BY DENISE MYSHKO

DEVELOPMENT

Models of CHANGE

IN THE FUTURE, SUCCESSFUL BIOPHARMACEUTICAL COMPANIES will be those that have reviewed R&D business models and implemented updated strategies for improving the development of new products.

The pharmaceutical industry is at a critical point in its evolution. The needs of patients are changing, regulators are more safety-conscious and risk-averse, physicians' roles have changed as a result of managed care, and technology and other advances are changing the understanding of diseases.

PricewaterhouseCoopers (PWC) analysts expect that by 2020 the clinical environment will marry the needs of patients, payers, providers, and regulators, sharing a common infrastructure and access to outcomes data and results. Furthermore, these analysts expect that by 2020 decisions about reimbursement will fall within the the regulatory body that conducts the quality, safety, and efficacy review and that this cumbersome, all-or-nothing approach will be replaced by a cumulative process based on the gradual accumulation of data.

Steve Jolley, VP and head of pharmacovigilance, Patni Life Sciences, agrees that one of the issues facing pharma companies is the danger of investing almost $1 billion in the development of a drug and then facing increasing hurdles by conservative, risk-averse regulatory authorities to obtain marketing authorization.

"Thus an appreciation of the likely safety issues, and the risk/benefit profile of the drug, is critical to the development process," he says.

A report from Deloitte points out that virtually every pharmaceutical company has executed re-engineering programs to increase the speed and effectiveness of its R&D operations. Integrated knowledge management processes have been established to aggregate, correlate, and assess the R&D information generated. Decision-support mechanisms to continually realign R&D efforts based on potential risk/rewards are now common across the entire process. To date, there are few aspects of the R&D process that have not been re-engineered, restructured, or realigned. Yet, while individual companies have achieved performance improvements in different aspects of R&D, no significant industrywide gain is evident.

EXPERTS

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Dr. Catherine Ley *CollabRx*

Big pharma is trapped in a business model that requires the type of large patient populations for blockbuster drugs that are directly countermanded by our increasing understanding of personalized medicine.

The pharmaceutical industry has reached a crossroads, says Catherine Ley, Ph.D., director of virtual biotech services at CollabRx.

"Big pharma is trapped in a business model that requires the type of large patient populations for blockbuster drugs that are directly countermanded by our increasing understanding of personalized medicine," she says. "Orphan and neglected diseases are rarely considered. The model is further constrained by a lack of mutually beneficial information sharing and outmoded intellectual property controls. Young biotechnology companies may offer revolutionary new platform technologies, but they tend to be valued solely on the basis of whatever blockbuster they manage to wring from it while their funding persists."

But Martin Mackay, Ph.D., president of Pfizer Global Research and Development, says changing an organization's structure alone fixes nothing unless it is supported by changes to other elements of the business, such as the underlying decision-making processes.

"Our newly announced business unit structure will allow Pfizer to be more innovative for a number of reasons," he says. "Keeping research as a separate organization from the business units will give us the best of both worlds, which is necessary in a business where the time frames for research are much longer than the longest commercial time horizon. Organizing research into smaller units should allow similar benefits to the units, more control over resources, more accountability for scientific decisions, more flexibility, and the ability to find the breaking science more quickly. All of these smaller units will work with our platform lines in areas where scale and cutting-edge science are best consolidated, which will allow us to maintain cutting-edge science, links to the best outsourcing options, and cost-competitiveness."

Experts say it's important that the ways new medicines are researched and developed change to meet the needs of all stakeholders.

"Today, pharmaceutical companies must deliver improved productivity and innovation, while maximizing return on their enterprise information investments," says Christian Marcazzo, senior director of life science analytics at Tibco Spotfire. "To achieve future success, they must fundamentally review R&D business models and exploit new strategies for improving core drug discovery expertise."

A recent study by the Tufts Center for the Study of Drug Development and PRTM Management Consultants found that for the large pharma segment, leading innovators were able to translate innovation into operational performance, surpassing their average competitors on

psychiatric, and pain disorders. For more information, visit marinuspharma.com.

