDITOR'S BLOG

Our Chief Editor, Rob Wright, has been pondering naming his blog. How about "Rob's Rants" or "Wright Writes?" Or, maybe you have a good idea for a name. If so, send him an email at rob.wright @lifescienceconnect.com. He writes about a variety of issues such as recent shows attended, conversations with industry experts, and irritating business buzzwords. And don't forget about your opportunity to pick the brains of our editorial board. Send your questions for our monthly "Ask the Board" section to atb@lifescienceconnect.com.

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Q: What are the most important things to consider when developing/redesigning a company's leadership/mentoring program?

Leadership and mentoring are two different but related things. A good mentoring program requires training for its participants so there is a shared understanding of who mentors are and who their protégés might be. Most of the literature on mentoring cautions against using persons in the direct reporting line as mentors as there is often conflict between the role of mentoring and supervising. With the anticipated onslaught of about-to-retire baby boomers, some progressive companies are beginning to develop mentoring programs for their retiring talent. Rather than letting them disappear, they are asking them to stay on as part-time consultants and often using their experience to mentor the next wave of replacements. The connection to leadership can be made in the selection of the best about-to-retire persons to serve as mentors.

Dr. David Frew
Frew is a visiting professor at Mercyhurst College in the Graduate Organizational Leadership Program. He is also professor emeritus at Gannon University. He has served as a consultant to dozens of regional, national, and international clients.

Q: How will the new reauthorization act impact VC funding in life sciences?

As part of the reauthorization act (H.R.1540), small businesses that are majority-owned by VC firms are now allowed to compete for small business innovation research (SBIR) funds. Participation in the program assumes that VCs will be on board with the full disclosure of ownership information, the effort to meet the eligibility criteria, and the alignment of the VC's goals with those of the SBIR agency. The initial effects may be positive: VCs can now invest in SBIR-backed companies in initial rounds without affecting the company's momentum in the program. Additionally, VCs will certainly push their portfolio companies to obtain nondilutive SBIR dollars, which would generate data that could decrease risk and increase the probability of success. But this may trigger an overall decrease in VC funding in subsequent rounds, as the VCs may expect the government to take more of the risk.

Dr. Laura Hales
Hales has more than a decade of experience in biologics discovery research and is currently a founder of Extend Biosciences and The Isis Group.

Q: Why aren't Big Pharma companies striving to rediscover manufacturing as a competitive advantage instead of just outsourcing?

Pharma manufacturing efficiency might not yet have reached optimum levels, but the considerable efforts of Big Pharma in this area should not be underplayed. For example, the partnership between MIT and Novartis to develop continuous manufacturing strategies points to ambitious long-term aspirations, while in the United Kingdom, the recent announcement of substantial investment in the GSK manufacturing site at Ulverston underlines ongoing commitment to in-house production.

In the area of powder processing, QbD (quality by design) and PAT (process analytical technology) have helped focus attention on manufacturing, stimulating interest in instruments and technologies that accelerate and optimize successful process development. It seems Big Pharma plans to play a vital role in transforming production, both with in-house action and through collaboration with trusted partners.

Tim Freeman
Freeman is director of operations for powder characterization company Freeman Technology. He has 10 years' experience in understanding and characterizing powder behavior and works closely with the pharma and powder processing industries.

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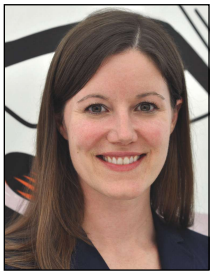

OUTSOURCING INSIGHTS

What's The Buzz Around Oncology?

By Kate Hammeke, research manager, Nice Insight

Heightened interest in developing cancer treatments, combined with R&D efforts during the past decade, contribute to the type of positive news that was aired at the American Society of Clinical Oncology's annual meeting in June, where the emergence of a class of "smart bomb" therapies was reported as one of the most hopeful developments in the field. These drugs use antibodies, which bond to specific cancer cells to deliver a very toxic ingredient directly to the cancerous cell while leaving healthy tissue alone. The second major development reported to have demonstrated some success uses the body's own immune system to fight cancer — an idea that has been around for a century. But training the immune system to recognize cancer cells as an "enemy" and attack them had previously met with limited success. These potential new types of therapies, combined with progress in diagnostic tests that will help to more accurately predict which medicines will work for which patients, are important tools in reducing cancer deaths — and consequently carry huge potential for developers that can bring them to market. What does this momentum mean for the outsourcing market?

Between January and the end of April 2012, the FDA approved 6 oncology drugs — a faster pace than 2011, when 12 oncology medicines were approved, comprising 1/3 of new drug approvals for the year. The large number of oncology therapies being investigated and developed should come as no surprise, considering cancer is a leading cause of death in the United States, second only to cardiovascular diseases. The vast market for cancer treatments has promoted this disease to a major therapeutic area of focus in the drug development pipelines of 1/3 of all pharmaceutical and biotechnology businesses.

FILLING PIPELINES WITH ONCOLOGY TREATMENTS

Looking at the different sponsor segments, Nice Insight research data show that 45% of Big Pharma companies have oncology drugs in their development pipeline, consistent with the 46% who indicated so in the Q1 survey. Biotech sponsors follow Big Pharma, where 40% include oncology medicines in their drug development pipeline — an 8% increase from 32% in Q1. Specialty pharma showed a slight drop from 29% to 26%, as did emerging biotech, down from 31% to 29%. However, emerging pharma sponsors demonstrated an increased interest in oncology as a therapeutic area of focus, rising 5% between Q1 and Q2 to 18%.

The results from the Nice Insight pharmaceutical and biotechnology outsourcing survey show that sponsors typically have two to three different therapeutic areas of focus in their drug development pipelines (2.2 in Q1 and 2.31 in Q2). Among the businesses whose pipeline includes oncology medicines, 82% are engaged in the development of biologics-based therapeutics. These respondents are heavy outsourcers, averaging 6.9 different services in 2012, as compared to the overall average of 5.3 different services outsourced this year.

This heavy outsourcing is accompanied by substantial outsourcing expenditure. Forty-one percent of businesses whose therapeutic area of focus includes oncology diseases indicated they will spend more than $50M this year, compared to 26% of the overall respondent group. Thirty-six percent will spend between $10M and $50M, versus 41% of the overall, and 22% had an outsourcing expenditure under $10M, significantly lower than the overall at 33%.

As such, sponsors with a therapeutic focus in oncology have considerable influence over the market size of the services they outsource. Looking at spending across each service included in the quarterly survey, data showed that for 12 of the 25 services, projects related to oncology therapeutics accounted for the greatest percentage of the service's market size. The next tier of expenditure can be attributed to services outsourced for the development of cardiovascular therapeutics.

Despite extensive focus, the American Society of Clinical Oncology states that the cancer community is still experiencing severe and worsening shortages of many critical therapies for a myriad of reasons. So demand and advocacy appear set to continue to promote opportunities and interest in the development of new therapies to counter the scourge of cancer.

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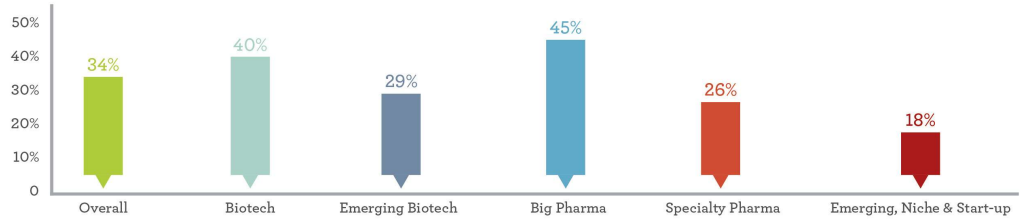
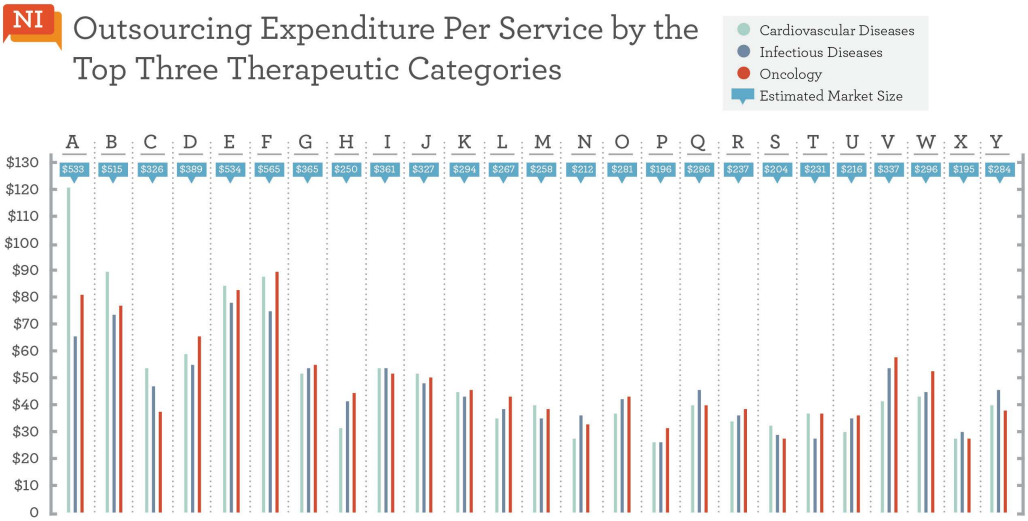
NI Oncology as a Therapeutic Area of Focus Among Each Sponsor Group



NI Outsourcing Expenditure Per Service by the Top Three Therapeutic Categories



A Analytical testing
B Bio-analytical testing
C Blending projects
D Chemical synthesis projects
E Clinical research
F Consulting services
G Custom Manufacturing
H Cytotoxic projects
I Data management
J Drug delivery systems
K Fill & finish projects
L High potency compounds
M Logistics & distribution
N Lyophilization projects
O Packaging services
P Formulation/Pre-Formulation
Q PEGs
R Product characterization projects
S Process optimization projects
T Regulatory support
U Stability, storage & testing projects
V Sterile compound research & development projects
W Toxicology testing projects
X Drug metabolism
Y Environmental testing

Survey Methodology: The Nice Insight Pharmaceutical and Biotechnology Survey is deployed to outsourcing-facing pharmaceutical and biotechnology executives on a quarterly basis/four times per year [Q2 2012 sample size 2,402]. The survey is composed of 750+ questions and randomly presents ~35 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 than1,200 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, Innovation, Regulatory Track Record, Affordability, 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

Can Single-Use Technologies Solve Downstream Bottlenecks?

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

Downstream operations continue to be a source of bottlenecks in the bioproduction process, with much of this attributable to an inability to keep up with increased upstream productivity and yield. Our just-released *9th Annual Report and Survey of Biopharmaceutical Manufacturers* evaluated ways in which the industry is tackling this problem, specifically with regard to new downstream processing (DSP) technologies being considered.

Topping the list of 21 different new technologies under consideration this year are disposable ultrafiltration (UF) systems, with close to half (47.1%) of the more than 300 global biomanufacturers we surveyed indicating they are at least considering this as a solution this year. After disposable UF systems, the next tier of solutions being considered include buffer dilution systems/skids (42.6%) and use of high capacity resins (41.2%). Following these were 18 other alternatives, many of which are single-use.

At least a quarter of the respondents are evaluating single-use technologies such as prepacked columns and membrane technology, while relatively fewer are drawn to chromatography alternatives, precipitation, and simulated moving beds, among others. It is interesting to note that single-use/disposable solutions continue to be prominent, accounting for 4 of the top 10 technologies being considered by the industry.

ANNUAL TRENDS

A comparison of this year's data to last year's shows interest in disposable UF systems (47.1% as mentioned above), which continues a strong multiyear rise, from 36.8% last year and 26.1% in 2010. Buffer dilution systems/skids, which took the number two spot this year at 42.6% of respondents, also sees a year-over-year jump, from 36.8% in 2011.

Beyond these top two, though, we have to move down the list to find solutions that are seeing active growth in the percentage of respondents evaluating each new technology. This year's seventh-most considered solution — online analytical and control devices — saw a modest rise in interest from last year. And membrane technologies, in the #9 spot, also saw a slight gain.

When we limit our analysis to evaluation of single-use technologies, the picture is clearer. Interest in disposable UF systems and single-use disposable tangential flow filtration (TFF) membranes both grew. Although a slightly smaller proportion of respondents this year said they are actively considering single-use prepacked columns, this appears to be simply a leveling off of interest after a large jump in 2010. In fact, the only single-use technology to see a marked drop in interest this year was single-use filters, which fell from 43% last year to 36.8% this year.

The drop-off in consideration experienced by the majority of downstream processing solutions does not necessarily mean the industry is any less invested this year in tackling the persistent problem of downstream bottlenecks. Rather, the hikes in interest in some technologies, coupled with the marked decline of others, might simply mean that the industry is either beginning to develop solid preferences for some technologies over others or figuring out what works and what doesn't.

GLOBAL DIFFERENCES

Clearer differences are in view when sorting the responses on a regional basis. We compared answers from U.S. and Western European respondents, finding these groups agreeing on relatively few new technologies. Significantly, a majority of U.S. respondents are actively considering technologies such as disposable UF systems, use of high capacity resins, and in-line buffer dilution systems. By contrast, Europeans' level of interest for disposable UF systems, buffer dilution systems/skids, and single-use disposable TFF membranes, although at the top of their new technology list, stand at a somewhat lower level compared with U.S. biomanufacturers.

These regional differences also can be seen, though to a lesser degree, when we look at how U.S. and European respondents are actually implementing new downstream solutions. In a separate question, we found that a far greater percentage of U.S. than European biomanufacturers are cycling columns more frequently (64.1% vs. 16%) and developing more efficient harvest/flocculation operations (30.8% vs. 12%). On the other hand, Europeans are far more likely to have used or evaluated membrane-based filtration technologies (52% vs. 35.9%) and investigated process development to shorten cycle times (44% vs. 33.3%).

CMOs AND BIOTHERAPEUTIC DEVELOPERS SHOW THEIR DIFFERENCES, TOO

It's not only U.S. and European respondents who are looking at the downstream problem through different lens; CMOs and developers also differ on many downstream processing (DSP) technologies under consideration. For example, while two-thirds of the CMOs responding to our study said they were actively considering the use of high capacity resins this year, just 37.3% of developers said the same.

