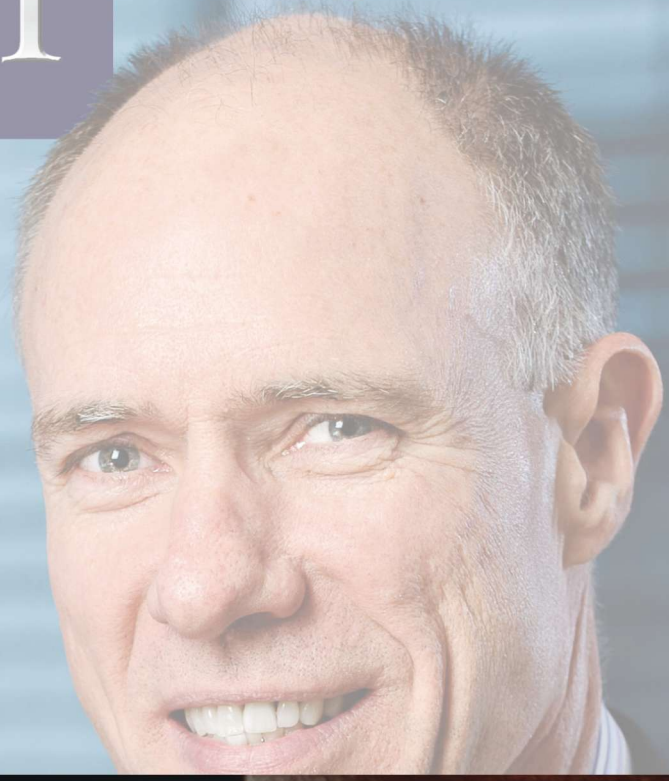
Life Science Leader
October 2012
LifeScienceLeader.com
The Industry's Essential Business Source

COMPANY TO WATCH: Synageva BioPharma

p. 10



Break From The Drug Discovery Crowd

p. 36

Venture Funding Drops

p. 42

Capacity Utilization Trends In Bioprocessing

p.16

Life Science Leader
October 2012
LifeScienceLeader.com
The Industry's Essential Business Source

COMPANY TO WATCH: Synageva BioPharma
p. 10

The Genzyme Way

Living The Patient-Provider Connection

p. 20

David Meeker, M.D., president and CEO, Genzyme

Leading the way in early drug and device development.

Your responsive CRO partner, delivering customized solutions and adaptability to changing needs.

Visit us at the upcoming shows:
AAPS booth 4215, SPS booth 100,
and ACT booth 102

With its emphasis on excellence in science, MPI Research works with Sponsors in developing solutions for all their drug and device development needs. From discovery to safety evaluation, analytical testing, and bioanalytical testing, you can count on MPI Research for quick quotes, frequent updates, rapid turnaround, and scientific rigor. At every stage and on every level, we adapt to your most exacting needs.

Explore the breadth of capabilities and knowledge that make us your CRO of choice at www.MPIResearch.com.

MPI RESEARCH

Customized. Responsive. On-Time.®

Call Acurian and clean things up.

We know best how to recruit the patients your sites need to fulfill enrollment, so you can put a stop to endless CRO change orders for more investigators and extended time lines.

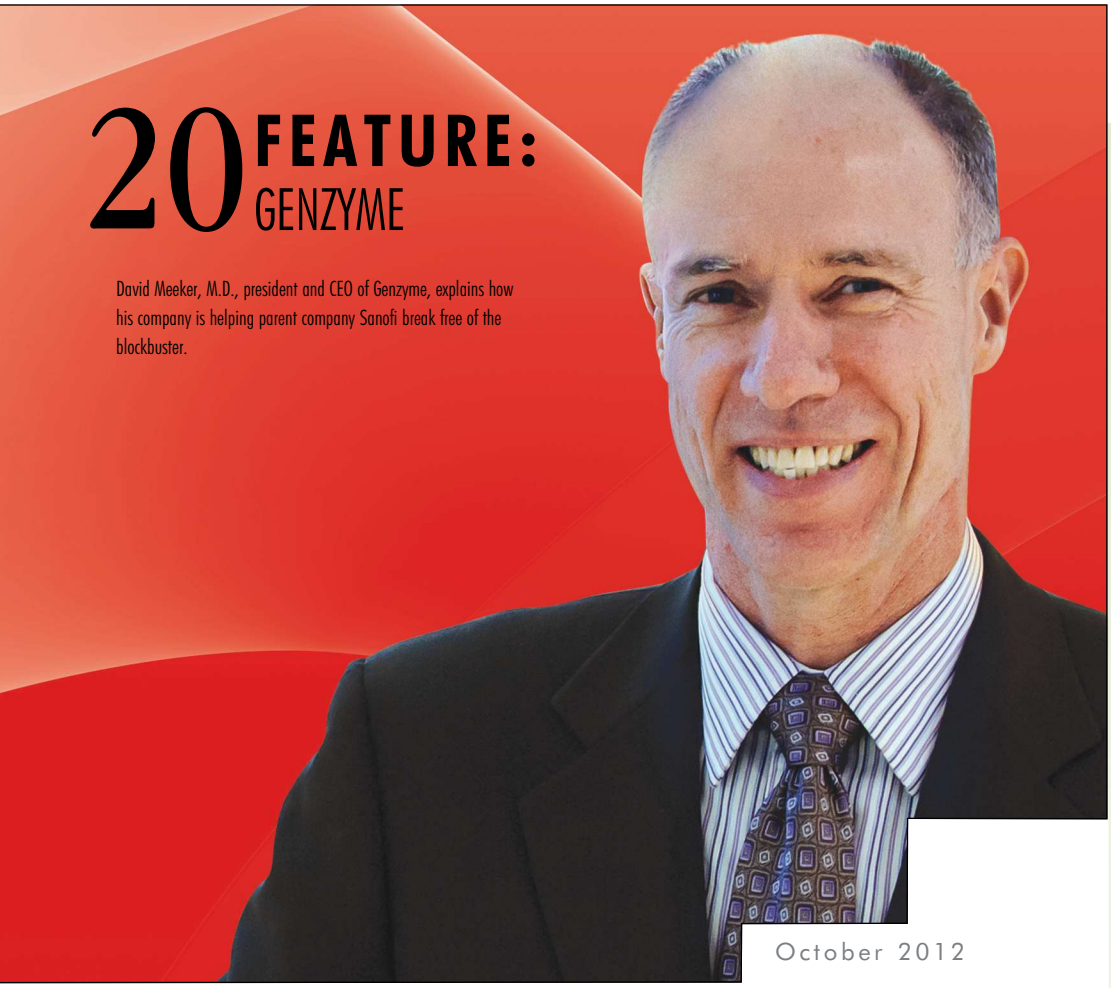
We increase your sites' productivity.
You complete enrollment without adding sites or time.

Acurian
The Enrollment and Retention Specialist

1-866-566-5966 ▪ www.acurian.com

TRUSTe CERTIFIED PRIVACY

Life Science Leader



20 FEATURE: GENZYME

David Meeker, M.D., president and CEO of Genzyme, explains how his company is helping parent company Sanofi break free of the blockbuster.

October 2012

Welcome to *Life Science Leader*

CONTENTS

DEPARTMENTS

Follow *LSL* on:

twitter

at twitter.com/LifeSciLeader

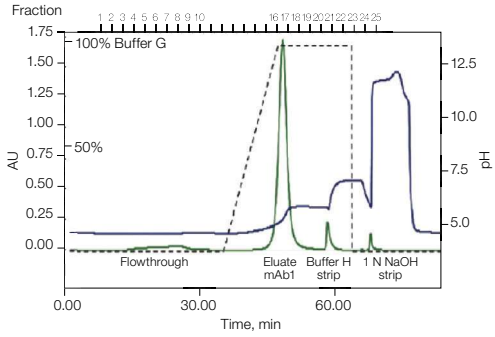
and

LinkedIn

Nuvia cPrime Media in a Three-Step Non-Protein A mAb Purification Process

In this three-step purification process, two high-capacity ion exchange chromatography media, Nuvia S and Nuvia Q, were used in the first two steps to efficiently capture target mAb1 from cell culture harvest and to effectively remove process and product related impurities. The high binding capacities of these ion exchange media make it possible to process increasing volumes of high titer feed with existing production facilities and minimal buffer consumption.

In the final polishing step, the orthogonal interaction modes afforded by Nuvia cPrime media offer unique selectivity for full-length monomeric mAb1 molecules. Furthermore, the sequence of the three chromatography steps has enabled an efficient process with minimal handling and requiring no buffer exchange for easy and straightforward transitions between steps.



OD_{280} pH Percentage of buffer G
mAb1 eluted from the column (fractions 17–19).

mAb1 purification using Nuvia media. With a unique balance between modes of interaction, Nuvia cPrime can effectively retain the full-length mAb at pH 5.0 while allowing a 25 kD L-chain fragment to flow through the column without any conductivity adjustments from the previous ion exchange purification step. Elution at pH 6.2 yields L-chain fragment and aggregate-free antibody collected under mild conditions and with high recovery.

Life Science Leader

OCTOBER 2012

EDITORIAL DIRECTOR: Dan Schell
(814) 897-9000, Ext. 284
dan.schell@lifescienceleader.com

CHIEF EDITOR: Rob Wright
(814) 897-9000, Ext. 140
rob.wright@lifescienceconnect.com

VP OF PUBLISHING: Jon Howland
(814) 897-9000, Ext. 203
jon.howland@lifescienceleader.com

ASSOC. PUBLISHER/BIOPHARM & LAB: Shannon Primavere
(814) 897-7700, Ext. 279
shannon.primavere@lifescienceleader.com

PUBLISHER/CONT. MFG. & INGREDIENTS: Cory Coleman
(814) 897-7700, Ext. 108
cory.coleman@lifescienceleader.com

GROUP PUBLISHER/OUTSOURCING: Ray Sherman
(814) 897-7700, Ext. 335
ray.sherman@lifescienceleader.com

BUSINESS DEV. MGR.: Mike Barbalaci
(814) 897-7700, Ext. 218
mike.barbalaci@lifescienceleader.com

SR. ACCOUNT EXECUTIVE: Scott Moren
(814) 897-7700, Ext. 118
scott.moren@lifescienceleader.com

ACCOUNT EXECUTIVE: Tim Bretz
(724) 940-7557, Ext. 123
tim.bretz@lifescienceleader.com

ACCOUNT EXECUTIVE: Becky Brown
(724) 940-7557, Ext. 164
becky.brown@lifescienceleader.com

ACCOUNT EXECUTIVE: Bill Buesink
(814) 897-7700, Ext. 119
bill.buesink@lifescienceleader.com

ACCOUNT EXECUTIVE: Sean Hoffman
(724) 940-7557, Ext. 165
sean.hoffman@lifescienceleader.com

ACCOUNT EXECUTIVE: David Ruler
(814) 897-7700, Ext. 157
david.ruler@lifescienceleader.com

PRODUCTION DIRECTOR: Lynn Netkowicz
(814) 897-9000, Ext. 205
lynn.netkowicz@jamesonpublishing.com

DIRECTOR OF AUDIENCE DEV.: Mindy Fadden
(814) 897-9000, Ext. 208
mindy.fadden@jamesonpublishing.com

Life Science Leader
2591 Wexford-Bayne Rd. Bldg. II, Level 3, Ste. 305
Sewickley, PA 15143-8676
Telephone: (724) 940-7557 ● Fax: (724) 940-4035

LIFE SCIENCE LEADER (ISSN: 21610800) Vol. 4, No. 10 is published monthly by VertMarkets at Knowledge Park, 5340 Fryling Road, Suite 300, Erie, PA 16510-4672. Phone (814) 897-9000, Fax (814) 899-5580. Periodical postage paid at Erie, PA 16510 and additional mailing offices. Print PP. Printed in the USA.
SUBSCRIPTION RATES for qualified readers in the US $0. For non-qualified readers in the US and all other countries $97 for one year. If your mailing address is outside the US or Canada, you can receive the magazine digitally if you provide a valid email address. POSTMASTER: Send address corrections (Form 3579) to Life Science Leader, Knowledge Park, 5340 Fryling Road, Suite 300, Erie, PA 16510-4672.

EDITOR'S NOTE

Harvesting The Network For Great Editorial

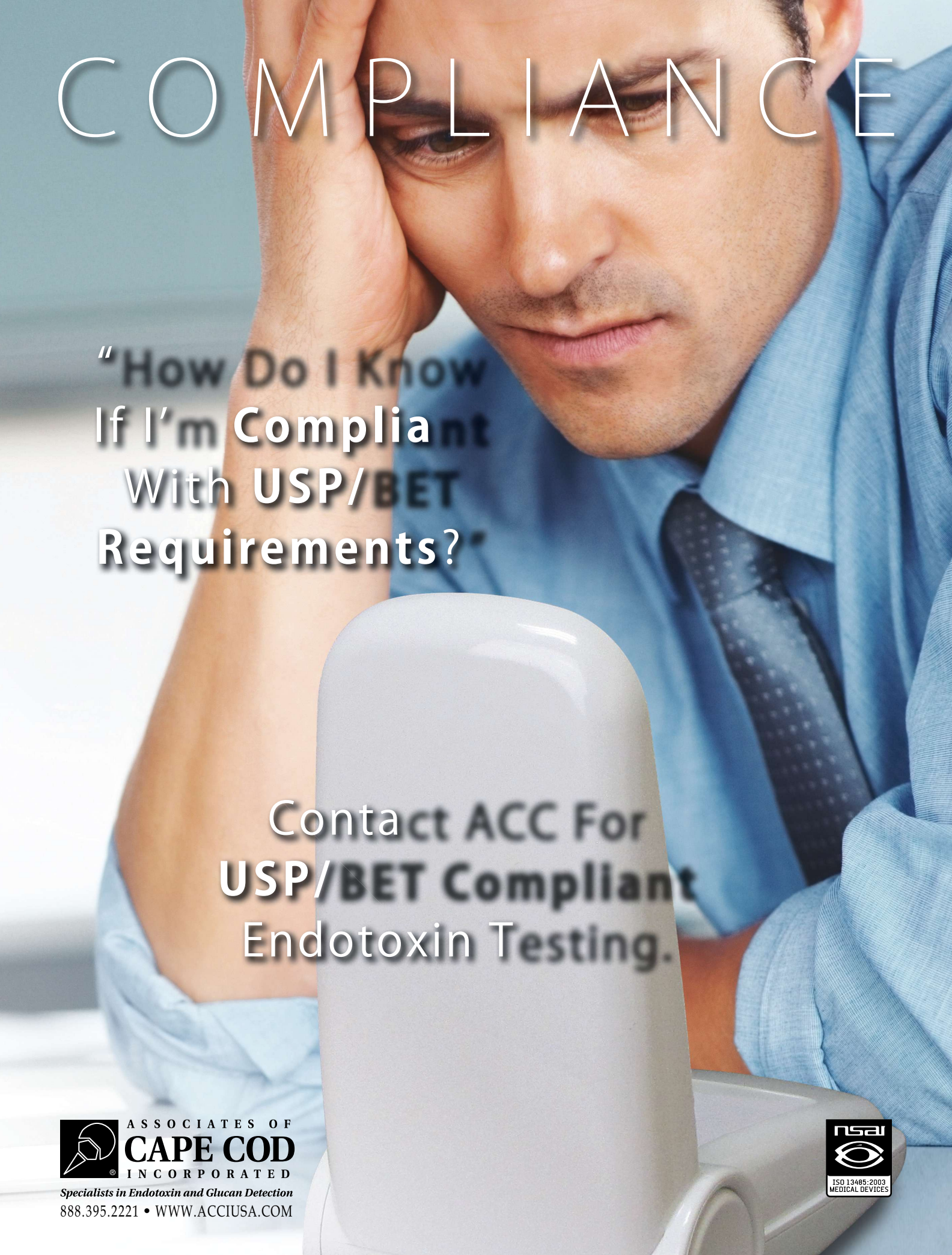
The month of October in the northern hemisphere is typically associated with the end of the growing season and the process of gathering mature crops — it's harvest time. In this month's issue of *Life Science Leader* magazine, I did my own form of harvesting, that is, the harvesting of people I met while attending conferences and trade shows and getting them involved in our editorial process. The business term we use to describe meeting people at events is networking. I find it interesting that the definition of networking — the cultivation of productive relationships for employment or business — includes the farming term cultivation. So let me share with you some of the relationships I was able cultivate and harvest for this issue through networking.

The Leadership Lessons article on page 58 is written by Mark Scharenbroich. He is the author of the award-winning book *Nice Bike – Making Meaningful Connections on the Road of Life.* He is also an excellent keynote speaker, whom I met at the 2011 Emerson Global Users Exchange in Nashville, TN. Mark came up to me before his talk and told me how he always gets nervous presenting to groups of smart people. He needn't have worried. Just my being in the audience skewed the IQ curve back toward the mean. His presentation was so good, I pestered him for months to put together an article for us.

On the cover of this month's issue is Genzyme CEO David Meeker, M.D., whom I met at this year's Bio International conference in Boston. I met Philip Haydon, Ph.D., at the state of Wisconsin's Bio networking event. Haydon and I discussed the challenges around the uphill battle one faces when going against established thinking. "Stay close to the literature," your Ph.D. advisor will tell you, when you are working on your dissertation. Doctoral training programs are one of the reasons I think researchers can get stuck in the rut of incremental innovation. As I listened to Haydon explain his work to me as president and founder of GliaCure, I was convinced we had a story (see p. 36.).

I am looking forward to continuing the cultivation and harvesting of people from upcoming networking opportunities for future editorial in *Life Science Leader*. For example, this month I am planning on attending CPhI in Madrid, Spain, as well as AAPS in Chicago. Now, some people have told me they have trouble networking. It is hard. They are shy. Well, the word does have the word "work" in it. So here's a tip. If you find networking difficult, make the time to read Thom Singer's book *Some Assembly Required: How To Make, Grow And Keep Your Business Relationships.* It will walk you through how to network. In case you are wondering, the answer is yes, I also met Thom while out "harvesting" at a show.