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Barry Cohen *Octagon Research Solutions*

Standard data are the underpinning of efficient information flow across the clinical data life cycle, from trial design upstream to submission of data downstream. Further, the use of CDISC standards in particular is critical to meeting existing and anticipated FDA requirements for submitted data.

the following metrics: 15% had more priority approvals on FDA product applications; 41% had a higher proportion of first-cycle approvals; they had a 17-month product approval cycle-time advantage; they had about three times greater revenue growth (14.1% vs. 5%); and they had a three times better operating margin growth (3% vs. 1%).

PRTM and CSDD analyzed the R&D operating models of 21 large and medium-sized biopharmaceutical companies to understand how the leading innovators structure their operating models and manage their business practices to drive improved performance. The survey found that medium-sized biopharmaceutical company best performers share some operating characteristics with the best-performing large pharma companies, including centralized decision making, maintenance of flexibility in operations, and adoption of a cautious approach to new technology. Specifically, they had: 50% higher average annual approvals of new molecular entities (NMEs) over a 10-year period from 1996–2006; a 20% lower average R&D spend per active investigational new drug (IND) in the total 2006 pipeline; better than three times the annual revenue growth rate (78% vs. 22%) as measured over a five-year period; and a 32% superior market cap growth rate (41% vs. 31%) as measured over a five-year period.

But the two groups diverged on the dimension of inventiveness. The best-performing large pharma companies tended to cast a wide net, working simultaneously on multiple therapeutic areas and modalities, including CE, biologics, devices, vaccines, and combination products. Large pharmaceutical companies place a higher priority on developing new therapies and high-risk novel drugs than on patent extension. They want to be first in class or best in class in each therapeutic area.

By contrast, medium biopharmaceutical leaders choose to focus more strongly on just one or two therapeutic areas and one primary modality. Best performers in this group excel at patent protection and product life-cycle management. Medium-size companies want to expand into new therapeutic areas, but they do so cautiously, incrementally, and opportunistically.

COLLABORATIVE APPROACHES

Some industry experts say significant changes have to occur in the development process if they are to be successful in the future.

"The entire clinical-research enterprise needs to work together," says Glenn Gormley, M.D., Ph.D., president and CEO at Gemin X Pharmaceuticals. "This includes the pharma and bio industries, as well as the academic, regulatory, and government-sponsored institutions."

Collaborative approaches such as the Clinical Trials Transformation Initiative (CTTI) — a public-private partnership that involves industry, government, patient advocates, trade organizations, professional societies, academia, and nonacademic investigators — can improve the clinical-research enterprise, he says.

"The aging infrastructure for conducting clinical research is in need of additional support," Dr. Gormley says. "Training for scientists interested in clinical research needs to be more available. An important step is to embrace initiatives such as CTTI as neutral forums where debate and challenge can occur that directly address these issues. Organizations like this can work to enhance efficiencies in clinical research by encouraging and evaluating more efficient ways to collect data and monitor the progress of trials, as well as advocate for improved training and support programs that encourage growth in the number of experienced clinical investigators."

Christoph Westphal, M.D., Ph.D., CEO of Sirtris, points out that pharmaceutical companies are turning their attention to the roots of medical innovation — academia and entrepreneurial biotechnology companies — to recruit talent and establish development collaborations to fill the gap being created by blockbuster patent expirations.

"There is broad recognition by large pharma companies that the direction of successful therapeutic development lies in understanding individual biological makeup and designing or identifying product candidates that will fill the blockbuster gap while leveraging demographic trends such as the aging population," he says. "The availability of a small number of one-for-all drugs is shifting toward a greater number of medicines that address particular disease populations or subpopulations based on an increasingly specific base of scientific, clinical, and demographic research."

Working collaboratively within organizations is important as well.

"A well-established company culture, with buy-in throughout the organization and exemplified by the senior management, is a critical component to employee satisfaction and incentive," Dr. Westphal says. "Couple this with recognition and reward programs for achievement, and innovation is inevitable. While this may sound clichéd, the concept that every individual's ideas are heard and respected is truly necessary to the success of an innovation culture."

Project management plays an important role in making this happen, says Chad Nikel, director of strategy and business development at Integrated Project Management Company.