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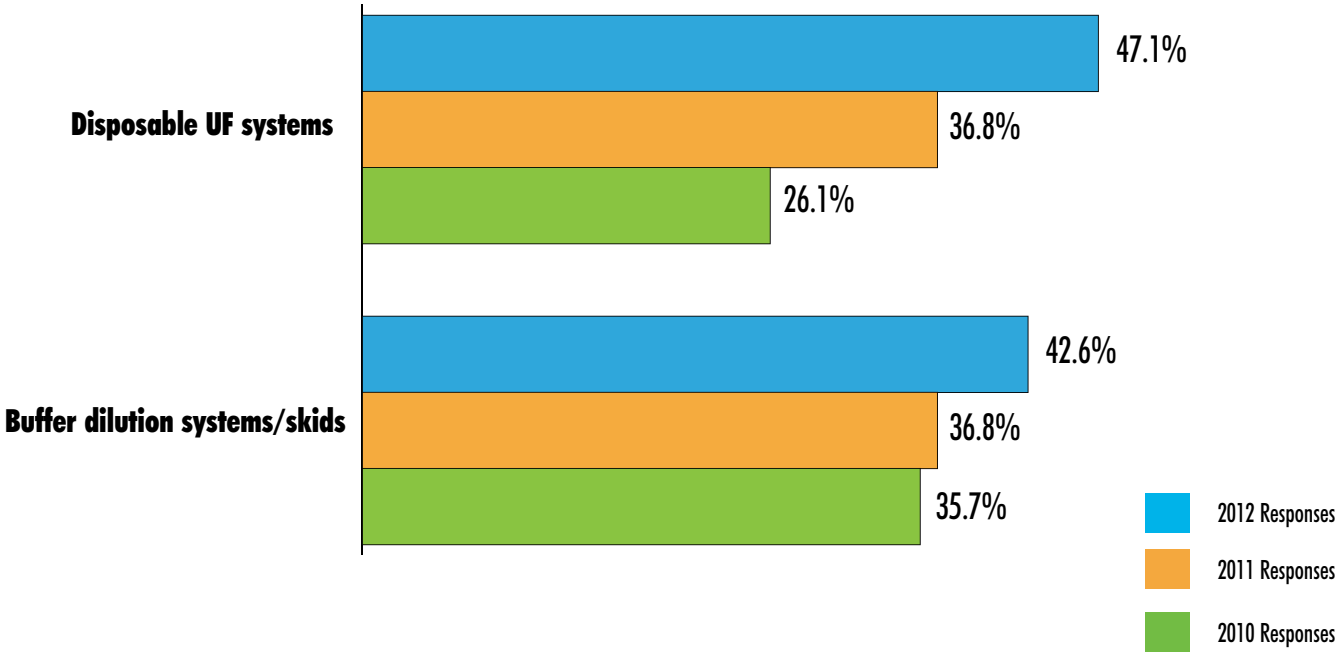
Adopting New DSP Technologies 2010 vs. 2012

Downstream purification (DSP) technologies being considered



Selected Percentages of U.S. vs. European Respondents Actively Considering New DSP Technologies (of 21 areas evaluated)

New Technology	% U.S. Respondents	% European Respondents
Disposable UF systems	54.2%	42.9%
Use of high-capacity resins	54.3%	38.1%
In-line buffer dilution systems	54.3%	28.6%
Centrifugation	28.6%	9.5%
Single-use prepacked columns	38.1%	22.9%
Development of MAb fragments	28.6%	11.4%

Survey Methodology: This ninth 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.

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Jose-Carlos Gutiérrez-Ramos,
Senior VP, BioTherapeutics Research & Development Group, Pfizer

The New Pfizer Research Strategy

Openness And Collaboration Replace The Old Imperial Model

by Wayne Koberstein, contributing editor

To any veteran observer, the words coming out of Pfizer research these days could stretch credulity. Words like "open" and "collaboration" were seldom heard throughout most of the company's buy-it-when-you-need-it-but-go-it-alone history — until recently.

In the past few years, the company radically overhauled its internal R&D organization. It slashed jobs, hired new research leadership, and cast its fate on external sources of new products, starting at the key transition from drug discovery to development. It also organized the four contemporary arms of biomedical research — proteins, small molecules, oncology drugs, and vaccines — into four separate but collaborative divisions, all united at the level of discovery, where the BioTherapeutics Research & Development Group, headed by Senior VP Jose-Carlos Gutiérrez-Ramos, plays a leading role.

Gutiérrez-Ramos here describes his mission to "entrepreneurialize" discovery and development at Pfizer through a rebalance of power from the company's internal R&D to a greatly expanded external network. He gives important tips and lessons for other companies dealing with the new Pfizer and looking to become part of its network, in particular, by the avenues now open through his group.

And he shows how his organization, working mainly but not exclusively with its new Centers for Therapeutic Innovation (CTI), is also incorporating academic researchers into the mix. CTI epitomizes Pfizer's quest for "biological probes" — novel active molecules at the right development stage for human proof-of-concept studies and ready to complete the translation of science into full therapeutic application.

Gutiérrez-Ramos sees his job as bringing together the three main forces or "constituents" in drug research: academia, biotechnology, and pharmaceuticals — all represented in his own professional background at biotechs Avidia, Millennium, and Amgen, as well as pharma giant GlaxoSmithKline. "Each of the constituents has its limitations," he says. "In the biotechs I worked in before coming here, there was a very entrepreneurial spirit and a strong focus, but we lacked the experience or the ability to take the big molecules all the way to the clinic. In Big Pharma, though, companies miss the entrepreneurial experience — not just on the market side or the technology side, but as a way of doing business, with small teams, very empowered."

CONFESSION TO PROGRESSION

On the surface, the new Pfizer sounds a lot like most other pharma companies these days, watching their block-

> "We had the tradition of approaching our partners like Big Brother, saying, 'Okay, we will tell you what is important.'"
>
> Jose-Carlos Gutiérrez-Ramos, Senior VP, BioTherapeutics Research & Development Group, Pfizer

buster patents disappear and their pipelines disappoint, despite decades of growth in R&D. Every company has in some way turned to the entrepreneurial life sciences sector as the most productive source of innovation.

So what makes Pfizer any different? Perhaps its own legacy as an unparalleled juggernaut that plowed through the industry devouring whole companies like no other, save Sanofi. Now, for Pfizer to champion an open, more egalitarian form of partnering and acquisition requires extraordinary effort. That may help explain its crash program to shrink internal R&D — some say to the point of abdication — and create an external network to replace the jettisoned capacity.

"We want to maximize the way that we generate value in research internally, externally, and in hybrid models," says Gutiérrez-Ramos. "We want to generate value with a spider web of activities and interactions that allow us to bring programs forward, not just in a binary way — that we do it or not do it — but in a range of risk and investment modes."

A range of modes means different financial and managerial terms for different deals and the resulting alliances. "In one case we might invest 20% of the cost of the program and the partner invests 80% because they have the top experts, or in another case we might go 50/50 or 70/30 if we have a better position. The driver is the constituent of the partnership that is in the best position to drive based on expertise and resources."

The driver of an alliance can be an academic, as in the exploratory projects of CTI, a biotech partner, or another pharma partner, he explains. "In a few words, we want to entrepreneurialize the way we operate, and that is mainly by partnering with the best people — the best scientific minds or the best business minds or the best medical minds — and empowering whoever is in the best position to drive the program intellectually, financially, or scientifically."

Gutiérrez-Ramos acknowledges that the open research model is a big departure for the company, not only in philosophy but in objective terms. Pfizer now has more programs that are externally derived than ever before, he says — a combination of outsourcing, strategic partnerships, programs like CTI, and other significant collaborations. "In the Pfizer of only a few years ago, if we saw something on the outside that we liked, we'd go ahead and buy it. Now we do alliances and limited acquisitions."

An example of "limited acquisitions" is Pfizer's purchase of Excaliard Pharmaceuticals, developer of an antisense oligonucleotide for wound healing and treatment of skin scarring, or skin fibrosis. "We retained the key people in the company, and they are driving it. We didn't try to reinvent the company ourselves; we kept the leaders as well as most of the staff running the program."

PRODUCTION HANDOFF

An often overlooked aspect of partnering is manufacturing. Scale-up from bench production to clinical batches presents an early challenge to many start-ups, especially in biotechnology. At the very least, it can take a significant amount of the active substance to obtain what many large partners now demand: early proof-of-concept in humans. But once a small company builds sufficient production capacity, the handoff of manufacturing to a larger partner can be complicated.

According to Jose-Carlos Gutiérrez-Ramos, head of the BioTherapeutics R&D Group, Pfizer is aware of the challenge, has created some solutions, and is working to develop others. "With any program that grows internally, the manufacturing team works together with the internal team from day one on. Any problems that a program might have, the pharmaceuticals manufacturing team is aware of them and works to fix them. In dealing with external programs, at times that interaction hasn't been as strong. But we are changing this to make it as strong as possible from day one and beyond, so that there is the same amount of feedback back and forth, and we can make a lot smoother transition." For some partners that have not scaled up to clinical production, Pfizer has created another option: It will produce a half-kilogram of the active substance for early human tests. "De facto, this is equivalent to a seed round or a Series A round of funding, say, worth $3M or $7M," says Gutiérrez-Ramos.

THE IDEAL DEAL

Openness, transparency, and entrepreneurialism among the internal R&D units is one intended outcome of Pfizer's transformation. The other main objective is a rebalance of powers between the huge corporation and its comparatively tiny partners.

"We had the tradition of approaching our partners like Big Brother, saying, 'Okay, we will tell you what is important,'" recounts Gutiérrez-Ramos. "For example there was no openness to discussion before a key milestone was achieved, even when the partner depended on it for a large amount of cash." A complete "change of attitude" has since taken place at Pfizer, he says — a change among company


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personnel that took more than persuasion. "In some cases, the headcount changes at Pfizer have been behavior-driven, related to each person's willingness and ability to interact, internally or externally. If we are to succeed in establishing connectivity — especially early connectivity between discovery, pharmaceutical sciences, and manufacturing — we need a different kind of interplay."

In contrast, though understandably, response to the change has been overwhelmingly positive among partners, according to Gutiérrez-Ramos. "If you approach partners, either academic or biotech, with an open spirit, they are delighted, because the fact is they usually don't have the expertise that we bring to the table."

Gutiérrez-Ramos uses his own experience in biotech to support the point: "We had a paucity of knowledge at the beginning — a lack of expertise in areas such as business, clinical trials, and manufacturing. To have a partner help us guide those programs to the clinic in an understanding way, not in a Big Brother way, would have been delightful. To make an advantage of that interaction, whatever the situation, that's what we seek with our partners as well."

A structural expression of the openness ideal is the option-based partnering agreement that Pfizer prefers — a form of alliance in which both parties share the risks, responsibilities, and possible rewards of the relationship. Pfizer no longer simply licenses in compounds for its own teams to develop, but most often continues to work to a varying extent with the compound originators.

"We recognize that, from very early on, an option-based deal is the best way to go. We have the freedom to adjust according to who is in the best position to drive the program. In some acquisitions, we retain members of the team, or keep the team intact — for example, Icagen, where we retained the team because they are experts in ion channel modulators."

Pfizer aims to operate its R&D as a "big collective matrix," he says. Each node of the matrix has to create unique value. In Icagen's case, because of the financial situation, the best way to make it part of the matrix was to acquire it. But in other cases, it makes more sense to make a partnering deal. So the matrix doesn't proceed through one particular pathway, technology, or asset.

WHY THE CTI WAS CREATED

The most visible example of Pfizer's new philosophy is the CTI. Gutiérrez-Ramos says the company created the program because it wanted to help more academic scientists translate their unique ideas into new therapies. "That piece of the discovery chain, translational research, moves novel compounds from early research into human testing. Most interaction in academia and in biotech tends to be in early research and then later on in chemical development. But in between, the unique ideas from bright scientists often go unnoticed."

Public grants and venture capital do not cover the translational research stage adequately, he says. Thus, Pfizer set out to fill the gap by first consulting with academic leaders, deans of medicine, venture capitalists, physician scientists, and ultimately its own internal leaders to answer the question: "How can we, the largest pharmaceutical company in the world, uniquely interact with them?"

First, the company defined what it would not do — fund start-ups or basic research, leaving those areas to the VCs and government funding such as NIH — then, what it would do: "The one thing we could do uniquely with CTI is to help develop clinical probes. By 'clinical probes,' I don't mean the final medicine — but really quality molecules, small molecules or large molecules, with which we are able to test a hypothesis in humans."

Small companies may have great chemists, biologists, and protein engineers, but very rarely do they have all the pieces of the puzzle — formulation, pharmacokinetics, pharmacodynamics, and so on — to go into human testing. "One unique thing we can bring to the CTI is that piece of the translational medicine,"

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PROFILE INFORMATION

Nice Insight survey respondents comprise people who work at the following types of companies:

- Biotech 27%
- Emerging Biotech 8%
- Specialty Pharma 16%
- Big Pharma 29%
- Emerging, Niche & Start-Up 20%

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OUTSOURCING TRENDS

Attributes of Outsourcing Partners Ranked in Order of Importance

QUALITY

When selecting partners, survey respondents ranked Quality as their number one priority.

