CLINICAL TRIALS ADMINISTRATOR

An essential resource for managers of clinical trials

THOMSON
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Advertising may be cost-effective, but liability lurks in the wording

IRBs looking for false promises and inducements

You can't have a clinical trial without volunteers, and clinical trial coordinators and investigators often find that recruiting human subjects takes some creativity. Enter advertising.

Advertisements seeking participants for clinical trials can be found in newspapers, on radio, in brochures, on public transit billboards, on television, and on the Internet. They can be expensive, but they have proven to be effective. They also can be subtly coercive unless careful attention is paid to what is promised and what is not said, say institutional review board (IRB) administrators and those who work to ensure ethics in research.

"One thing [clinical trial advertisers] have to keep in mind is that advertising meant to recruit subjects can't be used as a marketing tool," says **W. Parker Nolen**, MBA, IRB administrator for St. Joseph's Hospital in Atlanta.

While it's permissible for a drug approved by the Food and Drug Administration (FDA) to make certain claims about what it can do for the user, clinical trial recruitment ads must be carefully worded to make sure readers know that what is being advertised is research, not treatment, according to Department of Health and Human Services' guidelines published by the Office of Inspector General (www.dhhs.gov/progorg/oei).

And the line between permissible information and coercive inducement extends to other benefits that might come with participation in a clinical trial, Nolen says.

"My experience is that one of the most common mistakes people make [in drawing up advertising for clinical trials] is in the wording that describes compensation," he says. "Saying, 'You can make $500!' or 'You'll get a DVD player!' can cause the ad to be rejected [by the IRB]."

A research trial's IRB determines whether advertising is acceptable or not, and Nolen says IRBs handle that task in a variety of ways. Sometimes the administrator reviews and approves or rejects the ad; in other situations, a committee does. He adds that federal regulations governing

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IRBs specify that the chairman or an experienced designated reviewer may review and approve advertising. **(See "Advertising Do's and Don'ts," below right.)**

"Advertising and recruitment of subjects for research are considered an extension of the informed consent process," says **Alisa Irwin**, director of research protections, University of California-Irvine Office of Research Administration.

"Given that advertising often functions as the initial step in the informed consent process, the IRB must ensure all advertising includes a reasonable balance between the legitimate goal of recruitment and adequate disclosure about the nature of research," she adds. "Advertising must be clear that subjects are being recruited for research, be free of the potential to contribute to confusion between experimental research procedures and standard medical treatment, emphasize both the risks and benefits of participation, and disclose important features of the study design that may influence enrollment. All of these are expectations of federal regulations."

Advertisements need not include every potential risk and benefit, Nolen said, because that information is disclosed in the informed consent process prior to a subject being enrolled in a trial.

Advertising Do's and Don'ts

So what should an advertisement recruiting trial subjects say? **W. Parker Nolen**, MBA, IRB administrator for St. Joseph's Hospital in Atlanta, recommends the following:

Do include:

- that the trial is *research*, not treatment;
- age restrictions or other qualifications for eligibility;
- some benefits (if any);
- compensation (but without overemphasizing compensation);
- the time commitment expected;
- the name of the center doing the research;
- the name of someone affiliated with the trial who can be contacted for more information. The FDA suggests this should be someone knowledgeable about the trial rather than a general telephone operator without clinical expertise.

Don't include:

- claims, whether explicit or implied, that an investigational drug or device is safe or effective for the purposes being investigated.
- representations that the product under investigation is equivalent or better than any other drug or device.
- pejorative terms that could serve as inducements to the reader to participate (e.g., in a weight-loss trial, to use a term such as "fat" to describe potential participants). ■

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Editorial Questions

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Call **Alison Allen** at (404) 262-5431.

However, the major known potential risks and benefits should be mentioned.

Irwin says a trial's IRB should review all advertising with an eye toward avoiding the risk of undue inducement and social or therapeutic misconceptions (e.g., wording such as "groundbreaking treatment for advanced esophageal cancer" or "Suffer from debilitating headaches? A new treatment option now is available!")

Nolen adds that buzzwords such as "new and exciting," "cutting edge," or wording that indicates the trial is free treatment for a condition should be avoided.

Interesting aside

According to the FDA, research into recruitment advertising has indicated that expensive advertising is cost-effective only for studies in which the eligible population is large and widely dispersed (e.g., depression or heart disease), as opposed to rarer conditions such as cystic fibrosis. Internet advertising, Nolen adds, has been seen to attract "a more savvy and educated audience" than mass media advertising in some cases.

