AMERICAN HEALTH CONSULTANTS®

IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

INSIDE

Inserted in this issue:
✔ Pre-audit interview chart
✔ 2002 Reader Survey

APRIL 2002

VOL. 2, NO. 4 (pages 37-48)

IRBs can implement and adapt own auditing programs, depending on need

Time, staff, money are chief limiting factors

As public and federal scrutiny increasingly focuses on human subjects research, IRBs are becoming more interested in forming ongoing auditing/monitoring programs of protocols and principal investigators.

"It's obvious from federal regulations and guidance documents that there's a responsibility for IRBs to make sure researchers are meeting their obligations when conducting studies," says **Dennis Freeman**, MPH, director of the division of research compliance at the University of South Florida in Tampa.

Another good reason for initiating a formal auditing or monitoring program is that there will soon be accreditation standards requiring more detailed documentation of policy compliance and procedures, and an auditing program can help an IRB prepare for state and federal audits.

Also, it's just good practice.

"It's a philosophy that the university wants to follow and implement," Freeman says. "We recently completed a recruitment search for an individual who can implement and develop our program."

The IRB at Sentara Hampton General Hospital in Hampton, VA, also has implemented a monitoring program that will be handled on a contractual basis by a certified IRB administrator of a neighboring IRB, says **David Plummer**, MDiv, LMST, manager of the department of pastoral care.

"We wanted to make sure we're reviewing adequately the activities of our patients and of those who are undergoing research trials with research associates from the hospital," he says. "We're aware that the field of research in human protection is a rapidly growing area within the medical industry."

Since the IRB represents a small, community-based hospital, funding a full-time auditor isn't a feasible option, Plummer says.

Plummer met with the director of clinical research to discuss how the

third-party audit might be conducted, including parameters and time frames.

"For us, our audit needs to focus on Food and Drug Administration [FDA]-type compliance issues," he reports.

The consultant will monitor research protocols, conduct on-site record reviews, review enabling documents, memorandums, policies, and procedures, standard operating procedures, and the IRB's conduct. Other tasks will include:

- periodically attending IRB meetings to observe and evaluate compliance with federal rules and regulations;
- assisting the IRB in developing written critiques that identify program strengths and weaknesses;
- helping to formulate an action plan;
- monitoring the program on an ongoing basis, at least quarterly for the first year.

Since the auditor will be paid on a contractual basis, the financial investment is minimal to start and can be evaluated and changed as needed, Plummer says.

Another advantage to hiring an auditing consultant is that it ensures objectivity. Sentara's certified IRB administrator will have no conflicts of interest because her full-time work is with an IRB that has no overlap in research with the hospital's IRB, he explains. "She's doing her job, and we're grateful for it; we hope to improve upon our processes."

While small and medium-sized IRBs might find it most practical to hire auditing consultants for the monitoring program, larger IRBs could develop a highly specific and involved auditing program that utilizes on-line education and information.

A model-auditing program of this nature can be found at the University of Pittsburgh, which has developed dozens of auditing forms and guidelines. **(See story on University of Pittsburgh's IRB program, p. 39.)**

"What we try to do with our auditing program, as much as possible, is make it educational," says **Dennis Swanson**, RPH, MS, CIP, director of research conduct and compliance.

"We started auditing five years ago, and we got into it thinking we'd go out and find that everyone was doing things according to clinical research practices, and there'd be no problems," Swanson says. "What you actually find when you go out there is there's a background-noise level of problems, and there are certain things that principal investigators [PIs] are not aware of."

By this, Swanson means that PIs may forget to have a research subject initial each page of a consent document to indicate that he or she has read it. Or the audit might find filing problems in which investigators cannot readily reproduce records or have problems with source documentation.

These are minor problems that need to be resolved, but are not in themselves cause for a report to the Office of Human Research Protections (OHRP).

That's another issue that IRBs need to consider as they establish a monitoring/auditing program, Swanson suggests.

"I think it's important to realize that when you go out and do auditing and look for problems, you're going to find them," Swanson says. "Then the big question is whether you are obligated to report them to federal agencies where the problems are subject to the Freedom of Information Act."

The argument that must be made to the OHRP and other federal agencies is that having an IRB conduct its own audit is a positive step that must be encouraged. If IRBs voluntarily audit their programs and protocols, but then are required to report every single discrepancy to federal officials, then it will shed the institution in a bad light, Swanson explains.

"So there's a hesitancy for institutions to do audits because if they look for problems and find them, then they'll have to report them," Swanson says. "That's why it's very important when you put the auditing program in place that you have clearly defined the policies and procedures of what types of problems will be reported and what you will not report."

For example, all major violations, including those that result in the IRB removing a PI from a study because of noncompliance, should be

COMING IN FUTURE MONTHS

- IRBs manage operations with PRO IRB and iMedRIS software systems
- Determining subjects' ability to consent can be a problem
- OHRP updates stem cell guidance
- Recruiting 'community' IRB members
- What you need to know about MedDRA

reported to the OHRP, Swanson says. "But if you identify background noise-level problems, then you should be able to take care of those internally."