Rob Wright
rob.wright@lifescienceconnect.com
@RFWrightLSL


COMPLIANCE
"How Do I Know
If I'm Compliant
With USP/BET
Requirements?"
Contact ACC For
USP/BET Compliant
Endotoxin Testing.
ASSOCIATES OF
CAPE COD
INCORPORATED
Specialists in Endotoxin and Glucan Detection
888.395.2221 • WWW.ACCIUSA.COM
nsai
ISO 13485:2003
MEDICAL DEVICES

WIN A COPY OF THIS BOOK!

Ask the Board wants to hear from you. Have a question that you would like to pose to our editorial advisory board of experts? Send it to atb@lifescienceconnect.com. If we select your question for publication, we will provide you with a complimentary copy of a business book, such as Mark Scharenbroich's *Nice Bike — Making Meaningful Connections On the Road of Life.* Read Scharenbroich's "Leadership Lesson" on page 58.

ASK THE BOARD

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

Q: What type of economic incentives would you propose to spur antimicrobial drug development?

There is a growing (and appropriate) need for antibiotic stewardship, which is the reluctance to use new, powerful antibiotics when older ones might be used first (until and unless there is clear evidence of antibiotic resistance). This state of affairs is referred to by economists as "market failure." Thus, while we need a continuous supply of new antibiotics, because of evolving and inevitable resistance, pharmaceutical companies are reluctant to invest. Glimmers of hope, though, exist, among them the recently passed GAIN Act by the U.S. Congress as part of PDUFA V. The GAIN Act provides companies developing new antibiotics for serious and life-threatening infections due to resistant organisms an additional five years of marketing exclusivity along with FDA fast track and priority reviews, simulaneously helping the economic outcome and reducing the regulatory risk. This new act is a model for how government, at times of market failure, can intervene in helpful ways.

Barry Eisenstein, M.D.
Dr. Eisenstein is senior VP of scientific affairs at Cubist Pharmaceuticals and editor of *Antimicrobial Agents and Chemotherapy.*

Q: What is your opinion of the California e-Pedigree law and its impact on securing the supply chain?

The California e-Pedigree Law will certainly improve the security of the drug supply chain and make it more difficult to introduce counterfeit drugs into the system. However, full implementation is not scheduled until July 2017. Producers of counterfeit drugs, if so inclined, will figure out how to circumvent the system. The effectiveness of the law is also dependent on proactively checking the integrity of the pedigree through the supply chain. Either through laxity in vigilance — assuming someone else in the supply chain has checked the pedigree — or overt desire to source "cheap" drugs, the system could be subverted. While not necessarily the "final solution," the law is a major step forward and should improve traceability if and when a problem arises.

Norm Klein
Norman Klein is the principal at Core Results, LLC, which offers consulting in the areas of purchasing and supply chain optimization. He has more than 35 years of experience in purchasing, engineering, finance, manufacturing, and distribution.

Q: What impact do you think recent well-publicized drug failures will have on future research initiatives?

Today's investment for compounds in Phase 3 is enormous, and the FDA requires more long-term safety data before approval. In addition, they are asking for studies showing that a potential new drug does not just show an impact on a disease marker, such as lowering bad cholesterol or plasma sugar levels; they are also requiring drugs have a meaningful effect on slowing or halting the disease. In addition, payers are demanding that new drugs show benefits over existing medications. Such head-to-head comparisons also require expensive clinical trials. In some ways this will impact future research initiatives. However, the higher hurdles will not necessarily mean that high-risk projects will be abandoned. While more care will be taken before such a commitment, CEOs realize that pharma R&D is a high-risk/high-reward business.

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

Best overall brand value of any full-line manufacturer on the road today.[1]
IntelliChoice

Longest lasting vehicles[2] and most fuel-efficient full-line automotive manufacturer.[3]
Polk

Awarded more Vincentric Best Fleet Value in America awards than any other manufacturer.[4]
Vincentric

More vehicles named to the American-Made Index's Top 10 than any other brand.[5]
Cars.com

Best retained value of any full-line car manufacturer on the road today.[1]
IntelliChoice

#1 selling brand of hybrid vehicles in America.[6]
MotorIntelligence

Praise like this doesn't come around every day.

But it sure feels like it around here.

Time and again, the critics have spoken, and their message is always the same: For all your Fleet Vehicle needs, you can't beat a Toyota. Call 1-800-732-2798 or visit fleet.toyota.com for more information.

TOYOTA FLEET

Options shown. 1. 2012 IntelliChoice, www.IntelliChoice.com; Popular Brand. Based on 2012 model year study. 2. Longevity based on Polk U.S. Vehicles in Operation registration statistics MY 1987-2011 as of July 2011. Full-line manufacturer based on car, SUV, minivan, compact and full-size pickup. 3. Fuel efficiency based on NHTSA Final Industry MY10 CAFE data for Toyota Motor Sales. 4. Based on Vincentric Best Fleet Value in America awards from 2006-2012. 5. For more information about the 2012 American-Made Index, visit Cars.com 6. MotorIntelligence.com, CY 2011 sales.

By Wayne Koberstein

Synageva BioPharma

Returning to the roots of biotech and orphan drugs

SNAPSHOT

Synageva is a public company committed to invading unexplored therapeutic areas — aka, orphan diseases — while returning to biotech roots with its rDNA (ribosomal deoxyribonucleic acid)-based proteins for replacement therapy. It aspires to the kind of mission and model other orphan-drug companies like Alexion have championed successfully, yet it brings an exceptional amount of industry experience and practicality to the task. Underlying its development of lead product SBC-102 (rhLAL), an enzyme replacement therapy for Lysosomal acid lipase (LAL) deficiency, and others in the pipeline is a diverse team of industry veterans equipped for commercialization. The company's protein expression and production platform, as well as royalties from Roche for an acquired HIV product, Fuzeon (enfuvirtide), bring in cash for Synageva. It has completed a Phase 1/2 extension study of SBC-102 in late onset LAL D and plans to follow with a double-blind placebo controlled trial next year.

LATEST UPDATES

- February 2012: Presented interim SBC-102 clinical data
- July 2012: Closed $115 M public offering

WHAT'S AT STAKE

Companies have concentrated on developing therapeutics for a relatively few rare diseases where further development of the compound has big-market potential, as Tim Cote, longtime rare disease advocate and chief medical officer of NORD (National Organization for Rare Disorders), observed at an AAPS (American Association of Pharmaceutical Scientists) conference last May. Unfortunately, he noted, that leaves most rare diseases with no treatment options, now or in the foreseeable future. If companies lived up to the spirit more than the letter of the Orphan Drug Act, a different model would emerge — one based on orphan drugs for orphan diseases and rare conditions where the need remains unmet — because most companies developing orphan drugs have generally targeted only a relatively few rare conditions or indications, flocking around ones that have become popular for their potential to lead to large-market indications for the same drug. Actually, such a true or "ultra" orphan drug model has emerged, however imperfect in form, with successful companies such as Alexion (Soliris/PNH), and Genzyme (e.g. Cerezyme/Gaucher Disease), as well as with new orphan drug developers, exemplified by Synageva BioPharma.

Let's pause for a disclaimer: Pricing is the "fly in the ointment" for the "ultraorphan" model . All the company successes so far depend on the *orphan blockbuster* strategy; Gaucher prevalence is only about 1 in 75,000, but Cerezyme delivers around $800 million in sales per year with its price of $200,000 per patient. Synageva has not signaled a price for SBC-102 if approved, but the company's presentation to analysts cites Cerezyme and other high-ticket orphans to indicate potential revenue. The same presentation, however, dramatically illustrates the human stakes as well — describing an infant with LAL Deficiency (LAL D) surviving and growing well beyond the usual, dismal bounds of the disease after SBC-102 treatment. According to Synageva's CEO, Sanj K. Patel, both the late and early onset forms of the disease are greatly under- or misdiagnosed, and the chief challenge in its drug development is finding the right patients for its clinical trials. Anticipating a similar challenge once on the market, the company built its clinical and commercial teams in tandem, beginning early on. Finding patients requires extensive outreach to specialists, academic centers, and opinion leaders, along with medical publications, conferencing, and encouragement of investigator-sponsored studies, especially as it gears up for a double-blind placebo controlled trial in late onset LAL D. It is exceptional for a start-up to start out with the full complement of functions needed to reach those objectives. To whatever degree the company relies on high pricing to sustain its success, there is honor in its commitment to filling a truly unmet need. Synageva is not just developing drugs for rare conditions, but solitary hopes for patients with genuine orphan diseases.

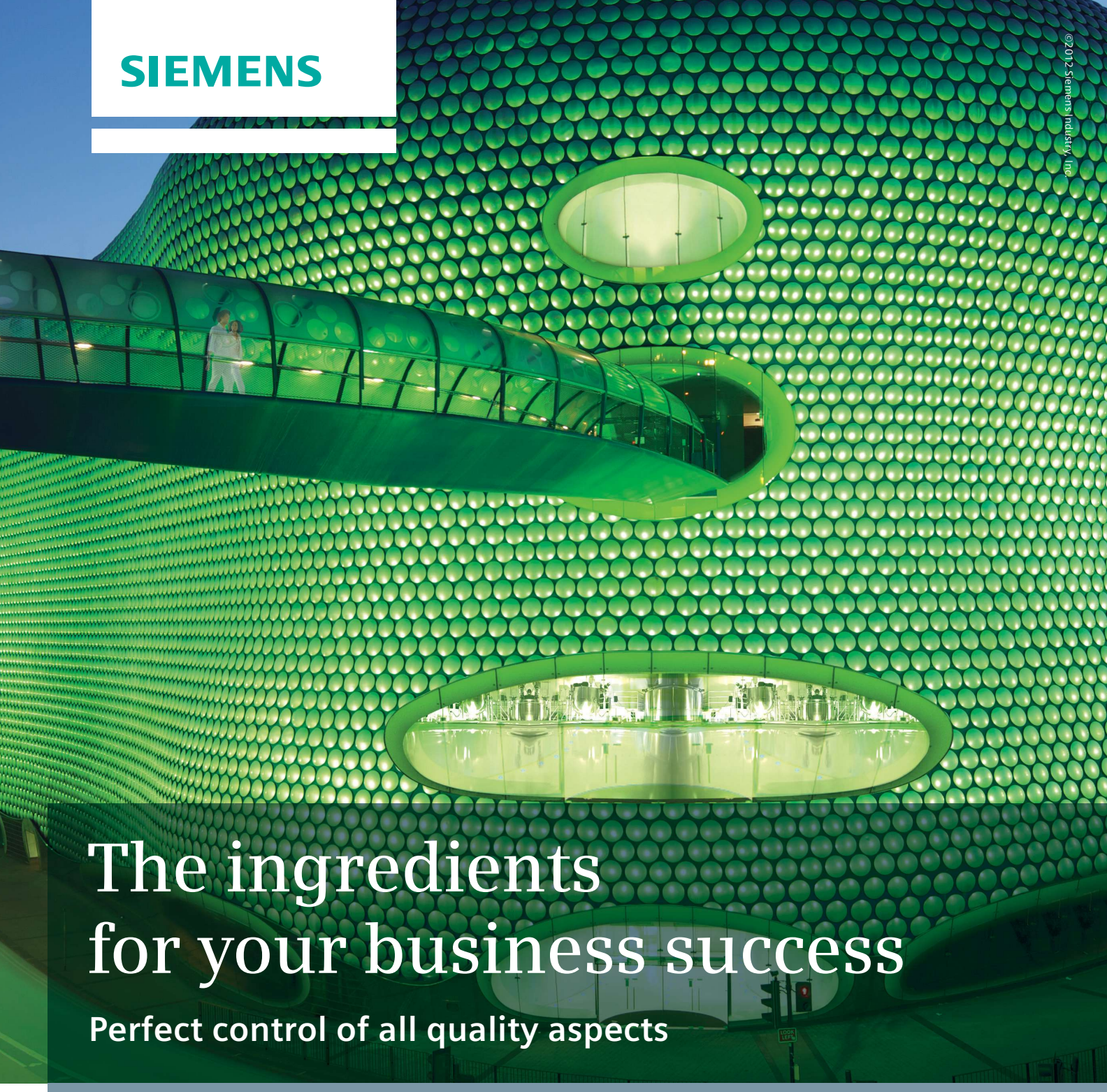
VITAL STATISTICS

■ Employees: estimated 110; Headquarters: Lexington, MA.

■ Finances:
Q2 2012 Cash: $139 M
2012 net operating loss guidance: $40-$45 M

■ Research partnerships:
Mitsubishi Tanabe Pharma: develops novel therapeutic for an undisclosed orphan disease
Morphotek: expresses and develops mAb (monoclonal antibody) therapies for cancer and infectious disease

SIEMENS



The ingredients for your business success

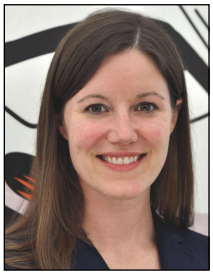
Perfect control of all quality aspects

Pharmaceutical and Life Science Industries

Companies in the pharmaceutical and life science industries benefit the most from a trusted technology partner that really understands their business. With its unrivaled portfolio in the fields of automation and drive technologies and its thorough understanding of the specific industry needs, Siemens is that partner.

Our expertise and solutions for research and development, manufacturing, utilities and business processes, as well as a commitment to the environment help the industry to minimize risk, increase efficiency and improve patient safety.

www.usa.siemens.com/pharma



OUTSOURCING INSIGHTS

Outsourcing Biomanufacturing

By Kate Hammeke, director of marketing intelligence, Nice Insight

A recent strategic partnering survey by Nice Insight asked participants working at midsize and large cap pharmaceutical companies about their business's long-term strategies for maintaining a strong drug development pipeline. Their responses confirmed a common practice that is continuing to grow in popularity — integration of biopharmaceuticals through partnerships or acquisitions to supplement a weakening pipeline. In fact, 56% of respondents indicated that their company is looking to partner with a large biopharmaceutical company to strengthen their development pipeline, and 51% stated the company they work for is looking to purchase a small biopharm company. Another 37% want to partner with a small biopharm company, and 22% said their company wants to purchase a small biopharm company's compounds. Only 13% stated that their company's drug development pipeline is strong.

The drug development industry is motivated to invest in developing biopharmaceuticals as a form of pipeline security because these products have demonstrated profitability. The practice of partnering with or acquiring biopharmaceutical companies is mirrored in the results of the Nice Insight Pharmaceutical and Biotechnology Outsourcing survey, where 71% of respondents stated the company they work for engages in the development of biologics-based therapeutics. Of these respondents, 77% will outsource biomanufacturing in 2012 and will spend just over half of their outsourcing budget on the development of biologics (54%) — compared to 46% of the outsourcing budget spent on conventional therapeutics.

This bodes well for contract service providers, both in terms of winning outsourced biomanufacturing projects and also for the long term, as CROs and CMOs will likely perform the R&D and manufacturing of new biosimilars/bioequivalents for biologics that come off patent in the coming decade. This means it may be a good time to start considering CROs and CMOs for biologics projects. The Nice Insight Brand Index includes 28 contract manufacturing organizations that offer biomanufacturing services. Five of these CMOs stand out from the rest, in that they have been consistently identified as businesses that the respondent pool considers for custom manufacturing projects throughout 2012. These standout companies are Baxter Biopharma, BioReliance, Boehringer Ingelheim, DSM Biologics, and GlaxoSmithKline Biopharmaceuticals.

5 COMPANIES TO WATCH

The data also showed five companies that shifted from being infrequently considered to frequent consideration for biomanufacturing projects. CMC Biologics, Cytovance Biologics, Laureate Biopharma, Lonza, and Paragon Bioservices* all increased their likelihood of winning a large molecule custom manufacturing project between Q2, 2011 and Q2, 2012. Nice Insight reviewed these companies' customer perception scores to see if there was a correlation between one of the key outsourcing drivers and this increased likelihood of being considered for a project. Interestingly, productivity scores tended to remain steady or show a slight decline, as did customer perception scores for regulatory compliance. However, the data showed that companies earning higher scores in 2012 with respect to reliability and quality also increased their likelihood of being considered for a custom manufacturing project. There was an occasional exception, such as when a company's 2011 score exceeded 80%. It is difficult to maintain scores in the "excellent" range (80%-100%), let alone improve. However, CMC Biologics — the only company with a drop in reliability and quality scores — still came out on top, receiving the highest customer perception scores for these drivers among the group.

With biotherapeutics expected to outpace conventional therapies in the next decade — S&P industry data predicts that biotechnology products will account for 48% of the top 100 drugs in 2016 — it is a good time to identify prospective outsourcing partners and begin developing relationships. Consideration of the companies mentioned above is a good start, but this may end up costing more than joining forces with a smaller, lesser-known CMO. In which case, outsourcers can start by looking for contract manufacturers with strong quality and reliability scores, as these attributes are continually ranked as the #1 and #2 drivers influencing partner selection by survey respondents.