The FDA advises that the mode of advertising is an important consideration when a trial seeks to recruit subjects with acute or severe physical or mental illness, or when the audience may include persons who are economically or educationally disadvantaged. ■

College students: Are they a captive audience?

Some strategies could cross the line

To clinical trial coordinators looking for study subjects, a nearby university campus looks like a godsend — large numbers of unemployed young people all in one place for a designated period of time.

But college students are more vulnerable to coercion, in some ways, than people in the general population, and IRBs may take a dim view of researchers who seem to be exploiting them.

"Students are generally unemployed and need money, and they are relatively easy to target with advertising around campus to solicit participation," notes **Jon Merz**, JD, PhD, MBA, assistant professor at the University of Pennsylvania Center for Bioethics. "But for this group, I would be concerned about how much money is being offered as an incentive to participation and whether the solicitation is forthright about what participation will entail."

Merz cites reports of bad outcomes in human subjects research where participants were paid considerable sums of money and consented to procedures that might seem unthinkable to someone not being paid.

For unemployed students in need of money, the amount that might be coercive could be lower than that for someone able to earn money in the work force, for example.

Good subjects — or, just easy to get?

Ethically, research subjects, to the extent that it is feasible, should be drawn from the population mostly likely to benefit from the results of the research, Merz notes. Therefore, IRBs might legitimately question why students are being considered as subjects for a given trial in the first place.

"If they're simply available and easily targeted, this might be an area of concern," he continues. "For example, we no longer allow research on prisoners unless it is therapeutic or is related to their status as incarcerated persons. So with students, research on students is more legitimate if it benefits the students themselves."

Frequently, students in health-related areas of study are recruited by their professors or medical leaders to serve as subjects in projects related to their field. However, this has the potential to be extremely coercive.

"Medical, nursing, or students in the related professions might be solicited because of their ready availability, need for cash, and usually, their willingness to participate in clinical activities," Merz notes. "It could also be argued that if they are doing research or will be in their careers, they should also be willing to be subjects. Nonetheless, the potential for coercion by professors or mentors or anyone of authority must assiduously be guarded against."

Many departments have rules that prohibit research on their own staff or residents, he notes. If individuals want to get involved in studies in other departments, they're free to do so. But persons of authority over the person considering participation should not solicit or otherwise be involved in such studies.

"This isn't always the case in the real world,"

he acknowledges. "I know of one case of a cancer researcher who proposed taking control bone marrow biopsies from staff in his department, asserting that the people were quite willing to do it because they do it to patients all the time, and they needed the $75. The IRB approved this."

Local IRB scrutiny

Some universities have policies that off-campus researchers attempting to recruit students must get the approval of the school. In some cases, this also means, getting the local IRB to review the protocol.

Members of the institutional review board at Towson University in Maryland have a policy of asking off-campus researchers to submit their protocols for review before they recruit on campus, says **Patricia Alt**, PhD, a professor in the department of health science and chair of the university's IRB.

"We don't do clinical research trials here but we do have a large, nearby medical center that frequently wants to recruit our students; and we have had people contacting faculty, wanting to use their classes."

University policy prohibits researchers from posting ads in the student newspaper or on university-sponsored bulletin boards without prior approval of the administration, but this policy is frequently flouted, and strict enforcement is difficult, Alt notes.

"The faculty are supposed to come to us if they get a request [to recruit students]. But we frequently find all kinds of things on the bulletin boards recruiting people to participate in studies for large amounts of money," she says. "We call them up and actually say, 'Has this even been in front of your IRB, much less ours?'"

A recent flier, posted without administration approval, recruited participants for an anthrax vaccine study. The protocol had been in front of the IRB of the sponsoring institution, but no one at Towson was notified.

"I think when you recruit on campus, especially on a campus-sanctioned bulletin board, that implies we are supporting it," she states. "When we spot one of those, we usually call the coordinator and ask them, 'Are you aware that we're talking about 18-year-olds here?' and try to get them to run it by our IRB. They are usually pretty graceful about it. Occasionally, you will find someone who doesn't see why they should bother — it's been through their IRB. We just ask as a courtesy. We'd like to see it."

Of course, IRBs have no real authority to restrict research not sponsored at their institution, both Merz and Alt admit, though some feel that solicitation and enrollment of students at their institution should be within their jurisdiction.

