Development delays lead to new trends in clinical trials industry

Trial experts discuss recent research trends

In 2005, major pharmaceutical companies are estimated to have spent $45-$50 billion on research and development. Yet only 17 drugs were approved for marketing by the FDA, says Dan McDonald, vice president of Thomson CenterWatch in Boston.

In fact, the pipeline of drugs in development has grown rapidly in recent years with a greater than 10% annual increase. This has combined with other market pressures to force new trends in the clinical trial industry, experts say.

"We're seeing an absolute explosion in the pipeline of drugs in clinical research and moving toward the market," McDonald says. "Most of this is due to new drug discovery technologies and science that make the process at the discovery, pre-clinical phase much more efficient. But on the cusp of that we're seeing an impact on our ability to get drugs to the market faster."

Ten years ago, there were nearly 70 drugs approved for market in one year, but the recent numbers have been low, averaging below 20 annually, except for the 30 drugs that were approved in 2004, McDonald says. "That year is looking like an anomaly," he adds.

"Industry in the clinical trial process is not very efficient," McDonald says. "So we have a lot in the pipeline, but they're not pushed through to the final phases."

The biggest problem is poor recruitment in phase II and III clinical trials, he adds. "The process has slowed down so much that 90% of clinical trials are delayed by at least a month because of an inability to recruit patients," McDonald explains.

Going global

Primarily for this reason, pharmaceutical companies have flocked to other countries to find new clinical trial sites, experts say. In recent years, U.S. companies have sent increasing numbers of clinical trial contracts to international sites, says Norman M. Goldfarb, CRCP, managing director of First Clinical Research and editor of The Journal of Clinical Research Best Practices. Goldfarb also is the chairman of the Model...
Agreement Group Initiative and chairman of the Clinical Research Relief Organization. (See story on clinical trials moving to India and elsewhere, p. 88.)

In 2002, about 76% of the 1,572 contracts that investigators sign with the FDA to conduct studies were submitted by U.S. investigators. Two years later, U.S. investigators submitted 62% of the FDA’s 1,572 contracts, and that same percentage was submitted by U.S. investigators in 2005, Goldfarb says.

“My guess is that the plateau is temporary,” Goldfarb says. “Studies aren’t moving to Japan and England; they’re moving to Poland, Brazil, India, and places like that where the costs are lower and, more importantly, it’s easier to recruit subjects.”

There always will be clinical trials conducted in the United States because the U.S. market constitutes 60% of the global pharmaceutical market, says Vijai Kumar, MD, global medical director for Neeman Medical International of Raleigh, NC.

About 80% of clinical trials are conducted in the U.S., and less than 5% are done in non-traditional geographies, including South America, Asia, Africa, and Eastern and Central Europe, Kumar says. “The rest are in Western Europe,” Kumar adds. “However, the trend is moving towards trials outside the U.S.”

U.S. investigators will continue to have as many clinical trials as they can handle, but pricing and offshoring trends may force them to become more efficient and produce trials faster with lower costs, the experts predict.

“U.S. investigators who are competing with other investigators in their area will now have to compete on a global scale,” McDonald says. “Companies won’t take a trial and put it all in one location; there will be sites in India, the U.S., Eastern Europe, and elsewhere.”

U.S. clinical trial sites will continue to do a majority of post-marketing studies because pharmaceutical companies want to conduct these in the countries where doctors write prescriptions, and the U.S. has a high prescription rate, Goldfarb notes.

Also, the U.S. has a more diverse population than do many other countries, and pharmaceutical companies need to show drug efficacy in the ethnic groups that will be using the drug, he says.

“You can’t find African Americans in Africa, for example,” Goldfarb says. “The diets, etc., are different, so the ethnicities are different.”

Cost, timeliness, and quality are the three main reasons pharmaceutical companies are moving more trials offshore, Kumar explains.