THE R&D MODEL OF THE FUTURE

- R&D strategies that support the assembly of treatment portfolios for the entire disease life cycle and the various genotype specific patient segments in the life cycle, rather than the traditional one-off blockbuster product.
- Focused R&D programs based on genotyped patients/subjects and biomarkers.
- Virtual, disease-specific R&D networks, incorporating patients, physicians, and the medical treatment infrastructure, which involve extensive partnering and collaboration with all the disease knowledge communities.
- Virtual R&D processes with significant outsourcing to maximize flexibility and manage development risk.

Source: Deloitte, New York. For more information, visit deloitte.com.

"Project management, by its very nature, enables interconnectedness across functions," he says. "By identifying interdependencies, project management facilitates seamless handoffs and eliminates inefficiencies. If teams can perform well within a function, the professional project manager can dedicate more time and effort to ensuring the best possible performance across functions.

"If basic project management skills, for example building and driving project plans, were cultivated on the team level throughout the organization, then professional project managers could focus more on systemwide, high-level problem-solving," Mr. Nikel explains. "For example, why is the clinical group always waiting for trial materials? Because the professional project manager has a systemwide purview, he or she can track down the bottleneck, while on the team level, staff with basic skills can ensure they hit their day-to-day targets. The entire system will become more efficient."

PWC analysts also predict the development process will become iterative, with data on a molecule for one disease subtype getting fed back into the development of new molecules for other disease subtypes.

In fact, companies will be forced to look at patient subgroups in an even more focused way, says Anthony DiTonno, president and CEO of NeurogesX.

"Statistical models that can be adaptive and offer interim analysis will become more popular," he says. "The biggest challenge is to stop projects earlier in the cycle. There are too many Phase III trials that fail. They need to be better 'de-risked.' The cost of late-stage clinical failures is not only measured in cash, but in the opportunity costs of spending all that time in a higher probability trial/therapeutic area."

Mr. Jolley agrees that drug-development programs needs to embrace the new paradigm of risk management as legislated by the FDA Amendment Act, a key provision of which allows the FDA to require a Risk Evaluation and Mitigation Strategy (REMS) for drugs associated with greater safety risks.

"This requires that development programs be designed to address potential safety risks, both known and unknown, that have been identified in preclinical development and that may be expected to occur in the target patient population," he adds. "Regular and timely review, appraisal, and communication of safety information are critical to risk management during the clinical development of drugs. Whereas the overall goal of a clinical-development program is to characterize the benefit-risk relationship of the product in a particular patient population, the risk to individual trial subjects is a critical consideration during product development, at a time when the effectiveness of a product is generally uncertain. By conducting an overall appraisal of safety data at regular intervals, risks can be recognized, thoughtfully assessed, and appropriately communicated to all interested stakeholders to support the safety of subjects."

THE VIRTUAL DEVELOPMENT MODEL

One solution, Dr. Ley says, is to shift the pharmaceutical industry from a system with intensive investment in vertical integration to a diversified horizontally integrated system, in which specialization and a marketplace of ideas contribute pieces to the puzzle of drug discovery and development.

"Such a system is exemplified by newly emerging virtual biotech companies, in which groups of researchers and service providers with aligned incentives in the form of shared IP or contracted services assemble to solve particular disease problems," she says. "Virtual biotech companies are being increasingly adopted as a new funding strategy for disease-focused foundations that want to advance drug discovery and translational research for their patient base as well as to generate good basic science."

Dr. Ley says virtual companies can be assembled and disassembled as the need and opportunity arises at different points in the drug discovery and development process.

"There is no reason that big pharmaceutical companies could not adopt similar strategies to manage their R&D processes, bringing in expertise from academia or biotech as needed, with the distinction between outsourcing and investment blurring," Dr. Ley says. "Lower initial investment costs and the ability to fail faster will reduce overall investment costs, obviating the need for the increasingly elusive blockbuster drug."