**Paragon Bioservices currently offers GMP manufacturing for clinical trials, with an eventual commercial manufacturing launch.*

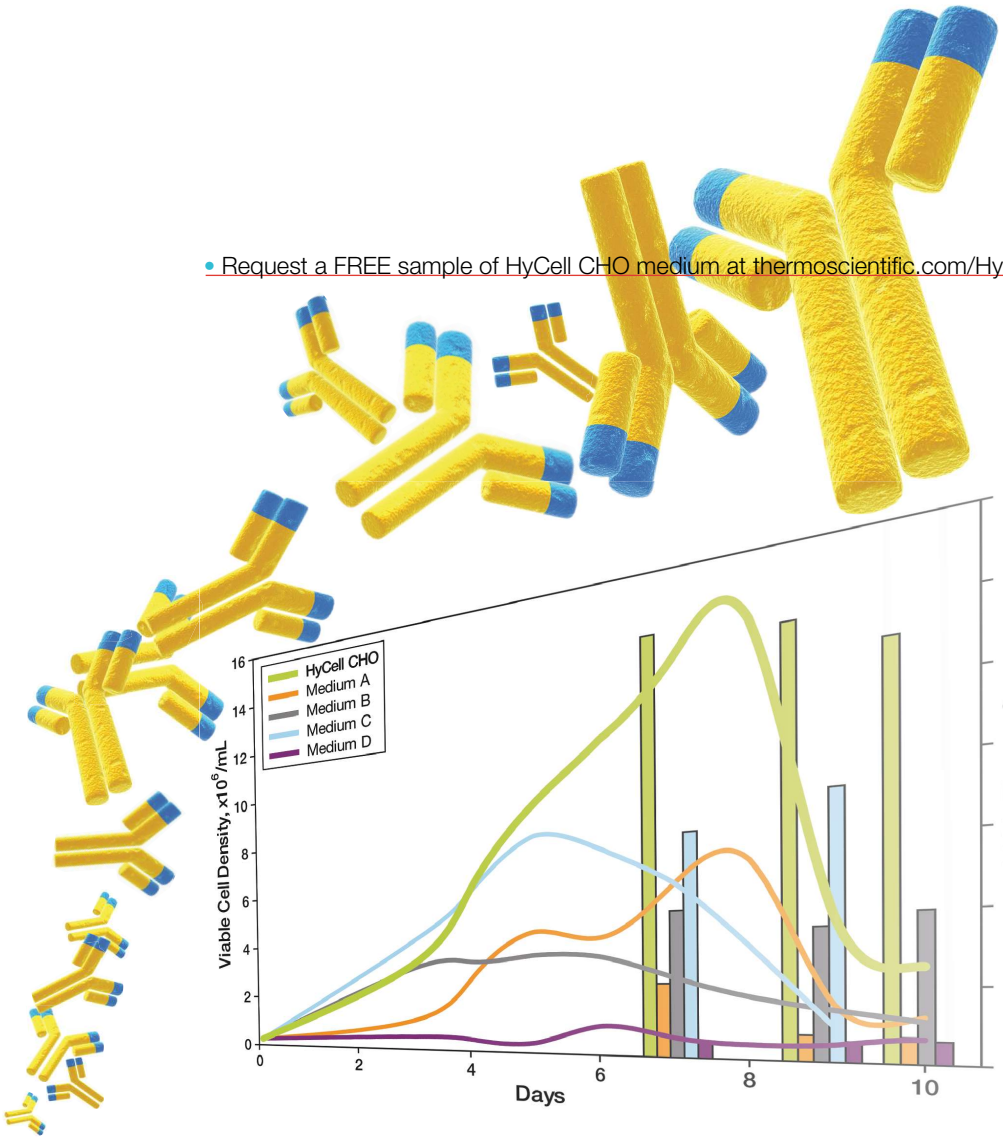
maximize cell culture

Thermo Scientific HyCell CHO medium **increases bioprocess yields up to five-fold** or more over other comparable CHO media. Higher product yields allow you to run smaller scale productions to achieve similar results, which equates to **significant cost savings**. HyCell CHO is a versatile, protein-free, chemically defined medium containing no animal derived components that can be used for a wide variety of CHO lines.

production and performance

Thermo SCIENTIFIC

- Request a FREE sample of HyCell CHO medium at thermoscientific.com/HyCell



- **Thermo Scientific HyCell CHO Medium:** Targeted for high cell density and productivity across a broad variety of CHO clones

NI Customer Perception Changes in Quality & Reliability 2011 – 2012

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 ~30 questions to each respondent in order to collect baseline information with respect to customer awareness and customer perceptions on 300 companies that service the drug development cycle. More than 1,200 marketing communications, including branding, websites, print advertisements, corporate literature, and trade show booths are reviewed by our panel of respondents. Five levels of awareness from "I've never heard of them" to "I've worked with them" factor into the overall customer awareness score. The customer perception score is based on six drivers in outsourcing: Quality, Innovation, Regulatory Track Record, Affordability, Productivity, and Reliability, which are ranked by our respondents to determine the weighting applied to the overall score.


Walker

If you want to learn more about the report or how to participate, please contact Nigel Walker, managing director, or Salvatore Fazzolari, director of client services, at Nice Insight by sending an email to niceinsight.survey@thatsnice.com.

FOCUSED RESOURCES. INTEGRATED SOLUTIONS.

Tailored Resource Solutions — Your Way.

We can deliver the full range of clinical development services customized to meet your objectives whether you need an individual or a team, help with a single function or a range of functions, use our tools and processes or your own.

Resourcing allows the flexibility to rapidly expand or contract a dedicated workforce as your development pipeline evolves. Control what you need - when you need it, and get the experience and expertise necessary for your development programs.

- All job functions
- Therapeutic expertise
- Global placements
- On-demand staffing
- Functional resourcing (FSP)
- Resource transfer
- Strategic alliances

1 609 951 6800 www.pharmanet-i3.com

PharmaNet|i3
Strategic Resourcing
INVENTIV HEALTH CLINICAL

Strategic Resourcing Phase I-IV Consulting Bioanalytical

BIO DATA POINTS

Capacity Utilization Trends In Bioprocessing

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

The biopharmaceutical industry continues to have underutilized capacity for all expression systems, according to results from our Ninth Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, where we asked 302 biotherapeutic developers and CMOs to estimate their average production as a percentage of their operating capacity. Capacity utilization information is important for planners as they determine whether capacity will be available for the production of pipeline drugs that may be reaching approval. For biomanufacturing capacity utilization from 2006 to the present, the industry rate has remained relatively stable at 61.7%.

Biopharmaceutical manufacturers have become increasingly adept at anticipating high production demands and avoiding capacity crunches. A certain amount of excess, "flex," or buffer capacity is important in biomanufacturing because the opportunity costs associated with not getting a company's drug product to market can be devastating. On the other hand, the cost of an idle biomanufacturing facility and costly excess capacity is also actively avoided.

Compared to last year, capacity utilization appears to be steadier for some systems than others. Mammalian cell culture — this year at 61.7% — is virtually unmoved from last year's 61%. Similarly, capacity utilization for plant cells — at 52.7% — has not changed appreciably from last year's 51.3%. Rates for other systems have seen more movement: microbial fermentation, down from 53.6% in 2011 to 49.5% this year; yeast, down from 46.8% to 35.7%; and insect cells, down from 59.3% to 53.9%. Looking back as far as 2004, there has been significantly more volatility, with capacity utilization generally trending downward during that time period.

Significant capacity utilization drops for mammalian, microbial, and yeast culture after 2003 are partly due to new large scale facilities going operational and following that, higher titers in upstream production. We note that the same equipment can be used for both microbial and yeast systems (yeast is a eukaryotic microbial system). So the differences between microbial and yeast capacities are likely due to respondents' accounting for actual processes being run at their facilities (rather than processes capable on the same equipment).

IS THE INDUSTRY PLANNING BETTER?

The current economic situation also has had a dramatic impact on global capacity utilization for all industrial segments, so it is likely to have some impact on biopharmaceutical products. However, despite utilization percentages having decreased in recent years, it is worth noting that a lot of new capacity and higher yields have been established during this period, so overall biomanufacturing levels (output) are up considerably.

Of course, a certain amount of excess, flex, or buffer capacity is important in biomanufacturing because the opportunity costs associated with not getting a company's drug product to market can be devastating. At the same time, the cost of an idle biomanufacturing facility and costly excess capacity is also actively avoided. So predicting one's own needs and overall industry capacity becomes a high-stakes game. Today, smoothed-out biopharmaceutical industry utilization rates are due primarily to improved planning by manufacturers and the lack of major new blockbuster products that might absorb substantial industry capacity. The leveling-off in biomanufacturing capacity suggests that companies are using their existing capacity more efficiently and are planning more effectively for shifts in demand for additional capacity.

CMOs SEE HIGHER CAPACITY UTILIZATION FOR NONTRADITIONAL SYSTEMS

Our study also compares drug developers to CMOs, finding that reported capacity utilization for mammalian cell systems in 2012 was higher for biotherapeutic developers than for CMOs, at 64.2% compared to 51.1%, respectively (vs. 61.3% and 52.5%, respectively, last year). Conversely, for microbial capacity utilization, the opposite occurs, with biotherapeutic developers at 48.2% capacity utilization, compared to CMOs at 55.9%. Biotherapeutic developers report slightly higher utilization than CMOs for yeast systems (36.1% vs. 34.6%), while CMOs are slightly higher for plant cells (55.5% vs. 50.8%).

THE OUTLOOK FOR CAPACITY UTILIZATION

The study's data agrees with most industry analysts who feel there is likely to be sufficient capacity worldwide to meet production requirements for biopharmaceuticals during at least the next five years. However, budgets for new capacity have or are being increased in 2012, and companies continue to consider CMO capabilities at the scale-up stage and beyond. With the continued increase in biopharm approvals, some industry capacity may be absorbed. Further, because blockbuster products, particularly monoclonal antibodies, can consume substantial installed capacity, the success or failure of one or two potentially high volume products in development can change the capacity utilization picture. However, this only affects those few companies with the largest capacity, and we are seeing fewer blockbuster-like products in the pipeline.

We'll take you down a better path.

See how the people behind the slide can make the difference in your research.

flexibility. innovation. people who care. | www.criver.com/people

charles river

Figure 1: Average Production As % Of Operating Capacity, By System, 2004 Through 2012

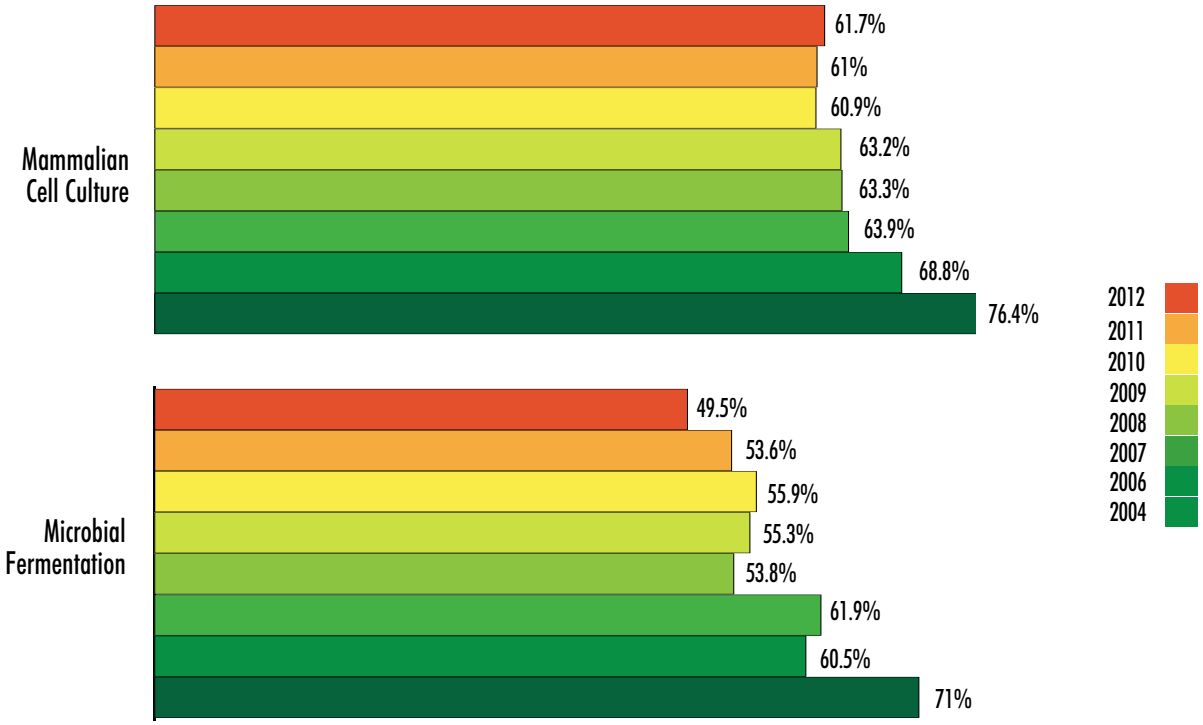
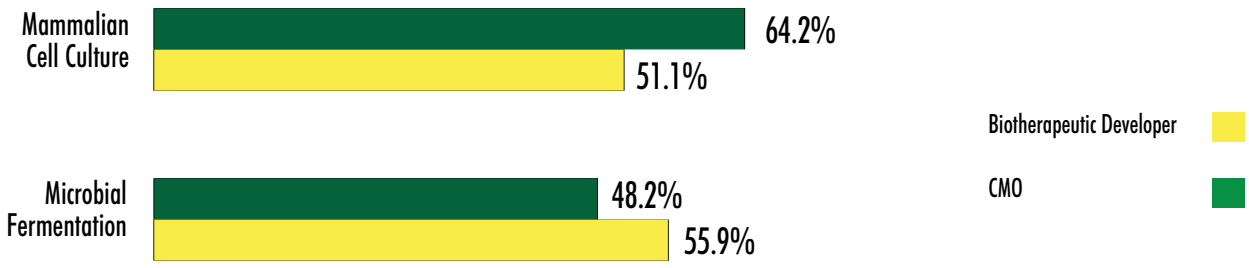


Figure 2: Average Production As % Operating Capacity Biotherapeutic Development vs CMO, 2012



Survey Methodology: The 2012 Ninth Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production in the series of annual evaluations by BioPlan Associates, Inc. yields a composite view and trend analysis from 302 responsible individuals at biopharmaceutical manufacturers and contract manufacturing organizations (CMOs) in 29 countries. The methodology also included 185 direct suppliers of materials, services, and equipment to this industry. This year's survey covers such issues as: new product needs, facility budget changes, current capacity, future capacity constraints, expansions, use of disposables, trends and budgets in disposables, trends in downstream purification, quality management and control, hiring issues, and employment. The quantitative trend analysis provides details and comparisons of production by biotherapeutic developers and CMOs. It also evaluates trends over time and assesses differences in the world's major markets in the U.S. and Europe.

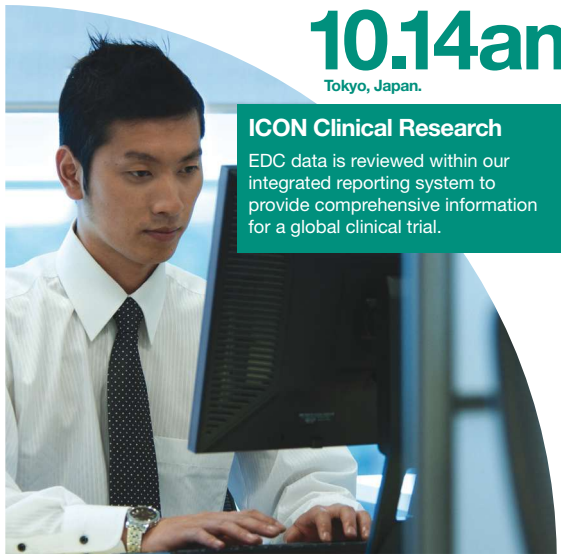
If you want to learn more about the report, please go to bioplanassociates.com.

9.15pm
San Antonio, U.S.

ICON Development Solutions
Pharmacodynamic specialists conduct complex models to identify early efficacy signals for candidate compounds.

10.14am
Tokyo, Japan.

ICON Clinical Research
EDC data is reviewed within our integrated reporting system to provide comprehensive information for a global clinical trial.



ICON Central Laboratories
Chemistry samples for a cardiovascular study are being tested in our Central Laboratory.

4.45pm
Tianjin, China.

ICON Medical Imaging
Patient information including Medical images, lab summaries and the eCRF are electronically hosted for remote review by a Clinical Endpoint Committee.

3.28pm
Zurich, Switzerland.

24 hours in the life of ICON

No matter the hour of the day, there's an ICON expert somewhere around the world working to deliver results for informed, timely decision-making.

www.iconplc.com

ICON
A Symbol of Excellence

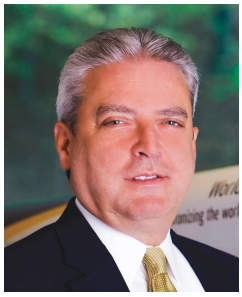
Genzyme:

Helping Sanofi Break Free Of The Blockbuster

By Rob Wright

Last year's acquisition of Genzyme by Sanofi was unusual, but probably not in a way you would expect. Once you look past the sheer magnitude of the acquisition (i.e. $20 billion+), you notice that, unlike many of the other companies acquired by the $48 billion-dollar behemoth, Genzyme continues to maintain its cultural identity. Indeed, instead of being assimilated into the Sanofi culture, Genzyme continues to maintain its own president and CEO in David Meeker, M.D., who previously served as Genzyme's COO. That's impressive considering Meeker is the only member on the Sanofi leadership team carrying the title of CEO other than Chris Viehbacher, CEO of Sanofi.

David Meeker, M.D., president and CEO, Genzyme



Mark Davis
HEALTHCARE LOGISTICS
PRODUCT MANAGER
UPS

The Benefit Of A Logistics Provider With A Healthcare Focus

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

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

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

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

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

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

PharmaPort 360

What's next in temperature-sensitive supply chain management?
UPS recently announced a very unique air freight container called the PharmaPort™ 360, which is specifically designed to transport temperature-sensitive pharmaceuticals, vaccines and biologics required to stay within 2–8 degrees Celsius. The PharmaPort 360 is really a game changer, offering a new level of in-transit product protection. The unit maintains a strict 5 degree Celsius set point within the container, plus or minus two degrees. And, it can do so for upwards of 100+ hours, depending on the ambient conditions. PharmaPort 360 is powered by an AC rechargeable battery and its technology eliminates the need for dry ice and the hazards and fees associated with its handling. This super-insulated container has an R factor of 70 and includes built-in GPS/GSM (Global System for Mobile Communications) capabilities which enable near-real time visibility and monitoring. Data is monitored by UPS's global network of control towers to not only track location, but more importantly to enable UPS to act on shipment alerts in-transit such as low battery life or temperatures that are going out of range, which helps protect against product loss.

Together with UPS Temperature True®, our air freight service, we're providing a whole new level of shipment protection and monitoring of temperature-sensitive products throughout the supply chain. Our service gives companies precise, measurable operating procedures backed by dedicated support and contingency plans for unexpected situations. With UPS, they feel confident that products are being handled with care and under the right conditions.

4 WAYS LOGISTICS CAN IMPROVE YOUR HEALTH.

The health of your supply chain, that is. UPS surveyed healthcare executives and found that their key concerns were compliance, expanding globally and managing costs. UPS understands the challenges of your industry. And has the resources to help you.

1) ENSURING RELIABILITY UPS runs the best integrated logistics network—freight and package—on the planet. As one of the world's largest air freight forwarders, we have the flexibility to help ensure a consistent and compliant supply of healthcare products.

2) GAIN GLOBAL ACCESS UPS serves over 220 countries and territories, and has 30 dedicated healthcare distribution facilities worldwide.