Just look at the statistics of U.S.-conducted trials, he says:

• 15%-20% of clinical trials conducted in the U.S. have zero enrollment, and 30% enroll just 5% of the patients, Kumar says.
• Another 20% of clinical trial sites are average performers, and 30% enroll 75% of the patients, Kumar adds.
• The amount of time a new drug or device spends in the clinical phase of research has increased from 31 months in the period of 1982 to 1999 to more than 70 months today, McDonald says. “So the process involved in testing drugs has become more extensive and complicated.”
• Clinical trials cost $50,000 a day on average to operate the trial, and the opportunity costs — measuring how much money is lost in potential drug sales as the product is delayed in making it to the market — is more like $1 million per day, McDonald says.
• Pharmaceutical company spending on phase III trials through bringing a new drug to the FDA for approval has had greater than 20% increases over the last three years, due, in part, to increasing recruitment costs and replacing investigators, McDonald says.
• At least one measure of clinical trial quality shows that the U.S. lags behind developing countries: In the U.S., clinical trial sites average 15 queries per 100 pages, while in some developing countries the number of queries is an average of five per 100 pages, Goldfarb says.
  “The research team is more motivated, and the compensation is relatively higher, so they can afford to spend the time on documentation,” Goldfarb explains.
• Patient retention in phase 2 and 3 studies is 70%, which is very low, Kumar says.
  In developing countries, there is less mobility among populations, and this contributes to a higher subject retention rate, Goldfarb notes.
  “Each patient who is lost costs a pharmaceutical company $45,000 a day,” Kumar says. “Therefore the drivers for off-shoring clinical trials are increasing patient costs, delays and drop-outs in the United States, and quality is slipping. It’s a vicious cycle because everyone goes to the experienced investigators; so they’re kept busy, and you have to find new investigators who are not as experienced and who don’t have the same level of quality.”

**Are changes in order for US trials?**

These problems may contribute to clinical trial outsourcing, but they also indicate a need for changes in how trials are conducted in the U.S., the experts say.

“Less than 3 to 5% of the entire U.S. population participates in clinical trials,” Kumar says. “We really have to go out to the community and find out why they’re not participating.”

This will require broad public education about clinical trials, but also education that targets community physicians, who could be discussing research with more patients, but are not, Kumar suggests.

“Most new investigators in the U.S. are tourists,” Goldfarb says. “They think research looks interesting, and they have the impression it will be easy money.”

Then they start a trial and reality strikes.

“They do a study or two and find out it’s a lot harder than they thought and more of a headache, and they lose a lot of money,” Goldfarb says.

This trend accounts for 60% to 70% of investigators who do one or two studies and then drop out, never returning to clinical trial research, McDonald says.

Giving incentives to investigators and clinical trial professionals to become certified is one way to improve education and training, Goldfarb says.

If sponsors were to reward sites with certified personnel by selecting them over competitors and paying a token amount above the average contract budget, it would pay for the training and certification and be a very inexpensive way to improve clinical trial quality, Goldfarb says.

Then there are the problems related to poor training of new investigators, particularly when it comes to the management and budgeting of clinical trials.

In CenterWatch’s 2005 annual survey of research sites, there was a major shift in what those surveyed reported as their number one cause of delay, McDonald says. “Contract and budget negotiation and the approval process are the main causes of delay in clinical trial sites at this point in time.”

Previously, budget negotiation was listed as the second or third cause of delay, McDonald says. New investigators often make the mistake of accepting the first budget a sponsor puts forth, and those typically are the inexperienced sites that will have difficult with subject accrual, Goldfarb says.

A logical solution would be for sponsors to keep track of the good performers versus the poor performers, but that does not always happen.

“I’m sure there are a lot of sponsors that are aware of this problem and attempt to cultivate relationships with good sites,” Goldfarb says. “But I can also tell you that sponsor study personnel are very focused on the current research project, because that’s what they’re paid to do.”
For example, when Goldfarb ran a clinical trial site, sponsors commonly would ask him if he'd ever done a study for them before, and he might be running another trial for that very same company at that time, and they weren't aware of it.

"It's very fragmented on the service provider side. Most research sites are small, part-time, and not long for the industry," Goldfarb says.

One trend that may improve this situation is the pharmaceutical industry's outsourcing to contract research organizations (CROs) for conducting clinical trials, McDonald suggests.

"CROs have the expertise to find the right doctors with the right patients or to venture into territory outside the United States," McDonald says. "We're seeing about 21% of research and development outsourced to CROs [including those in developing countries] today, and that will grow close to 30% in the next four years."

You're adding a population of 1 billion people, and the urban centers have around 400 million, so there's a better chance of meeting the accrual target," Ahmed says.

Although some experts predict that India will have nearly 20% of the patients in global clinical trials by 2010, Kumar says that is an unrealistic expectation.

India's share of trial subjects could grow to 200,000 within the next four years, but not the more than one million predicted by some in the industry, Kumar says.

"Probably India now has about 1,000 investigators, maybe 800 good clinical practice-compliant investigators, but this number has to go up to at least 4,000 for patient intake," Kumar says.