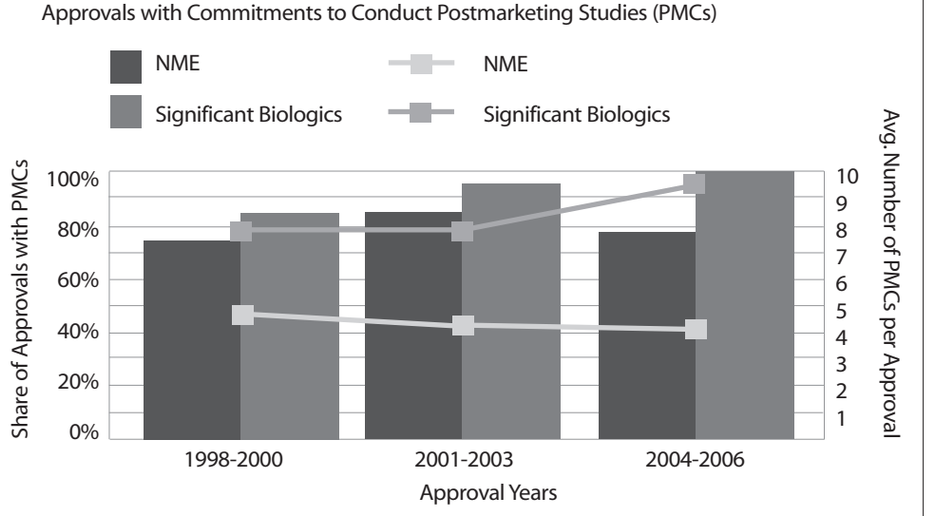
William Bertrand, executive VP, legal affairs, and general counsel and corporate compliance officer at MedImmune, says the newly evolving arrangements between big pharma and biotech — like those between MedImmune and AstraZeneca after AstraZeneca's acquisition of Medi — which have allowed the biotech company to remain somewhat autonomous is a reflection of big pharma companies' attempts to change their approach to reflect the entrepreneurial spirit and protect the spirit of innovation found in smaller biotechs.

"This approach is also being adopted within some big pharma companies where smaller research centers of excellence are being created to allow innovation, accountability, and a desire to advance the science quickly," he says.

Dr. Westphal says from the perspective of a small biotechnology executive and venture capitalist, he has long believed in building an organization around acutely focused goals and a concentration of internal efforts on core areas of expertise to enable efficient, effective drug discovery and development efforts.

"In areas supportive to these core areas of

POSTMARKETING STUDIES ARE EXPECTED TO STREAMLINE THE APPROVAL PROCESS



Source: Tufts Center for the Study of Drug Development, Boston. For more information, visit csdd.tufts.edu.

Rachael King *CRF Inc.*

In the coming year, the FDA and other regulatory agencies will likely take the recommendations of academics and professionals into consideration and will issue clarifications that will help accelerate the adoption of ePRO versus paper PRO.

excellence — such as preclinical validation work, regulatory know-how, manufacturing, or other specialty areas — outsourcing to external experts is not only time- and cost-efficient, but key to achieving corporate goals," he says. "In the future, I believe the industry will see an increasing number of win-win outsourcing collaborations that match talents for the most expeditious route to product approvals and marketing."

According to the Tufts Center for Drug Development, demand for CRO services will likely grow by 16% annually over the next three years as sponsors seek assistance in managing large, complex global projects without increasing their internal headcount.

A report from Kalorama Information, Outsourcing in Drug Development: The Contract CRO Market, 3rd Edition, reveals that in 2007, 34% of global R&D spending, or $26.4 billion, was committed to outsourcing, up from 22% in 2002, an increasing amount of which is going offshore.

Outsourcing can be a tremendous service to the industry, as these partners can play a role in training clinicians on GCP, record management, and so on. This provides value-added services to the sites and companies, including better trained sites with accurate patients profiles, says John Krayacich, CEO and president of Marinus Pharmaceuticals.

"The goal is to reduce the white space between phases of development and accelerate the decision-making process," he says. "Many holdups are the result of delayed decisions or lack of preparation for data readouts that require teams to start working on plans to move to the next step of development. Many decisions can be made by teams or middle managers to advance drugs through development. The effectiveness of teams and their leaders to drive the process is dependent upon providing them with the tools, budgets, and authority to advance drugs within agreed-upon parameters."