On a positive note, an internal auditing program is the one truly effective way for an IRB to efficiently investigate research problems, Swanson adds. ■

The ins and outs of Pitt's IRB monitoring program

As increasing numbers of IRBs consider establishing an auditing and monitoring program, there is at least one trailblazer from which they can learn, and that is the University of Pittsburgh.

The university's research conduct and compliance office, which oversees the IRB, established in 1997 an extensive auditing program for protocols submitted to the IRB.

"At the time, it was very unique to an academic medical center to have this type of program," says **Kelly Dornin-Koss**, RN, BSN, CCRC, education and compliance coordinator.

Initially, the program was developed in the Office for Research for Health Sciences. Then in August 1999, the research conduct and compliance office was created to separate compliance activities from the office of research, which is responsible for generating funds for research, she reports.

Dornin-Koss is in charge of an office of four employees who conduct all of the audits of human subjects research. One of the four staff members is in charge of education and computer-based training, and another is an auditor solely for an area Veterans Affairs (VA) medical center with whom the university is sharing office space and resources, she says.

"Most of the investigators who do research in the VA also are faculty at Pitt, so it serves two purposes," Dornin-Koss says.

Since the program began, the standard operating procedures (SOPs) and audit forms have been revised and expanded numerous times.

The auditors attended a lecture on the subject by the Greater Pittsburgh Chapter of Clinical Research Professionals and used their sample format in the development of SOPs, Dornin-Koss says.

"These were created over time, and I did audits before developing the SOPs," she explains.

As the audit and informed consent process SOPs evolved, it became clear that the process of educating investigators and others also needed to expand and improve.

"I went to the Public Responsibility for Medicine in Research meeting this past fall, and one speaker said the investigators should be aware of your SOPs," Dornin-Koss recalls. "We had them internally, but I didn't think about making them available to investigators until he said that, and so we put them on the web site, and it's been helpful."

Here is an overview of how the auditing program works:

• **Selecting protocols.** Auditors query the IRB database for protocols that have received federal or internal funding, an active approval status, IRB approval within the past five years, and have an expected subject enrollment of 10 or more people.

Once these protocols are identified, auditors focus on protocols with moderate to high risk, Dornin-Koss says. "For high risk, we'll look at it with 10 or fewer subjects, but we might choose a minimal risk protocol if there are 300-400 subjects enrolled," she explains. Other criteria considered during audit protocol selection are:

• **Involvement of a gene transfer intervention.**

• **Requirement of periodic review by federal regulations** (e.g., research protocols involving approval by the radioactive drug research committee).

• **Research terminated by the IRB due to failure by the investigator to submit a subject for continuation of IRB approval.**

• **Involvement of multiple study sites.**

Occasionally, the IRB executive committee will instruct the office to conduct 100% audits based on a particular criteria.

"A directive from the IRB executive committee last year told us to do audits on all gene transfer protocols, and we had about 10-15 of these," Dornin-Koss says. "Basically, these are all high risk, and they don't enroll very many subjects."

• **Auditing schedule and table.** The program's goal is to conduct one audit per week, but this will be difficult to attain because the audits are very detailed and time-consuming, she explains.

In preparing an audit table, coordinators will assess eligibility criteria, screening procedures, study procedures, and follow-up procedures.

"We develop audit tables that are specific to each protocol, and we are trying to find a way to do audits that are not so detailed," Dornin-Koss says. "Some of these protocols have 30-40 inclusion/exclusion criteria, and we look at every one of these and every follow-up procedure."

For example, some inclusion criteria may include:

— subject is younger than 18 years of age;

— subject is HIV-negative;

— subject does not have a history of invasive fungal infection within 14 days prior to procedure X;

— subject does not have a history of allergy or intolerance to medications "A," "B," or "C."

— subject is not pregnant or breast-feeding.

"We look at every admission from 1997 forward, if the protocol was in place since 1997," she explains. "We take into consideration if there have been modifications."

Get every step of the audit in writing

• **Selection and notification.** One goal is to have every step of the audit in writing. Researchers are hand-delivered the audit notification that they must sign, Dornin-Koss says.

Audits typically cover 20%-25% of the enrollment of a protocol that has fewer than 100 subjects; for those with 100 or more subjects, about 10% will be selected, she says.

"If it's a for-cause audit, then we do a 100% record review and a 100% informed consent review," Dornin-Koss adds. "We review the entire IRB file and look at when the protocol initially was submitted and look at the timeliness of the investigator's responses to the IRB and if there are any lapses."

When investigators are notified of the audit, they are asked to meet with the auditing coordinator within the next two weeks.

• **Pre-audit interview.** "We like to sit down and have a face-to-face conversation with the investigator or research coordinator or whoever they bring to this meeting," Dornin-Koss says.

At this meeting, which may last 30-60 minutes, auditing coordinators ask who is responsible for which protocol-related activity and how investigators handled subject recruitment. Other questions include:

— Do they have any training programs for their staff?