"So the emphasis in India will have to be on imparting quality training — not only to investigators — but also to build up a cadre of clinical research professionals," Kumar says. "If you focus just on the business end and compromise the science and ethics, the bubble will burst, so I think it's very prudent to start low and go slow — do it right the first time."

India's share of the clinical trial industry is very small so far, with only a $50 million investment, but this is expected to grow to $300 million by 2010, says Dan McDonald, vice president of Thomson CenterWatch in Boston.

"The intellectual capital in India is impressive," McDonald notes. "I was in central India in March, and there are 600,000 English-speaking physicians trained in Western medicine, which is very significant." Those physicians are a potential pool of investigators, he adds. In the U.S., by contrast, there are about 600,000 practicing physicians, says Norman M. Goldfarb, CRCP, managing director of First Clinical Research and editor of The Journal of Clinical Research Best Practices. Goldfarb also is the chairman of the Model Agreement Group Initiative and chairman of the Clinical Research Relief Organization.

The drawbacks are that India continues to have extreme levels of poverty and infrastructure problems, such as rolling black-outs on a daily basis in some places, McDonald says.

While sponsors go overseas to reduce costs, there is some offset of those savings in the additional costs for travel, shipping, and bureaucratic hassle, Norman says.

"Over time, those costs will go down as infrastructure improves with, for example, more labs in the countries and as the import/export process becomes more accommodating," Goldfarb notes.

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**Overseas trials: The trend has limitations**

*Experts discuss pros and cons*

Clinical trials in the United States have trouble recruiting subjects, completing on time, and maintaining high quality and efficiency, and these problems are why major pharmaceutical companies and other sponsors are offering more business to international research organizations, experts say.

At the same time, regulatory and media pressures are pushing for a greater emphasis on safety with new drugs, so in order for trials to make safety a primary concern, they need even more subjects, says Vijai Kumar, MD, global medical director for Neeman Medical International of Raleigh, NC.

This is where international sites, in countries such as India and China, come into the picture.

When India agreed to abide by international standards of patent protection in early 2005, the groundwork was laid for increasing India's share of U.S.-sponsored clinical trials, says Asker Ahmed, director of iProcess Inc. of Cincinnati, which has a large network of investigator sites across North America.

The benefits of conducting trials in India are that it can reduce the cost by 40 percent per patient, depending on trial and lab work, and the patient accrual rate is faster, Ahmed says.
The other issue involves regulatory approval, which in some countries can take up to six months, Goldfarb says. But this will be streamlined as the clinical trial industry grows internationally, he adds.

"The last issue, which is a concern, is the human research protection aspects of international clinical trial sites," Goldfarb says. "My understanding is there are some issues in some developing countries, and these are because of a lack of training and a relatively low percentage of FDA audits, and because of cultural aspects."

For example, in some nations, doctors are revered, and if a doctor asked a patient if he or she would like to participate in a clinical trial, then the patient interprets that almost as an order and he or she will do it, Goldfarb explains.

"Then there are the incentives," he adds. "If your family is living on a dollar a day and you live 30 miles outside a city, and bus fare is $1, it’s tough to buy that ticket."

But if the research site offers a bus ticket as an incentive, then that’s a big incentive for participating in the study, Goldfarb says.

This places clinical trial sites in a Catch-22: if they don’t provide bus fare, then they won’t recruit rural subjects, but if they do provide it, then it might be too big of an incentive for participation, Goldfarb explains.

Access to free drugs and treatment also are powerful incentives in developing countries, Goldfarb notes.

On a positive note, pharmaceutical companies will choose countries that have strong human subjects protections over countries that have loose ones because they don’t want to be hit by a scandal if something goes wrong in a trial, Goldfarb says.

"The race is not to the bottom in terms of protection, but to the top, and the trials will go to those who have the strongest protections," he adds.

The international business community’s perceptions of India also are obstacles to rapid expansion, Ahmed suggests.

"Some people are cautious, so it will take time," Ahmed says. "I feel the clinical trial industry in India is where the [information technology industry] was 10 years ago in India—not yet an accepted trend."

With education and time, people will begin to accept trial outsourcing to India, he adds.

"The other concerns are regulatory issues and the timeline," Ahmed says. "There’s some added padding to the time because you’re doing business in India."

While U.S. companies never will outsource all of the clinical trial business, the trend of trial sites moving to international locations will continue, and the work will be spread around the globe, the experts say.