"Technically, IRBs have jurisdiction only over researchers at their institutions," Merz says. "I always argue that the IRB has no authority and it is really an institutional question whether solicitation of subjects by off-site researchers should be permitted. But if that institution decides that their IRB should approve any such studies, then, that's the end of it."

The local IRB may have no knowledge of the off-site investigators, their reputations, etc., and has no institutional hook to assert authority over those researchers, he adds. But the local IRB may know its study population best and can even be helpful in getting the solicitation done in a way that is sensitive to the population's needs.

It's a moral issue

Although they have no legal jurisdiction over off-campus researchers, Alt says he believes that university IRBs have a moral responsibility to the students to monitor what types of trials are allowed to recruit students, she says.

"As a parent, I would hope that the colleges would not allow on-campus recruiting for things that might be dangerous," she says. "Obviously, if researchers refuse [to get local approval], I can't go stand outside their office and watch for Towson students. And if they are 18, in the eyes of the law, they are adults."

In the interest of providing true informed consent and protecting the safety of participants, Alt feels that IRBs and study coordinators should seek the input of review boards at the institutions they propose recruiting from.

"Last year, we had a person who was working on a doctorate at a university in another state but had gotten a job in Baltimore at a local clinical organization," she continues. "She decided on her own that Towson had this great big campus, and she had a friend here; she had her university back home approve her protocol to use some of her friend's classmates as subjects for her study, but she did not come to us. We were pleasant about it, but it sort of shocked us. If someone were to propose something similar here, we might say it was fine, but only if they got the approval of the other IRB." ■

Numbers indicate misconduct rising

But they don't tell the whole story

Research misconduct activity reported by institutions in 2002 reached the highest levels since 1997, according to a report in the quarterly newsletter from the Department of Health and Human Services' Office of Research Integrity (ORI).

In their 2002 Annual Report on Possible Research Misconduct, 107 institutions reported misconduct activity stemming from allegations received during or before 2002 — the previous high number of institutions reporting was 82. Seventy-one institutions, compared to the existing high of 61, received new allegations. At those institutions, the 83 new cases topped the previous high of 72 cases.

Although the reports do indicate an increase, they do not necessarily indicate a wave of misconduct sweeping through institutions receiving funding through the National Institutes of Health (NIH) — the research that ORI is charged with overseeing, says ORI director **Chris Pascal**, JD.

"In terms of actual numbers, the increase is not very large," he points out. "We have approximately 4,000 institutions that report information to us and, of that number, we have about 100 institutions in any given year reporting activity to us. More than 90% of our institutions report no activity at all."

Institutions receiving NIH funding are required by the ORI to file annual reports of allegations of research misconduct, Pascal says. That report is simply numbers — how many allegations, of what type, which allegations led to further inquiry, and how many were deemed unfounded, etc.

If an individual allegation progresses, at any point during the year, to the point the institution launches an investigation, a separate, more detailed, report to ORI is required.

"The annual report gives us a chance to make sure we are getting the required information. Occasionally, they forget to send us stuff and we see a disconnect between sthe cases we have reported to us and those that should have been reported," Pascal says. "In that case, we follow up with the institution."

Since 1989, the ORI has had a compliance assurance program in place that requires institutions that receive funding to develop a clear policy for managing reports of research misconduct.

The office develops and distributes model policies and guidance for developing policies and then uses the annual reports of research misconduct as a means of ensuring that institutions have appropriate policies in place.

"If the institution doesn't have a road map on how to process an allegation and investigate it, it is much less likely that they will do so," Pascal says. "They are more likely to make mistakes, and the employees and the staff at the institution that have a concern, the potential whistle-blowers, won't know how the process works and who to go to, etc."

In recent years, ORI has shifted from a strictly enforcement role to sponsor more educational efforts, offering conferences, seminars, and publications to help institutions and researchers understand what research misconduct is, how to avoid it, and how misconduct allegations should be managed.

"Partly as a result of that, I think the institutions have gotten a little more adept at identifying substantial allegations up front and taking them through the whole process, and maybe dropping those where there seems to be nothing wrong," notes Pascal. "Many institutions also now have more experience in doing an investigation so that they can determine whether misconduct actually occurred."

The office also has seen a slight increase in the number of investigations of misconduct that it pursues, Pascal says.

