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Trials On Fire: Clinical Research Takes Off

How Your Organization Can Profit From The Boom in Clinical Trials

Executive Summary

Despite potential benefits, and during a period of double-digit growth in the clinical research market, many health systems have not exploited the opportunities presented by clinical trials. In fact, large medical centers, health systems and other health-delivery organizations that conduct research have been losing ground to competitors that specialize in clinical research. Clinical research is a complex and highly regulated business, but with the number of trials and the number of patients needed to populate them undergoing explosive growth, health systems may find themselves becoming more attracted to it. By growing your clinical trial business—and part of the challenge is persuading some key participants that it is in fact a business—health systems can gain revenue and provide benefits to patients, clinicians and the organization. Health systems may also be able to work with drug companies on ventures to help tie physicians interested in research to their organizations.

This issue of *Information Edge* looks at the state of the clinical trial market, opportunities in the business for health systems, steps that can be taken to exploit those opportunities and overcome existing obstacles and emerging Web-based tools that will build tighter links among research sponsors, physician researchers and patients.

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The Market

Spending in the United States on prescription drugs is expected to rise 15% to 18% annually during the next few years, reaching an approximate $212 billion by 2004. Of nearly $20 billion spent by pharmaceutical and biotechnology companies on research and development in 1999, more than $3 billion was spent on clinical trials, according to the Pharmaceutical Researchers and Manufacturers of America (PhRMA). Of the balance, pharmaceutical companies spent $12 billion internally on drug development, while more than $4 billion went to contract research organizations (CROs), and more than $500 million went to site management organizations. SMOs, many of which were started by CRO veterans, focus more narrowly on patient recruitment and data collection than CROs, which often are their clients.

Global pharmaceutical research and development spending climbed to $72.9 billion last year from $40.3 billion in 1996. During that same period, clinical development spending, which includes clinical trials, nearly doubled to $28.4 billion from $14.5 billion.

Several factors are fueling the growth, chief among them the emerging body of genetic research that builds on the mapping of the human genome. Last year, 369 biotechnology medicines were in development, up from 81 in 1988, according to PhRMA. That's just the beginning. To gain a sense of the vastly larger scale of biotech research that is coming, consider that for the last 50 years, pharmaceutical companies have been developing medicines for about 500 biological "targets"—chemical entities in the body on which drugs act on a molecular level. One conservative prediction foresees a 14-fold increase in the number of biological targets that could yield commercially viable drugs.

Other emerging drug discovery technologies, including high throughput screening (HTS) and combinational chemistry, also will accelerate drug development, meaning that more trials will be launched. HTS combines basic biological research with robotics and computers to speed the drug development process, while combinational chemistry speeds the process of reacting chemicals in all possible combinations.

Pharmaceutical companies have an enormous financial stake in bringing new drugs to market as rapidly as possible and thus in running clinical trials quickly and efficiently. Only one in every 5,000 new chemical entities (NCE) ultimately becomes a successful drug. It takes eight to 12 years and about half a billion dollars to bring a drug to market from the initial discovery of a promising agent. This includes two to four years of lab research, two to six years of clinical trials, and six months to two years to receive FDA approval. All the while, a 20-year clock is ticking toward patent expiration. Typically, a drug company loses $1 million in revenue for each day that FDA approval is delayed.

Until the 1990s, most pharmaceutical companies conducted research and development in-house. Rising financial stakes have led trial sponsors to shift research from academic medical centers and other health delivery systems to CROs, many of which were spun off from academic medical centers and universities to enable a more entrepreneurial approach. CRO revenues from outsourced drug discovery efforts grew 19.9% in 1998, to more than $4.6 billion, according to consultants Frost & Sullivan. Today, more than 600 CROs operate worldwide, the largest of which are full-service, publicly-traded international companies. Many are diversifying beyond clinical trials by including both front-end research and back-end sales and marketing services. Another strategy is for CROs to acquire technology and expertise in specific disease categories. By 2004, Frost & Sullivan predicts that 42% of pharmaceutical drug development R&D expenditures will be outsourced to CROs.

