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Improve SAE reporting via electronic submission

Reduce unnecessary reports

One of the bigger headaches for IRBs is having to sift through hundreds or thousands of unanticipated problems submissions when most of these should never have been reported.

The Human Studies Committee at Washington University School of Medicine in St. Louis, MO, has developed an electronic submission process that has reduced this problem. Without the system, the IRB reviewed in 2003 more than 11,000 submissions of unanticipated problems, deviations, etc., says **Diane Clemens**, DC, CIP, manager of research.

"This is a problem in the IRB realm where we've historically gotten inundated with a lot of reports we didn't need to see and which should have just been reported to sponsors," Clemens says.

Thanks to the system's screening and review process, the IRB reviewed 6,664 fewer unanticipated problems than the previous year, a 60 percent drop in volume, Clemens says.

The first person to see the unanticipated problems that have made it through the screening process is one of the four reviewers — all of whom are RNs, Clemens says.

However, if the event is a death, it is automatically routed to the IRB chair, she notes. Previously, unanticipated problems submissions were reviewed by four volunteer sub committees, each consisting of 20 people who met once a month, so the implementation of the electronic system and change to staff reviewers is a more efficient and effective process because these individuals do reviews every day, Clemens says. (See story on how review process works, p. 9.)

"We've seen such a drop in the review volume because the system will screen out external events that do not cause a change in the protocol or consent or increase the risk to participants," Clemens says.

Here's how the system works:

- All initial serious adverse events (SAEs) go through the electronic system.

All initial SAEs go through the electronic system, where they are divided between internal and external SAEs, Clemens says.

"We still have a significant number of SAE follow-up reports that

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are submitted on paper, some 3,619, but these are dwindling," Clemens notes.

Investigators have access to the system and log in, following on-screen directions for reporting SAEs and other events, she says.

The on-line prompter will ask the investigator whether the risk to participants increased, whether there is a change to the protocol, and

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Editorial Questions

Questions or comments?
Call **Leslie Hamlin** at (404) 262-5416.

whether or not subjects need to be notified of additional risk, Clemens explains.

"Typically, we see if it's a long-term risk that's identified, then the participants need to be contacted," Clemens says. "If it's something where after the first dose you are at increased risk for this reaction, but all people taking it at our site have already taken the first dose, then the need to contact them is no longer there because they're no longer at risk."

When investigators log on, they'll see a screen that has a list of all of their studies, both open and closed. They select which study the report pertains to and the next screen asks them to identify the type of submission they will make, Clemens explains.

"The initial page will give the specific item, unanticipated problems, external SAEs, a follow-up report, data monitoring report, a deviation, and we have another problem section," Clemens says. "The most common thing we see is submission of unanticipated problems."

Investigators select the correct path and follow-it through the electronic process.

For instance, for unanticipated problems, the process requests information about the timing of the event, and the system will calculate whether or not the submission is being made within the appropriate time frame, based on reporting guidelines that are pulled from the regulations, Clemens says.

The idea of this lengthy screening process is to assess these reported incidents against a very narrow definition of what needs to be submitted to the IRB, and these are consistent with the recent guidance released by the Office for Human Research Protections, Clemens says.

- System establishes criteria for what should be reported.

The Web page following the prompt about time frame is the screening tool, which helps investigators determine whether or not the event they are considering reporting truly needs to be reported, Clemens says.

The screening form outlines three criteria to determine whether something is an unanticipated problem or serious adverse event that requires submission to the Human Studies Committee and the Office for Human Research Protections, as follows:

- The event is serious;
- The event is unexpected;
- The event is reasonably related to the research.

If all three criteria apply, the investigator is directed to continue with the submission, and if they do not, then the investigator is told that the event does not meet the institutional requirements for reporting and should exit the system.

Since investigators often report events not meeting these three criteria to the IRB per instructions from sponsors, the next prompt also says, "If the Sponsor of the study is asking you to notify the IRB of an event that does not qualify for reporting, please send the following letter to the Sponsor as notification of our review policy."

The investigator could click on the prompt for an SAE review policy screen and print a ready-made letter to send to the sponsor.