— Who is responsible for obtaining informed consent?

— What is a description of the informed consent process?

— Where are records stored?

— Who is responsible for storing records and analyzing data? **(See sample pre-audit interview form supplement, inserted in this issue.)**

• **Audit report.** Using auditing forms, coordinators document basic information about protocols, including:

— investigator's name;

— source of funding;

— level of risk;

— abstract of protocol;

— pre-audit interview;

— IRB correspondence;

— number of centers/sites;

— number of subjects enrolled;

"We ask for a list of all subjects enrolled to get unique identifiers and dates enrolled, and we look for any subjects who were enrolled during a lapse of IRB approval," Dornin-Koss explains.

The audit form mirrors the information that the auditors entered into the database after the audit, and includes inclusion/exclusion criteria, study procedures, adverse events, and the last section of the audit report is a description of the research records and study documentation. Altogether, the audit report could be anywhere from 10-50 pages in length, Dornin-Koss says.

• **Identifying problems.** "What we have found is that there is a certain level of background noise in the audits, and you're not going to find everything just perfect," Dornin-Koss says.

When problems are discovered, they are documented in the auditing reports and reviewed by the IRB executive committee, which makes the decision about how these will be handled, she reports. "They'll ask the investigator to respond to the audit and list a corrective plan of action that they're going to do, and it depends on how many mistakes we find throughout the audit," Dornin-Koss explains. "If we find several mistakes, the IRB executive committee might suspend enrollment."

The executive committee, consisting of the IRB chair, four IRB vice chairs, the director of research conduct and compliance, and legal counsel, also decides which problems should be reported to federal agencies, she adds.

• **Reviewing consent forms.** Auditors verify that the documentation of informed consent is performed according to federal policy and according to the university's policies. Files are audited for the following documentation:

— the signature of the subject or of the subject's legal representation;

— the signature of the investigator, who must be a physician investigator in protocols involving drug device or surgical procedures;

— witness' signature;

— dates written adjacent to each signature, in

the hand of the signatory;

— narrative documentation in the case history regarding the informed consent process;

— the research subject's initials on each page of the informed consent document, except for the signatory page.

Auditors also will assess informed consent documents for these items:

— Presence of the IRB approval date in the right hand corner of the informed consent document, along with the renewal date and, if applicable, the date of the most recent protocol modification.

— Utilization of the current version of the IRB approved consent form.

— Consistency between the type and frequency of side effects listed in the informed consent document to those that actually occurred.

— Presence of any extemporaneous modification to the informed consent document.

— Determination that informed consent was obtained prior to the initiation of any research-related procedures.

— Implementation of all study procedures outlined in the informed consent document.

Since the auditing began, there has been considerable improvement in the area of informed consent documentation, Dornin-Koss says.

"When we first were doing audits, we'd see extemporaneous modification of the consent form, and that's something we haven't seen now for a couple of years," she reports.

For instance, in previous years, an investigator might have crossed out the part that reads, "You have four visits," and written in, "You have three visits," and had the subject initial the change.

"That's wrong because every modification to the protocol has to have prior approval from the IRB, and the only exception is to avoid an immediate hazardous research incident to subject," Dornin-Koss explains.

• **Other audit goals.** "What we like to see is if the investigator has copies of all IRB correspondence and copies of correspondence with the sponsor," she says.

"We like to see if they have a status data safety monitoring board; we'd like to see the minutes of that," Dornin-Koss adds. "We like to see a section on training, and our university has implemented requirements, so we have our own computer-based training module that everyone involved in human subjects research is required to complete."

So every protocol submitted to the IRB must be checked to see if the investigator has completed the education.

Protocols that use drugs or medical devices must have records of receiving drugs and dispensing drugs and devices. This accountability should be a standard practice, Dornin-Koss says.

"We have an investigational drug service as well, and they do audits also," she adds.

• **Education and training.** None of the auditing forms are copyrighted, and they can be viewed by anyone who is interested in seeing how the university's auditing program works at the web site: www.rcco.pitt.edu.

For example, here is a list of the links to audit SOP forms:

— protocol selection;

— audit notification;

— selection of research subject records;

— preparation of protocol timeline;

— preparation of audit tables;

— pre-audit interview;

— review of investigator's consent form documents;

— review of research participant records and source documentation

— review of regulatory file;

— test article accountability;

— review of electronic records;

— audit report;

— reporting of serious noncompliance.

Then there are further links to the informed consent process SOPs:

— observation of informed consent process;

— investigator interview;

— subject evaluation of informed consent process;

— subject interview;

— audit of consent form for 24-hour adverse event contact information. ■

Should IRBs standardize payments to subjects?

Payments to research subjects is common practice, but a recent report appearing on the abcnews.com web site raises the question: When does the payment become coercive? Clearly some research subjects volunteer because of compensation. Take Bob Helms, for example, the subject of the abcnews.com story and author of *Guinea Pig Zero,* a book detailing

his and others' experience as research subjects in clinical trials. By his own admission, he volunteered for clinical trials as a way to make extra money. His case may be extreme, but it does raise interesting questions, such as when is compensation appropriate and how much is too much?

