BY DENISE MYSHKO

making investigators TOP OF MIND

Finding experienced and trained physician investigators will become more of a challenge in the future as new technologies and advances in genomics increase the number of drugs in development.

8,000

In just a few short years, this will be the projected shortfall of clinical investigators.

In fact, unless the industry starts to make the training of researchers a priority, development projects are likely to be stalled while the search for qualified investigators intensifies. A recent study confirms what a number of industry experts already suspected: there may not be enough investigators in the future to handle the number of projects in development. CenterWatch, which provides information about clinical trials to patients, pharmaceutical sponsors, and research centers, estimates there will be 48,000 principal investigators available for clinical research in 2005 — but 56,000 principal investigators will be needed to meet sponsor demand for clinical trials. The reason for the shortfall: genomics and advances in technology, which are leading to a greater number of potential development projects.

DR. GREGG FROMELL
Investigator training issues could lead the FDA to consider mandating that investigators be trained and certified.

"While the shortfall is something that the industry is becoming increasingly aware of, I don't think it has been enough to get companies to move faster," says Kenneth Getz, president and publisher, CenterWatch. "We're going to hit a wall if we don't do more than we've done in the past."

Even now, some project sponsors are struggling to find the necessary investigators, especially if the trial is to be conducted solely in the United States. Warren Stern, Ph.D., senior VP, scientific and medical services, Parexel International Corp., finds that between 10% and 30% of the time, his company has to reach beyond U.S. borders to find the appropriate investigators.

Broadening the geography of trials may be one way to help ease any investigator shortage for now. But many say the issue of having enough qualified investigators is not just a U.S. problem. Investigators in every country have to be knowledgeable about good clinical practice, trial protocol, and the regulations important to clinical research.

Many pharmaceutical companies have yet to experience such a shortfall, but realize that not to address the future supply of — or lack of — investigators would be shortsighted. Pharmaceutical sponsors and contract research organizations have to be willing to reach out to new physicians and those with limited research experience.

Reaching Out to Physicians

"In the future, investigators are likely to be new physicians who start to do clinical research from the beginning of their career," says Leslie Michelson, CEO, Acurian Inc. New physicians are likely to be more open to clinical research, he says, because they are excited about the new developments in biotechnology and genomics.

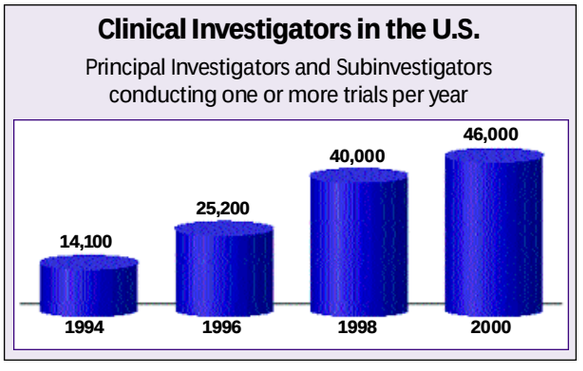
He says sponsors often don't do enough to recruit these new investigators. "The sponsors are quite good at working with the core of investigators with whom they have existing relationships. But they don't regard themselves as the best positioned entities to train new investigators. And in some ways, they are not in the best position to learn about new investigators."

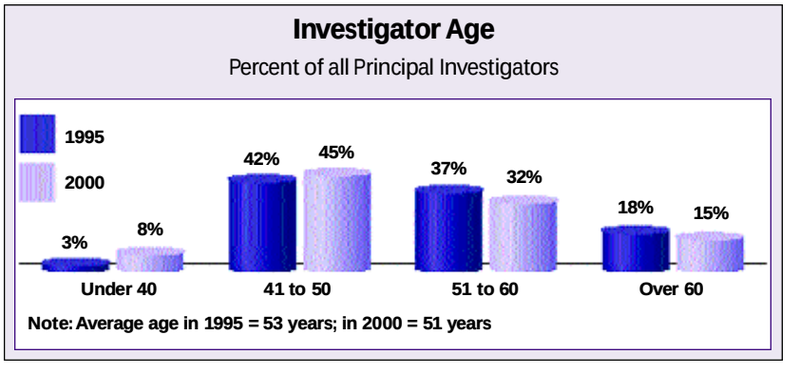
One place to find qualified investigators is at the point of patient care, says Bonnie Brescia, president, BBK Healthcare Inc. "If the study is for a diabetes drug, patients are being seen by their primary-care providers. I think we need more primary-care physicians as investigators because of where science is pushing the new medicines. These physicians work closely with patients and they understand their needs, fears, and concerns."

More physicians would be interested in doing clinical research, but don't know how or

Clinical Investigators in the United States and Their Age

SOURCE: CENTERWATCH ANALYSIS 2001, FDA, DATAEDGE





where to get started, says Dr. Consuelo Blosch, director of clinical research, NPS Pharmaceuticals Inc. "Going through my training, a lot of my peers said they wanted to get into clinical research. But unless they were with a private practice group already established in clinical research or a bigger well-established institution, the opportunity wasn't there."