3) KEEPING YOU COMPLIANT The movement of medical products triggers costly compliance issues. UPS's team of experts maintains hundreds of geographically specific regulatory licenses and registrations that can help keep your supply chain cost efficient and compliant.

4) PROTECTING TEMPERATURE-SENSITIVE PRODUCTS Many healthcare products require special handling. That's why UPS Temperature True® provides proactive global monitoring to help keep your shipments within strict temperature ranges and prevent costly excursions.

For healthcare industry insights, go to **thenewlogistics.com/healthcare** or snap the QR code.

UPS®

WE ♡ LOGISTICS™

thenewlogistics.com/healthcare

This move seems to indicate a desire to not only preserve the Genzyme culture, which Meeker describes as being highly purpose-driven, but also to incorporate that into Sanofi's revamped strategy. "It wasn't that we had a brilliant strategy," Meeker says about the Genzyme culture. "The disease areas where we work are so small that you cannot help but to come into close contact with the people who rely on and are benefiting from your drugs." Though your company might not be in the business of discovering drugs for rare diseases, Genzyme's forte, perhaps you can learn from some of Meeker's insights as to Genzyme's approach to rare diseases, why Sanofi decided to acquire the company, and how Genzyme is helping to transform Sanofi.

ACQUIRING A NEW R&D FOOTPRINT

In 2009, the decision was made that Sanofi would respond to the challenges posed by the pending patent cliff, generic competition, and cost-containment pressures from third-party payers and healthcare authorities by implementing a new strategy that would reposition the French-based pharmaceutical juggernaut for more stable and sustainable revenue earnings and growth. According to its annual report, the company needed to transition away from a reliance on blockbuster medicines and, instead, optimize its approach to R&D.

The first step in this process involved the reallocation of some of its internal infrastructure toward partnerships and collaborations. The second step involved redesigning its internal R&D footprint. For a company built on the backs of blockbuster drugs likes Ambien, Lovenox, and Plavix, this was no easy task. Remember, though, Viehbacher is a CPA with a decidedly business background, having started his career with PricewaterhouseCoopers. Meeker on the other hand, is a trained medical doctor, having practiced medicine at the world-renowned Cleveland Clinic for six years prior to joining Genzyme. Perhaps Viehbacher could help Genzyme with the business challenge surrounding its well-publicized production problems, while Meeker could help Sanofi continue to redesign aspects of its drug development approach.

THE GENZYME WAY

According to Meeker, the Genzyme way to drug development for rare diseases can be applied to drug discovery in general. "The general concept is that you are trying to solve a problem," he states. "You have no chance of solving the problem, if you don't thoroughly understand the problem." In the case of rare diseases, there is often very little information, and what information there is often involves very few patients. In order to best understand the problem, you have to get close to the patient. One

EMBRACING ADVOCACY GROUPS

Advocacy groups, charities, and research foundations have been playing an ever-increasing role in the drug discovery process. Many of these result from a family's desperation to find a cure and, in the case of rare diseases, may lack organization. Genzyme CEO David Meeker says, "One of the most valuable things that we can do is to create communities to connect people. We need to connect patients with other patients and connect physicians who are interested in a disease with other physicians who might be interested in that same disease. What's missing in these rare diseases is simply that community." Meeker has seen the benefit of facilitating these connections in what he describes as the multiplier effect. "Things like disease awareness become much easier," he affirms. "Communities enable research. They can support the creation of awareness. You can't do the trial if you can't find a patient." Meeker even credits patient organizations with being extremely helpful in terms of gaining government support, not just in reimbursement, but helping to establish centers of excellence, establishing diagnostic testing, and newborn screening. "Virtually every aspect of development can be aided by the community," he states.

According to Meeker, a number of rare disease organizations lack experience in knowing how to operate. But what they lack in experience, they make up for in determination and effort, making it fairly easy to partner with them. "As groups become larger, they often have professional management, who may or may not have a strong connection with the disease prior to joining the organization," says Meeker. He believes the key is to remember the patient who desperately needs a cure and wants to trust that everything is being done to solve the problem.

Lack Of FDA Social Media Guidance

The FDA has yet to issue guidance for the pharmaceutical industry on how it can use social media, a key ingredient to the successful formation of patient advocacy groups. This is not a problem with which Meeker gets concerned. "When you have a small group of individuals trying to do the right thing, you don't need a lot of rules," he shares. "That has been the nature of the rare disease communities. In that setting, we are focused on sharing information. Our whole purpose has been to create awareness about the prevalence of the disease and the problems associated with it." According to Meeker, the marketing of pharmaceuticals is becoming much more restrictive, and with that in mind, everybody in the healthcare equation needs to be much more attentive in trying to ensure that the patient/physician interaction is not manipulated.

way of doing this is helping to create organizations to help connect patients and providers. For example, since 1991, Genzyme has worked closely with the international Gaucher community to understand the disease's epidemiology, history, and long-term treatment outcomes, through the creation of the International Collaborative Gaucher Group (ICGG) Gaucher Registry. This organization includes more than 700 participating physicians, representing nearly 6,000 patients, with more than 40,000 patient-years of follow-up data, and has resulted in nearly 30 published papers on Gaucher's disease. The Genzyme investment in this organization is estimated to be over $50 million since 1991.

Meeker sees healthcare as much more intimate than other industries. "It is not like purchasing a washing machine," he states. If you are going to connect with and solve the problem a patient is experiencing, you need to care about that patient, and their problem. "I think failing to see these health problems as something you need to care about is often the gap between what defines success in development of innovative medicines," he states. That's why Meeker always seeks to include some healthcare providers for the Genzyme clinical and commercial teams who have had the opportunity to practice medicine, not just have a medical degree.

"I think failing to see these health problems as something you need to care about is often the gap between what defines success in development of innovative medicines."

David Meeker, M.D., Genzyme

"When it comes to applying medical training to the individual patient," he explains, "that is the art." For Meeker, successful drug development is taking the understanding of medicine's data-driven elements and combining these with the understanding of an individual patient, which gives you the best chance of getting the right answer for that specific patient. "You have to care about the people you treat or may be benefiting from your medication," he states.

Genzyme's culture has what Meeker describes as the patient-provider connection. "There is a remarkable level of connectivity throughout the organization with the people we are trying to help," he explains. Some of this connectivity Meeker attributes to the natural consequence of working with rare diseases, involving such small numbers of patients that it would be difficult not to become well-connected to their problems. In addition to supporting and helping to found such resources as the ICGG Gaucher Registry, Genzyme has taken other proactive steps to create connectivity, such as bringing patients in to visit manufacturing plants to speak with employees who actually make the drug or having patients visit Genzyme offices throughout the world to share their story. "We are a global company with a culture that is no different if you are in China or Cambridge, MA," Meeker attests. Genzyme is taking the cultural connectivity approach learned in discovering drugs for rare diseases and applying it to its emerging multiple sclerosis (MS) franchise. For example, for MS awareness day the company had advocacy organizations and patients come in to help employees better understand the symptoms and sensations the disease causes. Employees were given the opportunity to wear glasses, gloves, and

macaroni-filled shoes, simulating the vision, numbness, and pain challenges patients with MS experience on a daily basis. These types of initiatives help to create a culture whereby employees are better able to understand people who have a need, are ill, reliant, and want to trust. For Meeker, trust is one of the key components in the healthcare equation to successful drug discovery.

EARNING TRUST NECESSITATES BEING TRUSTWORTHY

At this year's BIO International conference, Meeker conducted a presentation entitled "Orphan Disease Forum — Orphan Markets are Different: Are They At Risk?" During his talk, he described a recent visit to his own physician, asking audience members to recall their last trip to the doctor. He prompted them to think about sitting in the waiting room, being ushered back, getting weighed, measured, taken to a room, removing clothing, putting on a gown, and waiting some more. He then solicited responses from audience members as to how it made them feel. One person said, "Vulnerable," while another replied, "Scared." Meeker says, "You expect your car salesman to not necessarily be the most trustworthy individual. But that is okay, because you are prepared for that. In the healthcare setting, you are vulnerable. You are sick. You need help. You are scared. You need to trust." Meeker is a

BRINGING BACK HUMANISM TO THE DRUG APPROVAL PROCESS

No one doubts that the people working at the FDA have a tough job. "It is truly one of those no-win jobs," says Genzyme CEO David Meeker. "They have to ensure safety. Nobody rewards them for taking a risk." Meeker believes safety is one of those things that is always hard to prove. "You might prove efficacy and safety in 100, 1,000, or 10,000 people, but the question, is it safe, always lingers," he states. Meeker would like to see a level of humanism brought back to the regulatory drug approval process. He believes the FDA needs more support from society and Congress for the work it is trying to do. Further, he believes the FDA realizes that the organization needs to engage with the patient community, particularly in new areas. "They need to understand the problem to apply the risk/benefit judgment in an optimal way," advises Meeker. "It isn't that there is no risk, and it's not that there is a perfect benefit. Weighing benefit and risk is the nature of the drug approval exercise." Assessing risk and benefit is easier when working in an area where you have many therapies that have been approved previously, as there is a model with benchmarks and metrics from which to compare. But what if you are working in an area where there is no therapy or a totally different transformative therapy? In this case, you need the ability to think differently. "You need some context," he affirms. "Context comes from understanding the patient and the problem." According to Meeker, "Everybody wants the same thing, which is to make the patient better. If I am a payer, I have no interest in paying you more for the same outcome. Therefore, we as developers need to be clear about the value that we are delivering from our side." So if you want to get humanism back into the drug approval process, the FDA, payers, and developers need to gain alignment on how best to achieve making people better — with acceptable risk — while being willing to think differently when a transformative therapy comes along. Take the 6-minute walk test, for example.

The 6-Minute Walk

The American Thoracic Society has issued guidelines for the 6-minute walk test (6MWT), considering it to be safer, easier to administer, better tolerated, and a better reflection of the activities of daily living than other walk tests. Regulatory bodies frequently use the 6-minute walk to assess a patient's level of improvement when being administered an experimental drug. They also often use this test's results as a criterion when considering approving a drug. Meeker believes the 6-minute walk to be an inadequate measure of improvement in many cases, and he thinks people need to entertain other options. "There is language within the regulatory framework — accelerated approval types of things — biomarkers — reasonably likely to predict clinical benefit — the whole question of validation," he states. "It comes down to the disease itself and being open to new endpoints that are most meaningful to that particular disease. This requires a high level of disease knowledge on the part of the FDA, which means bringing in disease experts. It requires involvement of the patient community which, if it is a rare disease, may not have a significant amount of information at the time you are starting to develop the drug." Meeker believes drug development companies, disease experts, and most importantly, patients, need to work collaboratively to help shape what a patient would view as clinically meaningful changes in their life. In rare diseases, it is not easy because the sample size may be as small as just one person.

proponent of creating an organization whereby employees not only understand their role as stakeholders, but as contributors. "In an equation that desperately needs to trust, we need to be trustworthy parts of this equation. You do that by saying, what is the problem? Who are we trying to help, and what is best for them?" To be a true partner in the healthcare equation, Meeker stresses the importance of working collaboratively with the patient, adopting a selfless approach, with no interest other than making sure the patient gets the best possible outcome.

Unfortunately, he sees this as something that sometimes gets lost in our industry. To avoid this happening in your organization, Meeker advises developing a healthcare mindset with the goal that every patient, with whatever disease, has a chance of being recognized, diagnosed, seen by an expert, and prescribed a therapy that is in their best interest. Meeker believes using these principles can be highly energizing to any organization because people can be motivated to do what they think is in the best interest of the patient. He cautions, however, "You have to bring something of value to the equation. This isn't about going out and trying to 'do good.' You have to create value, and then you have to bring that value in a way that it can be understood and utilized with a thorough understanding of the potential benefits."

The business model for Genzyme has always been to put the patient first, and the money will follow. Some have described this approach as taking the high road. However, Meeker believes that people gravitate to places like Genzyme because it is a comfortable place to work, not in the sense of being easy, but in terms of the philosophy. "People reading this and wanting to find out what the great secret is, already know it," he contends. "Any company can usher patients into their organizations, hang their photos on the wall, and include the word patient in their mission statement. And that is great," says Meeker. "However, the true definition of patient-centricity is an organization that will radically change its course based upon the input and evolving needs of the patient community they are there to serve. Unless you are willing to put the needs of the community first from an operational and business standpoint, then you are not patient-focused, and you do not have a sustainable model in rare diseases."

EMBRACING THE ACQUIRED

Sanofi has certainly embraced the Genzyme acquisition. For example, in 2008, 61% of Sanofi's sales originated from its top 15 products. In 2011, 65% of the company's sales originated from six growth platforms and Genzyme:

- Emerging Markets
- Diabetes Solutions
- Human Vaccines
- Consumer Health Care
- Animal Health
- Innovative Products

But there is another benefit to the acquisition beyond sales. Sanofi is now the largest life sciences employer in greater Boston, one of the hotbeds for biotech R&D. Why Boston? According to Meeker, being in Boston is another component and the final key to developing the next breakthrough therapy. Consider this — the greater Boston area is home to around 190+ biotech-related businesses, world-class academic institutions including Harvard and MIT, as well as a number of highly ranked medical centers, such as Massachusetts General, Brigham and Women's, and Boston Children's. "You need to have cutting-edge internal science that is interacting with an incredibly networked external world of academics, small biotechs, and other places where innovation occurs," he concludes. "It is not always easy to predict where it will be. If you are not out there looking and interacting with the community, you are going to miss it." By connecting and interacting with the community, Genzyme has been very successful with its commercial drug development. How successful? Nearly half the medicines Genzyme markets have originated outside the organization — helping Sanofi to break free from the blockbuster model.

Statement of Ownership

1. **Title of Publication:** Life Science Leader
2. **Publication Number:** 2161-0800
3. **Date of Filing:** 09/14/12
4. **Frequency of Issue:** Monthly
5. **No. of Issues Published Annually:** 12
6. **Annual Subscription Price:** $97.00/year
7. **Complete Mailing Address of Known Office of Publication:** 5340 Fryling Rd, Suite 300, Erie PA 16510-4672
8. **Complete Mailing Address of Headquarters or General Business Offices of Publisher:** Same
9. **Full Names and Complete Mailing Addresses of Publisher, Editor and Managing Editor:** Publisher, Jon Howland, 5340 Fryling Rd., Suite 300, Erie, PA 16510-4672; Editor, Rob Wright, same as above; Managing Editor, Dan Schell, same as above.
10. **Owner(s):** Terence C. Peterson, 5340 Fryling Rd., Suite 300, Erie, PA 16510-4672, Richard J. Peterson, same as above.
11. **Known Bondholders, Mortgagees, and Other Security Holders Owning or Holding 1 Percent or More of Total Amount of Bonds, Mortgages or Other Securities:** None
12. **Tax Status (For Completion by non-profit organizations authorized to mail at special rates):** Not Applicable
13. **Publication Title:** Life Science Leader
14. **Issue Date for Circulation Data Below:** September 2012
15. **Extent and Nature of Circulation:** Average No. Copies Each Issue during Preceding 12 Months/Actual No. Copies of Single Issue Published Nearest to Filing Date. A. Total Number of Copies: 27,611/29,228 B. Legitimate Paid and/or Requested Distribution: (1) Outside County Paid/Requested Mail Subscriptions Stated on Form 3541: 26,063/26,091 (2) In-County Paid/Requested Mail Subscriptions Stated on PS Form 3541: 0/0; (3) Sales Through Dealers and Carriers, Street Vendors, Counter Sales and Other Paid or Requested Distribution Outside USPS: 3/312 (4) Requested Copies Distributed by Other Mail Classes Through the USPS: 0/0; C. Total Paid and/or Requested Circulation: 26,066/26,403 D. Non-Requested Distribution: (1) Outside County Non-Requested Copies Stated on PS Form 3541: 0/0; (2) In-County Non-Requested Copies Stated on Form 3541: 0/0; (3) Non-Requested Copies Distributed Through the USPS by Other Classes of Mail: 419/375; (4) Non-Requested Copies Distributed Outside the Mail: 987/2,325 E. Total Non-Requested Distribution: 1,406/2,700 F. Total Distribution: 27,472/29,103 G. Copies Not Distributed: 139/125 H. Total: 27,611/29,228 I. Percent Paid and/or Requested Circulation: 94.88%/90.72%.

Clinical Trials Ontario: Harnessing Its Research Expertise

By Fred Olds, contributing editor

Ontario is taking an active approach to attract large multicenter clinical trials. As biopharm globalized clinical trials during the past 10 years, Canada's scientific community did not change to meet the opportunities. The result was that after peaking in 2008, clinical trial placements began to decline, with fewer numbers of sites, patients, and dollars. Recognition of this spurred collaborative initiatives among Canadian industry, science, academe, and national health to analyze the problem. Sober analysis made it apparent that scientific excellence alone was not enough to maintain Canada's position as a premier location to conduct trials. Ontario became the first Canadian governmental entity to fund an organization, Clinical Trials Ontario (CTO), to change the clinical trials landscape.

For sponsors of trials, this means there will be provincial support and active assistance in placing research projects. Ronald Heslegrave, Ph.D., executive director CTO, says, "It is our intention to take a businesslike approach to the conduct of clinical trials in terms of efficiencies and cost while maintaining the high scientific, regulatory compliance, and patient protections for which we are known." He says the approach is founded on three strategic pillars: 1. Improve speed and reduce costs; 2. Leverage partnerships to gain access to global decision makers; and 3. Improve recruitment.

Currently, sponsors placing research at multiple sites may have to deal with scores of different institutions, agencies, investigators, and companies individually for contracting, ethical reviews, and SOPs. Heslegrave says quite often these entities have not only conflicting, but contradictory requirements. It's an obstacle to getting situated and delays start-up. Through collaboration with all the research centers in Ontario, Heslegrave envisions CTO becoming a single portal for clinical trials. It will be a triage center for sponsors, industry, physicians, and patients looking for information on research studies. He says CTO will act as both an active outreach to decision makers making choices on site selection and as a welcome center when the sponsor arrives. Ontario can no longer just hope investigators will choose Canada and, in particular, Ontario.