U.S. companies also are turning to central and eastern Europe for clinical trials to save money and time, McDonald says. "There’s a 20% reduction in costs and 400 million treatment-naïve patients among a non-transient group across eight eastern European countries," McDonald says. "It’s not difficult to find patients, and there’s a significant and highly-trained and motivated investigator base over there that has been trained in western clinical practice guidelines."

For these reasons, there have been a number of contract research organizations that have opened their doors in Eastern Europe, he adds.

India and Eastern/Central Europe have moved beyond the infancy and discovery stage, but there are other places that are attracting a small number of clinical trials, including Singapore, Africa, and China, McDonald says.

"People see in China an enormous patient population and a lot of the same benefits you see in India with several million doctors, giant city hospitals that see 10,000 patients daily, and 1 billion treatment-naïve people," McDonald explains. "China has a good accreditation bureau, and it’s one of the few countries to have accreditation of research sites."

Most of the major pharmaceutical companies have established research and development enterprises in China within the past five years, and China is tightening its intellectual property laws, which was one of the major obstacles to companies moving there, McDonald says.

Also, China is planning to build a new biotechnology center and is actively courting businesses to buy development space, McDonald says.

The clinical trial industry also is looking at South America for new sites, Kumar says.

Costa Rica, Chile, Argentina, and Brazil hold promise for future clinical research sites, Kumar says.

"Regulatory changes have taken place, and more and more investigators are being identified and trained," Kumar says.

The timeline for trials still is a little slow, but the infrastructure rapidly is being built up, he adds.

As clinical trial sites move out of the United States, there is a need for careful follow-up and analysis of trials in emerging markets to see how many patients are enrolled and what the timeline
is for completion of clinical trials, as well as the impact on production, Kumar says.

Also, international sites need to follow the example of India and build capacity and tighten the regulatory process in accordance with ICH guidelines, Kumar adds. ■

Recruiting: A picture’s worth a thousand words

Men like gadgets; women like bright colors

Sponsors and clinical trial sites increasingly are turning to multimedia material for both recruiting subjects and for explaining particulars of a study during the informed consent process.

But how can investigators and trial sites know whether the recruitment material is helping or hindering their cause?

Investigators at Summa Health System in Akron, OH, decided to explore this question after finding some surprisingly negative responses to a mock-up of a patient education brochure.

“We sent the brochure around to some people to look at, and most people had no problem with it,” recalls Jere M. Boyer, PhD, director of research and research administration at Summa Health System.

But several people thought at least one photo was coercive, Boyer says.

It was a picture of a female health care provider who stood over a subject as the person signed a health care form, and it looked as though the woman had her hand on the subject’s shoulder, Boyer explains.

“One person said, ‘It looks like they’re lording it over them by standing while the subject is sitting,’” Boyer says. “Some people said the hand on the shoulder made it look as though the health care provider was pushing a subject to sign the document.”

Boyer and the others who selected the photos were curious about the response and decided to conduct a study of what potential subjects think about various recruitment/educational photographs.

They obtained IRB approval for the study and enrolled 68 volunteers, including 26 men and 42 women, who had a mean age of 52 years. They were shown 10 photographs, including two from a federal research brochure, and they answered questions about the photos from an interviewer. Questions included the following:

- Which of the 10 pictures would encourage you the most to participate in a research study?
- Do you like this photograph?
- Do you believe the subject in the picture has a free choice to participate (or not) in the research project?

“The results were quite interesting,” Boyer says. “There was a difference between male and female replies.”

For example, men tended to want to see photos that displayed instruments or equipment, even if these had nothing to do with the study, Boyer notes.

“They like gadgets,” he says. “And women wanted to see a perky setting where the subject looked happy and where the individual presenting the information seems to be actively involved with the subject.”

Women also were more interested in seeing bright colors, and they responded well to a sharp picture rather than a blurry picture, Boyer says.

“College-level individuals seemed to be attuned to whether there was actual teaching and learning occurring in the setting and whether it looked as though the health care provider was explaining the study to the subject, as opposed to doing something else,” Boyer says.

Also, all subjects were concerned about the dress appearance of health care professionals, wanting to see a neat appearance, regardless of the venue, Boyer adds.

Since Akron has a small minority population, the trial did not have enough African American subjects or others of minority backgrounds to make any cultural determinations, he notes.

Subjects also indicated a dislike for photos that looked staged, Boyer says.

“You can fake the health care scenes, but don’t let it look like it was faked,” he says. “Even with real pictures of health care providers, subjects didn’t like it if it looked faked.”