If an institution has a substantial allegation that leads to a full-scale investigation, it files a detailed report with ORI. In some cases, ORI reviews the institutional documentation and finds reason to visit the institution to conduct an oversight review, possibly asking additional questions and reopening parts of the investigation if it feels the institution missed something, he explains.

Recently, the office has averaged about 12-14 official findings of research misconduct per year, about 30% of all of the allegations of misconduct. In the past two years, the numbers, and therefore the percentage, has gotten higher, but the actual numbers are not that different.

With only about 100 institutions reporting allegations, and only 30%-40% leading to official investigations of misconduct, the percentage of research affected is small.

"Most of the activity comes from the larger institutions with the most grants," he notes. "We did a comparison of that at one point, you could

see the number of cases that come from the institutions with the most funds."

Mark Brenner, PhD, vice chancellor for research and graduate education at Indiana University in Bloomington, also thinks the recent statistics are not representative of a growing problem.

"I am not aware of, among the people I interact with, a huge wave or change or surge [in misconduct allegations]," he says. "I think institutions are becoming more informed on how to deal with allegations, and I suspect that, in general, the education programs are touching more people. To some degree, that awareness does bring out more allegations. People find out about the policies and the processes."

More and different education for research investigators and other personnel about responsible research standards still is needed, however, he adds.

With more private sponsorship of research and increased federal attention to the integrity of information gained from studies and the conduct of researchers, institutions need to be explicit about what they expect and what they will require from students, faculty and others who participate.

"I certainly don't want to be lurking in the corridors looking for instances of misconduct, interviewing students and staff, asking, 'Is there something going on here I need to know about?'" he says. " I am much more interested in having us engaged in promoting education programs. And my position is that this isn't just for graduate students, we need to have programs that touch all people engaged in research."

In recent years, it's not even been clear what different entities mean when they talk about misconduct.

In 2000, the federal Office of Science and Technology (OSTP) issued a standard Federal Policy on Research Misconduct, which was designed as the single federal standard, defining research misconduct.

Prior to that, different federal agencies and different institutions had widely varying definitions and policies.

The final policy adopted by OSTP defines research misconduct as the, "fabrication, falsification or plagiarism in proposing, performing or reviewing research, or in reporting research results." The policy further clarifies that:

- *Fabrication* is making up data or results and recording or reporting them.
- *Falsification* is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- *Plagiarism* is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- Research misconduct does not include honest error or differences of opinion.

This is the definition that ORI and other federal agencies use to define misconduct and breaches of conduct that fall under these categories are the allegations and investigations that should be reported to them, Brenner says.

However, investigators and research coordinators should be aware that individual institutions might have policies that include broader definitions of misconduct, he adds.

"For example, at my campus as we are going forward, without question we use include the fabrication, falsification and plagiarism in our definition, and that would be reported to federal agencies, but we continue to have in our definition the 'failure to comply with federal regulations,' which means then that if you failed in a reckless and intentional way to comply with the regulations governing human subjects research or animal subjects as an animal, we could consider that misconduct on our campus," Brenner explains.

Investigators who are found to be violating federal standards for protecting human subjects can have their research suspended by the institutional review board, and may lose research privileges, Brenner notes. But, at Indiana, and other institutions with similar policies, they would also be subject to disciplinary action for misconduct.

"The IRBs do not dispense disciplinary action, they can suspend or halt studies, take away research privileges, but that is about protecting the subject, not the researchers themselves," he says. "That is why we've chosen to leave the other available as a tool in our toolbox."

Researchers need to be aware both of the federal definitions of research misconduct and those used by their sponsoring institutions. ■

HIPAA authorizations don't require IRB review

FDA addresses questions, issues guidance

IRBs are not required to review stand-alone HIPAA waivers as part of their oversight of

research subject protections even if their written policies and procedures indicate they will review any written documentation provided to potential study participants, the U.S. Food and Drug Administration (FDA) clarified in a recent guidance document issued Oct. 21, 2003, and published in the Nov. 7 issue of the *Federal Register*.

"The Privacy Rule does not require IRBs to review these authorizations," explains **Catherine Lorraine**, director of policy development and coordination in the FDA's Office of the Commissioner.

The Privacy Rule section of the 1996 Health Insurance Portability and Accountability Act (HIPAA) establishes the right of individuals, including research subjects, to authorize the use and disclosure of their protected health information by signing an authorization form (also known as a waiver) for uses and disclosures not otherwise permitted under the rule.