The screening page also includes definitions of the criteria for investigators who are uncertain of whether their events qualify. For example, the definition states that an event is serious if it adversely alters the relationship between risks and benefits and includes events that either result in or require intervention to prevent the following:

- Inpatient hospitalization or prolongation of hospitalization;
- Life-threatening reactions;
- Result in persistent or significant disability/incapacity or permanent harm or disability (either physical or psychological);
- Jeopardize the subject;
- Congenital anomaly/birth defect in the offspring of research participant;
- Breach of confidentiality that may have a negative consequence;
- Death.

"Part of our system that's pretty nice is it's set up as a split screen with guidance to investigators on one side," Clemens says. "And on the other side of the screen they're working on questions we're asking them."

If an event meets all three criteria, then the investigator is given a link to a directory of events. They can choose whether it's related to allergy/immunology, general cardiac, etc., she says.

"Then there's a find button and it pulls up all the terms related to cardiac, for example," Clemens adds.

The idea is that the system limits the numbers of terms and helps investigators keep better track of events that have occurred in a study, linking them together as needed, she says.

"It provides some consistency and is especially helpful if you have several different coordinators who may be entering SAEs for one particular study," Clemens explains. "What the system will do is track the number of incidences of a particular event and calculate the percentage of occurrence based on the number of participants."

- Investigator adds pertinent information.

The electronic system's next prompt is for simi-

lar SAEs that have occurred at this institution, as well as other institutions, Clemens says.

"There may be events that are not exactly the same, but they have a similar process, or they maybe somewhat linked to this event," she says. "Also, the investigator may have gotten reports from other institutions, which are not something he had to submit to us, but it may be good information to have."

Likewise, the system asks investigators to provide additional comments, including descriptions of related events. For example, there could be a different study using the same drug, resulting in an unanticipated event in a different population, but the metabolic process could be the same, Clemens says.

"Investigators have the flexibility to elaborate on what has happened, which is extremely beneficial for our review," Clemens says.

Then the system asks for information about when the SAE occurred and when the principal investigator was notified of the event, and that tells the system whether the report is made within the appropriate time frame, Clemens says.

The next thing the system asks is what changes need to be made in light of the event, including possible changes to the informed consent form, changes to the protocol, and if these are changed they are sent to the IRB in attached Microsoft Word documents, she says.

"We have received reports from investigators saying, 'I intend to revise the consent form and I will submit it at a later date,'" Clemens notes. "The event is reported on time, and we've reviewed and considered it, but we'll hold it open until we receive the final piece of the revised consent form."

If an investigator chooses not to revise the consent form, he or she is asked to provide a rationale for why the change is not needed, Clemens adds. ■

When to inform about subjects' threats is unclear

Weigh laws, confidentiality, and severity of threats

Public health researchers studying sensitive issues — suicide, domestic violence, drug use — sometimes find themselves dealing with more than just the survey questions at hand.

In the course of interviews and surveys, they may learn about threats affecting third parties or participants' suicidal urges.

What is a researcher's duty to inform someone about these threats, which are not the direct

result of research but are uncovered by it?

David R. Buchanan, DrPH, a professor of community health education at the University of Massachusetts, Amherst, MA, says the answer isn't as clear-cut as one might think. Laws governing mandatory reporting are vague and vary widely from state to state. It's hard for a researcher conducting a simple survey to know how serious the threat might be. And reporting such information raises as many ethical problems as it potentially solves, since it breaches promised confidentiality to research participants.

Buchanan worries that IRBs are increasingly inclined to simply turn down proposals for this type of research, rather than wade into the murky legal and ethical issues involved.

He tells the story of a researcher he knows who was doing a longitudinal study of Vietnam veterans, one of whom committed suicide during the course of the study.

"Was that her responsibility?" he asks. "Nonetheless, the IRB shut down the research."

Buchanan says incidents such as this have made some researchers reluctant to discuss the ethical quandaries involved in handling non-research related risks for fear of drawing even greater IRB attention to it. But he believes a thorough airing of the problem is necessary, in part to show IRBs that the risks are small and shouldn't hamper important studies.

In a paper published in the *Journal of Public Health Policy*, he notes that public health researchers have a duty to study leading causes of morbidity such as suicide, homicide and AIDS, which can lead them to work with high-risk populations.

He argues that researchers doing simple surveys and observational studies have limited contact with participants, and aren't in a position to gauge the severity of threats. So, he says it makes no sense for an IRB to deny a proposal based on concerns the researcher and institution might later be sued.