SIX FACTORS THAT DRIVE INNOVATION AND PERFORMANCE

1. Operating Flexibility. For large pharmaceutical companies, flexibility means selectively pursuing strategic collaborations in areas where they lack a competitive advantage. Using a modular approach to developing a partner network, leading large pharmaceutical companies apply a library of distinct development strategies like in-licensing to develop their portfolios.
2. Centralized Decision Making. Leading large pharmaceutical companies centralize major strategic decisions while distributing operational decisions. Best performers make decisions with fewer, more streamlined committees. Decisions made centrally are rapidly disseminated and integrated throughout the business.
3. Open Innovation Strategy. Top performers are skilled not only at strategic in-licensing, but also at rapidly divesting low-priority compounds through out-licensing. In addition, leading companies use partners beyond development to manage risk and expand the organization's global footprint.
4. Structured Technology Adoption. When it comes to technology, the top players have a rigorous process for evaluating new technology by focusing not just on technical specifications, but also on anticipated business contributions. Rather than plunge into an unknown situation, they are likely to incubate and test technology through pilot programs.
5. Simple, Global Business Practices. Leading large pharmaceutical companies have learned that standardization and simplicity are vital to success. Such organizational simplicity enables a company to focus its energies on flexible workforce deployment, rapid scaling of promising initiatives, and sustainable regulatory compliance.
6. Continuous Improvement Culture. The best-performing large biopharma companies proactively set targets and constantly strive to improve performance. They optimize not only within functions, but across functions. They clearly define and document responsibilities in order to better track and reward organizational improvements.

Source: Tufts Center for the Study of Drug Development, Boston, and PRTM Management Consultants, Waltham, Mass. For more information, visit csdd.tufts.edu and prtm.com.

THE TECHNOLOGY PIECE

Industry experts agree that technology, especially Web-based solutions, will play an important role in creating a more efficient and effective research and development environment.

"Technology will continue to revolutionize the industry and will serve as the catalyst that drives us toward greater efficiency by allowing us to reduce paperwork and accelerate decision-making while ensuring regulatory compliance," says Glenn Bilawsky, CEO of i3. "And the more intuitive and interactive technologies will be adopted more rapidly by the industry, regardless of the clinical trial or its delivery model."

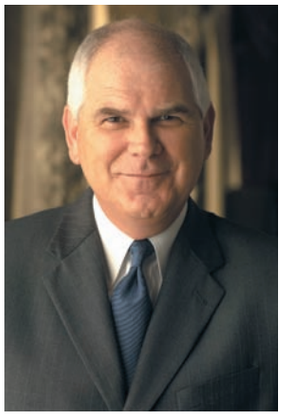
The industry, he says, needs to adopt and implement the most efficient and best-integrated technologies to streamline the drug-development process.

"E-solutions on the horizon that provide end-to-end automation will deliver unprecedented visibility into the information that sponsors need to accelerate the completion of clinical trials and navigate the development process with greater agility," Mr. Bilawsky says.

On average, life-sciences companies spend between $12 million and $17 million annually on mailings and copies of paper case report forms. With the implementation of e-clinical solutions, a company could save anywhere from $10 million to $15 million a year on paper and postage alone. This is according to a recent report by Datamonitor titled, In Pursuit of the Paperless

Steve Jolley *Patni*

One of the issues facing pharma companies is the danger of investing almost $1 billion in the development of a drug, and then facing increasing hurdles by conservative, risk-averse regulatory authorities to obtain marketing authorization.



Glenn Bilawsky *i3*

E-solutions on the horizon that provide end-to-end automation will deliver unprecedented visibility into the information that sponsors need to accelerate the completion of clinical trials and navigate the development process with greater agility.

Clinical Trial: A Look at EDC and CTMS.

For technology to make the improved inroads for better development processes, many believe that there has to be adoption of clinical-data standards.

Barry Cohen, senior director, clinical data strategies at Octagon Research Solutions, says standard data are the underpinning of efficient information flow across the clinical data life cycle, from trial design upstream to submission of data downstream.