For example, in the context of a clinical investigation, a HIPAA authorization explains the ways in which a subject's protected health information will be used and disclosed by the clinical investigator and permits the clinical investigator to use and disclose that information as specifically described in the authorization document.

A HIPAA authorization is different from a subject's informed consent in that a HIPAA authorization focuses on uses and disclosures of information that may be made, the FDA's guidance notes.

Informed consent, on the other hand, apprises potential subjects of the possible risks and benefits associated with participating in the clinical.

The HIPAA Privacy Rule permits — but does not require — clinical investigators to combine a HIPAA authorization with the informed consent documents. This is known as a "compound authorization."

Internal policies complicate the issue

Following final implementation of the Privacy Rule provisions last year, the FDA and the U.S. Department of Health and Human Services' (HHS) Office of Civil Rights (OCR) received many questions from IRBs about their obligations under the new law, Lorraine says.

On April 15, 2003, the OCR issued a guidance document clarifying that IRBs were not required to review stand-alone HIPAA authorization documents.[1] Obviously, IRBs are required to review compound authorizations because they still must review the informed consent documents.

However, some lingering questions remained.

Many IRBs, in adopting the International Conference on Harmonisation Good Clinical Practice Guidelines, have developed internal policies stating that they will review any written documentation provided by investigators to potential subjects.

Federal law governing protection of research subjects requires IRBs to adhere to their own written policies and procedures.

The new FDA guidance was issued to clarify that the agency would use "ongoing enforcement discretion" with regard to IRBs that decided against reviewing stand-alone HIPAA authorizations even if they have written policies that would seem to require them to do so.

"FDA is exercising this discretion in order to encourage IRBs to permit the continued enrollment of subjects in clinical investigations without IRBs' prior review and approval of stand-alone HIPAA authorizations," the *Federal Register* notice indicates. "FDA believes that enrollment in well-designed and well-conducted clinical investigations should not be interrupted for the purpose of IRB review and approval of stand-alone HIPAA authorizations even though the IRB's written procedures would otherwise require this review and/or approval."

In writing to the FDA and OCR in April, shortly before the regulations took effect, several institutions indicated that clinical investigations might be impeded because the IRBs would be backlogged with requests to review thousands of stand-alone HIPAA authorizations and some communications further stated that some IRBs intended to halt enrollment in some trials pending IRB review of the authorizations, Lorraine says.

The guidance document was written to clarify the FDA's position and make it easier for IRBs to focus their resources on overseeing and approving good, well-designed clinical trials, she noted.

Unless the situation under the current law changes, the FDA's enforcement discretion will continue, she says. Any changes would be announced in a new guidance document.

Copies of the FDA guidance are available online at: www.fda.gov/oc/gcp/guidance.html or by submitting a written request to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Requests should be identified with the docket number found in the Notice of Availability for this document published in the *Federal Register* (Docket No. 2003D-0204).

The HHS also has established an informational web site covering the obligations of the research community under the HIPAA Privacy Rule. The web site (http://privacyruleandresearch.nih.gov/) contains documents and lists of frequently asked questions (FAQs) covering the responsibilities of researchers and IRBs under the HIPAA regulations.

Reference

1. Department of Health and Human Services' Office of Civil Rights. "Privacy Guidance about Authorizations for Research and Institutional Review Boards." Available on-line at: www.hhs.gov/ocr/hipaa/privguideresearch.pdf. ■

Integrated systems keep all connected

Software reduces paper trails

It's pretty much a given that computer-based recordkeeping will play a part in a clinical trial. Someone, somewhere, has at the very least created a database to track protocols, participants, and IRB requests. In recent years, however, institutions have recognized the need for more integrated systems — those able to lessen paper output while enhancing the flow of information between investigators and IRBs. *Clinical Trials Administrator* is taking a look at three such systems. These web-based applications are designed to streamline the protocol submission and IRB review processes.

Baylor uses its BRAAN

Two years ago, Baylor College of Medicine had a dilemma: Double its staff to accommodate the increase in study protocols being submitted to its IRB or find an electronic solution to its problem. BRAAN, the Baylor Research and Assurance Network system, was born.

Developed by end users, BRAAN is a web-based application that allows investigators and IRB members to do everything from submitting protocols to tracking and reviewing studies on-line to training investigators on human subject protections.