Federal guidelines do not address the issue of compensation other than to state that IRBs must determine "whether the rewards offered for participation in research constitute undue inducement."[1]

Compensation matters need more review

"Most research involves some kind of compensation for the time and inconvenience that goes into it, particularly in drug development research," says **Greg Koski**, MD, PhD, director of the Office for Human Research Protections' Department of Health and Human Services in Rockville, MD. "Clearly, if you offer people money to do something they would not otherwise do, and if it's large enough, it could be coercive. What IRBs have to do is to consider what is appropriate compensation. It's an area where there could be further development."

Koski explains that most institutions have established guidelines concerning what's appropriate. For example, subjects submitting to simple blood draws may be compensated $10-$25.

Marc Rogers, PhD, associate professor of kinesiology at the University of Maryland and co-chair of the university's IRB, says that his institution's IRB does not have formal guidelines. Decisions regarding compensation are made on a case by case basis. "Typically, the payment is determined by the principal investigator [PI] based on whether the project is funded or not," he explains.

"We have never, to my recollection, ever said to a PI that the remuneration was excessive," Rogers says. "Usually, payments for the types of projects that we review are small — $15-$25 per study or per visit to a lab for testing. One project, the subjects were paid $700 for an experiment that lasted 12 months and required multiple visits to a lab for testing and three times per week for exercise training over that time."

He says they have also had several vaccine studies that paid participants $150-$220, "but again, the investment in time for the subjects is substantial in terms of visits to the lab, collection of biological specimens and filling our diaries, etc.," Rogers explains.

Cincinnati-based Schulman Associates' IRB has requested that PIs reconsider their payment plans in research involving children where they thought payments were excessive, explains **John Isidor**, JD, CEO, Schulman Associates IRB and a member of *IRB Advisor*'s editorial board. Another area where they have requested changes is in the area of compensation for screening visits.

"Sometimes for screening visits, principal investigators want to pay for completion of the screening visit only if candidates qualify for the study. We think it's inappropriate and ask them to reconsider," Isidor says. He explains that in all cases the PI does indeed change the compensation amount or parameters.

Kaiser Permanente Center for Health Research (KPCHR) views its research participants as volunteers and instead of compensating them for the value of their time, KPCHR seeks to "recognize" participants for their spirit of volunteerism.

"Part of our mission is to produce new knowledge, so it's part of the social contract [with Kaiser members] to be open to public domain research," says **Mark C. Hornbrook**, PhD, associate director. "What we're finding is people like to be recognized for what they are contributing, and birthday reminders, personalized thank-you notes, T-shirts, pens, coffee mugs all say, 'You're part of something important.'" For long-term studies, Kaiser may sponsor lunches and reunion parties to keep participants tied in.

Financial incentives are offered by Kaiser, but Hornbrook stresses that the amounts are modest, in the $15-$20 range. These "thank-you gifts" typically are in the form of gift certificates.

Kaiser's IRB does not have established guidelines regarding the types or amounts of incentives awarded to participants. "We try to recognize that every research project has different needs and comes from a different field. We look at it and say, 'What's appropriate for the kind of people who are going to be approached?' We always want to make it very clear that gifts should not be overwhelming, rather they should be modest and symbolic."

Regardless of the form of the remuneration, Isidor stresses that compensation to study subjects should be based on time and inconvenience and not risk related to the study.

"You should never base compensation on risk level," says **Ernest Prentice**, PhD, associate vice chancellor for academic affairs and co-chair of the University of Nebraska Medical Center (UNMC) IRB. "I think you're really getting into trouble when people enroll just to get compensation. The

more risky the study, the more the compensation would be, and the more enticing."

Compensation for time, effort acceptable

The UNMC IRB considers compensation acceptable if it's based on time and effort required of the research participant, Prentice explains. "It is not acceptable if it's based on risk levels of a protocol. We look at how much time is devoted to a procedure, travel time and post-procedure periods." For example, if a patient were to undergo a bronchoscopy, he or she would likely experience residual effects, so the UNMC IRB would allow that they be compensated for that.

"We will not base compensation on risk; we think that's coercive. We try to use a fair-market wage so that we'll compensate so many dollars per hour of time required of the research subject," he adds.

To that end, UNMC's IRB is establishing compensation guidelines. "We found that we were inconsistent and we found ourselves constantly debating on whether a compensation was reasonable. The pendulum swung from meeting to meeting," Prentice says.

The guidelines, which have not yet been finalized, will include a list of procedures and associated fees based on a rate of about $10 per hour. "We're basing compensation on a list of procedures such as routine blood draw, physical exam, and CAT scan, etc.," Prentice explains. "We have some general guidelines in terms of total compensation not exceeding $1,000 without significant justification," but individual procedures will be assigned a dollar amount, and principal investigators will be asked to adhere to the guidelines.