Nearly 80% of the subjects said they would be willing to participate in a clinical trial, Boyer says.

Investigators did not determine whether this high percentage reflected original bias or was the result of the study and recruitment photos, he adds.

However, it’s safe to assume that audio-visual materials presented to potential trial participants could help with recruitment and informed consent, Boyer suggests.

“I think educational film strips, as well as photos, may be better than just sitting down with 20-page consent forms and trying to explain a study
to the subject, who might tune out much of the information,” Boyer says.

“My biggest problem with the consenting process today is that consent forms are long, and cancer patients, for instance, may not be in a state of mind to read or understand them,” Boyer says.

In addition to providing visual aids to the consent process, the investigator or clinical trials professional should give potential subjects a couple of days to think about the study and to discuss it with their family, friends, and family doctor, Boyer says.

Research about how people learn suggests that visual stimulation and one-on-one education help with the learning process, he notes.

“The sponsors are getting attuned to the fact that they need to do more than explain a 20-page consent document to subjects,” Boyer says.

Since conducting the study, Summa Health System has changed its recruiting materials and has developed a brochure that uses pictures that have bright colors and display a health care activity, as well as health care devices and technology, Boyer says. These are distributed in hospital/clinic lobbies and other places where potential subjects might be found, he says.

Reference:

What do clinical trial participants want?

Collaboration with participant is key

Researchers increasingly are told they need to involve participants in clinical trial design, but most would agree this is a difficult ideal to follow.

For one thing, it’s hard to find people who are willing to imagine and talk about what they would do with regards to research if they had cancer or some other potentially deadly disease.

“The reality is many people are first faced with the notion of a clinical trial once they are diagnosed, so our conversations often start at a time of great emotional turmoil,” says Lidia Schapira, MD, an oncologist at Massachusetts General Hospital in Boston. Schapira speaks at national research conferences about respecting research subjects.

However, what can be achieved is collaboration between researchers and study participants in which the discussion of a clinical trial is a conversation and not a one-sided recitation of the informed consent document, Schapira says.

“The collaboration has to be around the possibility of this particular person, who is diagnosed with an illness, entering the study, with the expectation that he or she will gain something from it,” Schapira says. “And we should share the uncertainty if the outcome of the trial is uncertain.”

Perhaps a turning point in how the research industry collaborated with the community and potential subjects was reached in the last 25 years of the HIV/AIDS epidemic.

“Our experience in AIDS has taught research a lot,” says A. Cornelius Baker, a community health advocate and former executive director of both the National Association of People with AIDS and the Whitman Walker Clinic in Washington, DC.

“We’ve learned we can grant access to study drugs to people in need of treatment prior to the drugs being approved,” Baker says. “As a result of that, I think we’ve created a much more humane drug approval process.”

Early access and compassionate use of drugs also have resulted in greater respect for the pharmaceutical industry and scientists among AIDS advocates and others impacted by the disease, Baker notes.

“People don’t see it as just about the pharmaceutical companies and science using them as guinea pigs and not being in a partnership,” he adds.

Nonetheless, that trust still has to be built in other communities, and one way clinical trial sites can achieve this is through transparency, Baker says. Secrecy about trials leads to mistrust, particularly when a problem occurs and its public disclosure comes in the form of a media event, Baker explains.

Investigators and clinical trial professionals can improve transparency and build trust through consistent communication with participants, Baker and Schapira say.

For example, they can demonstrate respect for participants through education and even more casual conversations with them, Schapira says.

“We have at the cancer center a series of lectures that are offered to all patients and people with them,” Schapira says. “Some of these are general lectures about research, and we try to orient people by explaining how cancer clinical trials advance from ideas in a laboratory to being tested and offered in public.”
The educational sessions also discuss the various phases of clinical trials and the safeguards put in place to protect participants, she adds.

AIDS advocates worked on public education and treatment education very early in the epidemic’s history, Baker notes. “With John James’ book AIDS Treatment News and newsletter AIDS Alert, and the Project Inform work, we’ve had a number of different environments in which to learn about the science being created to treat HIV infection,” Baker says.

Also, when the pharmaceutical industry and academic research institutions ran into problems regarding public perception, they began to invite treatment advocates and educators to seminars where they could be educated about the latest science and research so these people could, in turn, educate the communities they represented, Baker explains. “That developed greater trust and greater transparency,” Baker says. “It also created a partnership so people with HIV could see the research being conducted as in their interest.”