The application is menu driven, providing pull-down selections for users in every aspect of protocol creation, submission and review. From the home page, administrators and investigators can select the appropriate path — animal or human protocol, existing or new protocol — and they then will be directed step-by-step through the program to supply information that must be included in the protocol application.

BRAAN is divided into sections, with each containing questions or prompts designed to gather pertinent information about the protocol. For example, investigators creating a new protocol must answer questions such as "What is the purpose of the protocol?" or "Will research data be tied to individual's names or record number?" They also will be asked to provide specific information on inclusion and inclusion criteria, sample size, potential risks or discomforts, and consent procedures (e.g., who will be recruiting subjects, how research population will be identified, and how consent will be obtained). Investigators can generate a preliminary informed consent form that contains autopopulated information provided in previous answers.

Required fields, such as risk categorization or a series of questions to determine whether a protocol qualifies for expedited review, are highlighted in red. The system will not allow investigators to move forward if those fields are left blank. There also is a "Review for Completeness" section that will list areas that require more information before submission.

If investigators would like to use information from an existing study, they can select the study from a drop-down menu, and all pertinent information will autopopulate in upcoming screens. Investigators then may revise or update autopopulated fields as they go along. Additionally, personnel information can be autopopulated with data provided by the human resources department.

IRB administrators can use the program to schedule meetings and report findings using templated memos. IRB board members can access protocols on-line and provide comments that can be viewed later by investigators.

"One example of a BRAAN feature that has made life easier is as an investigator, I have access to the protocol and all documents related to the protocol," says **Addison Taylor**, MD, PhD, associate dean for clinical research at the Houston-based medical college.

"These are stored on-line and can be printed for regulatory authorities or clinical monitors wherever needed. Also, as an IRB member, I can now review protocols off-line by downloading them to my laptop for review away from the office. I can access protocols from anywhere in the world as long as there is Internet access."

BRAAN contains education modules on research

ethics; investigator responsibility; the role of the IRB; and special topics, such as informed consent and scientific integrity.

The application won the 2002 Award for Excellence in Human Research Protection given by the Bethesda, MD-based Health Improvement Institute and sponsored by the Office of Human Research Protections.

For more information about BRAAN, contact API, 167 W. Main St., #210, Lexington, KY 40507; Telephone: (859) 233-2006; web site: www.api.md.

ImedRIS: Something for everybody

One of the challenges facing Texas Tech Medical Center several years ago was to start a clinical trials office that covered four academic health center campuses, located long distances from one other.

"We had identified that we would have to have some way to try and communicate from the business side with the clinical trials office here," says **Stacey Pugh**, RN, BSN, CCRC, director of clinical services in the clinical trials office of Texas Tech Medical Center in Lubbock.

"We made attempts at developing internal clinical trials software, but we didn't have the expertise to take it to the next level," she recalls. "We started on a quest, and we have searched out and talked with every clinical research system or software system that's out there for the past two years."

Then last year, Pugh met with representatives from iMedRIS Data Corp. of Yucaipa, CA.

"When we looked at their study assistance software and were looking at it from the patient management side, we thought their study assistance was far superior," she reports. "We knew we had to have an IRB component. We met with iMedRIS a few times and communicated by telephone; and the next thing we knew they were providing us with a product that allowed us to go to an electronic, virtual IRB," Pugh says. "That completely addressed our compliance program and systems program."

The iMedRIS product marries the site management piece with the IRB agenda, says **William Schroeder** of iMedRIS, which stands for Internet Medical Research Information Systems.

Pugh says the result of the cooperation between Texas Tech and iMedRIS has been a software system that is efficient and integrates every aspect of research management — from compliance to data collection. The application has these features:

- **Site assistant:** This provides the ability to manage all aspects of clinical studies, including patient data, study information, visit tracking, screening, etc., and incorporates data from individual clinical visits.
- **IRB assistant:** Site activities are directly integrated with the IRB. Meeting agendas are built from requests to the IRB, and this in turn results in automatic records attendance, voting results, and meeting minutes. Any meeting outcome is sent electronically to study coordinators, and all pre-meeting study information is available to IRB members.
- **Contract assistant:** Negotiations between an institution and sponsor are recorded throughout the process.
- **Compliance assistant:** Study audits are performed, and the software ensures compliance.

"We have found that by developing the software with Texas Tech, that this is a software that's available for multiple sites with everything flowing automatically right to the agenda for the central IRB," Schroeder says.