The challenge of finding experienced people will even be faced by companies involved in discovery and preclinical research, says John Flavin, executive VP and chief operating officer, MediChem, a contract research company.

MediChem has tapped into the resources of universities. In the Chicago area, MediChem has a partnership with the University of Illinois, which has a strong medicinal/computational chemistry focus, with the Illinois Institute of Technology in chemical engineering, and with Northwestern University, which has a formalized biotech program.

Training Issues

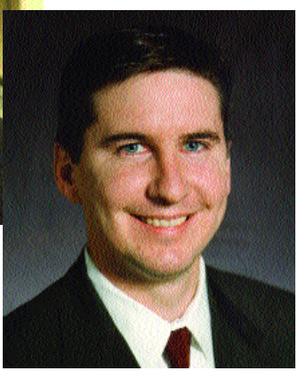
Professional organizations, such as the Washington-based Association of Clinical Research Professionals (ACRP), are making strides to address the issue of investigator training. Earlier this year, the organization hosted a summit to reach a consensus on the best approach to meet the training and certification needs of clinical investigators. The ACRP worked with the Janssen Research Foundation to develop a pilot program that includes training on good clinical practices, FDA regulations, and ICH guidelines.

But the industry needs to do more. Funding for investigator training, some say, needs to come from the sponsors. "In the long term, this will benefit the industry by providing more timely, more effective information as well as higher quality studies," says Dr. Gary Bloomgren, medical director and principal investigator, Northwest Kinetics LLC.

Some pharmaceutical companies are already stepping up to the plate. Merck & Co. Inc. for example, is in the process of developing an investigator training program and expects to implement that program sometime later this year. "The program is essentially a training workshop to take our clinical investigators through all the activities involved in conducting a successful clinical research program," says Mark Evans, Ph.D., executive director, clinical research operations U.S., Merck. "It is similar to the program we have implemented for study coordinators and is based on areas surrounding what's required from a good clinical practices perspective, what's required of federal regulations in conducting clinical research, the ICH guidelines, as well as issues surrounding the reporting of adverse events, etc."

But others say training needs to be more comprehensive. "For example, most of us are unaware that the Federal Aviation Administration has regulatory authority over some aspects of trials," says Dr. Gregg Fromell, medical director, Nexigent Inc., a subsidiary of Covance Inc. "That came to light late last year when a few sites were audited by the FAA. Biohazardous material is often shipped by air. There is a whole set of regulations for anyone handling, packaging, and shipping hazardous materials by air. Even dry ice is a material that can endanger the operation of a plane."

In fact, officials with the FAA in 1997 launched an aggressive program to uncover violations surrounding the transportation of hazardous materials in all industries. The rules are determined by the Research and Special Program Administration, an agency within



MARK EVANS, PH.D. Merck has a training workshop to take clinical investigators through the activities involved in conducting a successful clinical research program. The program is based on the federal regulations for conducting clinical research studies, what is required from good clinical practices perspective, the ICH Guidelines, etc.

JOHN FLAVIN. The challenge of finding experienced people will even be faced by those in discovery and preclinical research.

Building a Better Patient Population

A TARGETED APPROACH. Pharmacogenomics offers the potential to design new medicines that are targeted for specific patient populations. But pharmacogenomics presents its own unique challenges in terms of recruiting patients with a particular profile. Some companies — Merck & Co., Johnson & Johnson, and Pfizer Inc., to name a few — are addressing this challenge by developing partnerships with sites to help build the patient populations they need for their studies.

PARTNERING IS ANOTHER APPROACH. "In the last few years, we've had sponsors approach us, saying they'd like us to assist in trying to develop this population or that population for a long-term strategy," says Dr. Gary Bloomgren, medical director and principal investigator, Northwest Kinetics LLC, a clinical site located in Tacoma, Wash., that specializes in early clinical development.

PROCEEDING WITH CAUTION. But those sites that have developed partnerships say the industry has to proceed with caution. Covance Inc. a contract research company located in Princeton, N.J., had an initiative — now gone — to develop investigator alliances. "We were trying to develop relationships with what we thought were the cream of the crop so that we could activate trials quickly," says Dr. Gregg Fromell, medical director, Nexigent Inc., a subsidiary of Covance Inc. that provides clinical trial technology. "Unfortunately, what we found was that great sites weren't always great sites from year to year. Sometimes a site lost a coordinator or they broke up the practice."

SETTING NEW TARGETS. "It used to be that Phase I subjects were college students who had some free time to participate in studies," Dr. Bloomgren says. "Now, more and more of the focus groups involve senior populations. The pharmacokinetics may be different in people who are 55 and 32. The pressure is on to develop more focused populations. I think that will also increase as we do more genotypying and get more demands for more specialized populations."

the U.S. Department of Transportation. Since that time, the FAA has collected more than $24 million in fines for such violations.