References

1. Office of Human Research Protections. *Protecting Human Research Subjects: Institutional Review Board Guidebook.* Rockville, MD: Office of Human Research Protections; 1993. ■

UM takes proactive training approach

Human subjects protections classes taught weekly

The University of Miami last year launched an education program designed to inform and instruct researchers and IRB members on the protocols and regulations that impact human subjects research.

The program, called the Human Subjects Protections Educational Program, is the brainchild of Dr. Norman Altman, vice provost for research at the university, and **Jay Sosenko**, MD, professor of medicine, assistant provost for research standards, and former university of Miami IRB chair.

"When you have worked in an IRB setting, it becomes clear that human subjects protections education is very important," says Sosenko. "We wanted to try to have a broad outreach to our academic committee to better educate individuals at the university and also raise consciousness in the area of human subjects research protections.

The one-hour seminars have covered everything from the nuts and bolts of how to prepare research applications to be submitted to the IRB to ethical issues to data safety monitoring. All seminars are taught by university staff and are sponsored at no charge to participants or the university. "When I surveyed individuals working at the university, I found that there are a number who have expertise in the area of human subjects research protection," he says.

Instructors have varied backgrounds

IRB chairs, staff ethicists, IRB members, and attorneys have taught seminars, says Sosenko. "One of our surgeons led a seminar on standards of care and experimentation, with an emphasis on defining the boundaries between innovation and experimentation. One of our psychologists talked about the inclusion of students and employees as research subjects." Sosenko goes on to say that an HIV expert came in to talk about HIV research, and a faculty member who also serves on the National Bioethics Advisory Commission reported on its findings.

The seminars are held on campus each week, and attendance is voluntary. Since the program's inception, nearly 500 people have attended seminars, with each session averaging 15 participants. Sosenko stresses that the seminars are interactive, not lectures, so discussion is welcome. Past seminars have included "IRB: Behavioral Submissions," "IRB: Responsibilities of the Principal Investigator," and "Placebos, Parts I and II."

One of the most well-attended sessions was a five-week series on working with IRBs. "The idea was to try to give people, in a more practical way, some idea of how it all works," says Sosenko. The topics ranged from responsibility of the principal investigator to the proper way to obtain consent to forms, what kinds you need, and how to properly fill them out. ■

Special series: IRB Software for the Millennium

Georgia Tech designs on-line software for IRBs

Software permits complete system integration

The electronic race is on to develop an easy-to-learn and practical software that will help IRBs run more efficiently.

While homegrown electronic systems worked well in the past, many IRBs now are finding that these are too cumbersome or inefficient as the IRB's responsibilities and research needs grow.

"We're reviewing more and more studies every year, and when I started researching different software programs out there, I realized that they were able to offer a lot more than our current system does," says **Dana Susa**, MS, CIP, IRB administrator with the LeeCoast IRB in Fort Myers, FL.

Susa has collected business cards at research conferences and followed up with calls to software companies. While the IRB has not yet decided which software to purchase, the decision likely will hinge on how easily the system can be installed, how well it has been tested, and how much it costs, Susa says.

"I think we've narrowed down our decision to between two systems, but we also have the option of updating our homegrown system, which has worked well over the years," Susa says. "In my opinion, it's worth going ahead with a regular software program when you consider the amount of time and money spent to upgrade the current system."

A major reason for an IRB to invest in management software systems is to help the IRB staff eliminate much of the paperwork and minor details that keep them from focusing on their role in protecting human subjects. So while a software system might not enable an IRB to reduce staff positions, it will help the IRB make better use of the staff's time, suggests **Scott Sherrill**, software team lead for AIST at Georgia Institute of Technology (Georgia Tech) Research Institute in Atlanta, which has recently launched its own IRB software system called IRBWISE.

IRBWISE is a completely integrated, on-line system that supports on-line submission of applications, renewals, modifications, IRB meeting agendas and minutes, and assignment of reviewers. It has been under development since 2000 and now is fully in operation for research conducted at the institute.

"We decided to design our own system because we did not feel there was a product available on the market that met the needs of our IRB," Sherrill says. "We wanted to design a totally on-line IRB management system."

The paper trail that IRBs follow is time-consuming and limiting, he notes.

"In this day and age, we felt like the goal for all users of the system would be that they should be able to access the system anywhere, and they should be able to do their job at work or home or wherever they might be," Sherrill says.

Georgia Tech's IRB has been using the system since February, but the software designers always had a bigger goal in mind. "We built it with the idea in mind that it might have use in other universities," Sherrill explains.

So far, Georgia Tech's IRB and research community have found that the software makes the IRB process faster and more efficient, says **Barbara Henry**, manager of research compliance.

"We've got a system that allows us to manage protocols so much more effectively and efficiently than we were able to do before," Henry says. "It's like having another person on staff in many ways."