During the 1990s, academic medical centers lost more than $1 billion in research spending to dedicated research centers and community physicians. That erosion can be traced to several institutional handicaps facing academic medical centers. They are typically more bureaucratic than independent research sites, have higher overhead and take longer to complete a trial, due to multiple technology systems and administrative offices and additional clinical responsibilities of researchers.

Clinical Trials: A Four-phase Process

- In Phase I clinical trials, researchers test a new drug or treatment with 20-80 people for the first time to evaluate its safety, determine a safe dosage range and identify side effects.
- In Phase II clinical trials, the study drug or treatment is given to 100-300 people to see if it is effective and to further evaluate its safety.
- In Phase III studies, the study drug or treatment is given to 1,000-3,000 people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments and collect information that will allow the drug or treatment to be used safely. Following this phase, the FDA decides whether to approve the drug.
- Phase IV studies are done after the drug or treatment has been marketed. These post-market studies continue testing the study drug or treatment to collect information about effects in various populations and any side effects associated with long-term use.

Source: National Institute for Allergy and Infectious Diseases, National Institutes of Health

Even without those handicaps, many medical centers failed to pursue existing opportunities, says David Hardison, a vice president with First Consulting Group. "Some didn't take it seriously as a business," he says, "although that's starting to change as CEOs come to appreciate the benefits to their organizations." CEOs also are discarding an old view that only delivery systems that are affiliated with a medical school can conduct clinical trials.

There is a strong business case to be made for health delivery systems seeking a larger slice of the clinical research pie. Reducing cycle times, adding more randomized patients per trial and attracting additional studies can significantly increase revenue. A 1999 survey of 103 clinical trials sites conducted by CenterWatch Inc., a clinical trial information clearinghouse, found that the sites' operating profits averaged 11% of net revenue, or $115,000. If an organization that conducts 200 studies per year adds two more patients per study at $4,000 each and 10 studies a year at $50,000 each, it could bring in additional revenues of $2.1 million a year, which would represent $231,000 in additional income at the 11% average profit rate.

Beyond the direct financial benefits, clinical trials offer other benefits to clinicians and patients that include:

- Access to state-of-the-art drug therapies for patients while providing the highest level of care
- Enhanced national clinical reputation through published results of clinical research in peer-reviewed journals and the academic press
- Increased patient and physician recruitment
- Increased visibility with pharmaceutical sponsors

Yet clinical research has been a market that many provider organizations have left to others, says Dee Anna Smith, CEO of SiteWorks Solutions in Memphis, Tenn. SiteWorks provides customized, Web-based site management systems and process consulting for the clinical trials industry. "Given that many hospitals are under-resourced, it makes sense that they would focus on what they see as their core mission, care delivery and patient safety," she says. "As a result, the business processes needed to efficiently and correctly run clinical trials have not received the attention they need. Hospitals have tended to treat clinical trials as a stepchild rather than as a business."

Two crucial problems facing clinical-trial sponsors are a shortage of patients and inefficient performance by research sites, says Hardison. "There are problems and opportunities on the supply side, and a need for provider organizations that want to be active in clinical research to get serious in their approach," he says. Many organizations have no infrastructure to collect and analyze clinical data, and have confused policies and procedures. Clinical research has also been particularly paper-intensive and slow to adopt technology that will increase administrative efficiency. The Gartner Group estimates that clinical trials employees currently spend 60% of their time filing, searching, retrieving, managing and disseminating documents.

Some obstacles facing organizations that want to build their clinical research business are built into the regulatory structure that governs research. Federal law requires that clinical trials in the United States be approved and monitored by an Institutional Review Board (IRB). The IRB, an independent committee of physicians, statisticians, community advocates and others, reviews each research proposal in order to determine whether the risks to subjects are

minimized by appropriate safeguards; the risks are reasonable in relation to anticipated benefits; informed consent is sought from subjects and documented; and selection of subjects is equitable. Unfortunately, many IRBs create bureaucratic bottlenecks, says FCG Vice President Mitchell Morris, MD, an oncologist who was actively involved in establishing the University of Texas M.D. Anderson Cancer Center and Health System's research operation.