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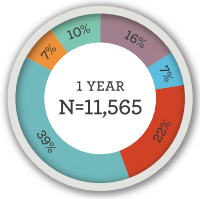
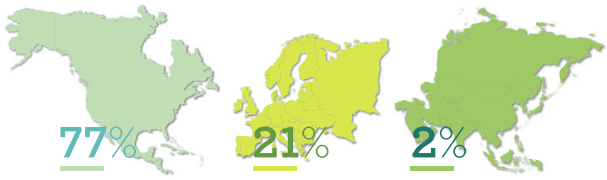
Within Pharmaceuticals and Biotechnology, survey respondents work in the following departments:

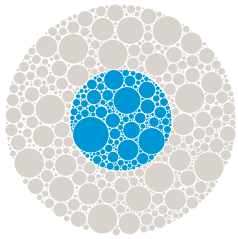


- Manufacturing 16%
- Regulatory 7%
- Operations 22%
- R&D 39%
- Purchasing/Procurement 7%
- Quality (QA/QC) 10%

Respondents' Business Location By Region



MARKETING COMMUNICATION UPDATES

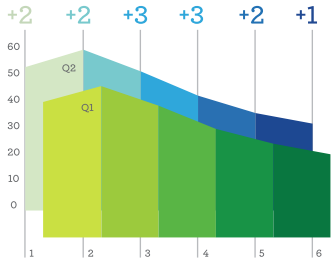


109 different companies had marcom changes

- 36% Marcom changes
- 64% No marcom changes

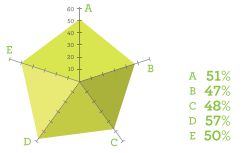
Phase Of Development When Outsourcing Partners Are Engaged
% engaging partners

		Q1 vs Q2	
1	Discovery	49%	51%
2	Pre-Clinical	53%	55%
3	Phase I	47%	50%
4	Phase II	39%	42%
5	Phase III	33%	35%
6	Phase IV / Post Launch	30%	31%



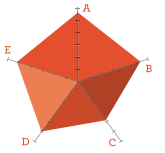
Q2 Breakdown By Sponsor
A: Big Pharma B: Specialty Pharma
C: Emerging Pharma D: Biotech
E: Emerging Biotech

Overall DISCOVERY 51%



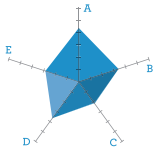
A 51%
B 47%
C 48%
D 57%
E 50%

Overall PHASE I 50%



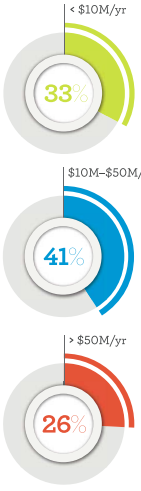
A 57%
B 52%
C 39%
D 50%
E 51%

Overall PHASE III 35%



A 44%
B 34%
C 21%
D 37%
E 29%

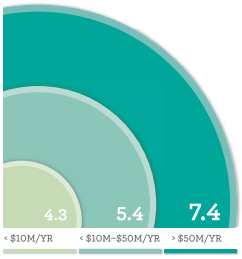
Annual Outsourcing Budgets



Average Number of Services Outsourced by Expenditure

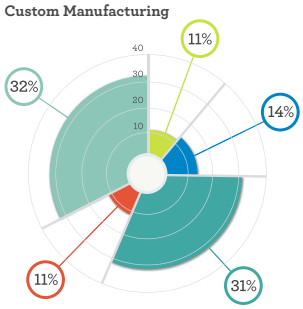
5.3 Q2 Overall

As outsourcing budget size increases, so do the number of different services outsourced.



SERVICE OUTSOURCING TRENDS

Custom Manufacturing



23% of survey respondents reported their company would outsource Custom Manufacturing services in 2012

- Big Pharma 11%
- Specialty Pharma 14%
- Emerging, Niche & Start-Up 31%
- Biotech 11%
- Emerging Biotech 32%

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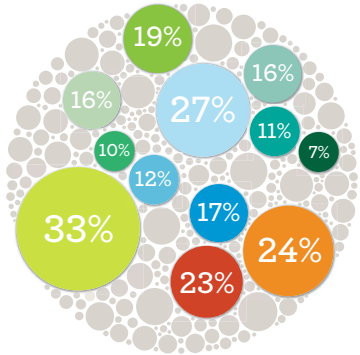
% of Respondents Who Plan to Attend the Following Industry Events



- AAPS 33%
- Bio International 27%
- Bio Europe 24%
- Contract Pharma 23%
- BPI 19%
- ChemOutsourcing 17%
- DCAT 16%
- DIA 16%
- CRS 12%
- CPhI Europe 11%
- Informex 10%
- Interphex 7%

Q2 Outsourcing Trends

19% of survey respondents reported their company will outsource Packaging Projects in 2012.

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Gutiérrez-Ramos says. "So we decided to bring to the biomedical discovery community of the world not just dollars, but operational dollars in the form of clinical probes."

Gutiérrez-Ramos sees the effect of CTI as positive for all players. "Deans of experimental medicine in the medical schools or the hospitals were telling us, 'We have great physician scientists but we have no chemists to support their studies because public money does not go in that direction and even if it did, they wouldn't know where to start.'"

CTI now has 22 academic centers and medical schools signed up with the program, with more than 300 proposals for experimental medicine studies. In all of the centers, the deans of medicine or experimental medicine are part of the governing bodies. "So the consequence of the CTI for the medical schools and the hospitals is that they will do much more experimental medicine research than before. As for the effect on biotech companies: We are building a complementary, not a competing, model to the venture-fund biotech model. I would describe the CTI as a self-propagating biomedical engine."

Among the 20 research programs accepted by the CTI, 1/4 are run by investigators with prior business experience. The ideal CTI candidates, however, are "the associate professors who haven't gone on a road show with venture capitalists, are intimidated by the process, or have an idea they believe is too risky. We can take an idea that has 20 to 30 academic papers that say this could be something fundamental in biology that shows some possible beneficial effect in humans and move it all the way to a human clinical study, in healthy individual patients, to test the hypothesis."

That journey includes discrete steps: 1) Pfizer works with the PI (principal investigator) to build an IP portfolio; 2) it generates half a kilogram of the active compound, whether antibody, protein, or small molecule, for human testing; and 3) a team of Pfizer "drug hunters" guides the key researcher through all of the details of the translational phase. "In our division, we are not giving out venture money; we are putting a team around that PI," says Gutiérrez-Ramos. "That's why cooperation with the PI at the academic medical center is very important."

Many of the agreements with investigators are, like company partnerships, option-based. If the company does not exercise the option, it retains only a "very small" royalty and shared IP. "In each one of the centers, we intend to do 15 CTI projects over the next five years. Pfizer co-invents the compound with you, and with it and the help of venture capitalists, you can still start a company."

Gutiérrez-Ramos adds that Pfizer management was very supportive of CTI and the open-research model because it places the company in a position to help drive innovation in the biotech companies. Even though Pfizer does not obtain the control over partners it once did, it places itself in the "pole position" for later partnerships or acquisitions — and for fulfilling its mission in R&D.

"Pfizer is the largest biomedical company in the world. Biomedicine needs a big push in terms of new options, and experimental medicine is one area where biomedicine globally hasn't been too fruitful. This is our way of generating more biomedical projects that focus on translational medicine — not completely in an altruistic way; of course, we have fiduciary responsibility to our shareholders. But we can really help biomedical research by generating clinical probes and initiating more experimental medicine. If biomedical discovery progresses, we will progress because we are in the best position to do it."

INNOVATION HEADWATERS: PFIZER'S BIOTHERAPEUTICS R&D GROUP

The Pfizer BioTherapeutics R&D Group headed by Jose-Carlos Gutiérrez-Ramos consists of four research units (RUs), including the Centers for Therapeutic Innovation (CTI), and global specialist function units with complicated names reflecting their functions: Pharmacokinetics, Dynamics and Metabolism - New Biological Entities (PDM-NBE), Global BioTherapeutic Technologies (GBT), and Pharmaceutical Sciences (global group). Together, the RUs discover and develop novel biologics and small molecules in inflammation and immunology, in another area the company calls biocorrection (correcting pathological function in metabolic disorders and genetic deficiency diseases such as hemophilia), and in tissue repair associated with various musculoskeletal conditions.

Specifically, the PDM-NBE tests NBEs for absorption, distribution, metabolism, and excretion (ADME) characterization, conducts preclinical pharmacokinetic/pharmacodynamic modeling, and develops quantitative biomarkers supporting the research units. The GBT works with the other RUs and therapeutic units to design and deliver biotherapeutic agents for development. Pharmaceutical Sciences supports early small-molecule development. But the BioTherapeutics division not only contains a collaboration of smaller units, it also maintains a cooperative relationship with the other main R&D groups.

"Our four R&D divisions are all interacting in a very collaborative environment, but we are each experimenting as well with different models," Gutiérrez-Ramos says. "We vary in the way we run our programs, the rates of externalization, how much we use the CTI model or other models in different collaborations, how much we partner, how much we do it internally — it's different in different divisions."

Although each division is large, staffed with hundreds or thousands of people with many programs and numerous sites, departments are relatively small, according to Gutiérrez-Ramos. Research labs are typically 30 to 100 people, he says. "Departments and labs are very autonomous, and the chief scientific officer in charge holds a budget for all the activities for many drug entities in lead optimization, process engineering, and so on. They act very much like a CEO on the outside. Such transparency of costs and decision making is something that typically did not exist in big companies because of their huge departments."

Lack of transparency causes inefficiencies and overhead costs because the key decision makers cannot gain a complete understanding of how much each decision is costing, he says. Nor can they balance the costs against the results. "You look at our dashboard operating plan now — every project has four to five key milestones in the program, showing what value those milestones generate compared to the investment in those milestones. With that information, the department heads can make decisions based on a business plan. So this is a fundamental departure from how we were operating a few years ago."

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Serialization And The Outsourcing Decision

By Rob Wright

In three previous articles in *Life Science Leader* magazine (April, May, June 2012), Gail Dutton discussed the long road to serialization and the serialization planning process for pharmaceutical manufacturers and built the business case for implementing serialization. In this article, we discuss the impact of global serialization on choosing outsourcing partners. In case you are unfamiliar with the serialization regulation, let me quickly get you up to speed.

The California ePedigree law will go into effect in 2015 and includes the need for pharmaceutical manufacturers and repackagers to serialize (provide a unique code) drugs, all the way down to the smallest level of distribution at the pharmacy. Companies throughout the drug distribution supply chain will need to make reference to the original manufacturer serial number and each subsequent ePedigree as they are updated through the process of distribution. Estimates on the time required to implement such a program vary depending upon the size of the company and range from an optimistic six months to a daunting three years. Although serialization initiatives have been in place in other countries for several years, California's serialization program is the most stringent, and it will take an act of Congress to prevent it from becoming the de facto standard for pharmaceutical serialization in the United States. This is not that far-fetched, as legislation may soon be included in bills relating to the Prescription Drug User Fee Act (PDUFA) reauthorization, which at the writing of this article, are in motion in the Senate and/or House of Representatives (see sidebar "The Delay Game"). Since other countries already have serialization regulations — and since the United States will eventually have them in one form or another — here is what you need to know about the impact of serialization on choosing outsourcing partners and the steps you should be taking (or observing your strategic partners doing) in order to be prepared.

THE IMPACT OF GLOBAL SERIALIZATION ON CHOOSING OUTSOURCING PARTNERS

If your company is a member of the pharmaceutical manufacturing supply chain and has taken a wait-and-see approach to implementing a serialization program, in some respects, the approach has paid off — up to this point. "Some companies who invested in solutions in 2008 eventually regretted it because the dates were subsequently pushed out so far," says Dirk Rodgers, U.S. healthcare supply chain consultant and co-chair of a number of key technical work groups including GS1, an international not-for-profit association responsible for developing the most widely used global supply chain standards. That being said, experts agree that taking the wait–and-see approach is no longer advisable. Virginia Herold, executive officer of the California State Board of Pharmacy, has repeatedly stated that the 2015-to-2017 deadlines are firm and that there will be no further extensions. Greg Cathcart, CEO for Excellis (an information technology consulting firm), believes that further procrastination toward developing a serialization strategy is placing your company at greater risk, noting that "Vendors which develop the serialization software and manufacture serialization equipment, as well as consultants with serialization implementation expertise, will be maxed out and in short supply the closer we get to 2015." M. (Ken) Kengatharan, a serial biotech entrepreneur and an experienced pharmaceutical executive who is currently a board member at Armetheon, Inc. (a California-based pharmaceutical company developing an anticoagulant drug currently in Phase 3) and also the president & CSO of Altheos, Inc., another California-based pharmaceutical company, sees this as an opportunity for companies in terms of a demonstrating competitive edge. In the late 1990s, one of Kengatharan's previous companies was developing an e-commerce system that was partly meant to deal with parallel as well as illegal drug import issues in Europe. "When I select a CMO, cost is not necessarily a key element of the decision making," he states. "I am looking for proactive companies, those I like to refer to as being future-proof, with people who view serialization not as a regulation requirement to be met but as an opportunity to provide added value and knowledge to their customers. These are the type of people I want to work with because they really understand the industry." Cathcart believes the law will result in manufacturers streamlining their contract packaging partners, with some com-

panies consolidating their partner portfolios to only those companies that are serialization-ready and eliminating sourcing to some of the mom-and-pop operations. Rodgers doesn't believe it to make much sense for a global manufacturer to retain multiple contract organizations just because each is capable of fulfilling the requirements of certain parts of the world. "The complexity and diversity of these regulations," he concedes, "may soon result in larger manufacturers deciding to outsource even more of their packaging and distribution components." Though all three differ as to the eventual end result of serialization's impact on industry, all concur that global serialization initiatives and supply chain member serialization readiness will impact the CMO selection process. So whether you are developing your own corporate serialization initiative or selecting an outsourcing partner, here are some steps to either consider implementing or observe being implemented by current and/or potential strategic partners.

STEPS TO SERIALIZATION

The first step in implementing a serialization initiative — if you haven't already begun the process — is the recognition that you have a problem. Kengatharan advises you to gain a thorough understanding of the problem by getting involved with the organizations at the forefront of setting up and implementing solutions.

The second step is to begin creating a dedicated team focused on developing and implementing a solution with pharmaceutical manufacturing, supply chain, logistics, IT, and legal experience. Given the size and scope that a serialization initiative can take, companies should seek a serialization team leader who ideally has experience in pharmaceutical manufacturing and supply chain management and, most importantly, has been involved at a very high level in the process of implementing and communicating a structured change management program (i.e. transitioning individuals, teams, and organizations from a current state to a desired state). This team will be responsible for identifying key stakeholders, coordinating stakeholder outreach initiatives, and developing plans and tools to strengthen alignment between all groups involved in the serialization program. If you are a small company with limited resources, consider retaining the services of consultants with the experiences described above. "In addition, a senior management member should be actively involved and part of driving the process," states Kengatharan. This type of thinking is not new. When e-commerce was considered a major avenue for businesses, several large companies had a CTO on their board if not on their executive teams. "Where we see people struggling," says Cathcart, "is when senior management doesn't give them the financial and people resources to be successful."

Cathcart sees the placement of a senior-level manager on the team as a mission-critical component to getting buy-in and support throughout the organization.

Step three to beginning the serialization process involves conducting a self-assessment. Cathcart believes this should involve the following. First, what products do you have presently? Second, what products do you anticipate having five years from now? Third, where are these products being, or anticipated to be, manufactured and packaged? Fourth, in what markets or countries are these products going to be sold? Fifth, how many different lines are being used to manufacture? Finally, how many regulatory bodies are involved? When gathering this information, it is not only important to note what you have, but in the case of assessing packaging lines, be sure to note what important equipment is lacking and necessary to be compliant.