Here's a look at how IRBWISE works:

• **Efficiencies, including automatic agenda lists.** The software has helped the IRB make all

In this issue of *IRB Advisor*, we will begin a special series on IRB software and how it is being used to make the jobs of IRBs easier, better organized, and to improve quality. This month, there is a profile of IRBWISE, designed by the Georgia Institute of Technology in Atlanta. Look in future issues for profiles of PRO IRB by ProIRB Plus Inc. of St. Petersburg, FL; iMedRIS by iMedRIS Data Corp. of Yucaipa, CA, and others. ■

processes automatic, including having agenda items immediately listed on the electronic agenda form and skipping the paper route, Henry says.

"It automatically generates minutes," Henry says. "And by doing minor keystrokes, we can enter things into the agenda and place items on different agendas."

For example, once information about a protocol or IRB meeting is put in the computer, it can be easily copied to various agendas and schedules, she explains. "Flexibility is very important, and having to not re-key information is wonderful."

The system handles time-consuming details, such as generating expiration notices and sending them by e-mail. It can send reminders to investigators to make certain they get their applications in for renewal on time, and sends out approval letters that indicate the type of review that was done and that approval was granted, Henry says.

Another major timesaver to the on-line software is that researchers will electronically send their protocols directly to the IRB. Some principal investigators (PI) have followed the on-line process without any training, but others will be given instructions on how to submit their protocols electronically and follow them on-line.

"At Georgia Tech, we have a lot of computer-savvy principal investigators, but there will be one or two who don't want to use a computer system, and we'll be glad to accommodate them with the same old paperwork we had before," Henry says.

However, the reception so far has been very positive, she adds. "We find most folks are able to log on and put in a protocol with no problem."

So far, there has been an open house to introduce the software to interested parties, and there was a special training session for IRB members.

• **Privacy and security.** "Anybody with a user name and password can access the system at the principal investigator level," Sherrill says. "If someone needs a higher level of privileges, then there is a tool we build into the system so that the IRB administrator can assign a higher level of privilege to the people who deserve that."

Since Georgia Tech is involved in department of defense research, a chief concern was to make the system as secure and private as possible. "That's why it's a 128-bit encryption with secure socket layer [SSL] in order to provide security as far as people being able to access it from outside," Sherrill says.

PIs can access from their home computers, as can anyone with an account with the system, but they are allowed only to see the protocols with which they are associated, Sherrill adds.

"Beyond that, security is handled by the IRB administrators themselves," he explains. "Details of protocols and things of that nature are restricted to board members and administrators, who assign the level of privilege."

• **Modifying forms.** Once a PI has submitted the protocol to the IRB and it is signed off on, then the original version of the form is frozen and can't be changed.

"If the PI realizes he wants to change something, or if a change is required by the IRB administrator, then it can be returned to the PI and modified," Sherrill says. "We maintain a history of every keystroke in the system, so we could say what the protocol looked like before and how it was changed."

Also, if a PI wants an amendment or modification to the approved protocol, it can be done with a prompt review and consideration by the board, he adds.

E-mail notification enhances system

• **IRB action.** The system works in a logical fashion so that whenever an action is taken, the next step of action is automatically triggered through e-mails or in-box notifications or whatever else is needed, Sherrill says.

For example, when a board member is assigned to review a protocol, an e-mail is sent to the board member along with a link directly to the protocol. When the board member logs on to the system, there will be a message in the in-box indicating that this protocol is on the to-do list, Sherrill says. "The goal is to keep the in-box empty, showing that you've done every task assigned to you."

The IRB administrator can easily append or change a message before it is sent out, and the customized e-mail is saved as part of the history of the protocol, Sherrill says.

"We defined the messages that we want to go out on a cue automatically, based on the feedback from a focus group," Sherrill says.

• **Web site and server.** Sherrill says the IRBWISE system was designed to work as a standalone application, but also is fully integrated within the university's WEBWISE system, which contains all administrative and contractual tools.

The system soon will be tested at other universities, which will need to set up their own web sites to support the system.

"It could be hosted from Georgia Tech, but

there'd be performance issues, so we expect the local universities to host it," Sherrill says. "We tried to build it in a way that it would fit within the normal expectations of the IT [information technology] personnel within the university."

[Editor's note: For more information, contact Scott Sherrill, Software Team Lead, Georgia Tech Research Institute, O'Keefe Building, Suite 139, Atlanta, GA 30332. Telephone: (404) 894-1190; e-mail: scott.sherrill @gtri.gatech.edu. Web site: www.irbwise.com.] ■

SPOTLIGHT ON COMPLIANCE

COE: Don't panic! Review compliance guidelines

By **J. Mark Waxman**, JD
General Counsel
CareGroup Healthcare System
Boston

The Office of Human Research Protections (OHRP) is the Department of Health and Human Services (HHS) agency chiefly responsible for compliance activities in human subjects research. OHRP is the agency that evaluates noncompliance with either the applicable regulations or any aspect of the Assurance of Compliance that must be submitted by entities receiving federal funds for human subject research.