Awareness of the large opportunity in clinical trials and the need to develop systems and processes to manage that business requires hospitals to take several steps, some of which require an up-front investment:

- Build a pool of certified clinical research coordinators
- Provide a focal point for marketing and contracting
- Provide a central coordination point for meeting regulatory obligations
- Streamline the institutional review board process without sacrificing quality
- Leverage IT resources to increase enrollment

These steps contribute to reducing cycle times, which is the best way to attract trial sponsors and generate repeat business. Key variables that affect site-cycle time in clinical trials are speed of contracting, speed of the IRB, speed of patient enrollment, volume of data clarification forms and the speed of resolution of queries between site and study sponsor or CRO.

The Physician Factor

No amount of administrative streamlining will make a difference without physicians who are committed to clinical research. "Number one, two and three on the list of things you must have to succeed in clinical trials is a medical staff with a strong devotion to clinical trials," says Morris. "Without that, forget it. It's not a case of 'If you build it, they will come.' Doctors have to push the process. Administration has to lubricate the process, by helping with internal marketing and clarifying policies and procedures."

To gain physicians' trust, starting with opinion leaders, hospitals need to demonstrate how an effectively managed clinical-trials business can mean more opportunities to conduct research, can increase funding and possibly generate capital for reinvestment in other hospital services. Administrators must provide the tools that make it easy for doctors to conduct trials and for pharmaceutical companies to have access to those doctors, Hardison says.

Imposing Order at M.D. Anderson

M.D. Anderson conducts more than 500 trials a year with a budget of more than $100 million. "Anderson's approach to clinical trials during the 1960's, 70's and 80's was highly entrepreneurial," says Morris, who was executive vice president and CIO at Anderson before joining FCG earlier this year. "Individual clinical researchers would find areas they wanted to explore, then go out and secure financing from pharmaceutical companies or in the form of government grants. That entrepreneurial approach got frayed," he says.

So M.D. Anderson created an Office of Research Administration run by an MD-MBA, centralizing functions that had been handled by individual researchers. These included documentation of regulatory compliance, "so that we would be bulletproof against an audit," Morris says. Centralized information systems perform biostatistical analysis, pool data and put research protocols in a common database, and online.

eHealth Survey—Update Opportunity

Those of you who took part in the Scottsdale Institute/First Consulting Group survey of eHealth readiness last spring have an opportunity to update your survey and obtain valuable comparative reports.

We have created a database of information from SI Members and other organizations that have participated. We can deliver a customized benchmark report comparing your organization's eHealth status to others'. This automatically generated report will be delivered immediately after you update your survey.

To access your report, just update the information that has changed since you last filled out the survey. If you have questions about accessing the eHealth database, please contact the Scottsdale Institute Membership Services Office for more information — 952/545-5880.

"We stressed the fact that we didn't want to do anything to detract from the creative or patient-care aspects of the work our clinical researchers were doing," Morris says. "Our goal was to make the process more efficient for patients, physicians and trial sponsors."

Another primary goal is strict compliance with Medicare billing rules. "One tricky aspect of Medicare regulations is that we can't bill for research, only for standard care," Morris says. "So we have to keep track of which diagnostic procedures are done for research and which as part of regular patient care." As one of the largest research facilities in the country, M.D. Anderson would be a ripe target for a Medicare audit. "If Medicare finds some accidental billing during an audit, in their view we're criminals. So we have a fairly extensive process during which we review bills line-by-line by hand."

Emory's Experience

Another organization that understands the benefits of running clinical trials as a business is Emory University's School of Medicine in Atlanta. "Emory made a commitment in 1997 to move into the top rank of research institutions among medical schools," says Larry Turner, assistant dean of research. Out of an annual research budget of $200 million, about $10 million is in clinical trials, he says.

A tricky aspect of clinical trials is that "they're neither fish nor fowl, neither classic bench research nor traditional clinical practice," Turner says. Emory's approach is to empower physicians where they are, provide them better tools and stay out of their way. Among the tools is what Turner describes as "a classic 1980's approach to information technology." The underlying philosophy and technology is straightforward and designed to get all pertinent data in one database where people can use it.

Emory gained physician support for the new system in a time-tested way: they paid for it. "Physicians expected that we'd slap a fee on them, but we didn't," says Turner. Another strategy was to make sure that the new system didn't complicate billing for doctors. Turner cites the example of a patient who gets admitted for pneumonia and two days later gets enrolled in a clinical trial. "The hospital tells us when they're ready to drop a bill, and we pay all charges that are part of the trial protocol. The bill then goes out to other payers."