The fourth step is to build a playbook based on all of the above gathered information outlining your serialization strategy. The playbook should prioritize the order in which manufacturing lines should be serialized. For example, if you have a product you anticipate selling in Brazil, that product should be the first priority since Brazil has a serialization law already in effect. According to Rodgers, "You will need a lot more time than you might initially think when it comes to fully realizing the successful implementation of a serialization program." How much time varies on the number of packaging lines a company owns, how much automation already exists in the operation, and how much downtime they can tolerate to endure a conversion. "Manufacturers are often caught off-guard by the fact that the California law isn't just a serialization law," states Rodgers. "It is a pedigree law that includes unit-level serialization, but you will find that neither you nor your downstream trading partners can fulfill the law unless you can make use of inference — that is, you need to be able to infer the unit serial numbers contained inside of a case by reading only the case serial number." Rodgers affirms that inference only works if you have a six-sigma casepacking automation system. "The point is, once you start looking at what needs to be done so you will be compliant at the deadline, you will very likely realize that you should have started much earlier," he concludes.

THE BENEFITS OF A PROACTIVE APPROACH TO SERIALIZATION

The experts interviewed for this article concede that many CMOs are working on very thin margins, and the cost of implementing serialization programs that meet the California requirement may seem cost-prohibitive. However, not doing so can result in being "penny wise and pound foolish." Rodgers reminds those involved that it is the manufacturer, distributor, and pharmacies that are responsible for compliance. Further, it will be these organizations at risk of losing business and being fined should they fail to meet the serialization requirement. According to Cathcart, a general rule of thumb to consider is by meeting the California standard, your company will meet every other serialization standard, as it presently represents the most rigorous standard. In addition to the benefits of avoiding fines, preventing the loss of business, and meeting the most rigorous serialization standard in order to facilitate future global expansion, Kengatharan sees additional benefits. First, he advises companies to consider the volume of data which would be produced by the implementation of such a program and what business opportunities having access to such data

THE DELAY GAME

For pharmaceutical manufacturers holding out hope that California's ePedigree law will be postponed, Virginia Herold, executive officer of the California State Board of Pharmacy, has stated that the 2015-to-2017 deadlines are firm and that there will be no further extensions. The California State Board of Pharmacy initially stepped into this area of regulation out of perceived need, in the absence of federal standards and in response to acts of counterfeiting and other threats to security, beginning the process of developing an infrastructure back in 2003. And yet, the delay game continues.

The most recent attack seeking to derail the implementation of California's ePedigree law (under review at this writing and anticipating a decision before the end of June 2012) was put forward by the Pharmaceutical Distribution Security Alliance, a consortium organized specifically to reach consensus on end-to-end track-and-trace rules, pedigree, and serialization. Their proposal, the Pharmaceutical Traceability Enhancement Code (RxTEC) Act, also referred to as the "Securing Pharmaceutical Distribution Integrity Act of 2012," is one more piece of legislation attempting to be attached to the reauthorization of the Prescription Drug User Fee Act (PDUFA) — essential to FDA funding in the new fiscal year, which begins Oct. 1, 2012. Henry Waxman (D-CA), ranking member of the House Energy and Commerce Committee, stated, "The User Fee add-ons are a long line," warning that as add-ons mount, complexity of negotiation deepens. So why the last minute move? Why the delay of course?

The proposal, which appears to be backed by PhRMA, was filed by the Washington-based law firm Faegre Baker Daniels. The hope is that by going to Congress with one plan, they can gain acceptance of a national standard, which would supersede the California law. The earliest date that the RxTEC Act could take effect is sometime in 2020. Since it is proposed to begin implementation five years later than the California ePedigree law, you might expect it to be more complex and more thorough. In an eight-page letter to Waxman, dated May 9, 2012, California State Board of Pharmacy President Stanley Weisser outlines the inadequacies of the RxTEC proposal. "While we agree in principle that a uniform national standard would be ideal, we would like to see that standard a much closer approximation of the California model than is reflected in the RxTEC proposal. We would encourage something closer to the Bilbray-Matheson model of H.R. 3026."

When I first became aware of California's position, I felt there was a need for a national standard. Further, I wondered why a state should be involved at all. Now that I have gained more information, I understand the benefits of California taking a leadership role. Had California done nothing, nothing would have been done. After having read Weisser's letter, I would argue that no national standard would be better than a substandard national standard. In typical pharma fashion, instead of seeing the opportunity to be gained by implementing a "Gold Standard" serialization program, which would result in the collection of tremendous amounts of data and the possibility of a wide variety of business opportunities, industry fell back on its own gold standard — the delay game.

could present. He believes if companies are implementing serialization just to meet a regulatory standard, then they are missing a bigger opportunity on which to capitalize. Finally, companies can strategically partner to meet the serialization initiative resulting in long-term strategic partnerships. "Once you've created this kind of tight relationship, switching becomes very difficult," he states. A proactive approach to serialization today will provide companies with strategic advantages which will serve as the foundational building blocks for the strategic partnerships of tomorrow — partnerships which may last a very long time.

WHAT NO ONE SEEMS TO BE TALKING ABOUT REGARDING TRACEABILITY

In February, Genentech, the maker of the best-selling cancer drug Avastin, issued a warning to doctors and patients, noting that the counterfeit vials of the distributed product did not contain the key ingredient used to treat cancers of the colon, lung, kidney, and brain. Charlotte Arnold, a spokeswoman for Genentech, said the counterfeit drug had been distributed to healthcare facilities in the United States, though it is unclear how many products are in circulation or where they may be concentrated. In addition, Arnold said the company was alerted to the problem by foreign health regulators. Unfortunately, this is not the first time Avastin has been the target of counterfeit. For example, in 2010, patients in China were given a drug thought to be Avastin which turned out to be saline contaminated with bacteria endotoxin. Another example of a deliberate drug contamination occurred in 2008 when contaminated heparin was connected with dozens of deaths and hundreds of allergic reactions across the United States. The FDA investigation concluded that the drug had been intentionally contaminated. Thirty years ago, Johnson & Johnson (NYSE: JNJ) experienced deliberate contamination of its market-leading product Tylenol. This event resulted in the death of seven people, resulted in the creation of industrywide tamper-resistant packaging, and cost J&J more than $100 million. Here is why all of these events are significant.

Tamper-resistant packaging has created a level of trust among U.S. consumers. Patients trust that the medication being injected by a healthcare provider is safe. Patients trust the person giving the injection. In a Gallup Poll, 84% of Americans rated nurses' honesty and ethics as "very high" or "high." That being said, when was the last time you asked the nurse (the person most likely to give an injection) if they checked the tamper-resistant packaging and if anything seemed amiss. Recent counterfeits of Avastin demonstrate the ability of counterfeiters to closely copy company drug labeling and successfully circumvent the current drug distribution system. For those people intent on launching a bioterrorist event, the best way to do so is to either tamper with a product prior to its being packaged or create a copy that looks just like the product and place it in the hands of trusted healthcare providers for administration. Bioterrorism remains a distinct possibility, especially without a program that involves the ability to trace medications back to their manufacture to ensure the contents have not been adulterated. So what is being done?

The Risk Of Legislation Procrastination

Recent legislation introduced in the House of Representatives would create a mandatory bar code system to monitor the authenticity of all prescription drugs moving through the U.S. supply chain. The legislation is known as the Pharmaceutical Traceability Enhancement Code (RxTEC) Act and was introduced earlier this year. But the importance of traceability is nothing new. In July 2003, U.S. FDA commissioner Mark McClellan established the counterfeit drug task force. In a report issued in 2004, the task force concluded that the adoption and common use of reliable track-and-trace technology based on radio-frequency identification (RFID) tagging of products was feasible for use by 2007, and the report recommended universal pedigree requirements to document all drug movements. And yet, eight years later, a federally mandated traceability program has yet to go into effect. The state of California's board of pharmacy began the process of taking action nearly 10 years ago, laying out an ePedigree law scheduled to begin going into effect in 2015. Its intent — to secure the drug distribution system from the threat posed by counterfeit, misbranded, adulterated, or diverted drugs. The problem with RxTEC is that it is not as robust as the California ePedigree law and, if passed, would supersede the California law. Finally, it won't go into effect until 2020. Traceability and serialization are not easy issues. But procrastination on legislation which leads to delayed implementation is simply providing those intent on causing harm a greater opportunity to do so.

Local Partnering: Two Views From China

By Gail Dutton, contributing editor

Partnering locally makes sense when it comes to gaining acceptance in new regions. Sometimes, it's even a requirement of doing business there. Naturally, any potential partners must be vetted, but when working in regions that lack a history of pharmaceutical regulation, local partnering can be fraught with peril.

China is a good example. HUYA Biosciences International and SciClone both are China-focused companies. HUYA has searched out innovative Chinese products since 2004, working closely with universities, research institutions, and young companies, maintaining operations in eight cities — Shanghai, Beijing, Guangzhou, Hangzhou, Shenzhen, Chengdu, Wuhan, and Taizhou. SciClone has worked with Western companies to bring innovative medicines to China since 1996, cultivating relationships with hospitals and key opinion leaders. Although these two organizations see different sides of the business environment, they both stress that China is changing rapidly and has many opportunities. "There are a lot of attractive things about China," says Friedhelm Blobel, Ph.D., CEO at SciClone.

IMPROVING RESEARCH QUALITY

Since HUYA entered China, the company has seen the quality of research improve. "The fact that our compounds come from China doesn't make them any more risky," says Curtis Tyree, VP of operations at HUYA. "Independently testing the molecule is a critical point. We have a due diligence process that is frankly skeptical. There are several examples of compounds in China that have gone head-to-head in clinical trials with those outside China with comparable or superior results." HUYA in-licensed HBI8000, a novel HDAC (histone deacetylase) inhibitor, just before it entered Phase 1. Tyree calls it "one of the first truly novel Chinese drug discoveries to enter U.S. clinical trials." The number of successful, international-quality compounds is not yet at Western levels, but it is growing.

From the Chinese perspective, Western companies offer the expertise that makes their programs more attractive globally. For example, HUYA may suggest experiments or models the local researchers may not be considering that can make their work more attractive internationally. "In discussions with our global partners, we've learned the gold standard models," Tyree says. "If the Chinese group doesn't have access to that model, we may know someone in China running it already, because we maintain ongoing relationships with investigators."

In China, as in other emerging markets, conventional wisdom advises partnering with companies with international experience. But, for companies bent upon accessing innovation, that's not always possible or practical. Increasingly, small Chinese companies are developing innovative products. Those companies, however, don't necessarily have the expertise or understanding of the international regulatory environment needed to deliver quality products. "In manufacturing, you have to be careful that they truly have the experience to manufacture to GMP standards. They call many things GMP that do not qualify in the Western sense," warns Blobel.

A CHALLENGING REGULATORY ENVIRONMENT

Because the government has a vested interest in building an international-quality pharmaceutical industry, it periodically cracks down on non-GMP manufacturers. That can be considered one of many growth pains of an industry that is evolving virtually from scratch. Another is the unpredictability of the SFDA (State Food and Drug Administration). For example, some biotech executives who have gained agreements with one SFDA official have seen those same agreements altered dramatically by the next person to fill that position.

That said, the SFDA is progressing closer to Western standards. Unfortunately, that increasing harmonization means the regulatory framework remains fluid. Approvals for products already commercialized in the West may take three to five years to gain SFDA approval, Blobel adds. Regional

governments also have great power. "They're like different countries, to a great extent. There are some overarching rules, similar to the situation in the EU, but those can change very quickly." Therefore, collaborations with organizations that understand the local business environment are critical to success in China.

Meanwhile, the government is providing substantial funds to support its scientists and research institutions. Indirect access to Chinese government funding is one of the benefits of partnering with Chinese companies.

Overall, according to the World Bank, China devoted 1.4% of its gross domestic product (GDP) to R&D in 2008. In 2011, however, China listed biotech as a developmental priority and China pledged to invest 2 trillion yuan ($318.5 billion at current exchange rates) — approximately 2.8% of its estimated 2011 GDP — on science and technology through 2016. Because of these resources, Chinese R&D projects are generally well-funded, well-equipped, and well-advanced when international companies begin licensing discussions. Consequently, the risk associated with specific projects is reduced.

A DIFFERENT KIND OF INTELLECTUAL PROPERTY

"IP is still a very special topic in China. There, they have a different understanding than the West of what constitutes IP," Blobel cautions. IP laws also are in flux. As Chinese companies are becoming innovators, the government sees an incentive to strengthen IP laws and their interpretation in an effort to protect the country's intellectual investment both domestically and internationally. Nonetheless, Blobel says, "It's not unheard of for a group of employees to leave, open a business, and file your patents first." Be cautious, he advises.

THE KEY IS THE RELATIONSHIPS

In view of such cautionary messages, it behooves potential partners to have a long courtship, working together on small projects before taking on the risks of larger, more formalized collaborations. Traditionally, businesses in China have been built upon the strength of relationships, because the force of law was unavailable. Although a legal framework is improving, the role of relationships remains strong. Because they are so important throughout Asia, they take longer to develop than in the West. The relationships HUYA began forging in 2004 are coming to fruition today, eight years later. So far, the company has in-licensed four products.

HUYA's embrace of Chinese-style relationships sets it apart from many organizations that focus strictly upon particular development programs. "We keep relationships, even if we can't license anything from them this year," Tyree emphasizes. By forming patient relationships with institutions and individuals, the company tries to help researchers' programs advance over time.

In return, HUYA gains the rights to license the potential products outside China, while the innovator retains domestic rights. The relationship also figures in the due diligence process, ensuring that questions regarding data aren't left unanswered. That attention to detail minimizes misunderstandings that otherwise can doom potential partnerships.

Because of its ongoing relationships, HUYA often gets the first look at promising projects, enabling it to match its database against the needs of some of its multinational partners. Consequently, some large pharmas have gained innovative compounds, and some Chinese start-ups have been able to advance their work beyond their internal capabilities or HUYA's interests.

There's another benefit, too. Because the Chinese version of the products usually advances faster than the international version, risk is lowered for products with a global market focus.

On the flip side, at SciClone, "We become interested in partnering once a company has some interesting assets or approvals in the West and is considering bringing them to China," Blobel says. Doing so involves conducting clinical trials at some of China's leading hospitals. In the process, SciClone has forged good relationships with key opinion leaders who have participated in trials for particular drugs and are convinced of their efficacy. "Without them, there's no chance of success."