QUALITY, SPEED, AND COST

"Placement of clinical trials is based on three simple principles," says Nita Arora, North American affiliate head for clinical affairs at Hoffman La Roche. "It is maintaining quality, low cost, and speed in getting an answer." She says there has never been any doubt of Canadian research quality. But while Canadian researchers felt their superiority in quality would continue to bring sponsors back to Canada, the rest of the world caught up. These other regions delivered quality more quickly and at a lower cost. She says these countries compete with a sense of motivation to get the funds to raise their standards of living.

So if sponsors can stipulate quality at a number of sites, that leaves Canada to compete on cost and speed. Arora says costs in Canada are among the highest in the world and would be difficult to reduce. Yet companies will still work with a location if that site can deliver enough benefits in the other two areas. "Canada," she says, "has all the assets necessary to encourage investment by biopharm." What she feels Canada has lacked is focus. Unlike some other countries, Canada hasn't yet decided to make a concerted effort to harness its resources in programs to attract and support multicenter clinical trials.

Heslegrave concurs, "It's more than making the paperwork easier. There needs to be reform of the current system." Speed certainly increases if you streamline start-up, SOP, and registration processes, but getting studies done quickly involves more. There needs to be programs to engage all the participants to improve collaboration, enrollment, retention, staff

sartorius stedim biotech

BIOSTAT® STR: The revolutionary single-use bioreactor.

Proven stirred tank design and full scalability.

- Cultivation volumes from 12.5 L to 1000 L
- Efficient oxygen transfer and CO_2 removal
- Optimised for high cell density cultures
- Single use or conventional probes
- User-friendly touch screen control unit
- Convenient installation and change over

www.sartorius-stedim.com/biostat-str

turning science into solutions

"Don't be trapped by dogma."

– Steve Jobs

T300 Open your mind… and your lab, to the next generation T300 universal controller.

And most important, have the courage to follow your heart and intuition. They somehow already know what you truly want to become. Everything else is secondary. – Jobs, 2005

At Finesse, we believe that nothing is impossible. Our first generation T300 platform could easily interchange glass vessels from Applikon, Sartorius, and NBS or single-use Millipore Mobius vessels. Now imagine plugging your second generation T300 into a Smartbag on a GE/Wave or Finesse rocker. Dream a little and listen to your inner bioprocessing voice. What do you want your lab to become?

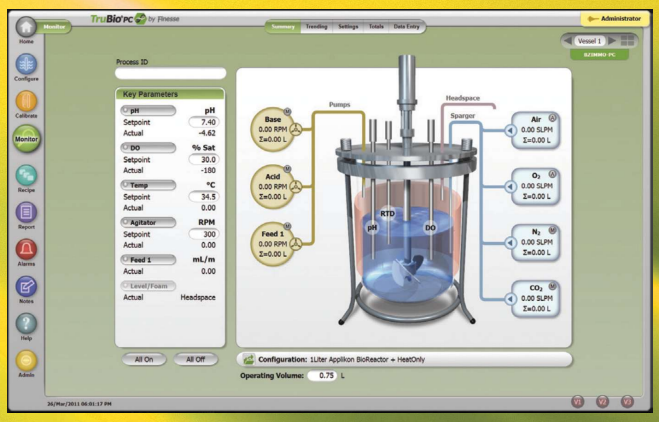
Freedom to do anything.

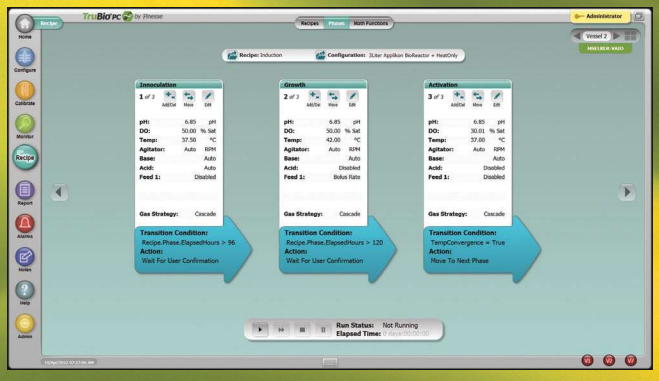
Today you don't need to bet your lab on one bioreactor platform. Contact Finesse and find out how our T300 systems can bring you bioprocessing flexibility.

800-598-9515
finesse.com

In Europe, call: +41 81 641 20 00. In Asia, call: +65 8322-8128.

Finesse





“Design is not just what it looks like. Design is how it works.”

– Steve Jobs

TruBio µC Don’t be fooled by its looks. TruBio is not a video game.

Simple can be harder than complex: You have to work hard to get your thinking clean to make it simple. But it’s worth it in the end because once you get there, you can move mountains. – Jobs, 1998

TruBio® µC software took us over three years to develop. Why? We wanted to design a product that was intuitive yet powerful. We combined a bold user interface with robust control algorithms. We pre-characterized bioreactor vessels to eliminate loop tuning. We captured popular TruBio DV features, but simplified data graphing and extraction. And then we created RecipeManager to automate runs and simplify batch design.

Simple is smart.

Call us for a TruBio µC demo and harness the power of simplicity.

800-598-9515
finesse.com

In Europe, call: +41 81 641 20 00. In Asia, call: +65 8322-8128.

Finesse

training, and a sense of urgency.

COSTS — MORE THAN TAX INCENTIVES

Canada and the province have tax incentives and financial supports available like many other countries competing for clinical trials. These are issues over which CTO has no control. Heslegrave views costs in a broader sense. If you look at the cost of conducting a clinical trial, time is money. Anything done to reduce time can greatly reduce the costs to the company. While it may be difficult to shrink direct costs, CTO can cut indirect costs by shortening approval time, speeding enrollment, and standardizing processes. "For instance, if a trial goes on for a long time beyond its expectation, the company is paying oversight and operational costs it didn't plan on. For a $100 million pivotal registration trial, those additional funds could equate to as much as $1 million every week, or some very large sum. Secondly, and equally important, is patent life. Any delays shave time off patent protection," says Heslegrave.

SPEED — STREAMLINING & ENROLLMENT

CTO's first initiative is streamlining regulatory and ethics review barriers to entry into Ontario. The goal is to establish a single ethics review board to provide standards mutually acceptable to all sites in Ontario and shorten approvals from months to weeks. Heslegrave is basing the CTO model on the successes of the Ontario Cancer Research Ethics Board (OCREB), which has a single ethics review process for all oncology research centers in Ontario. As an example, Heslegrave says that while he was associated with OCREB, Pfizer approached Ontario for placement of a study. Because of the centralized ethics review for oncology, Ontario had its first patient enrolled before other sites had approvals, and Pfizer-Canada lobbied its home office to get more sites in Ontario.

Slow recruitment is frustratingly unpredictable and can add months to a trial. Roche's Arora says that 20% to 30% of the physicians/sites recruit almost all of the subjects for clinical trials. That means that a sponsor spends millions on setting up sites that are slow or highly unproductive. This, she says, is an opportunity for Ontario to establish itself as a place where recruitment is reliable and time is saved.

Heslegrave recognizes that physicians pose two issues in recruitment — first, their own as investigators, and second, as recruiters of patients. Many physicians are finding the rewards of conducting investigatory work are outweighed by the barriers. Compensation may be low or nonexistent. Research time may not be allotted. Administrative requirements may be overly burdensome. For instance, investigators may have to attend good clinical practices (GCP) repeatedly to satisfy the needs of each sponsor and institution involved in a trial. Heslegrave says issues like these are the opportunities for CTO to promote collaborative solutions from industry and sites to reduce barriers and make research attractive to industry.

CTO plans to speed patient recruitment through education. An easily remedied problem is that many physicians are not aware of studies or the need of their assistance in identifying patients. Similarly, convincing patients to join a study is tougher, but pilot studies have demonstrated that both physician and patient groups participate at much higher rates when presented with information on the benefits for themselves and the common good. According to Heslegrave patients receive closer medical attention when they're in trials, and standards of care improve in hospitals that participate in clinical studies. Participation keeps the medical community abreast of current and new practices in medicine, which helps the entire province.

Investigators will also have access to patient registries to help them identify subpopulations for enrollment. CTO is compiling these registries through the national health system with voluntary support from physicians and patients. CTO is also working with patient advocacy groups to gain acceptance of and participation in studies. These groups have the networks and contacts to disseminate information and encourage support of research projects. They offer investigators a direct connection to patients.

WHERE DO THEY STAND?

CTO received provincial funding in June 2012. It established working groups with a year-end deadline to have a framework for legal and liability issues across all institutions and to have an IT strategy to link information among the institutions. Heslegrave says it will run a pilot program on the ethics review process in early 2013.

CAN ONTARIO HARNESS THE EXPERTISE?

Ontario has proven expertise and quality in medical research. It is, however, expertise that is siloed and independent. The costs are high, and analytical research attitudes lack a sense of urgency. Heslegrave says Ontario got the message. "Ontario has invested in reforming its clinical trials infrastructure, and that is unique. That investment should pay off by making Ontario a more efficient and effective location to carry out clinical trials. Companies should benefit directly from those efficiencies."

Arora says that despite what appears to have been difficulties in conducting clinical trials in Canada, Roche has increased its resources there. She says, "Canada provides a stable environment in which to build a framework. Ontario has a great talent pool and a density of knowledge. In a relatively small area, there is multidisciplinary expertise." Other countries once thought to be low-cost solutions to research are now enacting regulations and requirements that burden investigators and are not a "known quantity" like Canada.

She says there is also more consistency of care from practice to practice due to the nationalized healthcare system. That care is attended on one of the most diverse populations in the world. Both of these, she says, make studies easier to provide statistical significance for broader populations.

To a courier, this is just another box.

To Marken, this is a crucial specimen in a $20 million clinical trial

Most couriers work within their guidelines, not yours. But at Marken, Life Science is our business, so we know that the supply chain is different for every clinical trial. That's why top laboratories trust Marken to support over 6000 investigator sites globally. Our pharma experts have a deep knowledge of worldwide logistics and pharma regulations, providing our customers with the training, materials, and support needed to maintain specimen integrity, both at the site and on the shipment back to the lab. With preclearance of customs, a wide range of temperature control and logging systems, and more packaging solutions than anyone, Marken ensures that your specimens arrive on time and within specification.

When it's out of your hands, it's in ours.

MARKEN®

Global Life Science Supply Chain Solutions

Call (800) MARKEN1 to speak with a Marken specimen logistics expert today.

marken.com

Real-Time Alerting Is Changing The Dynamics Of Clinical Research

By Rick Morrison

The next several years are likely to be significant ones in the evolution of clinical trials. A number of new technologies are coming to the market that have unprecedented potential to improve trial efficiency, correctness, and, most importantly, safety. At the forefront of these developments is real-time alerting, a powerful new technology for helping each member of the research process do their job better at each stage of the research process. Although alerting is still a relatively new feature, many sponsors are already beginning to see the efficiency and safety benefits of incorporating them into their standard procedures.

UNLOCKING THE POWER OF EDC + MOBILITY

Alerts have been made possible by two related advances in technology: the digitization of clinical trial data through developments like electronic data capture (EDC) and the prevalence of Web-enabled mobile devices like smartphones and tablets. Alerts are the key to unlocking the combined power of these two technologies because alerts allow a clinical trial system to be configured to recognize relevant information as soon as it is entered digitally. In turn, the data can be sent to the right person on their mobile device via text message or email wherever they are whether or not they are logged in to their computer workstation.

Alerts are highly customizable in a number of ways, including in terms of timing (i.e. immediate versus aggregated once per day) and the information they include. Alerts are also relatively easy to adopt with little investment in hardware or training as many people already have mobile devices and are comfortable using them in everyday life. Because of this flexibility and ease of use, alerts can bring improvements to many facets of the clinical trial process, including in safety, efficiency, and patient interactions, as described in more detail below.

REACHING THE HOLY GRAIL WITH THE SAE ALERT

Perhaps the most compelling use for real-time alerts is in the case of serious adverse events (SAEs). An alert that is configured to notify all relevant stakeholders as soon as an SAE is entered into the system can drastically reduce the delays currently associated with identifying, evaluating, and reporting SAEs. This is a benefit both to patient safety, as potential dangers can be addressed sooner, and to trial managers, who will be better equipped to comply with their SAE reporting requirements. In extreme cases, studies can be suspended faster before more participants are harmed.

Sponsors can also consider other types of safety-oriented alerts. For example, if a study has an overall patient deceased rate of 20%, an alert could be configured to notify the appropriate stakeholders if a particular site has a significantly higher or lower rate. Such alerts could broaden the way trial safety is monitored, quickly identifying problems even where an SAE has not occurred.

SECURING EFFICIENCY GAINS WITH THE OPERATIONS ALERT

Alerts can be used to improve trial operations in a number of ways. For example, financial officers could be notified if spending starts to exceed the trial budget so that they can bring the trial back on budget. Concurrently, operations managers could be alerted if a clinical site is running low on certain supplies so that they can have additional supplies delivered, or a sponsor could be alerted if a certain patient screening question is disqualifying a large portion of potential study participants so that they can reassess if the screener is working properly. In each of these cases, alerts mean less time and less money goes to waste because potential issues are automatically brought to

the attention of the right people much sooner in the trial process.

HEADS UP, PATIENTS — THE SUBJECT SIDE OF ALERTING

Alerts need not be exclusively sent to sponsors and managers. Alerts can also notify patients when they need to take action, which improves the research process and creates cleaner data. The most straightforward patient alerts are ones that remind patients that they need to provide data, either by entering an electronic patient-recorded outcome (ePROs) or visiting a clinical site. ePRO reminders are particularly powerful because they can be combined with other mobile applications so that the patient can take action immediately with little effort. For example, a patient in an antidepressant trial may receive a text message reminder to provide an assessment of their mood, and then the alert can automatically open another app on their phone with a mood survey to complete.

Alerts may also be combined with other developing mobile technologies. For example, some blood pressure monitors can now be continuously monitored by a smartphone app, so a patient who experiences an unexpected drop in blood pressure could be alerted to visit a clinical site immediately for further evaluation.

THE FUTURE OF ALERTS

Clinical trial alerts are still relatively new, but they are likely to rapidly become commonplace in the industry. The industry should also expect to see a great deal of innovation in the use of alerts. Forward-looking sponsors will likely find beneficial uses of alerts we can't even imagine today. As a result, alerts are likely to remain at the forefront of new clinical trial technology for the foreseeable future.

About the Author

Rick Morrison is the cofounder and CEO of Comprehend Systems. Prior to founding Comprehend Systems, he served as the chief technology officer of an Internet-based data aggregator, where he was responsible for product development and operations. Morrison has more than a decade of experience writing software for clinical trials.

The Only Path To *True* Innovation In Drug Discovery

By Philip Haydon

Going against established thinking can be an uphill battle, but the payoffs can be huge in both academia and business. To achieve such payoffs, a scientific leader needs conviction, tenacity, and perhaps a slightly stubborn streak.

When I took my first faculty appointment in neuroscience in 1986 my work focused on neuronal signaling. In 1992 we had an experimental result that seemed to make no sense — in a dish of cells in which we had killed all of the neurons, we could still measure chemical signals. How could this be? I could draw only one conclusion: glia cells, the only cells left in the dish, must be releasing the same chemical transmitters as those released from neurons.

Glia. Even the name — Greek for "glue" — suggested that these were merely support cells. But why had no one questioned this assumption? As is so often the case, scientific inquiry was limited both by established thinking and by the tools and techniques available to ask the novel question. Electrical recording and stimulation techniques had allowed great insights to be made into neuronal function and the development of the field of "neurosciences." Glia, by contrast, are electrically mute. Their signals could not be picked up using these techniques.

NOT A POPULAR CONCLUSION

Our suggestion that glia not only release chemical transmitters but also play a key role in the modulation of synaptic transmission was not well accepted for a long time by neurocentric scientists. Fortunately we were confident in our glial hypothesis and ignored this advice. Along with other groups, we went on to identify how glia can play an active role in the brain and how different subtypes of glia serve different functions. Astrocytes, for example, which are the most plentiful glial cell in the brain, modulate synaptic transmission, plasticity, learning, and memory and play pivotal roles in the control of sleep. Microglia, another glial cell type, hold promise as therapeutic targets for Alzheimer's disease.

In the past 20 years skepticism has turned into success. The study of glia is now recognized as vital in understanding brain function. Our research has been so successful that we have formed a company — GliaCure, Inc. — to identify and target glial-based signaling pathways for the development of new drugs. As we gain an understanding about the biology and put this in the perspective of translationally relevant disease models, we have then been able to ask whether such targets have the potential to offer therapeutic opportunities. This strategy has already led to the synthesis of novel chemical entities targeting Alzheimer's disease that we will soon take into IND (Investigational New Drug)-enabling studies. Further down our development pipeline, we have identified new targets for sleep disorders and fast-acting antidepressive therapies.

We identify those new targets by looking for glial-enriched receptors that are preferentially expressed in this cell type. For example, it is known that the pressure to sleep is controlled by the accumulation of the extracellular signal adenosine. Through our basic investigations of glia and the use of molecular genetics, we have discovered that a subtype of glial cell called astrocytes is the cell that is responsible for the regulation of the amount of adenosine in the extracellular space and, as a consequence, homeostatic sleep responses. Due to these insights, we are now identifying the signaling pathways which control the release of adenosine from astrocytes with the long-term idea of specifically activating these pathways to control adenosine release and consequently sleep.

A FRUSTRATING APPROACH

Our approach to drug discovery — going against the literature — has at times been very frustrating. However, we believe that, while a healthy respect for the past has its place, innovators have to have the courage to break away from the crowd. It is essential to take risks away from the common focus so you can make quantal jumps forward. However, one of the difficulties of going against dogma is to find backers who will invest in this approach. Thus, it becomes important to recognize that there is a need to invest outside of the mainstream in high-risk high-payoff areas.

Our approach doesn't guarantee success, but the success it does lead to is truly rewarding.

About the Author

Philip Haydon, Ph.D., is chair of neuroscience at Tufts University and president and cofounder of GliaCure, Inc.

EXPERT GUIDANCE FOR PERFECTLY ALIGNED TRIALS.

When planning your next drug, device, diagnostic or combination product trial, think Theorem. We apply a team of experts with a steadfast degree of experience where you need it, every time. From start to finish, no matter the scale or setting, we have the strategic insight you need to simplify the complex, advance your trial and prepare your submission for success. When you need a CRO to customize solutions to get you to completion on time and within budget, don't give it a second thought. **THINK THEOREM.**

- Specialist in complex Phase I-IV clinical trials
- Advanced clinical analytics capabilities
- Expertise in complex medical device and combination studies

P 1-800-290-5766
W www.TheoremClinical.com

Simplifying the most complex CLINICAL TRIALS.