"Is it reasonable to put a burden of a duty to warn on researchers, or post hoc hold them liable, when any reasonable person would say there's no way they could have anticipated (a violent act)?" he says. "If it's not reasonable to expect that a researcher could have anticipated this event, then they should not be held to some standard of a duty to warn."

Buchanan says he first became concerned about the issue of non-research-related risks when he was working on his doctoral dissertation.

He distributed a confidential, but non-anonymous survey questionnaire to a group of adolescents asking about their future intentions to engage in risky behavior such as smoking marijuana. He says that one respondent crossed out one item in the list and wrote in the words "commit suicide."

"I was really torn about what to do," he says. "And I did go talk to a school counselor who, ironically, just shrugged his shoulders and said, what you do you think?"

Buchanan says public health researchers can discover other similar threats to health and safety in the course of conducting studies. The researcher may see an HIV-positive subject sharing a needle with someone he knows to be HIV-negative. A participant in an interview about contraceptive practices could express his intention of beating his partner because he suspects she is unfaithful.

Buchanan had written other articles examining these issues, and a few years ago was invited to participate in a workshop sponsored by the National Institute of Drug Abuse. There he found a number of researchers dealing with the same sorts of questions.

"They were all wrestling with it individually, wrestling with their individual conscience, and deathly afraid of calling further attention to it," Buchanan says. "Because, particularly these days, of the potentially chilling effect it could have on this research."

"But that seems to me to be the wrong direction to take," he says. "Right now, with less known about these issues, the fears are probably overstated and exaggerated. It is an exceedingly rare occurrence. We could do a good job of just documenting the things that could happen and documenting the circumstances in which they're going to happen, if people would be willing to talk about it."

Laws vary, are unclear

Legally, researchers and IRBs confronted with a non-research-related risk must consider several issues:

- Mandatory reporting laws, which vary from state to state, both in terms of who is covered and what kinds of threats they must report. Buchanan says that because these laws tend to cover those health personnel delivering care, it can be confusing as to whether researchers must report threats.

"Say a nurse is doing an interview," he says. "As a nurse, they're a mandatory reporter, but as a researcher are they?"

- The researcher's (and the institution's) liability in the event the threat is carried out. The 1974 case most often cited as laying out a duty to inform is *Tarasoff v. the Regents of University of California*, in which the California Supreme Court ruled that a psychiatrist should have breached doctor-patient confidentiality to warn a woman that his patient intended to harm her. The woman was later murdered.

Buchanan points out that in the wake of *Tarasoff*, psychiatrists have been found to have a poor track record in correctly predicting a patient's violent episode. He says a researcher with more limited contact to a subject could be expected to have even less success in correctly gauging the threat the subject poses.

- Informed consent assurances of confidentiality. If there are circumstances under which confidentiality may be breached, the subject must be informed ahead of time in the consent document.

From an ethical standpoint, Buchanan says the researcher's duty to inform hinges on how much he or she knows about the seriousness of the threat. The researcher must weigh that risk against the potential harm involved in breaching confidentiality.

He says that if a researcher's contact with a subject is sustained and in-depth, it might be reasonable to assume that the researcher would be able to make an informed determination about how serious the threat is. But if the subject is merely filling out a questionnaire and handing it in, the researcher wouldn't be in a position to make that judgment.

Ways to assess true risk

Buchanan argues that IRBs reviewing studies that raise questions about non-research-related risk should consider the same question: Will the researcher be able to gauge the seriousness of the threat? If not, it's unlikely he or she could be held legally liable, and so the research shouldn't be hindered.

He suggests other steps that could help in reviewing these types of studies:

- Assessment tools for threats such as suicidality. Buchanan says the tools currently in use have improved to the point where they can be useful in a survey setting.

"You can build into protocols these triggering questions," he says. "If somebody responds 'yes' to the question, then ask the following two questions. If they say 'no,' then skip to the next section."

- Informed consent documents that spell out

under what circumstances confidentiality would be breached.

"Basically, it's the same rule of thumb," he says. "If, in assessing the instruments that are going to be used, it looks like the researcher is likely to gain sufficient information that they can make a better than 50/50 assessment that some adverse event is likely to happen, [the IRB] should definitely stipulate that the researcher has to put that into the informed consent:

'Under the following circumstances, we will take actions to try to prevent harm.'"