New Tools

The huge and growing demand for patients to take part in clinical trials has created a bottleneck. In 1998, for example, while more than 40,000 people were enrolled in cancer clinical trials, there was demand for 170,000. Several Internet sites provide clinical trials information and services and a way to reach potential trial participants. Patient applications for clinical trials can be found online at *DrKoop.com*. Sites including *centerwatch.com*, *clinicaltrials.gov*, and *drugstudycentral.com* publish information on current drug trials. *AmericasDoctor.com* offers advice, links to CenterWatch information and interactive services like real-time chats with healthcare professionals.

Software tools, crucial to clinical trials success and that will help recruit patients and reduce errors, are also emerging, says Morris. Without sound information management techniques, clinical trials are hobbled by:

- *Errors and discrepancies in data*. Thirty percent of respondents to an international survey of senior pharmaceutical executives conducted by Phase Forward in 1999 moderately or strongly agreed that transcription errors during data entry were a contributor to poor-quality clinical trials. Eighty percent moderately or strongly agreed that time spent resolving data discrepancies led to delays in completing the trials.
- *Compromised patient safety*. Ineffective information management can lead to serious errors for patients involved, often in the area of informed consent. Five clinical trials offices at major medical centers were shut down in 1999, partly because of problems with informed consent, according to CenterWatch. Other problems include monitored errors and underreported side effects and adverse events. For example, in an adenovirus study with 691 side effects in patients, only 39 were reported immediately to the National Institutes of Health.
- *Longer cycle times.* Manual entry of thousands of pages of clinical trials data can take up to three months. That translates into three costly months of delay in presenting the information and getting approval from the FDA.

Among the software companies that have entered the clinical trial management business in the last few years in an effort to attack these problems, three—HopeLink, iKnowMed, and Acurian—are representative of the new entrants.

HopeLink

HopeLink is a syndicated Web service designed to help patients find clinical trials. "We seek to bridge the various constituencies of the clinical research ecosystem," says Hugh Hempel, a cofounder and the COO of the Menlo Park, Calif., company. HopeLink's service is a hosted application—not a destination Website—presented as "Powered by HopeLink" through the Websites of HopeLink partners, which include non-profit organizations, patient advocacy groups, for-profit healthcare sites and Web portals.

"We try to be to clinicaltrial.gov what FedEx is to the post office," Hempel says, by providing information faster and more clearly. HopeLink's Internet-based Clinical Trial Service provides an open, searchable directory of trials that can be viewed in standard and more detailed medical formats, aimed at laypersons and physicians respectively; tools for increasing process efficiencies in clinical development; and partnerships for creating exposure and access to trial information. HopeLink's service is free to people searching for information on clinical trials. The directory currently includes cancer trials, from both government and industry sponsors, and will offer trials for other disease areas later this year, starting with diseases of the central nervous system. Patients and their advocates can find trials currently open for enrollment, learn where the trials are located, what the basic eligibility criteria are and how to contact the organization conducting the trial. Healthcare providers can stay informed of the latest treatments being studied and can also search for trials on behalf of their patients. Sponsors can post trials and receive real-time contact information on potential participants. Health-related Websites that partner with HopeLink can present the service within the framework of their own sites.

IKnowMed

IKnowMed, in Berkeley, Calif., makes iKnowChart, an Internet-based patient charting technology that includes tools for identifying candidates for clinical

trials. During the physician-patient encounter, the patient's clinical profile is analyzed using an embedded logic database.

The system has three crucial features, says Arthur Gertel, the company's senior director of clinical trial services. "It identifies candidates for clinical trials at the point of care, provides real-time feedback on trial eligibility and does not interfere in the physician-patient relationship."

Physicians are presented with diagnostic and treatment options and patients are informed about any clinical trial for which they may be appropriate candidates. It does this by comparing the patient's profile to inclusion and exclusion criteria of ongoing clinical trials in its database. If the patient agrees, informed consent documentation is printed on the spot.