MINIMIZE YOUR CHANCE FOR CORRUPTION CHARGES

The commercial culture in many emerging regions, including China, is different than in the West. Partnering with organizations that understand the culture is an obvious advantage. Unfortunately, it also has a dangerous aspect.

"For many, business is still done with red envelopes [i.e. monetary gifts]," Blobel observes. Regardless of the local custom, American organizations and their international partners must adhere to the Foreign Corrupt Practices Act (FCPA). Additionally, if they have any business dealings in Britain, they also must adhere to the United Kingdom's Anti-Bribery Act. What is considered a usual business practice locally may be considered a facilitation payment under the FCPA and a bribe under the Anti-Bribery Act.

Minimizing the risk of corruption charges from either of those acts requires training partners' staffs as well as your own, with rigorous follow-up to ensure the training is understood and implemented and that the consequences of not complying are thoroughly comprehended.

Partnering in China can be a very profitable, worthwhile endeavor for organizations with the patience to understand the business environment and the tenacity to endure rapidly changing regulations (along with a host of other risks and vagaries inherent in building an industry). Remember that, above everything else, in China, relationships matter.

Partnering With A Big Pharma

By Wayne Koberstein, contributing editor

At a recent industry conference I met with Shaun Grady, AstraZeneca's head of strategic partnering and business development, who gave me his advice for small life sciences entities looking to partner with his company. Grady was eager to extend an olive branch from AstraZeneca to companies and academic centers on the other side of deal making, playing against the arrogant and aloof stereotype of Big Pharma business development. Grady heads the gatekeeper group for most of AZ's partnering, licensing, and mergers and acquisitions. But, he says, his company is now pursuing a much more interactive policy toward the community of smaller players that create most of the innovation AZ and other large companies need so urgently.

HOW CAN AZ IMPROVE THE PARTNERING EXPERIENCE FOR SMALL COMPANIES?

GRADY: That is actually where we're focusing our time and effort, because it shouldn't be daunting. For companies with good science, good technology, and good people, it should just be a lot easier to interact. My group includes about 150 people around the world, and we are focused this year on getting our people to speak with the right scientific experts and the right geographical experts, expeditiously. We are having more peer-to-peer engagement and getting good feedback. In the industry, there can still be a sense of arrogance about deigning to be with the smaller companies. So, we're trying to recalibrate that whole relationship. In November 2011, we set up a meeting between our R&D and business development leadership with all the key academic and biotech leaders in the greater Boston area. At our annual CEO Conference, we invited executives from current and prospective partners to give us candid feedback on what it felt like to interact with Big Pharma generally and AZ in particular. As a result, amongst other things, we have set specific targets for turnaround times and responsiveness to external opportunities. These will be included in everyone's individual performance targets in the business development function.

HOW EARLY IN RESEARCH CAN SUCH A RELATIONSHIP BEGIN?

GRADY: We all recognize that we need to talk to each other much earlier, even if there isn't a deal in sight, just to get a better sense of what we need, what we think, what's impacting and influencing the science, and what the university researchers and start-ups are doing at the early stage. In our areas of high interest we are prepared to offer our feedback and advice — and in theory — even services to companies on a no-commitment basis just to get to know them and their management and to put AstraZeneca in a good place when the time does come for partnering discussions.

DURING DUE DILIGENCE, ARE THE SCIENTIFIC PEOPLE MORE CONSERVATIVE THAN THE BUSINESS STAFF?

GRADY: Well, when you say conservative, you might just say, realistic. Listen, it's true we've had some cases where a supposedly advanced project was not quite so advanced after we got a closer look at it, and the company needed to do a lot more work on it. But it's not just about the due diligence; it's more about the feedback we give and get. If we like things, we'll tell people why, but if we don't like things, we try to give full and proper accounts of how we see the opportunity as well as any obstacles. We gave some very specific post due diligence to a prospective partner in China about a year ago around the regulatory pathway, dosing, and formulation. The company recently approached us again to say it had taken our advice, and we are now engaged with them to review the opportunity again.

WHY DO YOU PREFER TO PARTNER WITH COMPANIES THAT HAVE PRODUCTS READY FOR LATE-STAGE TRIALS?

GRADY: We are looking to partner and collaborate all along the value chain. Sure, our priority right now is later stage assets, but if you don't attend to the earlier opportunities you will always find yourself prioritizing later stage. Big Pharma has the experience to run the global Phase 3 trials and has the ability to fund them. So actually my job — our job — is to find those programs at the point where we can apply

our specific skill set, or as we refer to it, our "edge." We want to get into a discussion, help design those trials, and execute them in Phase 3 because that's an area we are comfortable operating in.

HOW DO YOU DIVIDE YOUR INVESTMENT BETWEEN EXTERNAL AND INTERNAL RESEARCH — AND BETWEEN EARLY VERSUS LATE-STAGE PROJECTS?

GRADY: We set ourselves a target of having 40% of our pipeline and portfolio coming from programs that began life outside AstraZeneca — and we are broadly at that level today. It varies a bit across the different discovery and development phases and is currently higher at the later phases. What's important is that it isn't about doing deals to meet a particular percentage target if the quality isn't there. Equally, we won't stop if we reach that target and still see attractive opportunities. It is all about quality.

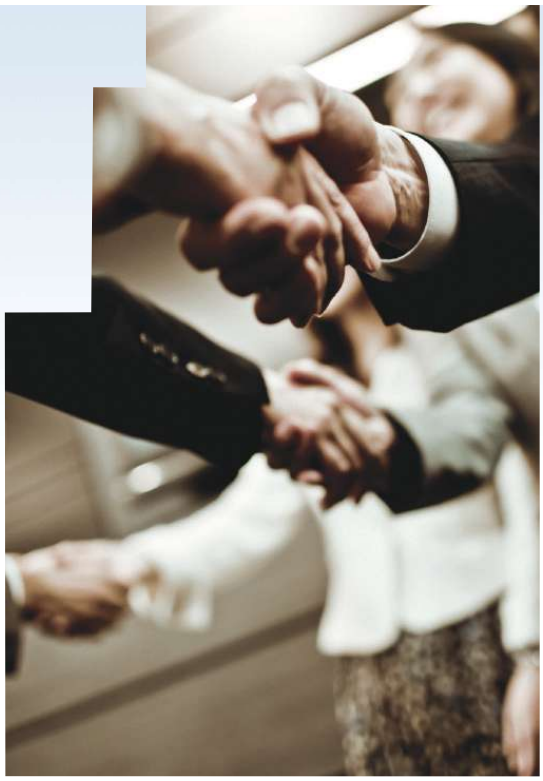
WHAT CAN COMPANIES DO TO AVOID THE COMMON PITFALLS OF SEEKING AND SECURING PARTNERS?

GRADY: As a small company, my advice is that you should talk to pharma companies early and be open, honest, and willing to listen. I'd talk to multiple pharma companies and hear what they've got to say — hear their feedback. And then on the pharma side, we need to be more open to giving and hearing feedback from the small companies, recognizing that we need to accommodate what is important to them and that, if we steer them in the right direction, they could come back to us at a later stage with a more attractive opportunity. There is still some residual "them-and-us" mentality in the industry — an old pattern we just have to forget and break out of. Everybody needs to be a bit more open with each other. The Pharmas who break out of that the quickest have a real opportunity to differentiate themselves from their peers.

WHEN DO YOU START THINKING ABOUT AN ACQUISITION RATHER THAN PARTNERING OR LICENSING?

GRADY: We pretty much look at any project potentially from an M&A perspective as well as a licensing perspective. All things being equal, you do a licensing deal because you get the risk profile aligned properly with your financial investments and risk is shared. We are open to considering acquisitions if the asset is strategically important to us or there is a bigger portofolio that fits well with our strategy. More often you're seeing acquisitions with deferred considerations or other contingencies — a kind of licensing deal by another name.

M&A Payback In 100 Days



By Matthew McCreight and Wes Siegel

Acquisitions and mergers are central to the strategies of many companies in the pharmaceutical and related industries. Some companies view M&A as a way to increase their cost competitiveness, for example the merger of Roche and Genentech. Others see M&A as a way to gain access to new channels and markets, as with Bausch + Lomb's recent market acquisition in Argentina. And still others use acquisitions to reinforce pipeline strength, as exemplified by the merger of Merck and Schering-Plough in 2010.

Whatever the underlying reason, M&A is seen as a major way to create value and strategic success. Given the vital importance of such activities, why is the track record of achievement so uneven? For every success story, there seem to be multiple examples of unrealized potential or of outright failure.

The shortfall is not for lack of trying. The effort expended to integrate two companies is often unprecedented in the life of an organization. Armies of people — from inside and outside a company — are involved in a broad array of activities to create unified structures and systems, take out costs, build integrated brands, harmonize R&D, and more. Time horizons, "temporary teams," and financial charges can stretch for years, as with Pfizer's $600 million impairment in its Q1 2012 reporting for its acquisition of Wyeth two and a half years ago.

STEPS TOWARD M&A SUCCESS

So, what does it take for leaders to ensure that their companies capture significant value from mergers and acquisitions? From our work with many pharmaceutical companies, as well as in other industries around the world, there are several key steps leaders can take to ensure a high and rapid ROI from M&A:

1. Keep your eyes on the strategic prize: The transformation of your company's future is the reason for the merger, not the integration of two organizations.
2. Don't settle for passive acquiescence — build the entire top team's commitment to the goal of achieving the aggressive value-creating aspirations underlying the merger — or get a new top team right away.
3. Champion a different kind of merger integration — where your focus is on rapidly multiplying talent and results at the front lines of the company, not on tracking a gantt chart of project activities. Speed of results achievement is crucial — major results should be delivered in the first 100 days, if not faster.

LEADERS SHOULD FOCUS ON THE TRANSFORMATION

Perhaps the most important role for leaders of newly merged entities is to focus attention during all stages of the merger on the strategic goal of the transformation of the company. The reason for the merger is not (or should not be) to "bring two companies together into one" — that describes a marriage, not a strategic merger. The reason for the merger is (or should be) to create a synergistic dynamo, a new company that is more competitive, capable, and successful than either of the predecessor companies could ever have been on their own.

Focusing on transformation means driving for new levels of performance from the very start, even before "nuts-and-bolts" integration issues like organizational and systems integration are complete. For example, commercial leaders at Merck challenged managers of their top markets to drive incremental growth from inline brands from both Merck and Schering-Plough's legacy portfolios. They created a rapid-cycle engagement strategy where local sales and marketing resources identified and committed to $500 million in recurring revenues, with minimal additional investments. This effort generated new revenue from the integrated portfolios and engaged the markets in a strategically important diversification of products that includes launch, growth, and inline brands.

Focusing on transformation also

means investing the time and effort required for true leadership team alignment and commitment to realizing the sources of intended value. Many leaders end up making Faustian bargains about the commitment of their leadership teams, believing that with enough time even the most recalcitrant of team members will "get onboard" and support this all-important effort. Unfortunately, there is little relationship between length of time to "think about it" and the extent to which dissenting leaders make the required change of heart. Instead, the lack of commitment from top members can continue for months or years and erode the progress not just of the integration of the merged companies, but toward the much more difficult and important goal of transforming how the new company works. One marked difference in how company leaders typically carry out their second major merger over how they drive their first is that senior team issues get addressed and leadership changes are made much faster the second time around.

How does a leader build top team commitment to the transformation of the company? While there is no one way, it is important to start with an honest assessment of the team members' views and the transformational goals and areas for performance improvement that underlie the merger. Developmental and performance expectations and commitments then must be discussed explicitly with the leadership team. Once this is done, it is essential to translate these commitments into action quickly, so leaders start to learn how to work in this new mode and drive real value creation from the merger.

Driving real success in transforming the company requires leaders to take a much more active role as champions of value achievement. They must demand progress on key strategic, commercial,

and operational goals while facilitating the learning and adaptation required to realize them throughout the integration. And they must support the development of a new culture, one that involves people working differently and breaking down previous silos, so the transformation can take place rapidly. Clarity about expectations and steadfast commitment to their realization will help to create the conditions where people learn how to collaborate to drive the transformation.

This can be done by demanding focused, rapid action initiatives that spearhead the realization of intended benefits through cross-silo collaboration. At the heart of this approach is a focus on driving for significant results in rapid-paced waves of 100 days or less. Our experience over the last 50 years has shown that this is the way companies break through long-standing barriers to change and create exceptional levels of performance. For example, J&J's Regulatory Quality & Assurance group started its integration of two very different global quality groups by setting an aggressive goal to create common global processes for three major activities in 100 days. Previously, up to five different processes existed in the various groups. The initiative had a stretch goal to remove 25% or more of the effort from the processes, have them all fully documented, and all staff trained and working in all locations within the 100 days.

Initiatives like this can be applied in a variety of areas. Rapid-cycle customer conversion and channel penetration efforts can establish beachheads of initial success that can then be scaled across the enterprise. Throughout an integration, leaders need to hold fast to cost-reduction commitments and timelines — while insisting that the affected areas maintain or surpass benchmark performance levels. These demands for breakthrough performance levels bring the transformation to life and develop a culture that is consistent with the strategic vision that originally inspired the merger.

EMPOWERING YOUR STAFF IS KEY

Another key step toward transformation success is to frame the merger integration as an opportunity to multiply organizational talent. Talent can be developed by tasking high-potential managers to contribute to the realization of intended merger value. Putting talent on the front lines of the rapid-action initiatives described above has several benefits:

- Leaders can test capabilities of legacy and acquired talent.
- Managers who participate can be educated more deeply about the merged entity's strategy and enrolled in communicating and distributing the strategy more broadly.
- Key opinion leaders are tasked to work across boundaries, promulgating a culture that fits the strategy of the new entity — and leverages the best of both legacy cultures.

By recognizing a merger as an organizational transformation, insisting on top team enrollment, and pursuing rapid results that both realize strategic value and develop talent, leaders can dramatically increase merger ROI. These shifts in mindset and behavior move beyond tactical integration management, recognizing the integration as a vehicle for organizational transformation and strategy execution. But to make this transition, leaders must recognize the opportunities that mergers present to renew and revitalize corporate strategy and engage people in executing and realizing it. Pharmaceutical leaders and their teams who build these capabilities will prevail in the new biopharmaceutical landscape.