The principal means by which OHRP investigates possible violations is a Compliance Oversight Evaluation (COE). A COE is designed to determine the factual basis for any allegations or indications of noncompliance. Absent a situation where "sound ethics" dictate a need to act immediately, advance written notice of a COE is provided and the institution is allowed to submit detailed information directed to the specific allegation being made.

Though the information provided (and the allegation) will be treated confidentially while the investigation is pending, once the COE has been completed and a determination letter is issued, that letter will be made accessible on the OHRP web site shortly, within 10 days, after its issuance to the institution.

Once the determination is made to initiate a COE, OHRP may communicate directly with investigators in addition to the institutional personnel. It is OHRP policy where an allegation involves a specific individual to notify that individual directly.

Following receipt of the responsive report concerning the allegation at issue, OHRP will determine whether more information is required, and where appropriate, conduct in-person or telephone interviews. As this process goes forward, the quality of the Assurance of Compliance filed by the institution is also being evaluated.

If a COE determines that a violation of the regulations has occurred, there are several types of actions that may follow, all principally designed to bring the institution into compliance and protect human subjects, which include:

- Development and implementation of a plan of correction.
- Mandated improvements to the Assurance of Compliance to enhance processes designed to protect human subjects.
- Restricted approval of an Assurance of Compliance, allowing affected research projects to continue to be supported only if the restrictive terms are being satisfied (e.g., requiring prior OHRP review of some or all research projects, requiring special education for IRB members or research administration personnel).
- Withdrawal of approval of the Assurance of Compliance, thereby effectively shutting down all research activities.
- Suspension or permanent removal of the right of an institution or researcher to participate in specific projects.

In extreme cases, OHRP may recommend to HHS that the institution or individual be subject to "debarment," an order declaring them to be ineligible to participate in HHS-sponsored research. It is noteworthy that these compliance steps are similar to those an IRB may take when IRB requirements on a research project have not been met.

One of the interesting questions institutions face when individuals are the subjects of OHRP review that determines that a violation has occurred is the extent to which other disciplinary processes within the institution are implicated. Specifically, two questions may arise:

- Is the peer review committee at the hospital to be notified and the matter processed there?
- Has there been a violation of the institution's

rules such that "employee" discipline should be involved?

If no policy or guidance is provided, then such policies should be considered and created. Because of the overlap between confidentiality and patient protection requirements with employment and peer review processes and protections, these policies should pay close attention to ensure all of the necessary institutional and regulatory privileges and requirements are considered. ■

NEWS BRIEF

Training CD-ROM designed for IRBs

Institutions with OHRP-approved FWA (federalwide assurance) or MPA (multiple-project assurance) can receive *Investigator 101,* a new CD-ROM training program at no cost.

The tool, developed by Public Responsibility in Medicine and Research (PRIM&R), incorporates a number of interactive features, including videos, slide presentations, ethical and research guidelines, and federal regulatory documents, to deliver guidelines on conducting human research and protecting human subject. There also is a search engine and note-taking function. The CD-ROM operates on both Macintosh and Windows platforms.

Non-FWA or MPA nonprofit entities can purchase Investigator 101 for $1,200 per copy. For-profit organizations will pay $3,000 per copy. For additional information, contact Rebecca Leroux at (617) 423-1185 or visit the web site at http://ohrp.osophs.dhhs.gov. ■

CE/CME objectives

The CE/CME objectives for *IRB Advisor* are to help physicians and nurses be able to:

- establish clinical trial programs using accepted ethical principles for human subject protection;
- understand the regulatory qualifications regarding human subject research;
- comply with the necessary educational requirements regarding informed consent and human subject research;
- apply the necessary safeguards for patient recruitment, follow-up, and reporting of findings for human subject research;
- have an understanding of the potential for conflict of financial interests involving human subject research;
- understand reporting adverse events during research. ■

IRB Advisor (ISSN 1535-2064) is published monthly by American Health Consultants®, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodical postage paid at Atlanta, GA 30304. POSTMASTER: Send address changes to **IRB Advisor**, P.O. Box 740059, Atlanta, GA 30374.

American Health Consultants® designates this continuing medical education activity for up to 15 credit hours in category 1 toward the Physician's Recognition Award of the American Medical Association. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

American Health Consultants® is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

This continuing education offering is sponsored by American Health Consultants®, which is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation. Provider approved by the California Board of Registered Nursing, provider number CEP 10864, for approximately 18 nursing contact hours.

Subscriber Information

Customer Service: (800) 688-2421 or fax (800) 284-3291, (customerservice@ahcpub.com). Hours of operation: 8:30 a.m. - 6 p.m. Monday-Thursday; 8:30 a.m.- 4:30 p.m. Friday.

Subscription rates: U.S.A., one year (12 issues), $299. With CME: $299. Outside U.S., add $30 per year, total prepaid in U.S. funds. Two to nine additional copies, $269 per year; 10 to 20 additional copies, $239 per year. For more than 20, call customer service for special handling. **Back issues**, when available, are $50 each. (GST registration number R128870672.)