Biopharmaceuticals \\ Medical Device \\ Diagnostics

THEOREM
CLINICAL RESEARCH™

The Importance Of Streamlining Content Management

By Shannon Zimmerman

An increasing number of global life sciences organizations are adopting a content management system in order to improve the quality and consistency of their content translations. While a changeover of this magnitude poses some difficulties, business leaders are discovering that an effort to streamline their content management for global-spanning markets is not only beneficial but essential.

CHALLENGES THAT GLOBAL ORGANIZATIONS ARE FACING

Significant difficulties arise when content storage is decentralized. It ends up costing a company more, not just in terms of expense, but in staff resources as well. Productivity decreases because of squandered time and potentially duplicated efforts. Lack of controlled management also exposes life sciences companies to greater risk, since regulation becomes more difficult to track and measure — a state that is untenable. To remain current and stay competitive, business leaders need to embrace better content management practices even while they pursue global growth.

"Life sciences companies that need to launch content such as manuals, IFUs (instructions for use), or product labels into global markets experience exponential growth in the amount of content and the number of touch points involved," says Shannon Rose Farrell, an enterprise program manager in the life sciences translation industry. Managers are aware of this, and so they are taking steps to streamline their document production and control process to reduce costs, streamline efforts, and ensure message consistency — all while decreasing liabilities. Integrating a content management system into the current workflow allows for greater version control, easy content access for all involved individuals, a transparent audit trail, and overall diminished risk.

WHAT MOTIVATES LEADERS TO MAKE CHANGES

Due to regulatory compliance, it takes weeks, months, and even longer to get documents approved by all required individuals. Every piece of content must be approved by each stakeholder. As a result, it is not unheard of for organizations to still be using documents that received the green light more than 10 years ago. Operating a highly regulated business using out-of-date content increases the amount of risk they face.

Even so, the decision to centralize business data is not taken or arrived at lightly. Many business leaders are hesitant, sometimes even paralyzed, into inaction when faced with the prospect of overhauling the entire content management process. Some of the world's largest medical device companies are still trying to optimally centralize and streamline their content management and localization paradigm.

Despite the ultimate advantages of undertaking such an initiative, changing the current system and storage infrastructure entails a considerable shift in thinking and operations. Yet it is a beneficial shift, especially when an organization is localizing materials for international markets. Ensuring the highest quality in the source language will result in effective translated content that adheres to the original document messaging. A document only needs to go through the approval process once; going forward, the document can be rendered in additional languages and retain consistent wording.

ADDITIONAL STREAMLINING

Global organizations requiring localization are finding that it makes sense to link up their content management system to a translation management system. As a next step, it goes a long way toward ensuring complete centralization. Messaging consistency is assured across all languages; quality control and tracking are transparent.

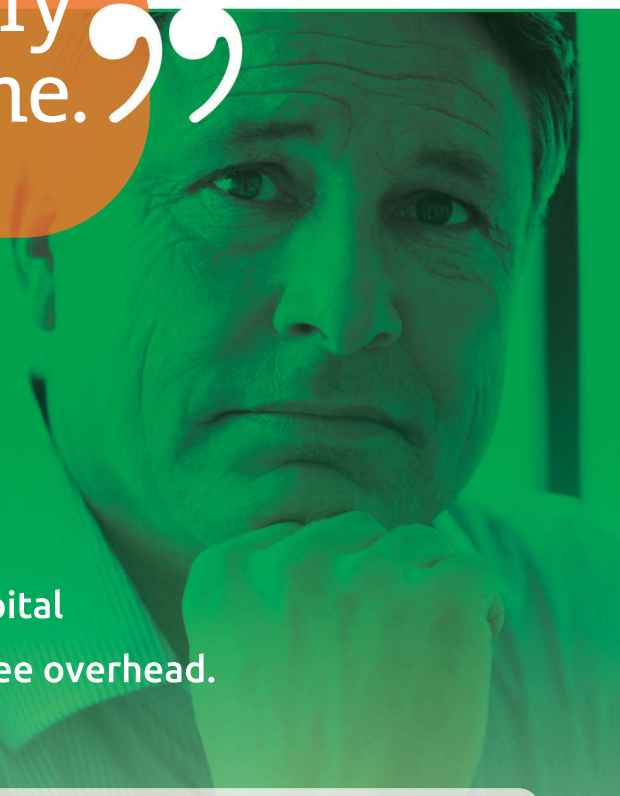
While adopting a centralized content management system is not yet a mainstream practice, some organizations are implementing this solution. These life sciences companies are at the forefront of this space. Over the next few years we may be seeing a more universal shift in this direction with how content is accessed, rendered, and controlled. For now, it signals a trend toward more streamlined, consistent, and accurate multilingual content, benefiting not only life sciences organizations but ultimately the end users of their content all over the world as well.

About the Author

Shannon Zimmerman is the CEO of Sajan, a language translation services company. A third of the company's business is dedicated to the life sciences industry.

"We *need* an automated visual inspection system.

We simply can't justify the capital to buy one."



At Visionspect, contract visual inspection is all we do. Our service offers all the advantages of automated visual inspection without the capital outlay or employee overhead.

We furnish your site with Viswill (formerly Kanebo) vision systems, the industry's premier visual inspection technology. Our skilled operators and technicians run, maintain, and service the equipment, freeing you to focus on what you do best.

With Visionspect, you have the flexibility of pricing by batch, by unit, or by volume…*and all our inspection results are guaranteed.*

Contact us today to schedule a free verification batch test. Call 630-776-2459 or email us at info@visionspect.com.

visionspect
contract visual inspection

630-776-2459 | info@visionspect.com

A Biotech Structure For A Tough Financing World

By Joe Comeau

The current world of biotech start-ups is experiencing a real crunch obtaining financing. VCs are very particular, having investors who may not have the patience for very long times to commercialization and payday. Big Pharma appears to be all over the place, with money to spend on good IP, but with huge bureaucracies and infrastructures that can sometimes stifle good science and often choke entrepreneurial spirit. Bio is unique as a business space because so many companies are driven by people who are brilliantly creative *and* who have ideas about how their science can change the world in good ways. Often those dreams fail, but so do many start-ups in any space. However, bio company founders also remain undaunted by the fact that they typically take considerably longer than other start-ups to get to commercialization events that allow investors to see a return on their investments. This confluence of factors has distinguished the bio world as being especially leading edge when it comes to creatively financing their projects. Based on the unique characteristics of the bio world, it is time for these companies and their founders to take a look at a page from big business — with a modern twist.

There was a tech-oriented company in greater Boston called Thermo Electron (now called Thermo-Fisher). The company had many people investigating many different discoveries, including people who came over in acquisitions. However, the discoveries led to technologies that were not all best applied in the company's core business. Management distributed promising tech into subsidiaries and took those subsidiaries public, keeping a majority stake for the parent. As an early pioneer in what was essentially a public venture investment, the company was able to finance good ideas and give its investors access to public market liquidity. Bio can use a variation on this theme with very powerful results.

APPLICATION IN TODAY'S WORLD — HUB AND SPOKE

The proposition is that a new bio enterprise be formed as an LLC, *not* as a regular corporation. That LLC would own the core IP and the founders would be LLC owners. The LLC will be a holding company for all IP — the hub for all future expansion. On day one, it will contribute a specific subset of the core IP to a subsidiary LLC (Sub1) in exchange for its equity. This would be the first spoke of potentially many. Then, external investors will contribute cash in exchange for typical preferred equity financing in Sub1. Sub1 will perform the development activity — and any other activity that an otherwise single corporate entity would accomplish. Other applications for the core IP will be contributed to sister subsidiaries from the holding company LLC, as the times and markets develop demand for those applications (additional spokes). The same or other investors could participate in those new subsidiaries, and the pricing, financing, and terms could all be specifically tailored to the value proposition of that subsidiary.

WHY DOESN'T EVERYONE DO IT?

Why is this worthwhile? The founders can concentrate investment dollars on specific applications without needing to convince existing investors to participate and without requiring expensive taxable separation of valuable IP components. Furthermore, if BIGCO comes by and wants to pay up for the first IP slug, the other applications — in which BIGCO may not even be interested — can be further developed and harvested with different players. The structure gives the operators and the investors incredibly more flexibility than a single entity for the entire package.

This is a more tax-effective approach than the one used back in the day by Thermo and others. With a traditional corporate structure like theirs, if StartupCo had investors that wanted to harvest value from one IP but not others (because, for example, the others are in different fields for which current buyers of the extant IP are not willing to pay), its investors would likely experience double taxation. With the LLC model, that does not need to happen, and that means more after-tax cash for all.

SO WHY DOESN'T EVERYONE DO THIS?

First, traditional corporations are simple. Companies have been started in that way for decades. "Keeping It Simple Stupid" is an easy approach to take when all you really want to think about is the IP development. Second, most founders focus on their "best shot" within their IP, with the hope that they can develop the rest later. Having it all in

one corporate pot is easy to understand. Finally, LLCs are different tax animals, and some investors shy away from them for that reason. Although most VC funds are LLCs or their rough equivalent, the funds themselves are used to investing in traditional corporations, and they usually eschew anything more tax-complex.

However, the laws have evolved, and more importantly, the vast majority of start-ups focus on one product/suite of tech for their value proposition. Bio is more diverse, at least right now. There are fascinating caches of IP that have the potential for application to widely diverse therapies, and those applications could have very different ultimate consumers and ultimate interested buyers. This represents an opportunity for investors and founders to maximize their value with very little brain damage due to structure. Nowadays, any investor reluctance to invest in LLCs for tax reasons can be very effectively managed, and, in the end, the advantages will likely outweigh any added complexity.

Some other flexibility advantages for this approach include:

- Companies can issue "cheap stock" to key employees even when subsequent financing rounds value the company higher. This helps the company attract and retain key people more effectively than a traditional corporation.
- Traditional corporations in the bio world can lose their ability to carry over their tax losses due to ownership changes or simply length of time. The LLC approach fixes that by stapling any losses to the investors present when they are incurred.
- The LLC vehicle can allow the company to position a sale of one or more of its component IPs to a buyer in such a way that the buyer can eventually tax deduct its purchase price.
- If "public venture funding" becomes a viable prospect for a given IP, this approach easily allows a SubX LLC to legally become a traditional corporation and do an IPO.

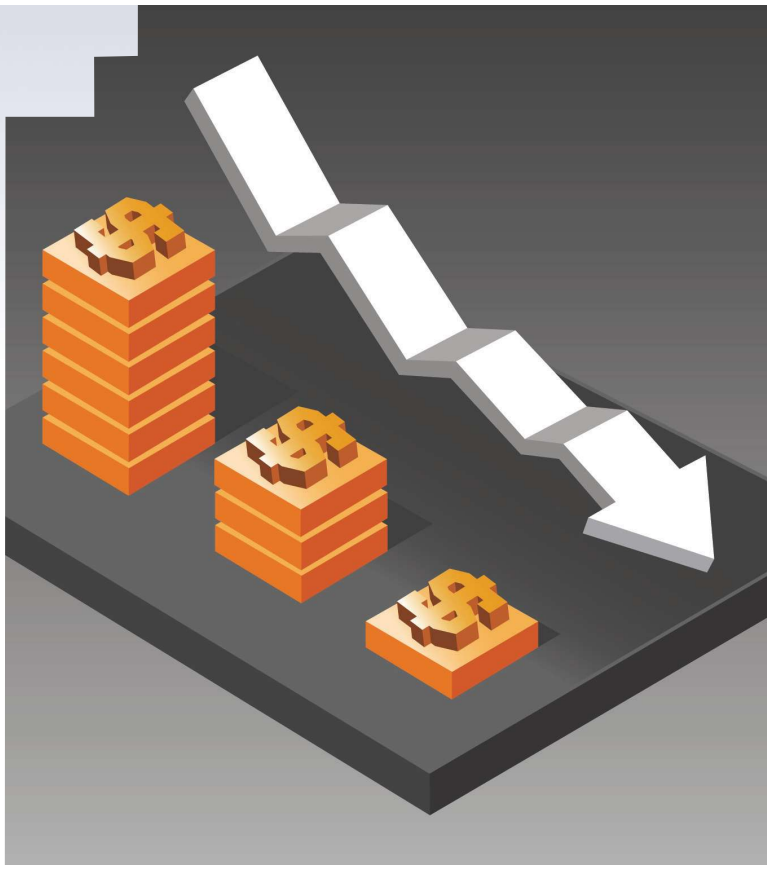
TIMES THEY ARE A CHANGING

The old Bob Dylan song couldn't be more apropos to the bio world today. All things considered, bio has demonstrated an excitingly creative bent on financing that appears to be far ahead of the curve in the overall start-up space. It is time to consider adding something like the hub-and-spoke approach to the bio toolbox.

About the Author

Joe Comeau is the office managing director for WTAS' New England practice. He has more than 30 years experience working on the tax and financial needs of entrepreneurs, their families, and their businesses.

Life Sciences Venture Funding Drops



By Cindy Dubin, contributing editor

In today's economy, capital is much more difficult to raise, and the various sources of investment, from private angels to larger VC firms, are understandably much more cautious and conservative about where they place their money. "The economic recession made its impact on life sciences investments, as there have been negative returns on investments for the last 12 years. Venture funds have been pared back, and until there is a change in the economy, the funding will not be there," says Tracy Lefteroff, global managing partner of the VC practice at PricewaterhouseCoopers (PwC) U.S.

This somewhat bleak picture is drawn out vividly in *Dollar Drought*, a new *MoneyTree* report from PwC and the National Venture Capital Association (NVCA), which addresses VC funding in the life sciences sector. The study, based on data from Thomson Reuters, found that the life sciences share of total venture funding fell to 20% during the second quarter of 2012, the lowest level since the third quarter of 2002. Funding for life sciences, which includes pharmaceutical and biotechnology, dropped during the second quarter of 2011 as compared to the same quarter in 2012 (pharmaceutical fell 13% to $89 million in funding and biotech research fell 96% to $3 million).

Early-stage deal volume declined by 16% in the second quarter of 2012 compared to the same quarter last year, and the average deal size shrank to $6.1 million. This drop in early-stage funding could have implications for the life sciences sector well into the future, as there will be less capital available to support start-ups, says Lefteroff. Late-stage funding also declined, dropping 41% year over year to $798 million.

"Overall, the sector has not delivered returns," says Doug Cole, M.D., general partner, Flagship Ventures, a VC whose portfolio consists primarily of seed and early-stage investments, with some later-stage value investments; healthcare investments; target therapeutics; and medical technologies. "The longer-time horizons, higher regulatory barriers, pressure from payers, and uncertainties around government healthcare policy have all combined to increase the potential capital needs for start-up life sciences companies. At the same time, public markets have become more difficult to access, and the cost of going public and being public has increased. Many funds are focusing primarily on supporting and building companies that are already in their portfolios. In recent years, the apparent success of some social media companies has diverted some venture investors' attention from life sciences investments, as well."

OBSTACLES TO FUNDING

The PwC report states that it will continue to be a challenge for life sciences to raise funds until the regulatory environment becomes transparent for firms trying to move new products into the market. Lefteroff says that the time frame to get through the FDA has significantly lengthened in the last five years. "There really is nothing that a company can do about the regulatory pathway except maybe lobby to streamline the process," he says.

"The FDA has gotten in the way for sure," says Adair Newhall, an associate with Doman Associates, a VC firm with an exclusive focus on life sciences. "Companies have to demonstrate quality and efficacy of their data, and many are told to go back and conduct their Phase 3 trials again, which can be too costly. As a VC, we are looking to back companies whose models are not too lengthy and not too costly."

James Smith, Ph.D., president, NanoSmart Pharmaceuticals, Inc., which is developing next-generation drugs to treat cancer, understands the FDA regulatory approval process all too well. NanoSmart is developing an immunoliposomal drug delivery system capable of targeting a wide variety of solid tumors. By reformulating drugs that are already approved for marketing, Smith believes his company can commercialize these products both

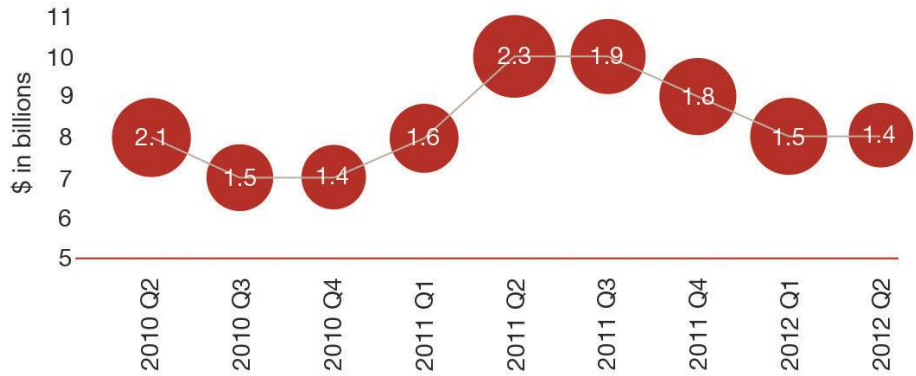
rapidly and economically. Due to the lower patient population for rare diseases, the FDA may also allow commercialization of the new drug product following successful Phase 2 clinical studies (typically larger Phase 3 clinical studies are required prior to market approval). In addition, subsequent NDAs (new drug applications) will have a reduced regulatory burden, since much of the analytical and nonclinical safety data for the drug delivery platform will already be available.

"Our regulatory strategy is specifically designed to take advantage of well-established regulatory incentives for commercializing orphan drugs," Smith adds. The FDA offers several key incentives to companies that endeavor to develop drugs intended to treat rare diseases (these drugs are termed "orphan drugs"). These incentives include tax credits to help offset the cost of development, FDA fee waivers, an Orphan Drug Grant program to support clinical studies, and seven years of market exclusivity.