Since they see research as something that benefits them and since they see researchers as people who listen to their concerns, HIV-infected people are much more willing to participate in research, Baker adds.

It’s a misperception to think people don’t want to participate in clinical trials, Baker says.

But the problem is that a few well-known examples of blatant ethical violations in clinical research have made it difficult for some people to trust researchers, he says.

The only way to resolve these fears and concerns is to be totally open and transparent during the research process, to hold to high ethical standards, and to directly involve the community, Baker says.

Baker and Schapira suggest these strategies for building trust among potential subjects:

**1. Hire a patient advocate.**

Research institutions should have a patient advocate whose role is to be the voice of the patient or participant from the recruitment stage on, Baker says.

The patient advocate’s role also could include helping the clinical trial site ask and answer these questions:

— How do we recruit people?
— How do we educate people who are in the trial?
— What is the benefit of the trial?
— How do we educate people in the larger community?

“As a result, you build the capacity to truly be engaged with the community,” Schapira says. “It’s the importance of representing those who are participating in research and those who will be impacted by the research.”

**2. Develop better educational strategies.**

There are many Web sites and written material available about clinical trials, particularly when it comes to cancer and HIV.

Schapira recommends sharing with patients a video that was designed to answer many of their questions. It’s called “Entering a Clinical Trial — Is It Right for You?” and it can be downloaded for free off the web site of the Dana-Farber Cancer Institute of Boston, MA at http://www.dana-farber.org/res/clinical/trials-info/.

Also, the National Cancer Institute has many publications and videos about clinical trials, which can be found online at www.cancer.gov.

Research sites need to build up the scientific literacy of communities to help people understand how difficult it is to develop drugs and how the process includes a lot of dead ends, but the only way to learn what works is to keep at it, Baker suggests.

It’s important to inform the larger community about research projects, and this doesn’t mean just issuing press releases when the news is good, Baker says. For example, when a proposed drug is found to have some safety concerns, it’s important to let the public know about these findings and to explain why a trial has been discontinued, if that was the result of the concerns, Baker says.

When a company has been upfront about the study all along, people will accept the bad news and move on; it won’t become a media sensation or scandal, Baker adds.

“We do not yet do a very good job of explaining to the community or public at large when a trial does not succeed and what we learned from it,” Baker says. “When we only publish the good news and hide the bad news, people believe there’s more bad news out there, so they don’t trust everything about the drug or treatment.”

**3. Make clinical trials inclusive.**

One of the problems with clinical trials and the public perception of research is that often trials are too exclusionary, Baker says.

Some research institutions and sponsors only want what they consider the best population and this often ends up being white men, Baker says.

“The real world includes women who can get pregnant, people who are not white, people who use drugs,” Baker says.
People are more likely to trust research when trials include participants who look like themselves, he adds.

"Given the demographics of the HIV epidemic, it would be horrendous for a trial to not look like all of the people who are infected," Baker says.

"You don’t want to have a situation where black people will look at a new drug and say, ‘We don’t know if that drug will work with us — that drug isn’t for us,’" Baker adds.

"I think we still have challenges to having truly inclusive clinical trials," Baker explains. "Even diseases that impact heavily on minority populations, like hepatitis and HIV, still have treatment trials that are not representative enough, and I think that’s not acceptable."

4. Respect clinical trial participants through words and action.

Respect for participants is a flexible goal that must be adapted to different scenarios, but it also must be a part of every single conversation within a medical clinic, whether it’s about the research or clinical care, Schapira says.

Clinical trial professionals and physician investigators should promote the real spirit of research in which there’s a sense of shared responsibility for the research enterprise, she adds.

"The patient and possible research subject would, hopefully, feel some excitement about participating in a trial," Schapira says. "The patient would be reassured that he or she would be ethically offered either the best-known treatment or something that might be better."

A clinician’s bedside manner can be learned and improved, and that’s an aspect of clinical trial research that could be improved, Schapira says.

People feel at ease with physicians who listen to them respectfully, elicit their concerns, present information fairly, and who respond to them with empathy and other appropriate emotions, Schapira says.

"All of those things are teachable skills, and we do have packets, seminars, workshops, and classes where we teach nurses, physicians, and nurse practitioners to do this well," Schapira says. "We teach them to really form respectful relationships and how to communicate in clear ways."

5. Work on the consent process.

Consent forms need to be more user-friendly, including shorter versions which are easier for patients to read, Schapira says.