About the Authors

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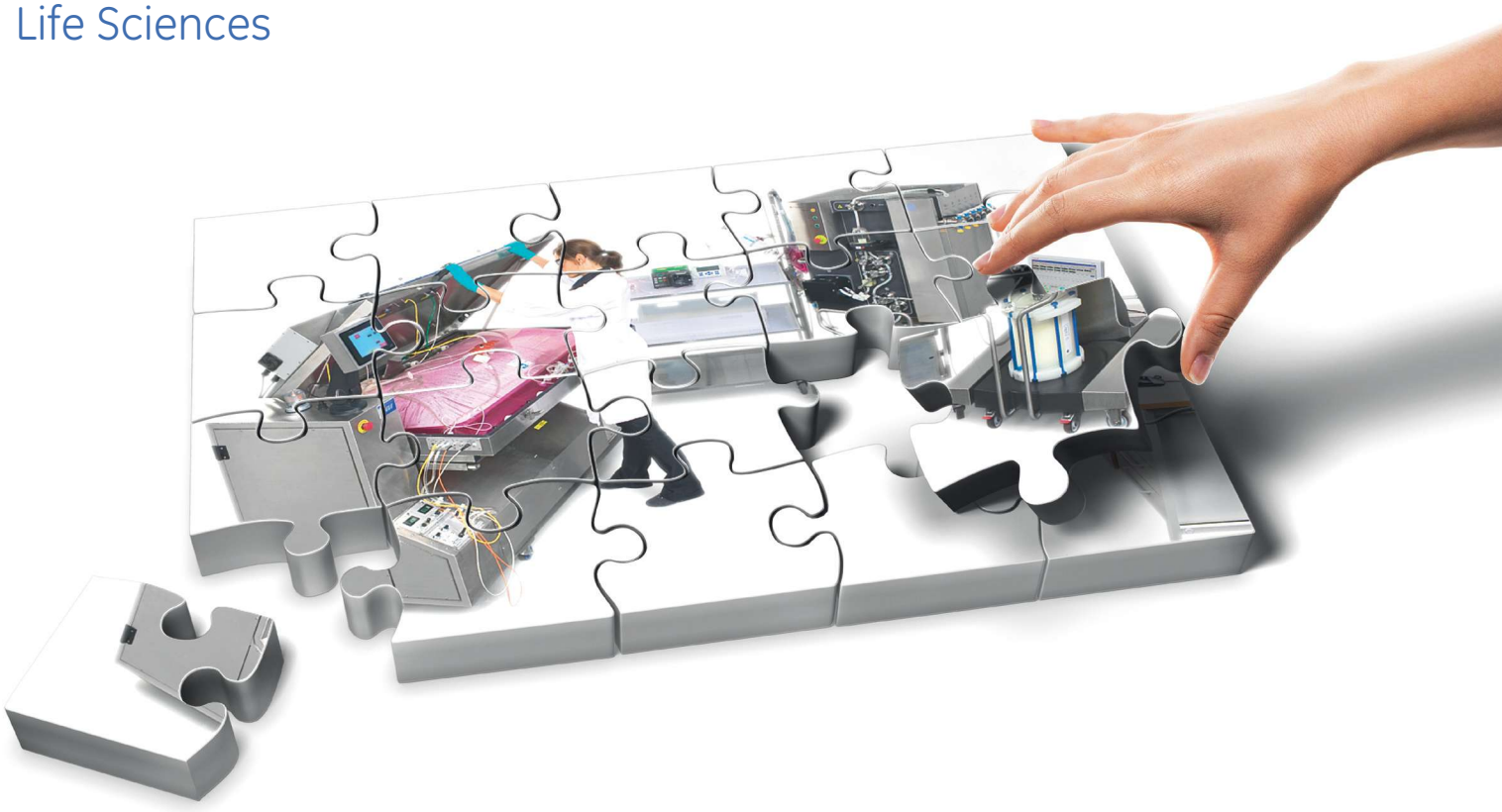

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Advice For Biotech Start-Ups From Someone Who's Been There

By Fred Olds, contributing editor

Larry Lasky, Ph.D., partner at US Venture Partners, will tell you it's hard to get venture capital to fund a project. Then, he will tell you it's not hard if you have good data. By "not hard," he means to make it easy for VCs to see a compelling plan backed by data and directed by a team that inspires confidence. Preparation and timing are critical. It's hard enough to get in to present a plan. He says make sure your plan is good enough to get you taken seriously. Getting it right requires expertise.

Lasky is a biotech pioneer. In 1981 he was a founding scientist in Genetics Institute, one of the first biotech start-ups. In the following 30 years, he conducted research at Genentech in its highest scientific position, Genentech Fellow. In 2002 he moved to venture capital, where he launched a number of successful companies. He also teaches a course in biotech start-ups at UC Berkley. Here are his observations on the state of biotech and venture capital and some advice on approaching the start-up process.

THE DARWINIAN ENVIRONMENT

Founders frequently blame venture capital for turning down so many plans. Lasky agrees that venture capitalists are very risk-averse. "The current environment is Darwinian," he says, but he disputes that the fault lies with the VC. "Most proposals are turned down because they should be." The blame for failure lies most often with a plan that lacks the scientific foundation or business understanding to warrant support.

"It's very 'squishy' stuff," says Lasky in describing the biotech start-up process. "There are lots of components to it, and I think it's hard to teach." It's challenging to lay out precise instructions for founders to follow to get noticed, sell their ideas, and set up shop. Nonetheless, he says it's easy to identify a plan that might work. You know it when you see it. He says it's fairly easy to read a proposal and tell very quickly whether it should get further consideration by the amount of scientific backing and the details of the plan. Lasky offers this formula to get consideration: "It's about a good team, a compelling plan, and interesting science. That's how a company gets started."

INTERESTING SCIENCE

"What will catch a scientist's attention," says Lasky, "is a novel target in a hot area of medicine." Novel doesn't mean a new, isolated discovery. It means a target that hasn't been commercialized. It's a target backed by scores of papers supporting its importance in human disease. He says too often researchers get excited about the science. The real issue is its relevance to humans.

"The problem with novel targets is eponymous," warns Lasky. They are inherently very risky, but the rewards could be very high, as well. Founders have to mitigate those risks with solid evidence. They have to provide research demonstrating a positive effect in an important human disease. They will need to identify the sets and subsets of patients they feel will benefit from the compound. Next, they have to develop assays to measure those effects. Most importantly, they have to propose how all of this can be translated into a compound that can be administered safely to humans and make a difference.

Lasky's particular "hot area of medicine" is oncology. He feels it's a field in which he can help the most people, but there are other hot areas. He suggests carefully selecting VCs with an experienced scientist on staff who will understand the esoterica of the founders' research. He warns that there is naïveté on both sides of the VC equation. Usually, scientists don't

appreciate how important and difficult the business aspects are to the venture. The funding partners are likely to lack the scientific expertise in cellular and molecular biology and pathology. They may have a young Ph.D. on staff who can explain the science, but who lacks the experience. "It's not the same thing. Biotech is much more complex than other ventures," says Lasky.

THE BUSINESS PLAN

The business plan has to persuade VCs that the founders can return value on the investors' capital. The plan should be about the business of making the science a commercial success. Lasky says all too often the founders get caught up in their excitement over the science, and they forget that the VC is focused on business.

He says, "My best advice is to talk to someone else who's done it before." There are just too few opportunities to get an audience and too many possibilities to stumble. Rely on a mentor for sober advice and introductions in the community. Get an introduction to a potential mentor the same way you will to VCs. Search for someone with success in biotech start-ups and with the clinical expertise to understand your science. It becomes an exercise in networking. Begin to work for introductions to VCs, as well, but don't pitch your work too soon. Get to know investors as you build the evidence for the research. Put out feelers. Describe the science, and ask if they might be interested at a later date.

The starting point for the plan is the exit point for the company. Lasky says virtually all biotech companies exit with a buyout from big pharma as the compound is in or heading to the clinic, "It's just too expensive and too long a timeline to try to launch a commercial operation." Plan the company backwards from the exit. Visualize what the patient population is, how many will be needed for clinical trials, what assays need to be designed, what statistical models are needed to measure outcomes with significance, what the desired endpoint of trials is, how the target will be translated into a compound for human administration, what preclinical studies need to be conducted, what space and equipment will be required, who has to be on the team, how the basic research is to be presented to show it's a good candidate for commercialization, and to whom the company should be pitched. Finally, ask, "What will this cost?" Designing the plan, then, is a matter of explaining how the team will direct the company to that end.

Lasky advises, "Try to get all the funds you think you will need to get to the clinic. Leaders underestimate the time they will spend trying to get series funding." He says getting it all from the beginning will require a consortium of some sort to aggregate enough funds. The team will have to plan for series funding and valuation. Determining funding out to 18 months is generally feasible. Beyond that requires some extrapolation and comparisons to other ventures. The important issue is that just like the business plan, the team must project with some confidence an ever-increasing line of valuation over time. Valuation has to be optimized so that at every tranche the company returns value to the previous investors while promising future value to new VCs. A level or losing series demoralizes the investors and makes any future series of funding nearly impossible.

Finally, the presentation is about and for the investors. It's the founders' opportunity to instill confidence in the VCs. The team has to convince investors that the company leadership is competent and resourceful enough to be trusted with the investors' money. Founders can't view and act as though the presentation is getting their ticket punched on their way to success. Show how the founders can make everyone — investors, partners, staff — successful.

Also, expect to fail often. There can be a lot of reasons for rejection, and it's critical to understand each one. Use the feedback to improve your plan.

THE TEAM

The team and the reputation of each member will influence the decision of an investor. Lasky says scientists from top research institutions as well as company officers with prior successful experience will improve chances for funding. While they may not conduct background checks on the suitors, VCs may conduct inquiries as to the team members' ability to get along and work congenially in a team.

The team should be science-heavy. Lasky explains that about 95% of the operation is research-based initially. It's important to have a CEO who knows the science as well as the business. Additionally, investors may look for flexibility, synergy, and complementary skillsets among the team. A start-up comes with the unexpected, and whatever needs to be done is in everyone's job description. Resourcefulness is imperative. The place to show this is in the presentation. Each team member should have time in front of the investors to give them a sense that the team is knowledgeable and competent.

PERSEVERANCE

Lasky says the biotech industry is always dealing with the new and interesting. You have the opportunity to make a drug that saves someone's life. Keep that in mind, because perseverance is a necessary ingredient to do it. Founders have to be steeled for rejection. However, Lasky believes good ideas have lasting power and will bubble to the top. He says Proteolix was a huge success in the end, but was a tremendous struggle to get off the ground. "It's like anything else that's important. If it's good, you just can't give up."

Cloud Computing Reduces Time And Money

By Cindy Dubin, contributing editor

It's a pharmaceutical given: Expect to spend $1.3 billion and 15 years to bring one drug to market. So, when cloud computing came along a couple of years ago with the promise of reducing time and money, large biopharma companies began moving their major business processes and applications to the cloud.

Cloud computing is rapidly growing in importance as life sciences R&D organizations are deluged with data from multiple sources. Simultaneously, demand for computationally complex modeling and simulation studies continues to rise dramatically. Limited funding and budgets make it difficult for many organizations to build the IT infrastructure necessary to keep pace with these challenges. Cloud computing appears, for many, as a promising alternative to in-house expansion of IT services. The trend in pharma toward more outsourcing, combined with restricted budgets and the increasing attractiveness of cloud computing offerings, has created a highly dynamic, yet nascent, market, writes Ken Rubenstein, Ph.D., in his book *Cloud Computing in Life Sciences R&D*.

The main impact to pharmaceutical companies of increased usage of cloud computing is a reduced dependence on their own IT infrastructures. Cloud computing offers the ability to implement services in a matter of minutes, by self-service from a Web platform. Cloud computing also provides the ability for companies to move away from intensive capital expenditures to an operating expenditure/pay-as-you-go business model. The business advantages of cloud computing include the standardization and streamlining of operations and stronger collaboration among external entities and the healthcare ecosystem as all parties have access to the cloud.

Lower costs are the result. By only paying for the computer power that you are currently using, you can lower the costs of meeting variable or unpredictable demands. However, the cost advantages of moving to cloud-based computing may not be as profound as some declare. Transition costs need to be taken into consideration. It is clear that organizations that already have in-house data centers will have to look at an investment in cloud computing as another cost or will have to merge their internal world with the cloud-based world and manage the switching costs. Even in this situation, the cloud model provides an attractive mechanism for rapid provision of high computational or storage capabilities when demands exceed existing infrastructure capacity.

Cloud computing is identified by SAFE-BioPharma Association as one of three IT trends that will shape the life sciences industry in 2012. The ability to create new alliances and get trial sites up and running more quickly, as well as analyze data more rapidly because it is standardized and centralized, could yield substantial financial advantages. Reducing time to market by just one month for a product that generates annual sales of $300 million could deliver $25 million in extra sales.

OPERATING COSTS DOWN 30%

According to IBM Global Business Services, cloud computing allows pharma to operate more efficiently by cutting IT costs and accelerating the deploying of new technologies and processes. Sharing an IT platform with other entities means an organization can use computing resources more efficiently and reduce the amount of data it needs to store. IBM's research suggests that life sciences organizations can save as much as 25% of their annual operating expenditures on clinical IT systems by using cloud computing.

At GlaxoSmithKline (GSK), that number is closer to 30%. GSK spends more than $5.9 billion each year in research. Back in 2010, GSK was searching for the ability to collaborate with external partners, support growing markets, move away from customized IT solutions, decrease operating and investment costs, and access the work environment from anywhere at any time with any device.

GSK chose to replace its existing Lotus Notes, Domino, and Postini services with the Microsoft Business Productivity Online Suite, which included Microsoft Exchange Online, Microsoft Office SharePoint Online, Microsoft Office Communications Online, Microsoft Office Live Meeting, and the Microsoft Deskless Worker Suite. The company deployed the solution to 96,500

employees worldwide, with everything being hosted by Microsoft at Microsoft data centers around the globe. "Rather than spend a ton of money to upgrade our old system, we chose to move to an external host," says Adam Raeburn-James, senior VP of end user and infrastructure services at GSK.

Through online services, Microsoft offers the ability to have fully functioning applications with a lean presence. The software will operate in the same capacity in a hosted solution as it would if it were implemented on-premise. The global implementation of Microsoft Online Services at GSK is intended to have numerous advantages for the company, including reducing operational costs.