IKnowMed's screening and comparison to trial criteria also contribute to more accurate matches between patients and trials. This reduces the amount of unusable data that must later be thrown out of a trial. Data is transmitted over secure Internet links among trial sponsors, iKnowMed and physician offices. The clinical trial-screening tool is starting with oncology, with plans to add cardiology and infectious diseases.

Acurian

Acurian, Inc., of Horsham, Pa., helps identify, select and recruit physicians to work as clinical investigators and provides information to individuals so that they can make more informed decisions regarding treatment options and appropriate clinical trial opportunities.

Patients and their caretakers can use the company's Website, www.acurian.com, to search a database of clinical trial listings, register to be considered for specific clinical trials and keep abreast of advances in therapies for their condition. The company seeks to bring new therapies to market faster by speeding the exchange of information among patients, providers and drug makers.

Using Acurian's Clinical Trial Accelerator, Aculaunch (www.aculaunch.com), bio-pharmaceutical companies can recruit and select qualified physicians and patients for clinical trials and facilitate the completion and transmission of required regulatory documents. Aculaunch also enables physicians who wish to conduct clinical trials to present their services to trial sponsors free of charge.

Conclusions

Not every health-delivery organization will find that building a clinical research business makes sense. Such a strategy requires an up-front investment that might not be justifiable amid competing priorities. Organizations that lack a core of physicians committed to research lack the crucial element needed to succeed in medical research. The research business adds a layer of regulatory and administrative complexity.

Other organizations, particularly those that have physicians interested in research, and that are already somewhat involved in clinical trials, will likely see more opportunity. As the number of pharmaceutical agents under development climbs rapidly, so will the number of trials. Well run as a business, clinical trials can bring in important additional revenue and less tangible benefits for patients, physicians and organizations.

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Welcome New SI Member

Children's Hospitals and Clinics

Children's Hospitals and Clinics is the largest children's healthcare organization in the upper Midwest, with 268 staffed beds at its two hospitals in St. Paul and Minneapolis. Children's offers comprehensive, integrated medical and surgical pediatric care with more than half of their beds dedicated to critical care services. Children's has more than 1,500 physicians and nearly 3,500 employees.

Welcome to CEO Brock Nelson; COO and VP Care Delivery, Julie Morath; VP Medical Affairs, Terril Hart, M.D.; CFO and VP System Support, Jerry Massmann; VP System Advancement, Phil Kibort, M.D.; VP-Patient Care and Nursing Practice, Cheryl Olson; VP Human Resources, Walter Chesley and the entire Children's Hospitals and Clinics team.

Niches No More

Groups that have been historically underrepresented in clinical development—children, women, minorities, and seniors—will have access to an unprecedented number of medicines tailored to their needs. Here's a look at some of the opportunities.

Children

Eighty percent of drugs given to children have only been tested for adult use. New FDA rules require pediatric studies for new and existing drugs that could benefit children and offer a six-month patent extension as a bonus for completing them. From 1998 through this year, FDA requirements will result in approximately 2,500 pediatric trials involving 30,000 to 40,000 children per year.

Women

In 1993, the FDA revoked rules—promulgated in reaction to the thalidomide experience—that excluded women with childbearing potential from early-stage clinical trials. Drugs affect women differently because of pregnancy, menstruation, menopause and use of contraceptives. Some illnesses strike women more frequently than men: sexually transmitted diseases (twice as common in women), depression (two to three times more common), lung cancer (20% to 70% more common) and osteoporosis (80% of patients are women).

Minorities

African-Americans, Hispanics, Asian-Americans and American Indians will account for a third of the U.S. population by the year 2030 and suffer certain diseases at higher rates than whites. For example, some minorities in the U.S. have higher rates of adult onset diabetes and associated retina damage, and prostate cancer has higher mortality rates for some minorities than for whites.

Seniors

Demand for pharmaceuticals geared toward the health and lifestyle enhancement of America's elderly population has soared along with our life expectancy. The elderly population, which will double by 2040, has traditionally been under-represented in clinical trials. There are 28 new drugs in the pipeline for arthritis, 26 for diabetes, 24 for Alzheimer's disease, 19 for stroke, 10 for Parkinson's disease and 7 for urinary incontinence.