Dr. Fromell says investigator training issues could lead the FDA to consider mandating that investigators be trained and certified. FDA officials say while they have increased their monitoring activities, they have no immediate plans to require that investigators be certified. The National Institutes of Health does require that investigators be trained to receive grants.

"The regulations are considerable and they evolve and change constantly," agrees Jim Geddes, president of Barnett International, a subsidiary of Parexel. "Study site staff and investigators really need to understand the regulations and stay current with those regulations. This is one of the bigger challenges.

"It's an increasingly complex regulatory environment that we operate in," he continues. "It's important that the people doing these trials are adequately trained and knowledgeable. It's in everyone's interest to make sure that happens." ✦

AN INVESTIGATOR SHORTFALL
will have far-reaching implications across the healthcare continuum. Without qualified investigators, development projects will not progress as quickly, resulting in fewer new drug approvals.

PharmaVoice welcomes comments about this article. E-mail us at feedback@pharmalinx.com.

Time is Money

ACCORDING TO THE TUFTS CENTER FOR THE STUDY OF DRUG DEVELOPMENT

ECON 101. The sooner pharmaceutical companies terminate drugs in development that are unlikely to succeed — either clinically or economically — the better able those companies will be to finance the discovery and development of new drugs that will provide significant value, according to a recently completed study by the Tufts Center for the Study of Drug Development.

UNCLOGGING THE PIPELINE. "Drug companies are becoming more efficient in developing new medicines that are eventually approved for marketing, and they're doing it by terminating research on unpromising compounds sooner rather than later," says Dr. Kenneth I. Kaitin, director of the Tufts Center. "This is good practice, because the sooner unsuccessful compounds are terminated, the more quickly resources can be re-deployed to investigate other, potentially more promising compounds." He says delaying product termination increases costs, clogs the research pipeline with compounds unlikely to achieve success, and disappoints stakeholders, including company shareholders, project teams, service providers, and patients.

SOONER RATHER THAN LATER. "Although limited commercial markets or insufficient return on investment are gaining ground as the primary reasons for terminating compounds, killing off compounds for economic reasons still tends to occur relatively late in development," says Dr. Kaitin.

THE RESULTS ARE IN. The study, done under the direction of Dr. Joseph A. DiMasi of the Tufts Center, examined data provided by 24 parent pharmaceutical companies worldwide on new chemical entities (NCE) investigated in human subjects anywhere in the world, or on NCEs for which the company was the first to file a U.S. investigational new drug application. Current success rates were examined through the end of 1999.

- Economic-related and efficacy-related factors have become more prevalent as the primary reasons for terminating compounds
- Median time to research abandonment or marketing approval decreased from 4.9 years to 4.3 years over a 10-year period
- Attrition rates are greatest in Phase II of clinical development, where more than half of the investigated compounds failed
- Approval success rates vary by therapeutic class, with anti-infectives enjoying the greatest likelihood of eventually obtaining marketing approval

Experts on this topic

DR. GARY BLOOMGREN. Medical director and principal investigator, Northwest Kinetics LLC, Tacoma, Wash.; Northwest Kinetics specializes in early clinical development

DR. CONSUELO BLOSCH. Director of clinical research, NPS Pharmaceuticals Inc., Salt Lake City, Utah; NPS Pharmaceuticals is a biotech company

BONNIE BRESCIA. President, BBK Healthcare Inc., Newton, Mass.; BBK is a patient recruitment and healthcare advertising agency

MARK EVANS, PH.D. Executive director, clinical research operations, Merck & Co. Inc., Whitehouse Station, N.J.; Merck is a pharmaceutical company

JOHN FLAVIN. Executive VP and chief operating officer, MediChem, Woodridge, Ill.; MediChem is a contract research organization focused on discovery and preclinical research

DR. GREGG FROMELL. Medical director, Nexigent Inc., Princeton, N.J.; Nexigent, a subsidiary of Covance Inc., provides clinical trial technology

JIM GEDDES. President, Barnett International, Media, Pa.; Barnett, a division of Parexel International Corp., is a consulting company

KENNETH GETZ. President and publisher, CenterWatch, Boston; CenterWatch provides information about clinical trials to patients, pharmaceutical sponsors, and research centers

DR. KENNETH I. KAITIN. Director, Tufts Center for the Study of Drug Development, Boston; Tufts Center is a part of Tufts University

LESLIE MICHELSON. CEO, Acurian Inc., Horsham, Pa.; Acurian maintains online databases of investigators and patients

WARREN STERN, PH.D. Senior VP, scientific and medical services, Parexel International Corp., Waltham, Mass.; Parexel is a contract research organization