"Moving to Online Services enables us to reduce our capital input and our total cost of ownership by 1/3 over the next five years," says Raeburn-James. The ability to introduce a variable cost subscription model for these collaborative technologies allows GSK to more rapidly scale or divest its investment as necessary. That translates into putting more money back into the business. In addition to using the cloud for email and collaboration, Raeburn-James says that GSK will likely make more use of cloud computing in human resources and infrastructure in the near future. "As the online service industry matures, the cloud will be used in more of our business," he says. "It is foreseeable that the whole clinical process could be running on software in the cloud."

R&D PRODUCTIVITY AND LOWER COSTS

Bryn Roberts, Ph.D., global head of informatics for pharma research and early development at Roche, agrees that cloud computing will enable science, R&D, and collaboration among the pharma community. And, that the goal is to increase R&D productivity while decreasing costs. "The main drivers for moving to the cloud for R&D are enabling science and collaboration while controlling or reducing costs."

"The main drivers for moving to the cloud for R&D are enabling science and collaboration while controlling or reducing costs."

Bryn Roberts, Ph.D., global head of informatics for pharma research and early development, Roche

Roberts, along with his colleagues at The PRISM Forum Association, a nonprofit organization that facilitates cross-industry discussions on hot topics in R&D informatics, recently published a paper about the relationship between the cloud and life sciences. The paper states computer-based technologies will underpin all R&D activities and that next-generation sequencing (NGS) will produce unprecedented volumes of data that might best be stored, shared, and analyzed in a cloud environment. To handle the NGS data explosion, Roche expects to have to leverage data stored in the cloud as well as within its own internal high-performance computing environment.

This past October, Roche purchased the Provantis Preclinical SaaS solution from Instem to consolidate several key application areas and harmonize Roche sites worldwide. Roche will access the integrated General Toxicology, Pathology, Clinical Pathology, and Protocol & Report Assembly modules using the SaaS delivery model from a U.S.-based data center. A data import solution allows Roche to import data from external sources.

"Rather than spend a ton of money to upgrade our old system, we chose to move to an external host."

Adam Raeburn-James, senior VP of end user and infrastructure services, GSK

"With the rising cost of R&D, consolidating the number of IT systems and vendors allows us to focus on science, reduce IT complexity, and speed up the R&D process," says Roberts. "Cloud computing will enable us to harmonize our system landscape for the nonclinical safety departments and help our scientists optimize laboratory processes with one fully integrated solution." Roche is still evaluating whether current cloud computing services for functionality, such as virtual screening, offer advantages over in-house high-performance computing in tests, such as protein folding.

Regarding the recent announcement that Roche will source email and calendar services from Google, Ken Wilcox, senior VP and global head of pharma informatics at the company, explains that Roche had been using traditional on-site software from multiple suppliers but felt that a cloud-based model would lower infrastructure and support costs.

When it comes to handling an unlimited number of users, Wilcox believes cloud computing has potential. Hundreds or thousands of servers can be up and running in less than an hour and scaled down just as quickly, and Roche only pays for the time it uses.

Costs do decrease with cloud computing, but Roche has yet to total all project numbers to determine its total savings to date. However, Wilcox is convinced that cloud computing will improve mobility options, equip workers in the field, enable global business integration, and also be a cost and time saver for Roche.

Roberts adds, "We will use cloud where it makes sense. The selective use of cloud services accelerates work and research and reduces the time it takes to analyze large volumes of data. More collaboration among scientists means greater success not just within a pharmaceutical company but across the scientific community."

The Three Words That Can Determine Patent Ownership

By Cathy Yarbrough, contributing editor

Three words — "and hereby assigns" — could determine whether a patent is owned by the company at which the invention occurred or by the employee or consultant responsible for the invention, said Philip Strassburger, VP of intellectual property counsel at Purdue Pharma. In a presentation at the Drug Delivery Partnerships conference, Strassburger noted that these words too often are missing from the agreements that life sciences companies require staff and consultants to sign as a condition of employment.

Strassburger said that the employer-employee/consultant agreement should include text similar to the following:

"All ideas, discoveries and inventions ('Inventions') discovered by employee in the course of its employment shall be and remain the exclusive property of Employer. Employee agrees to assign ***and hereby assigns*** all right, title, and interest in such Inventions to Employer."

"It's surprising how many companies do not have this language," Strassburger said, referring to "and hereby assigns," which is known as "present assignment" terminology. In a contract calling for a "present assignment" of inventions, the employee's or consultant's signature shows that they agree that the company owns any invention that they make during their employment.

Without the inclusion of a "present assignment," the contract may be legally interpreted to mean the employee promised that at a future date they will assign ownership of the invention to the company. Strassburger refers to the promise-to-assign as "future assignment." An agreement that includes "present assignment" as well as "future assignment" terminology "gives companies rights that otherwise that they may not have," Strassburger said.

The inclusion of "present assignment" terminology strengthens the company's ability to successfully assert its ownership of the IP, as illustrated by several court cases. For example, in *DDB Tech v. MLB Advances Media*, even though an employee had assigned his rights to the IP to his employer, he filed his own patent application and then assigned the patent to another company (DDB). Subsequently, DDB sued a third company for infringement of the patent, but the third company had acquired all rights to the IP as well as a retroactive license from the employee's employer. The case was dismissed because the third company, not DDB, legally owned the rights to the patent. "DDB had paid for the patent application but ended up with no rights," said Strassburger.

ENSURE A SOLID CHAIN OF TITLE EXISTS FOR YOUR INVENTION

In determining ownership, IP and real estate are very similar. "When people buy real estate, a lot of attention is paid to ownership," said Strassburger. "They obtain a chain of title to make sure they're getting what they think they're paying for and because a bank is not going to lend money to purchase the real estate unless a clear chain of title exists on the property. "However, even with a clear chain of title, the bank will require that buyer to obtain title insurance," Strassburger explained.

Because title insurance is generally not available to protect owners of IP, companies must be very vigilant to ensure that a solid chain of title exists for each invention and that they have the constitutional standing needed to effectively assert ownership if challenged. "We've learned from several court cases regarding IP that a company must get this right. It affects a company's standing in court and the damages and injunctive relief that it may seek," he said.

If a company sues, its failure to have standing may result in dismissal of the case, which may result in a pharmaceutical company losing the 30-month stay that is granted in patent infringement suits. "This is not rocket science, but it is complicated," added Strassburger, who

recommends that life sciences companies:

- **Conduct due diligence investigations to confirm IP chain of title** prior to purchase and prior to filing suit. For a company's most important IP, due diligence should be periodically conducted to confirm that the chain of title remains intact.
- **Structure agreements to address business needs** and objectives, including potential future litigation and the business needs for that litigation. For example, will the company need to be able to sue under the patent or is freedom-to-operate sufficient?
- **Review all employee and consultant agreements** to ensure they include both a "present assignment" and a "future assignment" of ownership of inventions to the company.
- **Confirm that the company's IP has a clear chain of title** before mergers, acquisitions, and new affiliations, including those with affiliates, prior to the transfer of patents.

"A company must be sure that the ownership of patents is being passed through from one company to another so that the IP can be asserted effectively."

Philip Strassburger,
VP of intellectual property counsel, Purdue Pharma

"A company must be sure that the ownership of patents is being passed through from one company to another so that the IP can be asserted effectively," said Strassburger. "At the time of any transfer, a company should ensure that all necessary assignments are made at that time and do not rely on future transactions."

Strassburger noted that there are cases in which the lawyers failed to execute all the documents needed "to put everything in the right place," during mergers and acquisitions.

Company officials who discover that their patents were not properly transferred can often rectify the mistake with amendments, he pointed out. But, such corrections should be completed before damages occur or before litigation.

Strassburger cited a "real world" example in Abraxis v. Navinta, a patent infringement lawsuit about a patent that was originally owned by affiliates of AstraZenica (AZ). The affiliates had not made a timely assignment of the patent to AZ for the company's anesthetic Naropin when the company assigned the IP to Abraxis.

Under the Hatch-Waxman Act, Abraxis filed a patent infringement lawsuit against Navinta, which had submitted an abbreviated new drug application (ANDA) for a generic version of Naropin. When AZ discovered it did not have the rights to transfer the IP to Abraxis, the affiliated companies subsequently executed an assignment to the pharmaceutical company. However, since the assignment did not occur prior to the filing of the lawsuit, the case was dismissed for lack of standing.

"When the lawsuit was filed, Abraxis did not properly own the patents. It was a matter of timing," explained Strassburger. If the assignments had occurred prior to filing suit, there would have been standing, and the litigation could have proceeded.

- **Before filing a lawsuit to assert its IP, a company should conduct a due diligence investigation** to confirm that it legally owns the IP and that it has been properly transferred to the company.

"The company also should make sure the patent has not been reassigned," said Strassburger, who also recommends that an IP owner assign patents to the parties (i.e. affiliates) that are consistent with litigation strategy. For example, the affiliate that will be damaged should have an ownership interest in the IP, so it can seek to recover damages.

- **Understand the licensing rights that can be asserted in court.**

A company that is the sole owner of the patent or is the exclusive licensee and has all substantial rights has the constitutional standing to sue and settle, said Strassburger. To have standing, the exclusive licensee legally does not need for the patentee to join the suit.

If a company has a nonexclusive license, in which the rights to the IP are shared, it lacks constitutional standing to sue without the involvement of the owner(s). The licensing agreement, however, can state whether owners must join a patent infringement suit. "The licensing agreement should stipulate that each owner will become a party to any suit that the other owner or licensee wishes to file," said Strassburger.

Although the license acquired by a company may be exclusive, the licensee may not have all substantial rights. "Calling a license

exclusive does not necessarily make it an exclusive license," he explained. "The license agreement may not provide sufficient rights to be considered by the court as an exclusive license."

Also, the existence of only one licensee does not necessarily make the license exclusive.

"When negotiating an exclusive license, a company should confirm that it will receive all substantial rights to assert the patent. And, before litigation, the licensee should confirm it again to be sure that the license has not been amended," Strassburger said.

He also noted that often the licensee and patentee could amend the licensing agreement to improve the licensee's standing before going to court. "Courts look to the substance of the license grant to determine whether all substantial rights have been granted," said Strassburger, who added that courts consider the following factors:

- Exclusive right to make, have made, use, sell, offer to sell, and import
- Territory and field of use limitations
- Term limits and termination rights
- Rights to enforce against infringers
- Right to grant sublicenses
- Right to assign
- Understand the implications for an owner or exclusive licensee, that it is not practicing, asserting a patent

If the owner or exclusive licensee of the patent is not practicing the invention, it may only be entitled to reasonable royalties and not lost profits. Also, to obtain injunctive relief, a company often must prove irreparable harm, Strassburger added. "And, for permanent injunction, patent owners must show irreparable harm. It usually is not enough to show irreparable harm to a nonparty licensee."

Protecting IP is one of the most important issues that decision makers in the life sciences business can improve upon if they take a few disciplined measures in a timely fashion. Strassburger said that he hopes individuals who attend his presentations — or read this article — will dedicate time, effort, and resources to perfecting the status of their company's IP, so valuable inventions can be protected by the courts.

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Best Practices For Successful Collaboration

Laurie Mims (top) and Audrey Walton-Hadlock are trial lawyers at Keker & Van Nest LLP with substantial experience litigating business relationships gone awry. This article is not intended as legal advice.

Although collaborations between companies are often necessary to bring new drugs or devices to market, many such collaborations end in unexpected acrimony and litigation. Companies can protect themselves in case a strategic alliance turns sour, however, by drafting agreements to minimize potential disputes with partners and by keeping the possibility of future disputes in mind throughout the collaboration. Any company engaging in a collaboration should consult with counsel for specific legal advice about how the following best practices can contribute to a successful collaboration relationship — or to success in litigation, if the relationship fails.

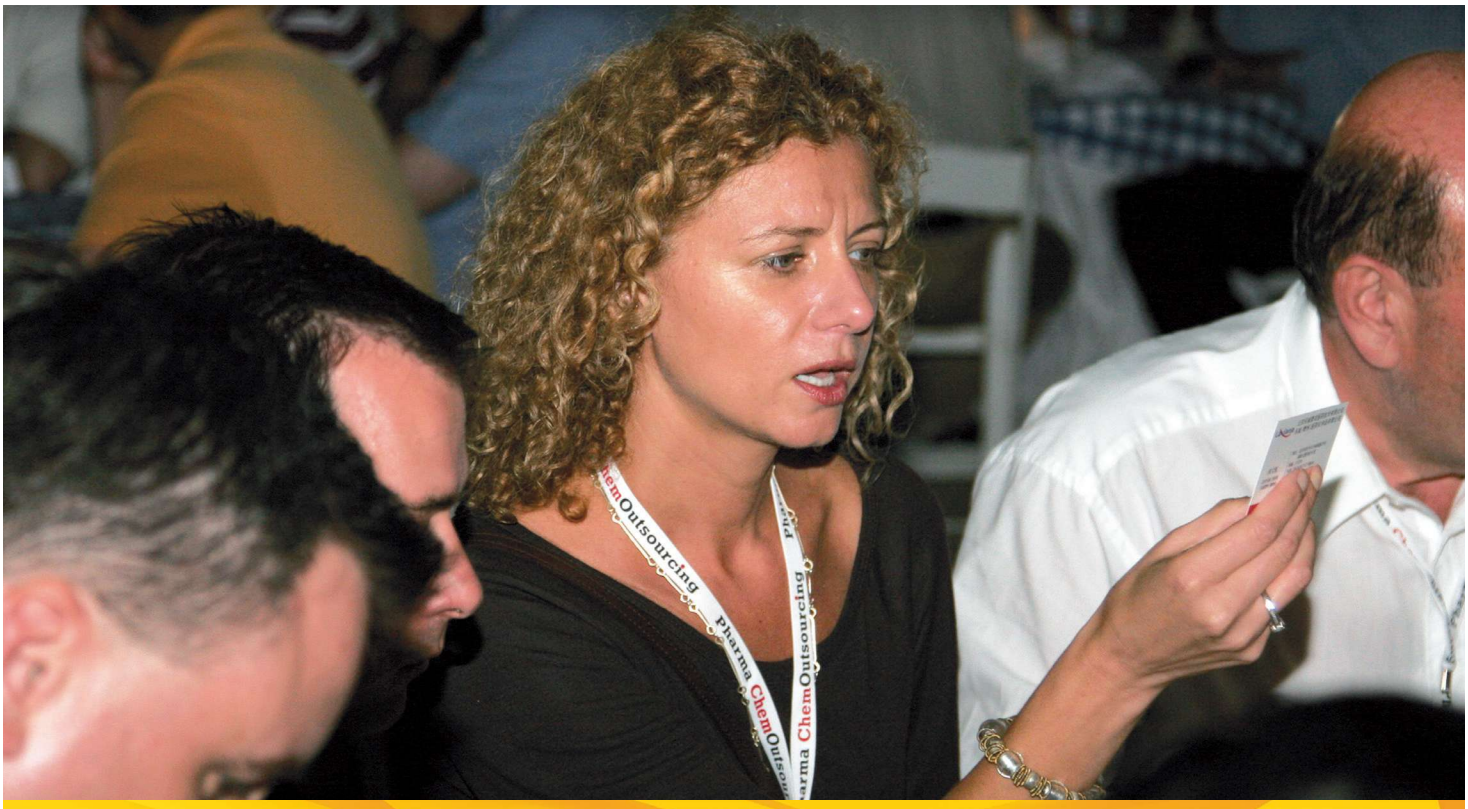
Make key contract provisions clear and objective. At the drafting stage, a company can reduce the litigation risk of provisions, allowing a collaboration partner to terminate the agreement or to prevent changes of control by defining the conditions for exercise of those rights as strictly and objectively as possible. For example, if a partner can terminate because of "safety concerns" regarding an investigational drug, clear language should define the types of safety concerns that can trigger that termination right (such as a death in a clinical trial, an FDA clinical hold based on safety issues, or a certain number or type of serious adverse events). Likewise, if a change-of-control provision restricts mergers with certain types of companies, defining those companies by name or by some objectively-determined criteria (e.g. Fortune 500 companies or NYSE-listed companies) can minimize later disputes about whether a particular merger can proceed. Using concrete, objective standards for these and any other contract provisions that impact critical business needs can make it easier for a court or arbitrator to reach a quick, cost-effective decision in related disputes, and may help eliminate disputes before they proceed to litigation at all.