- Necessary training to ensure staff safety. In addition to participants, IRBs also should consider the possibility that research staff may be exposed to threats because of their involvement in a study, Buchanan says. He says savvy investigators already make sure that staffers who deal with high-risk populations get additional training.

"It's certainly a concern among researchers in the drug world," he says. "I do think that's something that should be pretty routinely required of any research project that's doing field research with potentially dangerous populations."

Buchanan hopes to see the public health research community come up with its own set of criteria for evaluating possible harms encountered in this type of research.

In the meantime, he hopes to persuade IRBs not to dismiss studies too quickly over what he believes are exaggerated risks.

"We need to keep in mind the value of the research — that ultimately, this will have tremendous social value," Buchanan says. "We would be remiss to be overly conservative in failing to approve research with high-risk populations simply for very remote chances that incidents will happen."

"It would certainly be fair for IRBs to ask researchers to address questions of how well do they think they would be able to predict and anticipate some adverse event. But if it seems unlikely that the researcher will have sufficient information to predict some sort of event, then I would strongly urge IRBs to approve the research. Anticipate that their position will be upheld by the courts, which seems to be the direction the courts are going in the post-*Tarasoff* era." ■

Source

Buchanan DR. Policy needs regarding the duty to protect in epidemiological research with high-risk populations. *Journal of Public Health Policy*. 2006;27:293-308.

Virtual reality helps students with informed consent

Students learned informed consent facts faster

Students who did practice sessions with a virtual reality “human subject” learned better informed consent skills than did those who only studied consent rules from written material, according to a recent study.

The results of the study, published in the *Journal of Biomedical Informatics*, hold promise for using virtual reality (VR) applications to help research staff learn to work better with participants, and even practice informed consent for specific studies.

The study was an outgrowth of virtual reality work previously done by **Robert C. Hubal**, PhD, a senior research engineer at RTI International, a nonprofit research institution in Research Triangle Park, NC.

Hubal says he had students interact with simulated characters to train them in interpersonal skills such as interviewing and negotiation.

Wendy Visscher, PhD, director of RTI International’s Office of Research Protection, notes that a previous project of Hubal’s involved training interviewers to conduct household surveys.

“The first thing interviewers have to do is to see if they can get people to even talk to them,” Visscher says. “There was a virtual reality simulation in which interviewers could practice going up to a door and interacting with the character at the door to talk to them about their concerns right up front, which is sort of the beginning of informed consent.”

Developing ‘subject’s’ questions

Visscher obtained a Human Subjects Research Enhancement Award from the National Institutes of Health, and asked Hubal to employ the same technology to train and assess informed consent skills.

The program developed by Hubal runs on a regular personal computer and creates a virtual environment on the screen as the setting for an informed consent discussion — a suburban kitchen, with a 30-something woman seated at a table.

“I come from the technology side, and so what I do is work with the experts to say, ‘What would happen in this scenario?’” Hubal says. “What kind of questions would be asked? How would you respond appropriately to these questions? How would the person respond in response to that, and etc.”

He set up a series of questions the subject

would ask about a generic study: Do I have to participate? Will my answers be kept private? Will I get anything from the study?

The user answers, speaking into a microphone, and the subject asks another question. If a user gives an incorrect or incomplete answer, the virtual reality character replies “Please repeat that,” or “I am not convinced.” She might repeat a question.

“The questions come up in random order, which is very lifelike,” Visscher says. “People aren’t going to ask the questions in the same order every time.”

Each interview would end with the character either agreeing to participate or declining.

Hubal tested the application on a group of Duke University undergraduates who were fulfilling a psychology research requirement. He says they were not experts in human subjects research.

The entire group was given training materials about informed consent, which they had eight minutes to review. Then, half the group went on to a virtual reality training program, while the others continued to study the written materials.

Those in the VR group were seated in front of a computer featuring the VR character and told to attempt to answer as many of her questions correctly as possible and “convince” her to participate. During the student’s session he or she could run through the interview several times, with the order of the questions changing each time. VR participants averaged 6-7 interviews with the VR character during their 12-minute training phase.

Afterward, all of the students conducted another mock interview, this time with a real person. This interviewee asked all of the questions again, order to test how well students had learned the material.

In the end, those who had used the VR application did better in that final interview, answering questions more quickly and more accurately than the control group.

Enhancing lecture-style training

While the VR informed consent so far has not been used outside of this study, Visscher says that it could have real use in interviewer training.