NanoSmart's proprietary platform technology utilizes a unique antibody that is capable of targeting a variety of tumor types. When attached to a liposome or other nanoparticle, it can improve accumulation of the drug product at the site of a wide variety of cancer tumors. The antibody is human-derived and targets nuclear material found in areas of necrosis associated with all solid tumors. This allows the antibody to target tumors without having to target disease-specific markers. "Our technology was developed with the intent of mitigating the typical challenges associated with drug development (e.g. our use of a human-derived antibody vs. an animal monoclonal antibody, our selection of already-approved cancer drugs, and the use of well-known excipient materials in our final drug formulations are designed to mitigate regulatory risks and burden)," Smith explains. "We believe investors today will appreciate and support those companies that have the ability and willingness to reduce the risks inherent with any start-up operation."

Clinical trials for orphan drug products typically require fewer patients and are generally significantly shorter than nonorphan drug products. This translates into more rapid market approval of the orphan drug product. Smith says that by adopting this faster-to-market strategy for NanoSmart's initial pipeline products, the

Figure 4: Life sciences average deal size by quarter 2010–2012



company ultimately increases the inherent value of its drug delivery platform, substantially reduces the risk of the investment (by demonstrating an ability to commercialize), substantially reduces the overall cost of commercialization (and therefore investment needed, which in turn leads to lower investor dilution), and creates the revenue-generating opportunities from product sales and additional product collaborative opportunities with other products in the pipeline. "All of this should lead to substantial increases in the value of the investment and provide for exit strategies or investment liquidity that is also attractive for today's investors," he says.

The recently passed user-fee legislation (i.e. Prescription Drug User Fee Act) contains some incentives for companies to develop breakthrough therapies for infectious and rare diseases. These include extended market exclusivity for qualified infectious disease products and expedited FDA review for therapies that address unmet medical needs to treat rare and life-threatening diseases and conditions. Such incentives could pique the interest of investors in companies developing these products, as they might have a shorter path to market, says Lefteroff.

Mergers and acquisitions also affected VC funding. Life sciences companies closed 15 venture-backed M&A deals during the first quarter of 2012; 7 of them had an aggregate value of $1.7 billion. "The pace of venture-backed exits we saw for life sciences companies during 2011 should encourage investors going forward," says Lefteroff. If M&A activity picks up during the second half of this year, investors could see a clearer path to returns, which could potentially attract more money to be invested in the sector, states the report.

"M&A is often the outcome of choice for venture-backed companies," says Cole. "We view this as a great opportunity for win-win scenarios. Larger companies can get access to start-ups' creativity and novel assets, and the start-ups and their investors can realize attractive returns. A healthy M&A market is critical to all the stakeholders and the health of the industry."

The new Jobs Act might spur more confidential IPO filings, creating the opportunity for more exits, states the PwC report. The act makes it easier for start-ups with less than $1 billion in annual revenue to go public by relaxing Sarbanes-Oxley requirements for five years.

HOW TO FUNDRAISE

The concentration of VC dollars in the hands of fewer firms will dictate the flow of investment, which translates into less capital available for life sciences, according to NVCA President Mark Heesen. But, the VC pros do offer some insight into how to raise some funds.

"Discipline is critical in any investment environment, but especially now," says Cole. "We look for investments that combine indisputably leading people, ideas with real potential for disruptive impact on significant markets, strong scientific validation, tractable development paths, clear regulatory expectations, and receptivity among researchers and companies. This convergence only happens occasionally."

Assembling the best team possible is also an essential prerequisite for success. "Additionally, have a clear value proposition, and be able to articulate it incisively," continues Cole. "It is necessary to adapt quickly to changing circumstances and new data. Capital efficiency is essential to building value that also has the potential to provide meaningful returns to investors."

Like many innovator companies, NanoSmart Pharmaceuticals started with an innovative idea and a compelling story that it believed would be viable and important to the industry. Its key drug delivery platform technology patent was issued in 2009 internationally and in 2010 in the U.S., providing the room to innovate with secure IP and a good demonstration of its ability to execute on established goals. Since last January, NanoSmart has raised approximately $1.5 million in private investment.

"We have focused our approach to fundraising around the idea of selling progress, not promises," says Smith. "Anyone can share a vision of how great things would be if they just had enough of someone else's money. We felt that, by demonstrating that NanoSmart is a place where efficient progress is continually made on an aggressive development strategy, investors would view us as

an investment opportunity where the risks have been mitigated."

In that respect, NanoSmart developed a rapid and economical plan for development of its lead pipeline products and established a solid management team with expertise and track records in drug development, product commercialization, regulatory strategy, and business development. "We believe that building and maintaining investor confidence is critical to ensure continued funding. In that respect, NanoSmart operates as transparently as practical and openly communicates with its investors to ensure that they can see our successes as well as how we deal with the inevitable challenges that all development-stage companies face. If measures of success include current investors investing more and friends-telling-friends about a good opportunity, then we feel that our approach to fundraising is working very well."

THE SILVER LINING

"Although conditions certainly ebb and flow over time, it is likely that the paradigm in which start-up life sciences companies raised a few tens of millions of dollars, established a platform with one or two early stage programs and a corporate deal, and then went public is unlikely to reemerge. We expect funding will continue to be difficult," says Cole.

That being said, there is a silver lining. Advances in biology, ongoing unmet needs, development of new markets abroad, and increasingly well-educated consumers all create opportunities. The market will continue to recognize and pay for real value. "That is where venture investment should focus," adds Cole.

Are Big Pharma Companies Dangerously Limiting Their Supplier Options?

Missed opportunities for quality and value in supplier relationships are the price companies may pay when they use outsourcing only for efficiency and risk management.

By Wayne Koberstein, contributing editor

Simple questions often have complicated answers. In this case, with no sarcasm intended, the simplest answer to "Are Big Pharma Companies Dangerously Limiting Their Supplier Options?" is "It depends…"

What is the first thing that comes to mind when someone asks the question? Doxil? Drug shortages? Plant closures? Warning Letters? 483s? But don't allow transient events to cloud the picture; internally, the companies of Big Pharma have been cutting back big — not just in manufacturing, but in R&D and other areas. Externally, with suppliers, the situation is more nuanced. Companies may have boosted their outsourcing in quantity, though recent growth in the sector has flattened, but they have paid less attention to the quality of outsourcing relationships as a strategic asset. If anything, they have downgraded their priorities and purposes for outsourced goods and services of all kinds, relying on too few suppliers and largely failing to communicate and collaborate with the suppliers they do have to create a competitive edge. Dangerously so? It depends.

It depends on the product, the patient, the competitive position, and the many other alliterations that characterize what's at stake when the limits companies impose on their supplier options produce insufficient or unsatisfactory results. Consequences can range from inconvenience to the worst of all corporate fears — lost revenue and profits.

By all accounts, Big Pharma companies have been transferring more of their production to CMOs for some time, supposedly to be more efficient. So how is it that a company can find itself blindsided by a catastrophic shortage of a widely used drug, due to a single CMO plant closure? Have they never heard of backups? Do they even care about the condition of the CMO facilities? Why do they seem so surprised and overwhelmed? Those are questions only a layperson would ask, of course; people like us, working in or close to the industry, are supposed to understand the realities of fiduciary responsibility and its attendant frugality. Does that mean professional industry knowledge trumps common sense? No, something is seriously, strategically wrong with companies' thinking here, and we know it by their works.

Executives have a way of delegating doubt. If any area of the company represents risk without an obvious reward attached, as it is in sales, corporate management will typically departmentalize it or, if internal costs rise too high, outsource it. In large part, pharma companies unfortunately use outsourcing mainly as a risk-avoidance tool. They want the problem to go away, not to become another problem they have to manage. So if you tell them they need to have better oversight of their suppliers and put greater value into "collaborative" relationships, they'll probably want you to go away, too.

Okay, as everyone says, it's "harder" for pharma companies to widen their

> The most common reasons for outsourcing — efficiency and risk management — may not be the best ones.

ONE 2 ONE™

Parenteral Contract Manufacturing Service of Hospira

Our comfort zone is global parenteral manufacturing

- **Biologics**
- Highly Potent Drugs
- Cytotoxics
- Betalactams
- Controlled Substances
- Sterile Compounding
- Single-Use Technology
- Lyophilization
- Global Regulatory Services
- QP Release

Discover your comfort zone at one2onecmo.com

Get your custom report online or contact One 2 One.
Call +1-224-212-2267 or +44 (0) 1926 835 554 or e-mail one2one@hospira.com

ONE 2 ONE™

Parenteral Contract Manufacturing Service of Hospira

Your Parenteral Comfort Zone

P11-3517A-R1-Jul., 12

supplier options because their industry is so much more regulated than others. But when the regulators are out in front, pushing you toward new technologies, systems, and solutions, you can't just go on hunkering down and clinging to your old Victorian ways — says that pesky but informed layperson. You keep talking about innovation, so why can't you innovate your way out of nasty problems like sudden drug shortages or botched trials?

This is monumentally unfair, of course. I can already hear the corporate version of howling coming from the C-level offices of Big Pharma: "We do so care about our suppliers — and we have this and that program to prove it! We want our suppliers to be our partners!" All I can say in return is that I hear a different story coming from the "floor" and from manufacturing experts, who generally regard Big Pharma production as antiquated compared to the advanced technologies and systems used in other industries.

WHAT ARE YOU OVERUSING/UNDERUSING REGARDING OUTSOURCING?

But I won't waste any more time talking about why the pharma industry isn't doing more to avoid supplier-related problems. Let's just look at some of the things companies could do if or when they have the will to go further than they've gone before. Although the examples I cite apply mainly to manufacturing, they have implications for R&D and other outsourced activities.

First, how are companies generally underusing outsourcing? Here is just a short list of widely ignored options:

- innovation/access to new technologies and processes
- capacity sharing
- quality by design (QbD) and serialization
- preparation for regulatory actions and changes
- risk management and accountability
- strategic compound management — from characterization to clinical development
- backup supply.

Next, how are companies overusing outsourcing?

- risk/responsibility avoidance
- cost cutting/resource rationalization
- "blind" buying of expertise and capacity
- virtualization without participation.

Some of those points require more explanation. I've touched on technologies and processes. Capacity sharing opens up a new vista entirely. When MedImmune and Merck signed a deal to swap their excess but complementary production capacity, they made history in the world of CMOs. I hear from one well-placed source that many CMOs also have excess capacity in production dedicated to Big Pharma products. At some point, someone will likely put 2 and 2 together to configure a capacity-sharing model involving CMOs and their pharma clients.

THE DRIVERS OF QbD AND SERIALIZATION

Similarly, a combination of external pressures and internal needs will continue to drive pharmaceutical manufacturing into QbD and serialization. Regulators want both, and the auditing/consulting side of QA/QC is also lining up to support their speedy adoption. In fact, QbD and serialization illustrate the next underused option for collaborating with suppliers — keeping up with regulatory actions and changes. Pharma companies bear primary responsibility for any regulatory problems with their products, outsourced or not. Both suppliers and their clients have a mutual interest in avoiding regulatory censure. Let's suppose a pharma company could win a critical competitive advantage by being the best at collaborating with its suppliers for the cleanest possible regulatory record. Too "intangible?" Hire an accountant. Do the math. Show how much you can cut costs by lowering the rate of supply disruptions below historical levels.

> Pharma companies unfortunately use outsourcing mainly as a risk-avoidance tool.

The most common reasons for outsourcing — efficiency and risk management — may not be the best ones. What is so efficient about relying on a single supplier for a key product when you factor in the worst scenario — a total interruption of supply guaranteed to happen at some point by the great law of Murphy? And the risk actually "managed," i.e. avoided, is about the same as walking blindfolded along a narrow plank, not knowing what lies at the end. If you want to make important parts of your company "virtual," at least participate as one side of the virtual partnership. It's about more than avoiding supply disruptions; it's about strategically managing your product from characterization through development and, ultimately, as therapeutic agents inside the bodies of real human beings.

"By applying a unique bottle ID at the beginning of the line, we can track critical operations throughout the packaging process, resulting in a higher bottle integrity profile and a more consistent product for our customers. For this, we trust the Thermo Scientific Versa Rx checkweigher."

- Glenn R. Siegele, President
Omega Design Corporation

Scan to watch video

Visit us at Pack Expo Booth #1230!

motivated by challenge

When it came to finding the right partner for integrating key checkweighing equipment into their pharmaceutical demo line, Omega Design Corporation chose Thermo Fisher Scientific. Omega Design's dedicated serialization lab required a reliable solution to demonstrate data sync on their line; Thermo Fisher Scientific rose to the challenge, delivering a reliable, accurate solution.

driven by commitment

- For more information on Thermo Scientific pharmaceutical product inspection solutions visit: www.thermoscientific.com/checkweighers

your partner in product and process improvement

Thermo
SCIENTIFIC

Thermo Scientific
Versa Rx Checkweigher:
High accuracy and high rate to meet demanding pharmaceutical applications.

In Pharma-Academia Partnerships, Who Will Lead?

Pharma companies and academic medical centers (AMCs) have collaborated in various forms for decades. However, in the past few years, the number and extent of those partnerships have multiplied, driven by several forces. Most importantly, pharma and AMCs have shown that they need each other as never before, driven to collaborate by ever-shrinking academic research budgets and a dearth of viable therapeutics in the pipeline. Meanwhile, the rise in popularity of the "open innovation" model has led both pharmaceutical firms and academics to view partnering as a win-win opportunity.

The challenge for organizations that wish to partner will be to create a business model that protects both parties, is flexible enough to propel innovation through proof of concept, and addresses what kind of structural leadership will be most effective in running these combined ventures. Several high-profile partnerships have emerged over the past three to four years that are emblematic of the open innovation model, which is characterized by the idea that shared IP and the creation of a better business model through partnered innovation can trump internal, proprietary invention. Each of these examples has some form of shared IP, shared profits, and milestone arrangements. Where they differ is on control and leadership structure.

The broadest example is that of Pfizer's Centers for Therapeutic Innovation (CTI), led by Anthony Coyle, VP and chief scientific officer. Pfizer has formed alliances with multiple AMCs in the hopes of creating an environment of open innovation, whereby the company shares its tools and development expertise with investigators and post docs housed at the country's top academic research centers in an effort to spur development of biotherapeutics.

GlaxoSmithKline (GSK) has also embarked on a "Discovery Partnerships with Academia" initiative. This partnership, like that of Pfizer's, is driven from the pharma side. It does, however, go to some lengths to give academic partners a measure of control. For instance, the agreed-upon terms state that GSK will give research partners a year's notice if it chooses to end a collaboration and, if that happens, the academics would be free to continue with the project.

Sanofi has recently chosen an alternative path, putting C. Ronald Kahn, professor of medicine at Harvard Medical School and chief academic officer with Joslin Diabetes Center (a Harvard affiliate), in the lead of a joint project between Sanofi and Joslin. From all accounts, this has created added enthusiasm among Joslin researchers surrounding the possibilities for representation as well as commercialization of research.

Bristol-Myers Squibb (BMS) and the Duke Translational Medicine Institute have pushed the boundary of partnership even further. The two are looking beyond discovery or early-stage work and instead seek to foster a collaboration across all research and development stages.

HYBRID LEADERS NEEDED

The decision as to who will lead and control the direction of these types of partnerships is arguably as critical as how they are structured. Pfizer's CTI and BMS/Duke, among others, initiate their partnerships by forming joint steering committees with equal representation from both parties. These committees are charged with the selection and oversight of promising projects.

As the number and complexity of projects rise, so will the need for better and more direct oversight. These partnerships will increasingly need to be managed by individuals who understand both the academic and industry mindset and can leverage the best elements of both types of institutions. These leaders will also need the ability to anticipate conflicts that may arise between partners from the corporate and academic worlds.

Some of the concerns perceived by an academic partner may include the fear of a loss of control, the potential for conflict of interest, and compromised academic credibility. On the industry side, concerns include whether academic partners will have unrealistic expectations for financing, raise contractual issues, or fail to adhere to strict timelines and deliverables.

Leaders best-suited to address these issues will preferably have first-hand knowledge of both environments. Thus it is likely that a hybrid executive will lead the next generation of industry-academia collaborations. As the collaborations themselves increase in complexity, it will be critical to have such leaders at both the director and VP levels. While the success or failure of these partnerships will not be determined by a single driver, having the right leaders in place for a new and rapidly evolving R&D model will be pivotal.

Lisa Flavin

Lisa Flavin is a consultant in the life sciences and healthcare practices of the executive search firm Witt/Kieffer. She has more than 15 years of executive search experience in the biotech, pharmaceutical, and medical device industries.