Craft dispute-resolution provisions to reduce potential litigation expenses. Collaboration agreements typically require binding arbitration of disputes, which can benefit all parties by reducing costs and resolving disputes more quickly than litigation in court. To maximize these benefits, a company can craft an arbitration clause that defines the timing and scope of the arbitration process. For example, an agreement can expedite arbitration by setting fixed deadlines for completion of the arbitration or for the "discovery" process used for fact investigation. An agreement can also restrict the scope of discovery by limiting the number of depositions (or prohibiting them entirely) or limiting written discovery to an exchange of documents. Parties may also benefit from a mandatory mediation prior to arbitration, in which an unbiased third party can evaluate each side's position and preview the likely outcome of arbitration.

Document progress and interactions during the collaboration. Once collaboration begins, a company can protect its interests in future litigation by remembering that the partnership may end and keeping written records of the parties' work and important interactions. For example, if a joint steering committee or similar group oversees the collaboration, it should document its actions completely and accurately in meeting minutes or other records. Likewise, anyone who shares important information or makes decisions with a collaboration partner in person or by telephone can send a follow-up letter, email, or memo to the file to memorialize that fact. Documents predating any dispute carry great weight in litigation, and good record-taking may prevent he-said-she-said arguments on important issues years later.

Raise problems and issues in real time. If a collaboration does not proceed as expected, raising concerns promptly with collaboration partners can help a company's position in eventual litigation. Addressing problems directly as soon as they arise may let a company resolve them without litigation, getting the collaboration back on track. If not, documenting the issue and the company's position promptly in writing may prevent an arbitrator from later deciding that the company agreed to the objectionable conduct through its "course of dealing" under the agreement.

Most partnerships begin in a spirit of optimism and cooperation, but almost half of biotech alliances terminate prior to a successful product launch. Clear, concrete agreement terms and cautious performance during the partnership can help minimize disputes and protect a company in litigation if — or when — a collaboration goes wrong.



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Shared Quality Responsibility Pays Off For Sponsors, CMOs

With contract manufacturing on such a rapid rise, the industry needs to identify best practices for maintaining and improving quality and process management across outsourced manufacturing networks. However, many sponsor-CMO contracts are inadequate in the quality data-related provisions as they fail to properly address the rights of a sponsor or its contractors to directly monitor processes and receive process data.

Historically, sponsor-CMO contracts have been written and/or negotiated by colleagues outside of manufacturing/quality roles who are focused on pricing, legal aspects of the relationship, and technical product specifications. Agreements may not always provide the sponsor the right to proactively monitor processes and access the process data necessary to conduct the level of analysis needed for investigative analysis and quality by design (QbD) and process improvement initiatives. Without those rights, tech transfer to another CMO or a captive sponsor facility may be quite difficult. The sponsor's manufacturing and quality teams will be challenged after the contract is signed to obtain process data if it was not provided for in the agreement.

OBSTACLES TO AVOID

There are several obstacles to data sharing in the sponsor-CMO relationship. The most common is that many CMOs view the process data as their own intellectual property and are reluctant to share raw process data and "their" analytical reports with the sponsor. In addition, CMOs may not have the data aggregation and analytical tools necessary to support the sponsor's desired efforts around QbD, process understanding, and other quality-related initiatives. Lastly, there may be IT challenges that impair the ability to share agreed-upon data in the appropriate time frame.

As the FDA continues to clarify the need for sponsors to demonstrate control over their CMOs, it is imperative that sponsors and CMOs agree on the appropriate level of data and analytical collaboration as well as the adoption of the appropriate supporting technologies. As the contract manufacturing business grows, some CMOs are differentiating themselves by advertising their 1) investment in leading data aggregation and analytical tools and 2) willingness to be transparent with their sponsors about all aspects of their process and products.

CONSIDERATIONS FOR SPONSOR-CMO AGREEMENTS

CMOs and sponsors both will benefit from contracts that provide for data sharing and analytical collaboration. Given timely access to the right process data, a sponsor can collaborate with a CMO to identify process trends and apply corrective actions that serve both parties' interests.

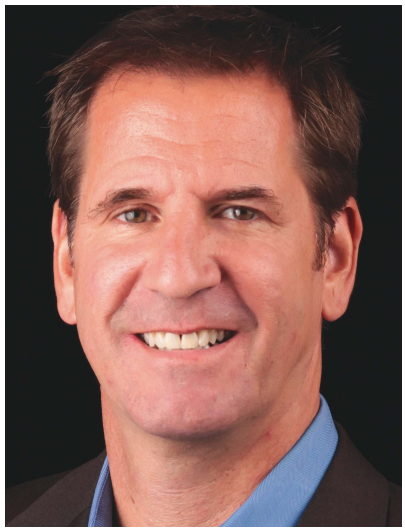
Specific contract provisions that support the enhanced collaboration include:

- **Data ownership:** Specify who "owns" the quality and process data.
- **Data access:** Specify who can access the data and what types of data are required (e.g. discrete, continuous, event, etc.) to enable better process understanding. Agree upon the frequency and format of the data exchange to avoid "spreadsheet madness."
- **Build in flexibility:** Specific data parameters for monitoring may not be clear at the start of a sponsor-CMO relationship. Critical process parameters (CPPs) and key performance indicators (KPIs) may need to be based on hypotheses and refined through monitoring. The contract should allow for dynamic and continuous changes in data-sharing requirements. Build flexibility into the contract for modifying data requirements and include the ability to retrieve and review historical data.
- **Determine data review timelines:** Specify how often the organizations will reevaluate and revise parameters and processes (e.g. every six months).
- **Consider requiring technological improvements:** Encourage migration from paper-based data records to electronic solutions that gather data from disparate systems. Both parties will benefit from lower staff costs and more reliable data upon which to base decisions.

Agree on confidential data elements. CMOs work with multiple sponsors and have to be sensitive to safeguarding proprietary information while providing reasonable data access to sponsors.

- **Process intellectual property:** Specify who "owns" enhancements to the original process.

Most regulatory agencies want outsourced manufacturing to be integrated into the operations of the sponsor organization. Including comprehensive collaboration and data-sharing provisions in the sponsor-CMO contract can help satisfy regulatory requirements across disparate manufacturing networks.



Robert Di Scipio

Robert Di Scipio is president and CEO of Aegis Analytical Corp., which licenses its Process Intelligence software platform to manufacturers of biotech, pharma, and chemical products.

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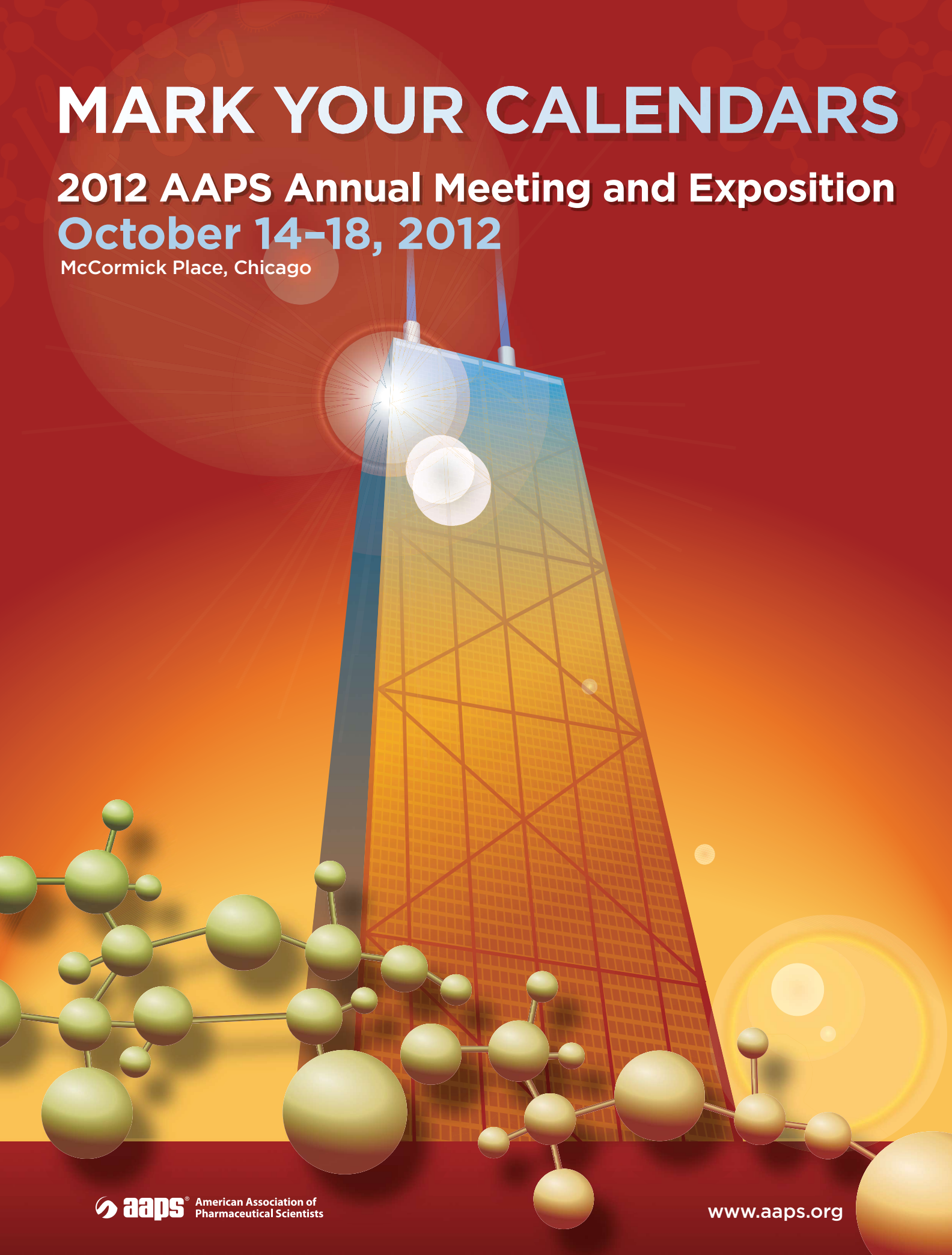

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To Align Senior Leaders, Find a Common Thread

By Dennis Goin

What will it take to unite my senior team around a new strategy? That's a question I've heard countless executives ask as they begin leading their organization down a new path, because they know that change takes much more than any one individual's efforts. And the answer I give is simple: find a common thread.

Before a leader embarks on an innovative course or seeks to transform the organization, it is essential for senior team members to be clear about the opportunity ahead of them and enthusiastic about their role in helping to achieve it. Without that clarity and without that sense of urgency, change is bound to be hampered by hasty, haphazard, and misguided activity.

To be successful, new approaches require focus. They require commitment. They require alignment. To get there, I typically encourage leaders to take these four steps:

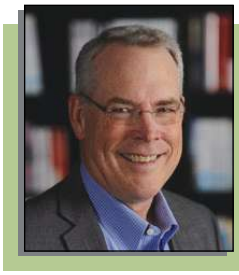
Gather. Convene senior team members and collect input from all of them about how they view the business, what they believe the company's key strengths and weaknesses are, and where they see — and hope to see — the organization in the future.

Credit. In order to create an open atmosphere where team members feel comfortable sharing their candid views on the organization, credit each individual's belief system. Explain there are not right or wrong answers, simply diverse perspectives — all of which are crucial to arriving at a winning strategy for the organization.

Explore. Display the feedback gathered from senior leaders, and search for common themes. Do not be fazed if they seem hard to come by; more often than not, there will be little initial agreement among team members. Each individual has their own responsibilities, goals, and job-specific priorities, all of which color their vision for the organization. Still, words and phrases like "growth," "employee involvement," and "acceleration" may appear repeatedly and can help reveal certain widespread aspirations — the common threads that will help unite the group.

Align. With the common thread established and shaped around people's hopes, each senior team member will begin to see how their unique skills, expertise, and function fit like puzzle pieces within the larger strategy. They will gain a sense of personal ownership of the new initiative, a stake in the game, not feeling as if they "have to" take on additional responsibilities, but that they "want to" help move the organization in a new and exciting direction. This is the significance of alignment.

A unified, motivated senior team is an essential ingredient in any campaign to quickly and effectively implement new strategy. When employees at other levels of an organization sense their leaders are aligned, they move toward them, eager to help drive the new approach forward. It is the leader's job to focus those efforts. They can do so with one simple tool: the common thread.



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