“Generally, when you do an interviewer training session, you go over human subjects issues and, in particular, informed consent, but it’s generally in a lecture setting,” she says. “You go over the consent form, and then they will generally have some role-playing with each other.”

But she notes that the role-playing encompasses the entire process, from gaining permission through the mechanics of the interview, rather than focusing on the informed consent portion.

"So there are a lot of things that they're practicing, and they don't generally have enough time to ask the sort of questions that this simulated character might ask about informed consent," Visscher says. "I think it's true that they don't get enough practice actually answering [informed consent] questions, and this helps them do that."

Hubal says that adapting the program to include more specific questions about a study is fairly easy, requiring only that the actress who recorded the initial dialogue be brought in to record more material.

Visscher says that other training programs that have included video have proven more expensive and difficult to amend later.

Hubal says that while he sees this program as being useful for helping students practice their skills, he doesn't anticipate that it would entirely replace a face-to-face interview with another human being to ensure that the student knows how to administer informed consent effectively.

"What we say is that there are stages of training, and along that continuum, you would use different sets of technologies," he says. "This virtual environment is particularly useful for acquiring and practicing these kind of skills. But I'm not sure we would ever suggest that for validation, before we sent somebody out in the field, we would want to use just a virtual environment."

Hubal says there currently are no plans to produce this program for sale as a training product. But he would like to take it further, if more grant money were available.

"We have some ideas of other populations and other areas where this type of technology might be really useful," he says. "There are some ideas in the works that we'll be pursuing."

Visscher agrees that the approach has real promise. "I think it's a neat application." ■

Source

Hubal RC, Day SD. Informed consent procedures: An experimental test using a virtual character in a dialog systems training application. *Journal of Biomedical Informatics*. 2006;39:532-540.

Review process for unforeseen problems is simple

Four reviewers handle bulk of work

The two-part process of electronic submission of unanticipated problems at Washington

University School of Medicine in St. Louis, MO, requires investigators and clinical trial staff to enter information about the events after passing the chief screening criteria, and then it requires a reviewer to look at what has been submitted.

Four reviewers who have registered nurse backgrounds look at the nearly 1,000 submissions sent to the university's IRB, says **Diane Clemens**, DC, manager of research for the Human Studies Committee at Washington University School of Medicine.

If an unanticipated event involved a subject's death, then it's routed to the IRB chair, Clemens notes.

Reviewers see both the electronic information submitted and the paper file that contains a history of the study, since the electronic submission process is still too early for everything to be on the system, Clemens says.

"The reviewer assesses the risk to participants and looks at the rate of occurrence before determining whether or not the consent form has been adequately revised," Clemens says.

Reviewers also assess whether the investigator has proposed adequate changes to the protocol to minimize newly-found risks, she says.

The system compiles all the information into one area for the reviewer and a reviewer's sheet, and the reviewer can add comments when necessary, Clemens says.

"Sometimes it will be that they send an email back through the system, asking for clarification or further justification, and the system keeps track of all that documentation," Clemens says.

When the nurse reviewer believes a particular event needs additional review then the reviewer can refer it to the full IRB, Clemens notes.

Submission of deviations is more free-form than unanticipated problems, Clemens says.

"Deviations can encompass a wide variety of things," Clemens explains. "Generally, the submission includes, 'Here's what we're supposed to do, here's what happened, here's why it happened, and here's what steps we're taking to prevent it from happening again.'"

For example, a deviation might be that someone was supposed to have a blood draw five days after the procedure, but the person cancelled the appointment and didn't get the blood drawn until the sixth day, Clemens says.

"Or maybe the person missed a scheduled dose," she says. "At that point the charge of the reviewer is to identify when a deviation may be indicative of something more serious where maybe a research team needs additional education, or maybe there was a communication

breakdown between two different processes.”

When deviations seem to indicate a communication problem or organizational problem, the IRB will work with the principal investigator to correct the situation, Clemens says.

Also, deviations might be discovered during an internal documentation audit, Clemens says.

So the investigator will submit notice of maybe five instances in which an activity took place a day later than it was supposed to have, according to the protocol, Clemens says.

The investigator’s report will note that the problem involved a misunderstanding that was discovered during an audit and now is being corrected, Clemens adds.