Integrating a new software system is not easy, but the cost and effort can be worthwhile, Pugh says. "It has been a real struggle for us to get to this point, but we just made a light-year transformation here," she says. "A year ago, if someone had said, 'How many human subjects do you have on any protocol now?' I would say, 'I don't know,' and I'd have to pick up the phone and ask the principal investigator how many people were on the protocol."

Now, if Pugh is asked to obtain the same information, she could ask them to hold a minute while she pulls up the report on the computer. "It'd take me all of 25 seconds to requisition that information," she says.

The financial investment was considerable, but it was money well spent, Pugh says. "It addresses so many of our problems in one fell swoop. How do we know whether we have a system oversight without an electronic system that ties in like this one does?"

Previously, investigators could be late in reporting serious adverse events (SAEs), and it would be difficult for the IRB to learn that this was a problem. Investigators now submit SAEs electronically as soon as they occur. The IRB has real-time data of what is going on, and the compliance officer can do audits with current information, Pugh says.

Also, the electronic documentation system allows PIs to amend the protocol as they go along. For instance, they should note how many people have withdrawn from a study each time the tally changes, and doing so is a great deal simpler than with a paper documentation system, Pugh says.

For more information about iMedRIS, contact iMedRIS Data Corp., 1960 Chicago Ave., Suite E9, Riverside, CA 92507; Telephone: (909) 784-1013; Web site: www.imedris.com; E-mail: info@imderis.com.

PRAMS saves on staff and time

Penn State University of University Park, PA, began to develop a web-based electronic documentation system in response to recent growth spurts at the same time that the university needed to keep staff growth relatively stable.

"We needed to find a way to use our resources more efficiently, and that prompted us to look at electronic data systems," says **Candice Yekel**, director of research protection at Penn State.

"Our hope is that this will ensure that not only will we have an efficient system within the administration, but that we can provide electronic data to investigators who are submitting and provide more efficiency within the review process," she explains.

The university stands to benefit a great deal from the university's homegrown electronic documentation system, which is called Protocol Review and Approval Management Systems (PRAMS). PRAMS development began March 2001, says **Kenneth Forstmeier**, director of the office of research information systems. By March 2002, PRAMS was rolled out in its first phase. Other institutions will have an opportunity to purchase and use PRAMS, which is being marketed by ERA Software Systems of Monterey Park, CA, Yekel reports.

"The application we developed is not only for the human side of things, but for all protocol types used at Penn State," Forstmeier says. "So we had to bring in data from five different regulatory systems and bring these into the new applications."

Yekel and Forstmeier offer these details about how PRAMS works:

• **Eliminates most paperwork.** The paperless system will eliminate the need to send paper documents to IRB members, who simply will log onto the system and see protocols ready to review, Forstmeier says.

"All of it will be stored electronically — all records — and any documentation that comes in," Forstmeier adds. "We'll receive paper from time to time, and those records will be scanned into the system and indexed and placed in a nonvolatile storage where it will be available for audit in the future."

• **Protocols may be submitted and reviewed electronically.** There are up to 3,000 protocols that the university tracks at any time, and the Hershey Medical Center, which is within the Penn State system, also has 2,500 protocols to track, Yekel says.

With PRAMS, the computer will search the protocol database for expiration dates, find e-mail addresses for investigators who have studies that are about to expire, and send them a notice via e-mail along with a form they'll need to complete, she notes.

"When the expiration date arrives and nothing has been received or entered in our system, PRAMS will prepare a report that says the following protocols are set to be inactivated," Yekel adds. "It's just a matter of pushing a button. We see this as a big plus in making sure we're not missing deadlines."

Principal investigators also are able to submit their protocols electronically. "We'll do a distribution of protocols electronically," Forstmeier adds. "And the other thing the system does do is audit all transactions, so as things change, we know who made the change, when, and so on."

This way, the system keeps track of what went wrong in the event something doesn't work, and the electronic data can be used to figure out which areas of business processes need to be bolstered with more resources and changes, he says.

• **IRB and research training and other data electronically tracked.** PRAMS will track adverse events and whether investigators and IRB members have had the required training and when the training expires.

A list of training credentials will appear with the principal investigator's name, and this information can be updated when people receive new training or continuing education credits, Forstmeier says.

The system will load data into the protocol application rather than having someone reload the entire protocol with the updated information, he adds.

With more than 9,000 faculty, staff, and students conducting research at Penn State, this electronic ability to track their training will save the university significant time and money over the years, Yekel says.