"These are for patients who don’t have the patience or educational level to read through a consent form, but who still deserve to know what they are signing up for," Schapira says. "We also need better language, especially when talking about randomization, and we need better training in how to have these conversations with patients."

One suggestion is to have the researchers who do very well with informed consent videotape their process and share it with colleagues, Schapira says. "Or they could have workshops to help new researchers improve their skills," she adds.

A simple way to improve the informed consent process is to build-in extra time, Schapira suggests. "I always give the informed consent form to the patient and ask them to take it home and read it and to not sign it until they’ve thought about it for at least a day or two," Schapira says. "You need to give them time to process the ideas and concepts."

Master’s degrees are gaining acceptance

Industry changes require more education

Master’s degree programs in clinical research administration or management, as well as certificate programs, are gaining ground as training vehicles for people who work in health care or another professional field and would like to switch to clinical trials and research.

The pioneering clinical research administration program at Eastern Michigan University in Ypsilanti, MI (<http://www.emich.edu/hs/cra>), is only a decade old, and one of the first master’s degree programs for nurses specializing in clinical research management at Duke University School of Nursing (<http://www.nursing.duke.edu/page/crm_home>) in Durham, NC, is just seven years old. Both institutions also offer a non-traditional track in which students can obtain a certificate after completing clinical research curriculum.

Duke started the clinical research management degree because administrators perceived a need for research training within the Research Triangle Park community, says Elizabeth E. Hill, RN, MS, DNSc, assistant professor and director of the clinical research management specialty. Hill is also on the editorial board of Clinical Trials Administrator.

"We’re the only group in the school of nursing where we have something where we admit people who aren’t nurses," Hill notes. "We offer a post-graduate certificate for people who have at
least a master’s degree in some other field, but who want to get into clinical trials.”

Advanced education in clinical research is becoming more widely available at a time when the clinical trial job market is booming.

“The job market’s phenomenal right now,” says Stephen Sonstein, PhD, director of clinical research administration program for Eastern Michigan University. “Clinical trials are getting larger, there are more of them, and they are more complex; the graduates of our programs have the depth of knowledge necessary to deal with this level of change.”

Previously, clinical trials staff would gain experience on the job, often moving into the field of research by more luck than design, he says.

“In the past, people became clinical trial managers or clinical research associates on an ad hoc basis, by being in the right place at the right time,” Sonstein says. “They had the skills and trained on the job.”

These degree programs in clinical research developed because this is the traditional way people in health-related professions become qualified entry level professionals, and clinical research has become as specialized as any of the other medical fields, he adds.

Sonstein estimates there are about 35 clinical research administration degree programs in the United States and perhaps 100 world-wide.

“With everything going on with clinical trial regulatory issues and the growth of drug companies, clinical research administration no longer is a job where you can learn on the job,” Hill notes. “You need an education just like you do with other specialties.”

Even clinical trial professionals who are experienced find it difficult to keep up with the changing regulations and requirements, as well as stay ahead of industry shifts and outsourcing trends, Hill says.

“There is a base of knowledge you need to really become an expert in managing clinical trials,” she adds. “So this program gives graduates the well-rounded education they need to start out well ahead of the other research professionals who have on-the-job training.”

Duke clinical research graduates have gone on to have residencies with the FDA and have been hired by contract research organizations, she notes.

As universities increasingly add clinical research degrees programs, the industry is beginning to accept these degrees and/or certificates as proof of entry-level job qualification, Sonstein notes.

Job hunters who have earned either the university’s master’s degree in science, clinical research administration, or the post-baccalaureate certificate in clinical research typically can find good jobs after completing the program, Hill and Sonstein say.

“It’s taken us a little while to demonstrate to people, but now I think it’s definitely helping people get jobs,” Hill says. “What we’re really trying to show people is how people who have this master’s degree don’t have to start out in the hospital as a clinical research coordinator and can start out at an advanced level.”

Duke’s master’s program is for nurses and provides 39 credits for an MSN degree in clinical research, and students complete a 200 hour residency; the post-graduate certificate program involves 19 credits, Hill says.

Duke’s post-graduate certificate and Eastern Michigan’s post-baccalaureate certificate programs have attracted students from a variety of backgrounds, including lawyers, veterinarians, statisticians, and even physicians who received their doctorates in foreign nations, such as China, Hill and Sonstein say.

“We’ve had a lot of people who were medical doctors in China, but who aren’t qualified to take the boards here,” Hill says. “They want to stay in the medical arena and have gotten the post-graduate certificate.”