“The reviewer determines which events qualify to be submitted to the Office for Human Research Protection (OHRP),” Clemens explains. “We send a report once a month via email to OHRP.” ■

IRB streamlines process to improve IRB response time

Reviews went from 24 days to 17 days

Intermountain Health Care Urban South Region of Provo, UT, revamped its IRB process with a goal of reducing its lengthy response time and to improve quality in IRB submissions.

After making changes that included hiring an IRB staff person, purchasing new software, and improving education, the institution was able to reduce the 24 days it took on average to bring a protocol from submission to IRB review to 17 days, and the average number of days from the IRB meeting to IRB correspondence was dropped from 22 days to five days, says **Katreena Collette-Merrill**, RN, a nursing practice and research coordinator at Intermountain Health Care.

The decrease in the days it takes the IRB to respond post-meeting was directly related to having the process computerized and the hiring of a dedicated IRB coordinator, Merrill says.

“And we had the expectation that we wanted to have a quicker turnaround,” Merrill says.

Merrill describes how the institution improved its process with these guidelines:

- **Address problem areas:** When Merrill became the research coordinator at the institution, there were no formal policies, procedures, or checklists, she says.

“And not only was the initial response time from when they submitted the application slow,

but the quality of submissions wasn’t very good because investigators didn’t know what we were looking for,” Merrill explains. “So we went at the problem from a myriad of approaches.”

First, a goal was set to reduce the time from submission to review by the IRB, and an IRB staff person was hired, Merrill says.

Then, the IRB purchased software and began an electronic system and then changed the entire filing system, Merrill says.

“We were still using hard copies at first, so we organized the filing system by year and the number of the study, and the first study submitted in 2005 was labeled 2005-01,” Merrill explains.

- **Develop checklists:** Checklists are used to help reviewers find omissions and mistakes in IRB submissions.

One checklist includes information about protocol submission related to National Institutes of Health (NIH) guidelines, and it asks questions, such as these:

- What was the stated hypothesis?
- What was the design of the study?

Another checklist relates to the Food and Drug Administration (FDA) and it goes through all of the different FDA requirements.

A consent checklist asks whether the consent document indicates that the subject has the right to withdraw, Merrill says.

“Does it have the contract number for the principal investigator,” she adds. “What is its readability on a readability scale?”

The consent checklist contains standard information of what should be on a consent and in the protocol, including the following, Merrill says.

- If someone is going to use pediatric patients, is there an assent attached?

- If someone is going to be working with patients who do not speak English, is there translation service available?

“We would take those checklists and give them to our primary reviewer, and the primary reviewer uses the list to check off items and say, ‘They don’t have this or that,’ or ‘I couldn’t find this information,’” Merrill says. “It’s a much, much easier process.”

The IRB coordinator has received training, and now she understands the submission process and can use the checklist to make certain investigators have completed their information before protocols are submitted to the IRB, Merrill says.

“She can tell them, ‘I can send this to the IRB, but you don’t have this information, and you

might want to do this before you submit it," Merrill says.

Some of the IRB review process bottlenecks were caused by repeat mistakes on the part of investigators.

- **Make changes as necessary:** As an IRB process is revamped, it's important to make adjustments and changes as new issues arise, Merrill notes.

For example, one physician who worked on newborn intensive care unit studies would omit an approval signature from the ICU manager on the submissions, and so a section was added to the submission form, saying that the investigator needs to obtain approval from these people prior to submitting the protocol to the IRB, Merrill says. "We've made a lot of changes," Merrill says.

The IRB coordinator, for instance, was a part-time position at first because the IRB is small, with only about 75 open studies, Merrill says.

Now, the IRB coordinator handles IRB work for the entire Intermountain Health Care system, which includes 22 hospitals, she says.

"With a central system, the IRB coordinator is half-time for us, and the other half of her time is for another region," Merrill says.

- **Move to an electronic system:** "We've created a virtual system where the IRB coordinator sends me all of the information and types the expedited review letters electronically, creating a pdf document, so it can't be changed," Merrill says. "It still has my signature, and no one can attach or unattach it."

Everything is available on a Web site, as well, she says.

Although the IRB coordinator is located an hour from each of the two research offices, the electronic system makes it as easy for the coordinator to work with investigators, IRBs, and research staff through telecommuting, Merrill says.

"If someone submits electronic data, then it's all electronic from the beginning," Merrill says. "But if someone submits a hard copy, it's copied and scanned and made into a pdf file."