• **PRAMS will cover all research and regulatory information.** Another unique feature of PRAMS is that it will cover all human subjects research, as well as all research involving biohazard materials, animal use, regulatory changes under the Health Insurance Portability and Accountability Act, and conflict of interest issues, Yekel says.

"This system is built to integrate all of those areas," Yekel says. "We keep data on animal use protocols and biosafety information. What's neat

about the system is if I have a human subjects protocol that involves some pathogen, then this system will alert me to that issue."

The system also will provide continuous documentation from a study's in vitro and animal trials, following the study as it moves into the arena of human subjects research.

If an IRB member or coordinator would like to learn more about a particular investigator who has not conducted human subjects research before, but will soon start, then it would be easy with PRAMS to call up that investigator's name and learn about all of the investigator's animal research, use of biohazardous materials, training, and funding, Yekel says.

For more information about PRAMS, contact ERA Software Systems, 1255 Corporate Center Drive, Suite 305, Monterey Park, CA 91754; Telephone: (323) 980-4900; e-mail: dianne@erasoftwaresystems.com. ■

Hastings Center issues report on 'reprogenetics'

Ethicists at the Hastings Center have issued a guidance document on the need for and potential of public oversight of "reprogenetics" research, their term for research that involves the intersection of reproductive medicine and the manipulation of gametes and embryos.

The report, *Reprogenetics and Public Policy: Reflections and Recommendations*, is the culmination of a two-year research project by the center. In it, authors Erik Parens and Lori Knowles argue that the complex ethical questions this type of research raises should not be resolved by market forces alone but need to be addressed by broad public discussion and oversight.

The report makes three policy recommendations:

1. The ban on federally funded embryo research should be lifted in order to allow federal oversight of such practices as preimplantation genetic diagnosis, ooplasm transfer, cloning and embryonic stem cell research. If the ban is not lifted, the market will remain the only mechanism regulating development of these technologies.

2. A commission should be established to consolidate the data on this topic and make legislative recommendations about statutory authority for an oversight group. The commission would be able to frame issues through engaging the public and experts and articulating ethical commitments. Ultimately, it would present legislative initiatives to Congress.

3. The commission, when established, should consider calling for a federal Reprogenetics Technologies Board that would have oversight authority of both public and private sectors.

The consequences of reprogenetic practice could be far reaching, the authors note, extending from the alteration of individual physiologies to reconfigurations of how a society views and treats its members. For these and other reasons, the direction of the research must not be left up to the market alone and an oversight system is needed.

Copies of the report are available on the center's web site at www.hastingscenter.org. ▼

NIH expanding distance learning programs

The National Institutes of Health (NIH) Clinical Center has extended its clinical research training programs to reach more than 1,000 physicians and other health professionals this year, in locations as far away as Peru and Puerto Rico. Improving clinical research training is a major initiative of the NIH roadmap, introduced by NIH in November.

This year, 1,426 students are enrolled in three core courses, "Introduction to the Principles and Practice of Clinical Research," "Principles of Clinical Pharmacology," and "Ethical and Regulatory Aspects of Clinical Research." They are available not only to NIH researchers, but are transmitted by satellite or web videocast to remote locations.

Additional information on these courses can be obtained from the Clinical Center Office of Clinical Research Training and Medical Education (director Frederick P. Ognibene, MD, and deputy director, DeNedra McPherson) at (301) 496-9425. ■

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CE/CME objectives

The CE/CME objectives for *Clinical Trials Administrator* are to help physicians and nurses be able to:

- review pertinent regulatory mandates;
- develop practical clinical trial oversight strategies;
- review best practices shared by facilities that successfully conduct clinical trials. ■

CE/CME *questions*

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

The semester ends with this issue. You must complete the evaluation form provided and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you. ■

21. Which of the following is allowed in advertising?
A. Information on risks and benefits
B. Information on compensation
C. Information on time commitment expected
D. All of the above

22. IRBs have legal jurisdiction only over researchers at and protocols sponsored by their institution.
A. True
B. False

23. The federal definition of research misconduct includes:
A. falsification, fabrication and plagiarism.
B. falsification, fabrication and violation of federal regulations.
C. falsification, plagiarism, and misrepresentation.
D. None of the above

24. IRBs are required to review stand-alone HIPAA waivers as part of their oversight of research subjects protections.
A. True
B. False

Answers: 21. D; 22. A; 23. A; 24. B.