The master’s degree in clinical research administration at Eastern Michigan has attracted dietitians, medical technologists, and others in health care, as well as nurses, Sonstein says.

“People come into this program when they want to transition into a different kind of health care profession,” Sonstein explains. “They may be burned out or lost their job, but they want to use their skills in another profession, and this program has provided them with the opportunity.”

Others entering the master’s degree program are bench researchers who had worked in research labs and now want to move into clinical trial work, Sonstein says.

“The third group is foreign physicians who came to this country with skills, but cannot practice their profession because of the regulations here, and this gives them an opportunity to get a good job utilizing their skills in this country,” Sonstein adds.

The Eastern Michigan master’s program involves two to 2.5 years of study and a master’s thesis or research project, and the post-baccalaureate certificate program can be completed within
one year, Sonstein says. The certificate program includes coursework and a hands-on preceptorship. “The post-baccalaureate certificate program provides entry-level competencies for a person entering the field,” Sonstein says.

Sonstein is part of a group of university administrators who run clinical research programs and who have been meeting on a casual basis for the past six or seven years.

“We decided in 2002 to formalize this group and we received support from the Philadelphia-based Drug Information Association and created the Consortium of Academic Programs in Clinical Research,” Sonstein says. “We meet annually at DIA meetings, and the purpose of the group is to discuss common issues.”

The group wants to define the knowledge base that entails a clinical research administration degree and to analyze content competencies and work toward programmatic accreditation, Sonstein adds.

170 speakers from 34 states and seven other countries. Now there are more than 200 speakers enrolled, Goldfarb says. The speakers include study coordinators, clinical research associates, administrators, university professors, and company presidents. However, many more speakers are needed for the bureau to have full geographic coverage, he adds.

The speaker’s bureau web site has resources available for speakers, including slides, handouts, and public speaking tips in both Spanish and English. To learn more about the speaker’s bureau or to volunteer to be a speaker, visit the web site at www.firstclinical.com/resources/bureau/bureau.html or www.firstclinical.com.

FDA warns against use of unapproved drug products

The FDA is cracking down on unapproved drugs, which the agency says are surprisingly prevalent. To address the issue, the agency has issued a new guidance: “Marketed Unapproved Drugs — Compliance Policy Guide.”

Its estimates point to several hundred different unapproved active ingredients in prescription drugs on the market, which represent less than 2% of prescribed drugs. Such products have bypassed standard approval rules primarily because they were developed and marketed before successive changes to the drug approval process that is established in the Federal Food, Drug, and Cosmetic Act.

Steven Galson, director of the FDA’s Center for Drug Evaluation and Research, said that the newly issued guidelines are meant to encourage companies marketing such products “to comply with the drug approval process and ensure the safety and efficacy of their marketed products.”

Enforcement priorities will be given to unapproved drugs that pose safety risks, lack efficacy and constitute health fraud. Manufacturers that do not comply with drug approval requirements could be subject to enforcement action.

Community speakers bureau launched

First Clinical Research of Palo Alto, CA, a provider of clinical research best practices information, consulting, and training services, has launched a community outreach speakers bureau for the purpose of promoting clinical research to the public.

The bureau provides an international capability to tell the industry’s story face-to-face at the thousands of schools, community centers, churches, and other places where people gather.

Within four days of sending out an e-mail announcement, the speakers bureau had signed up

Coming in future months

■ Here are the challenges of research in non-traditional settings
■ Learn what sponsors want from trial sites
■ Check out these best practices on educating clinical trials personnel
■ Weigh the ethics of using existing data in human research
5. According to CenterWatch, how much time does a new drug or device spend in the clinical phase of research in the U.S. today? (The average amount of time was 31 months between 1982 and 1999).
A. 25 months
B. Nearly 36 months
C. 52 months
D. More than 70 months

6. Which of the following statistic about clinical trials is accurate?
A. 15% to 20% of clinical trials conducted in the U.S. have zero enrollment, and 30% enroll just 5% of the patients
B. 20% of clinical trial sites are average performers, and 30% enroll 75% of the patients.
C. Clinical trials cost $50,000 a day on average to operate the trial
D. All of the above are true

7. India’s share of the clinical trial industry is worth about how much today?
A. $50 million
B. $125 million
C. $230 million
D. $300 million

8. A study of potential research subjects found some differences between how men and women viewed recruitment photographs of clinicians and patients, but which of the following factor was important to all groups in the study?
A. Whether the photo had gadgets
B. The photo’s colors
C. The dress appearance of the clinicians
D. All of the above