Study changes that need expedited review can be seen by the IRB's chair or vice chair, Merrill says.

"We didn't have a vice chairman when we started all of this, and then we found out when the chairman goes out of town, you're stuck and can't do anything," Merrill notes.

Since this slowed down the system, a vice chair position was added.

- **Provide formal training and education:** After the first changes were made, the institution held a meeting for the IRB and staff and went over the

checklists, Merrill says.

All protocol and checklist templates were put on a CD, and there also were hard copies for distribution, Merrill says.

Now all of the information is available on a Web site, she adds.

The formal training was done at a two-hour meeting, offered several times so all investigators and coordinators could find a convenient time to attend, Merrill says.

"We introduced a whole binder of hard copy information and introduced all policies and procedures and checklists," she says.

The training session explained why the institution was making the changes and what the goals were, Merrill says.

"They weren't too happy at first about the electronic submissions because some were doing a lot of protocols and didn't want to submit electronically, but we reassured them that it would decrease the response time," Merrill says.

Investigators weren't required to attend the meetings, but they did have to pick up the training material and review it, she says.

And the institution also required every person listed on a study, including principal investigators, co-investigators, study coordinators, and the people handling informed consent, to complete on-line human subjects research training coursework and receive a certificate, or else their study would be closed, Merrill says.

"Now they can't get an IRB application without having the training," Merrill says.

Some of the future plans for the streamlining process is to improve the electronic submission system to make it more user friendly, Merrill says.

"We still want to do more training for new investigators," she adds.

For example, the institution could offer courses on how to write protocols, Merrill says.

Also, the IRB may eventually become entirely electronic with laptops for members, and the institution might provide its own research training classes for certification, Merrill adds. ■

Think far beyond ethical requirements set, expert says

IRB's need more intuition, compassion

One of the drawbacks for research conducted in this age of checklists and strong regulato-

ry oversight is that IRBs and research institutions do what they're required to do and sometimes neglect to address the bigger picture, an ethics expert says.

"I think that research with human subjects is governed by regulations, which set the bare minimum for conversations that need to happen," says **Nancy Neveloff Dubler**, LLB, director of the division of bioethics and vice chair of the Montefiore Medical Center IRB, department of epidemiology and population health, at Montefiore Medical Center in Bronx, NY. Dubler also is a professor of bioethics in the Albert Einstein College of Medicine in Bronx, NY.

"In addition to regulatory steps, an IRB needs to be thoughtful, intuitive, compassionate, and learned about the population in its area, so it can learn about vulnerable populations," Dubler says.

"These processes all are facilitated by the regulations," she says. "The regulations provide a platform, but they don't in fact demand that you go into these directions, which I think are ethically required."

Dubler has co-written a new book on research ethics, titled, *The Ethics and Regulation of Research with Human Subjects*, published in 2005 by LexisNexis Group in Newark, NJ.

The goal of ethical consideration is to delve deeper into issues and considerations before approving a particular research project, Dubler says.

A first step to a more thoughtful and intuitive IRB review is for the IRB member to read the protocol carefully and think about who the stakeholders are in the proposal and what their interests are, Dubler suggests.

"Then step back and ask, 'Who are the people being asked to become research subjects?'" Dubler says.

Other questions to ask are as follows:

- Are they insured or uninsured?
- Are they rich or poor?
- Are they in the community or in nursing homes?
- What is the situation of the possible human subjects?
- What could that situation mean for the quality of independent consideration of the protocol and for quality of the consent process?

IRB members can apply compassion to their review work by thinking about what it would be like to be a person in the place of this possible research subject, Dubler says.

These questions to ask oneself are as follows:

- What would you want to know?
- How might you want to be protected?
- What information would you want shared?
- How might the protocol change your life?

"So I think that what this requires is an in-depth, thoughtful exploration of who these possible research subjects are and what might be important to them," Dubler says.

For example, if an IRB is considering approval of a research project involving children, the regulations will require the board to address the various situations in which the children will find themselves during the study, as well as the nature of the research and the possible risks and benefits of the research, Dubler says.

"I would argue that you then have to step back and think, 'What is the quality of parental permission that we would require to enroll a child?'" Dubler says.