"Further, the use of CDISC standards in particular is critical to meeting existing and anticipated FDA requirements for submitted data," he says.

The beneficial impact of data standards will be broad and deep, Mr. Cohen says.

"Standard data will reduce the time and cost of internal data development and analysis processes as well as the time and cost of the many data exchanges with partners and the FDA," he says. "More specifically, trials can be designed and protocol documents authored more quickly when based upon a standard protocol model and an automated trial design system that employs the standard model. The same is true for authoring a statistical analysis plan. Study databases can be set up more quickly in collection systems when the study definition is based upon a standard model for the clinical data domains, and that definition is communicated to the collection systems electronically. Analysis and reporting will require less program development and will be completed more quickly because standard programs and processes, which rely upon standard data, can be developed once and reused across many trials. The work of publishing the study data and submitting the information to the FDA will be significantly reduced because the data are now developed according to the submission data standard and need not be reformatted at the end-stage to meet regulatory requirements. And, finally, standard data will mean the work at every stage of the clinical data life cycle will be more transparent and more accurate because everyone involved will understand and communicate the data the same way."

Rachael King, CEO of CRF, says pharma companies also need to accelerate their move toward collecting all trial data electronically, including patient reported outcomes (PRO) data.

"With the recent conclusions of the ISPOR ePRO task force, many of the outstanding questions surrounding the validation evidence required to move paper PRO instruments to an electronic device are beginning to be answered," she says. "In the coming year, the FDA and other regulatory agencies will likely take the recommendations of academics and professionals into consideration and will issue clarifications that will help accelerate the adoption of ePRO versus paper PRO."

The capture of PRO data in an electronic format, especially when CDISC-compliant, will allow the real-time review of patient subjective and quality-of-life data together with the remaining clinical data captured during a study, she says.

"This allows the patient's perspective to be taken into account in the same time frame as the other real-time data collected, and will facilitate better decisions when using adaptive trial designs."

POSTMARKET RESEARCH

A changing regulatory environment and concerns about the safety of new medicines have led to more postmarketing and Phase IV research, all of which are having an impact on development strategies.

The number of postmarketing studies is increasing. In fact, postmarketing commitments (PMCs), in which drug sponsors are required by the respective regulatory agency to study a new drug after it enters the market, have become an increasingly common condition of approval. Today, more than three-quarters of new pharmaceutical and biological product approvals in the United States and European Union, and half of those in Japan, come with PMCs attached to them, according to the Tufts Center for the Study of Drug Development.

In the United States, the FDA Amendments Act of 2007 granted the FDA authority to require postmarketing studies, and those studies will now have to be conducted throughout the life cycle of many products. The law is intended to create a more efficient and effective evaluation process.

"There are now more rules, more resources, and greater governance power in the postapproval realm of regulatory oversight," says Patrick Lindsay, executive VP of United BioSource. "From FDAAA and the re-authorization of PDUFA to the initiatives that bring funding, resources, and access to large public and private data sets, the postapproval market space is front and center, with an increased focus on ongoing product safety."

Mr. Lindsay says these initiatives will result in tighter regulations to ensure compliance and adherence and greater emphasis on developing new tools for proactive surveillance as demanded by REMS.

"Increasingly, the industry will be responsible for knowing how and when to address key safety aspects, defining appropriate product use, and submitting thorough supporting plans to the agency for evaluation earlier in the approval process," he says. "There is an imperative to implement risk management earlier in the development cycle and in relation to every protocol and study that exposes subjects and patients to a sponsor's products."

Big pharmaceutical companies conducted 145 (75%) of the 243 industry clinical trials publicly registered with the FDA between 1998 and 2007, according to Business Insights. Of these trials, 109 were independently undertaken by big pharma as strategic initiatives. Average big pharma patient numbers (1,743) far exceeded those of mid-tier biopharma companies (952).

Anthony DiTonno *NeurogesX*

The biggest challenge is to stop projects earlier in the cycle. Companies need to spend more time in Phase II trials to reduce the risk of late-stage failures.

Patrick Lindsay *United BioSource*

Companies should begin by looking at the differences between the intensive processes required for pre-marketing studies and the more streamlined procedures that can be used in post-approval research where the focus is on how products are used in actual clinical practice.