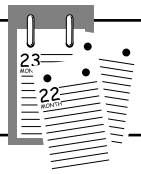
Vice President/Group Publisher: **Brenda Mooney**, (404) 262-5403, (brenda.mooney@ahcpub.com).
Editorial Group Head: **Lee Landenberger**, (404) 262- 5483, (lee.landenberger@ahcpub.com).
Managing Editor: **Alison Allen**, (404) 262-5431, (alison.allen@ahcpub.com).
Production Editor: **Nancy McCreary**.

THOMSON
AMERICAN HEALTH CONSULTANTS

Editorial Questions

Questions or comments?
Call **Alison Allen** at (404) 262-5431.

CALENDAR



• **Innovation, Inclusiveness & Informed Consent: Current Challenges for Institutional Review Boards & Researchers — May 13-14, 2002.** Hubert H. Humphrey Center, University of Minnesota, Minneapolis. Cosponsored by the Office of Human Research Protections, Department of Health and Human Services, Department of Veterans Affairs, and Department of Food and Drug Administration. For more information, go to web site at http://www.research.umn.edu/subjects/conference/.

• **Good Clinical Practices for Clinical Investigators — June 20-22, 2002.** Association of Clinical Research Professionals, Seattle. For more information, go to web site at http://www.acrpnet.org. ■

CME*questions*

Please keep your issues in order to take the CME tests given in June and September. A Scantron will be inserted in those issues, but the questions will not be repeated.

[For more information on the CME program, contact American Health Consultants at (800) 688-2421.]

13. Federal guidelines require that payments to research subjects:
A. not to exceed $100.
B. not be in an amount that would entice subjects to participate.
C. be any amount deemed appropriate by the principal investigator.
D. be established by IRBs.

14. Which of the following is not an example of inclusion criteria that may be included in a table designed to assess and audit protocols:
A. subject is younger than 18 years of age.
B. subject is HIV-negative.
C. subject does not have a history of invasive fungal infection within 14 days prior to procedure X.
D. all of the above

15. Which of the following describes a good reason for IRBs to conduct thorough and continual internal audits of protocols?
A. By having an internal auditing program an IRB may be exempted from FDA and OHRP audits.
B. An internal auditing program is the one truly effective way for an IRB to effectively and efficiently investigate research problems.
C. An internal auditing program can be done inexpensively.
D. all of the above

16. If a Compliance Oversight Evaluation determines that a violation has occurred:
A. research must stop immediately.
B. the principal investigator must undergo peer review.
C. a plan of correction may be requested.
D. the principal investigator and institution are automatically subject to debarment.

SOP #: I-A-6
SOP Area: Investigator Site Audit
University of Pittsburgh
Education and Compliance Program RCCO

Standard Operating Procedure
Pre-Audit Interview

1. PURPOSE

To define the procedures necessary to prepare for and conduct a pre-audit interview.

2. SCOPE

This procedure applies to all investigator audits performed by the Education and Compliance Office.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for preparing for and conducting pre-audit interviews for each audit performed.

4. PROCEDURES

4.1. A pre-audit interview is to be held prior to the conduct of an investigator site audit with a member or members of the respective research staff.

This interview is performed to identify the names of individual(s) responsible for various protocol-related activities, such as:
- preparing IRB protocol submissions;
- obtaining informed consent;
- recruiting study participants;
- reporting adverse events;
- maintaining study documentation;
- analyzing study data.

4.2. During the pre-audit interview, information is also obtained regarding:
- number of subjects screened and enrolled into the study;
- number of sites involved, if the study is multicenter;
- occurrence of adverse events;
- occurrence of site monitoring visit(s);
- presence of data and safety monitoring plans;
- difficulties in subject recruitment or in study conduct.

4.3. The pre-audit interview is to be utilized as an opportunity to clarify any questions or issues that the Education and Compliance Coordinators may have regarding the conduct of the study.

5. REFERENCES/DOCUMENTATION

Attached example of pre-audit interview form.

SOP #: I-A-3 Version # 1
SOP Area: Investigator Site Audit

Signature: _____ Date:_____
Director, Research Conduct and Compliance Office

SOP #: I-A-6
SOP Area: Investigator Site Audit
University of Pittsburgh
Education and Compliance Program RCCO

Standard Operating Procedure
Pre-Audit Interview

IRB # _____ QA# _____

Principal Investigator _____

Previous Principal Investigators _____

Study Coordinator_____

Previous Study Coordinators _____

Number of subjects screened to date: _____ Number of subjects enrolled to date: _____

If multicenter, number of centers: _____ Number of multicenter subject enrollment: _____

Procedure	**Responsibility / Comment**
IRB Submissions	
Recruitment Measures Advertising	
Screening	
Informed Consent	
Randomization	
Physical Exam	
Blood Draw Lab Used Blood Storage	
Questionnaires	
Record-Keeping Regulatory Records	
Storage of Records	
Drug Accountability	
Data Security	
Data Analysis	
Data monitoring	
Staff education	

Source: University of Pittsburgh.