Other ethical questions to consider in this example are these:

- Is it possible that parents will enroll their children as a way to gain access to care?
- Does that change how we think about the consent process?
- How might economic or social factors play on the willingness of parents to agree?
- How does the system for delivering care that forms the background of the protocol interact with this protocol?

"Those are not issues that naturally come to the fore when you read the regulations," Dubler says.

"You need to think about what are the larger sets of issues that we should be concerned with since it's clear that the regulations do provide a minimum basic framework," Dubler adds. "But then the research must be considered by the IRB in light of all the conditions that are in effect in the community in which the IRB sits."

Also, IRB members should give thoughtful consideration to the terms assent and consent when applied to research involving children, Dubler suggests.

Researchers need both permission from the parent and assent from the child who is capable of providing assent, she says.

"Those two ingredients are necessary, but I'm suggesting they are not ethically sufficient," Dubler says.

When research issues involving consent and assent are considered beyond the regulatory box,

it's more likely an IRB will avoid approving some of the research that later becomes controversial or the subject of lawsuits.

For instance, in the *Grimes v. Kennedy Krieger Institute Inc.* case in Maryland, a research institute created a non-therapeutic trial in which different levels of lead abatement modifications were performed in homes with children, Dubler says.

The families involved were mainly poor and African American, and investigators placed their children at risk for lead poisoning without clearly indicating the dangers to them, Dubler explains.

"They wanted to find out what was the cheapest level of lead abatement that would give them a safe home setting," Dubler says. "The critics of the research were parents who sued, and the court was very critical, and all of this could have been avoided by having greater sensitivity to the children, the setting, the family, and the issues."

Authors of the recent ethics book state: "Moreover, in our view, parents, whether improperly enticed by trinkets, food stamps, money or other items, have no more right to intentionally and unnecessarily place children in potentially hazardous non-therapeutic research surroundings, than do researchers. In such cases, parental consent, no matter how informed, is insufficient."¹

A similar issue recently arose with the Environmental Protection Agency's (EPA's) proposed pesticides study in primarily low-income homes inhabited by children, Dubler says.

The EPA's proposed research was shelved after media reports elicited widespread criticism.

"There are a lot of IRBs who think their job is to protect human subjects and that their obligation is completed if they respond to issues in the regulations," Dubler says.

The problem is that most IRB members probably don't really know the regulations, Dubler notes.

"So they use a sort of shorthand for quoting the risk-benefit ratio without most members of the IRB actually having grappled with the actual

language of the regulations," she says.

To make changes in an IRB so that it will more fully consider ethical issues, there will have to be a strong commitment on the part of the IRB chair and administrator, Dubler says.

"They have to find and educate nonaffiliated members of IRBs and give them the real education and tools they'll need to move forward," Dubler says.

"I think IRBs vary enormously in quality, largely because of the passions of their chairpeople," Dubler adds. "Chairpeople who care deeply about the quality of consideration given to protocols will over time change the culture of the IRB review — but it's a hard battle." ■

Reference:

1. Coleman CH, et al. *The Ethics and Regulation of Research with Human Subjects*. LexisNexis Group; Newark, NJ. 2005:1-746.

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;
- **apply** the mandated regulatory safeguards for patient recruitment, follow-up and reporting of findings for human subject research;
- **comply** with the necessary educational requirements regarding informed consent and human subject research.

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.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you.

COMING IN FUTURE MONTHS

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CE/CME questions

1. True or False: Mandatory reporting laws for the reporting of serious threats uncovered in the course of public health research make it relatively simple to know which threats should be reported.
 - A. True
 - B. False
2. How many mock informed consent interviews, on average, were students able to conduct with a virtual reality "research subject" during a 12-minute training program?
 - A. 1-2
 - B. 4-5
 - C. 6-7
 - D. 10-11
3. Before an incident can be reported to a human studies committee and the Office for Human Research Protections (OHRP), it should meet three criteria. Which of the following is not one of the three criteria?
 - A. The event is serious.
 - B. The event is unexpected.
 - C. The event is the result of a human error.
 - D. The event is reasonably related to the research.
4. IRB members need to think beyond the regulations, according to a research ethics expert. When they are considering a protocol, they should ask themselves which of the following questions?
 - A. Who are the people being asked to become research subjects?
 - B. Are they insured or uninsured?
 - C. Are they in the community or in nursing homes?
 - D. All of the above

Answers: 1. (b); 2. (c); 3. (c); 4. (d)