Analysts at Business Insights say the implementation of a networked model of stakeholder involvement has become crucial to the success of drug developers by enabling access to new development platforms and facilitating effective trial management/sponsorship.

"Companies should begin by looking at the differences between the intensive processes required for premarketing studies and the more streamlined procedures that can be used in postapproval research where the focus is on how products are used in actual clinical practice," Mr. Lindsay says. "For example, work-flow processes and technologies that might be ideal for preapproval programs can negatively impact speed, cost, or quality in postmarketing programs. For large postmarketing studies, specialized technologies are required for data capture, data cleaning, and data delivery to provide the flexibility needed to collect and analyze real-world data from healthcare professionals in a multitude of treatment environments."

Also important, he says, is building consensus among internal stakeholders.

"Team members from safety through medical affairs understandably come to the table with different points of view," Mr. Lindsay says. "Since a one-size-fits-all approach rarely works in postapproval, variations in potential tools and design options need to be explored, and then agreement must be reached on optimal study design. Finally, postapproval programs must compete for dollars that might have been allocated elsewhere; for example, to direct-to-consumer or direct-to-physician campaigns. Increasingly, as these programs demonstrate their value — in safety, efficacy, and cost-effectiveness — they will be seen as prerequisites for market adoption, while meeting regulatory and payer requirements.

Mr. Lindsay says because components of postmarketing programs can differ from country to country, and even within different regions, sponsors need to pay heed to several things, including: managing the interests of local markets' regulatory and legal infrastructures; obtaining support from local affiliates to develop a comprehensive understanding of the population and standards of medical care, so that program implementation can be successful; and preparing for differing local requirements for program conduct with respect to ethics committees/IRBs, regulatory issues, and legal mandates.

"Fortunately, there are tools that can support this variability, even in regions without experience in nontraditional clinical-trial approaches," he says. "For example, ePROs can provide significant benefit despite challenges like the requirement for translation."

Peggy Schrammel, VP of clinical research, Phase IV development, at PharmaNet Development Group, says sponsors need to be aware of the differences between typical Phase II-III clinical research and postmarketing research when selecting contract research companies.

"Issues of global safety and risk management change dramatically when a product moves from the controlled environment of early phases into the real world of Phase IV," she says. "The real world includes such confounding factors as spotty compliance, comorbid conditions, and concomitant medications. Evaluating safety and risks under these conditions requires experience in Phase IV. Since Phase IV is a relatively new territory for many sponsors, global safety and risk management are increasingly being outsourced to experienced providers."

Ms. Schrammel says successfully conducting late-phase programs requires a unique skill set that many CROs that excel in Phase II to Phase III programs do not possess.

"Key factors in a successful Phase IV program include the ability to apply technology, communicate with stakeholders, recruit and retain investigators, and collaborate well with sponsors," she says. "Size, communication, economics, and effective collaboration are the four gateways through which a Phase IV study must pass before it can reach a successful conclusion. Each of these factors exerts a strong influence on a program's eventual outcome."

The first key is to conquer a mountain of data through the intelligent application of technology.

"A clinical data management system (CDMS) that features true, hybrid data capture can greatly simplify the task of acquiring data in many forms, from many sources," Ms. Schrammel says. "Fortunately, there are competent, proven CDMS available that are well-suited to Phase IV studies. Unfortunately, there are also CDMS that are less competent, unproven, and poorly suited to Phase IV."

She says maintaining the interest of these stakeholders over the extended duration of a Phase IV study can be greatly enhanced by effective communication.

"For Phase IV studies, stakeholder communication can be greatly enhanced by branding the study and implementing a study Web portal as a central communication point," she says.

Suitable numbers of investigators can be recruited and retained for Phase IV studies.

"The solution lies in knowing what motivates them and then developing programs to leverage those motivations," she says.

The final key to success is collaboration between sponsor and CRO.

"A higher degree of collaboration is required for Phase IV programs because of the commercial sensitivities involved, the number and variety of stakeholders, and the relative newness and changing climate of the postapproval process." ✦

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