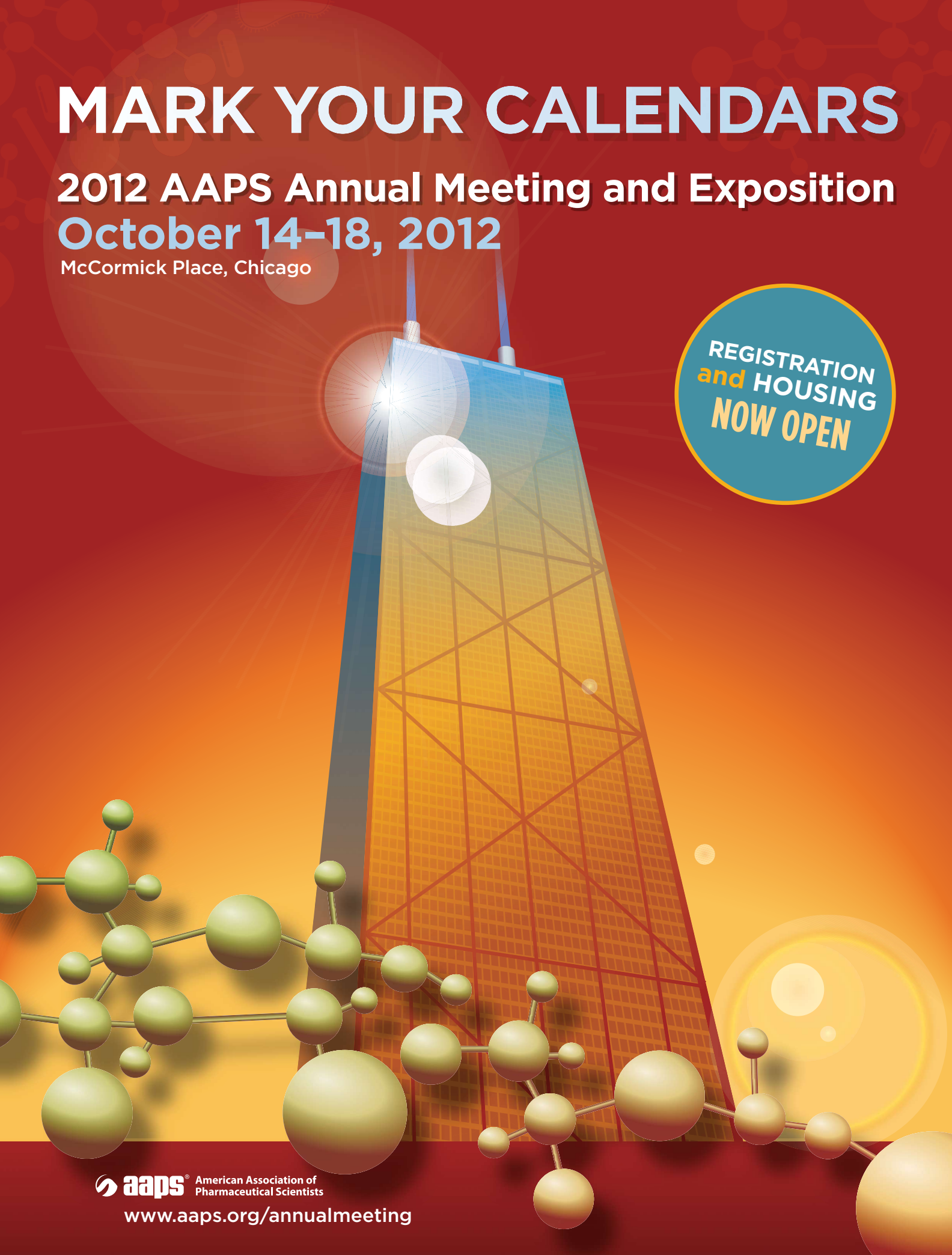
MARK YOUR CALENDARS

2012 AAPS Annual Meeting and Exposition

October 14–18, 2012

McCormick Place, Chicago

REGISTRATION and HOUSING NOW OPEN



aaps® American Association of Pharmaceutical Scientists

www.aaps.org/annualmeeting

SOT | Annual Meeting & ToxExpo™

San Antonio, Texas

March 10–14, 2013

HAVE YOU CONSIDERED ANNUAL MEETING SPONSORSHIP?

Show Your Commitment to the Society of Toxicology's Mission

Creating a Safer and Healthier World by Advancing the Science of Toxicology

Gain Valuable Exposure

More than 7,500 of the world's leading toxicology scientists and top executives from industry, academia, and government agencies gather at this one-of-a-kind event.

Sponsorship provides an opportunity for private, public, and nonprofit organizations to increase overall awareness of their services and programs by SOT members and Annual Meeting attendees.

Sponsorship also enables SOT to fund such programs as: Minority Student Program, Undergraduate Program, Student/Postdoctoral Scholar events, Continuing Education Program, Public Outreach, and much more!

Sponsors are recognized through numerous Annual Meeting print and web publications, as well as via banners and an acknowlegement presentation shown in each session room during the meeting. The level of recognition increases with the level of Sponsorship; *find out more at* ***www.toxicology.org/sponsor***.

For detailed information on the benefits of SOT Annual Meeting Sponsorship, contact Marcia Lawson, 703.438.3115, marcia@toxicology.org.

Photos courtesy of San Antonio Convention and Visitors Bureau. Photographed by Stephanie Colgan and Marks Moore.

Lead

Succeed

Learn

Grow

Connect

Transform

2012 ISPE ANNUAL MEETING

11 – 14 November

San Francisco,California USA

GLOBAL GMP SOLUTIONS

Through Innovation and Transformation

REGISTER NOW AND SAVE!

www.ISPE.org/2012AnnualMeeting

Your Suppliers Are Costing You More Than You Think

How many suppliers do you have that cost you millions of dollars per day? Your quick answer might be that none of them do. Think again. In 2010, the top 50 pharmaceutical companies had total revenue of $1.67 billion per day. That averages to over $33 million per company. If you are one of these companies and your production is down for a day, you just lost a chunk of that $33 million.

There are many causes of downtime in pharmaceutical and biopharmaceutical production. Your suppliers can be a major cause of downtime. When is the last time you had delays getting raw materials or replacement parts, and your production was down for a day, a week, or longer? Even a delay of a few hours can impact a production schedule and your bottom line. If your supplier or their supply chain is unreliable, it is you who foots the bill.

Even a delay of a few hours can impact a production schedule and your bottom line.

MITIGATE RISK WITH THESE STEPS

While you cannot totally avoid these interruptions, there are steps you can take to mitigate much of the risk you assume when relying on suppliers. You need to be aware of the many factors both inside and outside the control of your suppliers that can cause them to have delays in getting you the product or service you need. These can include validation issues, mergers and acquisitions among suppliers, natural disasters, problems with your suppliers' own supply chain, and even the suppliers' strategic plans.

Ben Franklin said "an ounce of prevention is worth a pound of cure," and this is true in mitigating supplier risk. Here are some best practices for choosing your supplier network:

- First and foremost, always have a backup supplier. It might cost more for this "insurance," but remember what Ben said.
- Make sure your suppliers have backup suppliers. Supplier agreements should have a change of materials notification clause, so you are notified when changes, such as the use of a backup supplier, are made that might affect your production.
- Understand how much control your supplier has over its supply chain. Is their manufacturing outsourced, and how well is it managed?
- Audit your suppliers.
- Push for open communication with your supplier regarding your own internal projections and needs so the supplier can plan properly. Involve your supplier in problem-solving on the production floor.
- Evaluate the supplier's investment in inventory. What is its inventory value? Is it changing and if so, why? If your projections increase, can your supplier react immediately?
- Get references.
- Understand your supplier's distribution model and how it can impact you. Can it ship direct? What is the average delivery time?
- Understand the long-term strategic plan of the supplier. Is it part of a merger or acquisition that could divert its investment in inventory or production? Is it serving other growth markets that might impact its available inventory for your market? Will it be discontinuing any product lines?
- Understand the employee turnover, especially key people in the organization. A company's success is due to its people. Is the company losing expertise or reliability through turnover?

If you can avoid even a few days of delay per year by improved vetting of suppliers, it can save you money, time, and relationships. The cost to you of establishing and executing a good process around vendor selection and management will be small compared to the problems you face when a supplier fails you.

Ken Baker

Ken Baker is CEO of NewAge Industries-AdvantaPure, a manufacturer of plastic tubing, reinforced hose, single-use manifold assemblies, and container closure systems for pharmaceutical, biologic, and food applications.

Getting The Most For Your Bioanalytical Testing Buck

The complexity of new chemical entities presents significant challenges in terms of developing and validating bioanalytical methods. When evaluating your analytical testing operation or even selecting a CRO to do your analytical testing, pay attention to the following considerations:

Invest in equipment that will improve how your analytical testing is performed. With ever-increasing drug potency, the level of analyte in systemic circulation continues to challenge the limits of instrument sensitivity. You should be investing in state-of-the-art instrument platforms, such as ultrahigh performance liquid chromatography (UHPLC) interfaced to modern LC-MS/MS instruments, for example, Sciex API 5000, Waters Xevo, or Thermo Vantage systems. If using a CRO, evaluate the equipment it utilizes.

Consider the latest innovations that can save you cost and improve performance. For example, many labs and CROs still use conventional ELISA (enzyme linked immunosorbent assay) methods for immunoassay analysis. Consider then the Gyrolab workstation and the Gyrolab CD format, which can enable immunoassays to be performed using only nanoliters of sample. The automation and unique flow-through design reduces "hands-on" time and significantly speeds up throughput. Moreover, the system offers an unprecedented four-log dynamic range, thus reducing the need for repeat sample analysis with additional sample dilution. Compared to conventional ELISA, the Gyros platform has shown equal or better overall performance, while exhibiting a wider analytical range and a reduction in matrix-interference effects. Look for these types of gained efficiencies in all areas of your operation as well as your service providers.

Don't ignore the impact of rising dose trials on patient safety. The nature of clinical bioanalysis requires high-throughput analysis to ensure patient safety for rising dose trials or first-to-file opportunities for generic drugs. Automated liquid handlers allow chemists to sustain a high level of productivity (e.g. 1500–2000 samples/day). For first-to-file opportunities, this may allow significantly reduced timelines for Clinical Summary Reports (even as few as 20 days from drug availability). You should pay careful attention to workflow and process, along with high-throughput analysis using state-of-the-art automation.

Are you using the most appropriate platform? LC-MS/MS is the standard platform for conventional small molecules, but it may not be the best platform for certain classes of molecules. Investments in GC-MS/MS and perhaps ICP-MS ensure that multiple detection platforms are available to meet all of your needs. For example, ICP-MS is the platform of choice for analysis of metals such as iron, potassium, calcium, and imaging agents in conventional biomatrices like urine, tissues, serum, or plasma.

Most modern immunochemistry groups will utilize MSD Imager 6000 readers as their core platform for performing regulated quantitative immunoassays, qualitative immunogenicity assessments, and cell-based assays for neutralizing antibodies. These systems are quite complementary to Gyrolab™ workstations that may then be utilized for nonregulated biomarker studies of novel biologics.

Roger Hayes, Ph.D.

Dr. Hayes is VP and general manager, laboratory sciences at MPI Research. He has held numerous leadership positions in the global life sciences industry and academia, leading teams in the development of state-of-the-art bioanalytical and analytical techniques.

Are you currently meeting bioanalytical regulatory challenges worldwide? The reliable reporting of data from the quantitative analysis of drugs and their metabolites is at the core of any bioanalytical laboratory. Both sponsors and CROs performing regulated analysis are routinely inspected by worldwide regulatory authorities. The regulatory agencies of different countries each have their respective guidance documents describing the requirements for bioanalytical method validation and the application of these methods to routine drug analysis. Involvement in organizations like the Global Bioanalysis Consortium (GBC) and the Global CRO Council (GCC) afford the sponsor and your CRO forums for addressing scientific and regulatory issues in their operations.

It is easy to continue to approach your analytical testing the same way it has always been done or use the same service providers you have always used. With the pressures of reducing costs and improving timelines, the impact to the overall bottom line of your drug development efforts makes looking for improved ways of operating worth the effort.

PERFORMANCE DEEP DIVE | Launching SEPT. 30

2,500+ Options for In-Depth **Industry Segmentation**

Create **Quick-View Reports**, with **Actionable Insights**

Quantify Market Penetration within Specific Segments of the **Pharma and Biotech Markets**

niceinsight

Marketing Intelligence by That's Nice

Visit That's Nice at AAPS or CPhI for a live demo of the product.

AAPS: Booth #1140
CPhI: Booth #7H33 (shared: Generic Pharma 2.0)

5 outsourcing buyers from sponsor groups

175+ in-demand outsourcing CMO/CRO companies reviewed

CA/CP SCORES

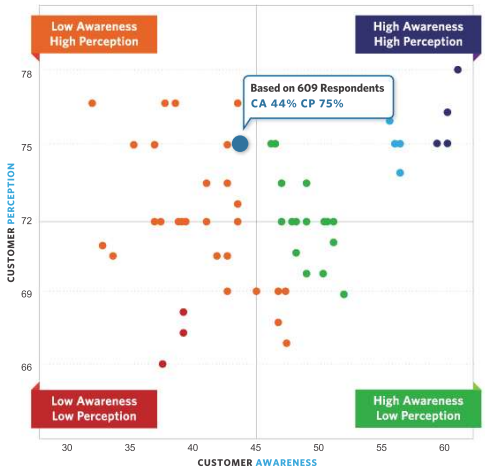
BY BUYER CATEGORY
Emerging Pharma
CA 56 CP 79
Benchmark 42 71

BY PHASE OF DEVELOPMENT
Phase I
40 76
50 74

BY THERAPEUTIC AREA
Cardiovascular Diseases
49 78
53 71

BY SERVICE CATEGORIES
Fill & Finish
70 80
56 71

COMPETITIVE LANDSCAPE



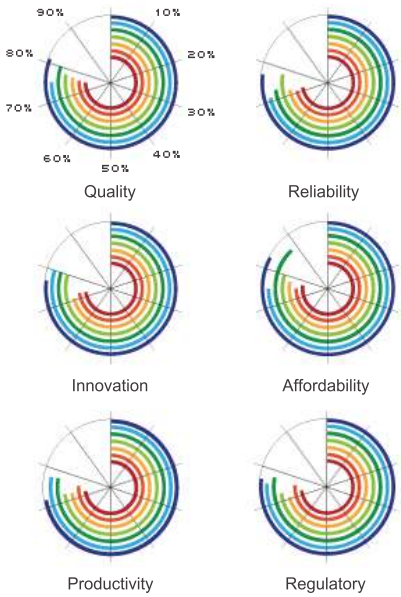
7 therapeutic categories

25 outsourced service categories tracked

6 phases of drug development

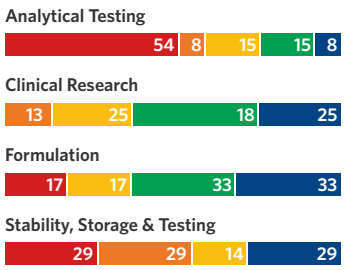
CUSTOMER PERCEPTION OUTSOURCING DRIVERS BY THERAPEUTIC CATEGORY

Cardiovascular Diseases · CNS Disorders · Endocrine Diseases · Infectious Diseases · Metabolic Disorders · Oncology Diseases · Respiratory Diseases



CUSTOMER AWARENESS BREAKDOWN

Never heard of them · Recognize logo/name · Know little about · Know them, haven't collaborated · Worked with them



BUY NOW, PAY NEXT YEAR

Nice Insight subscriptions are annual, running **Sept 30, 2012 to Sept 29, 2013.**

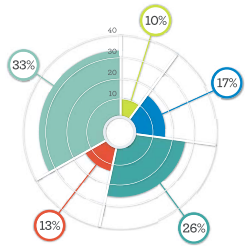
Sign up for September access but **defer payment until January 2013**.

To learn more about flexible subscription options, contact **Salvatore Fazzolari,** Director of Client Services:
Tel: +1 212 366 4455 Email: sal@thatsnice.com

www.niceinsight.com

CONSULTING SERVICE OUTSOURCING TRENDS

Big Pharma · Specialty Pharma · Emerging Biotech/Biologics · Biotech/Biologics · Emerging, Niche or Start-Up



6 key departments are represented

LIKELIHOOD OF WINNING A PROJECT BY SERVICE

⊕ indicates the profiled company has a greater likelihood of winning a project over other providers of the same service. ⊜ indicates the company scored at parity with the median. ⊖ indicates the company is less likely to be selected for the project than competing businesses offering the service.

"Nice Bike" — The Importance Of Making Meaningful Connections

By Mark Scharenbroich

I once flew to Milwaukee for a speaking engagement and rented a beige Ford Taurus for my trip to the event. Once under way, I was suddenly surrounded by thousands of black leather, bandana-wearing, hard-core Harley-Davidson bikers who had traveled across the world for Harley-Davidson's 100th year anniversary celebration.

I've never been on a Harley, dreamed of owning a Harley, or even thought of myself as a Harley kind of a guy. But that day in my bland rental car — I wanted a Harley. I wanted to be a part of the Harley gathering, part of the Harley tribe.

As I watched the interactions among bikers, two words surfaced that seemed to create a great connection. A stranger would walk by a rider, glance at their Harley, and simply say, "Nice bike."

It really hit me that once our basic needs are met, we all have two core needs. First, we need to belong to a family, a faith community, a great company, a united team. We need to feel connected. Second, we need to hear, "Nice bike," which translates to "I see you, I hear you, and I appreciate you. This world, this organization, or this community is a better place because you're in it. You belong."

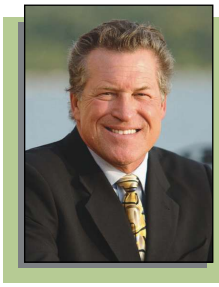
"Nice bike." It was the gold star on your paper in elementary school. It was being invited to sit at a lunch table in middle school. It was the high school teacher remembering your name on the second day of classes. It's the smile from a stranger during your travels. It's a manager taking the time to let you know how much you mean to an organization.

"Nice bike" is supported by three powerful steps:

1. *Acknowledgement* — let people know that who they are and what they do matters.
2. *Honor* — honor other people and know what's important — not to ourselves — but to them. It's serving others with a sense of passion.
3. *Connect* — Make a connection. Create a bond — large or small — that makes a difference in the life of someone else.

Here is a perfect example of "Nice bike" in the workplace. I spoke for Encompass, one of the largest personal insurance brands in America. My presentation closed out a three-day meeting of 200 key leaders and managers for Encompass. After my presentation, Cynthia Young, the president of Encompass, came back to the podium to close out the event. To thank the members of the meeting's planning team, Young went beyond the norm and gave each person their own "Nice bike." She shared something personal about each person — their hobbies, families, service to the community, etc. — something unique about each person. Why does Young have such a dedicated team at Encompass? She acknowledges, honors, and connects with each and every team member.

Find out about your team — know what they value and "Nice bike" them. It builds a better team and makes for a more meaningful ride through life.



Mark Scharenbroich is an award-winning author of the book, *Nice Bike – Making Meaningful Connections on the Road of Life*. He is also in demand as a keynote speaker and is an Emmy award winner. He has been inducted into the National Speakers Association Hall of Fame. Watch a clip of Mark's presentation at www.NiceBike.com. Reach Mark at Mark@NiceBike.com or (952) 939-9080.

To comment on this article, send an email to rob.wright@lifescienceconnect.com.

We'll earn your business with quality and value, not inflexible terms.

More value. More flexibility. More options.

Introducing P-Gels™ an innovative approach to softgel product development and manufacturing services for prescription pharmaceuticals. At P-Gels we believe in building strong relationships with quality and service rather than locking customers in with inflexible contracts. In fact, we won't charge you royalties, unless that's what's right for you.

You want quality, expertise, choice of technologies and flexibility. With P-Gels, you'll get it all for less – plus, we'll treat you right.

Find out just how flexible softgels can be.

P-Gels™

More value. More flexibility. More options.

Brought to you by Patheon™ and Softgel™

Scan the QR code • Visit www.Patheon.com
Call +1 866-PATHEON • Email doingbusiness@patheon.com