IRB ADVISOR
Your Practical Guide To Institutional Review Board Management

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Voluntary vs. compensated: New trend making inroads at some IRBs

Virginia IRB at VA hospital serves as model

As the scrutiny and duties of IRBs steadily increase, demanding ever more time from IRB members, it has become clear to some research universities and hospitals that there should be a change in whether and how IRB members are compensated for their time.

"IRBs are growing, and with that growth, there is an increase in the amount of work the members are required to do in order to protect the research participants," says **Laura Orem**, CIP, program manager of the Florida Hospital IRB in Orlando.

"We're fortunate to have the member commitment we do have; but as we add more to the members' workload, we have to remember their time is valuable, and some of the physicians have been volunteering for many years," Orem says. "They are dedicated, but busy, people."

For universities, IRBs are crucial to protecting the institution's research reputation, which makes it even more important that members are compensated in some way for their time, says **Anthony M. Boccanfuso**, PhD, managing director of the University of South Carolina Research Foundation of Columbia.

"The impact an IRB has on the university's reputation and stature is significant," he says. "It can really have a negative effect if your IRB is not professionalized."

At the University of South Carolina, faculty who serve on the IRB are recognized as providing an important service to the university, and their time spent on the board is recognized in some manner, Boccanfuso says. "Service should not be another box that gets checked."

Traditionally, IRB members have received token or no compensation at many institutions; but times are changing slowly, and more hospitals and institutions are making changes to improve IRB member compensation or to at least consider making these changes, Boccanfuso notes.

"I'm hearing a lot more about the IRB chairs receiving compensation," Boccanfuso says.

Florida Hospital has been looking at the issue, but no decisions

regarding changes have been made yet, Orem says.

"We are looking at other institutions who have already decided to compensate their members to see what programs they have in place and how those programs are working," she says.

One potential model for professional IRBs is the McGuire Research Institute, which is affiliated with the McGuire Veterans Affairs (VA) Medical Center in Richmond, VA.

The nine members of McGuire's IRB meet weekly between 4:30 and 8 p.m. and review copies of agendas that often reach a foot in height, says **Bob Dresch**, MSW, executive director of the McGuire Research Institute.

"This is work, and we pay people," he says. "We peg their salary to their VA salary."

For example, the IRB chair is a physician and head of a lab, so his salary is higher than the salary for the IRB's community member, Dresch adds.

Dresch says the pay is enough to make it worth the IRB members' time and is not a token amount as some IRBs pay.

Although there are eight IRB alternates who are compensated on a per-meeting basis, the IRB members are expected to show up for meetings, he says. "That's their job, and people have excellent attendance records."

As a result of having made the IRB professional, the IRB has had very little turnover, and members take the time to keep apprised of new regulations, Dresch says.

"This is serious work — there are thousands and thousands of pages of complex laws and ethics, such as dealing with prisoners, science, and the lists goes on," he says. "The IRB is the most important thing to our research operation."

Not encumbered by tradition

Founded in 1999, the McGuire IRB had the benefit of starting its work from scratch, taking no traditions for granted. It also had an advantage over most IRBs because the research institute had the financial resources necessary to make the IRB a professional one, Dresch explains.

Before the IRB was formed, the VA hospital shared an affiliated IRB with the Medical College of Virginia of the Virginia Commonwealth University (VCU), but this relationship came to an end when the U.S. Food and Drug Administration (FDA) sent a warning letter to VCU, Dresch says.

"That got our attention, and a month later, we started our own IRB," Dresch says. "It was very difficult at first, just getting established and getting investigators invested in doing something a little more rigorous."

However, the VA's investigators soon were enthusiastic for the new IRB when the FDA and Office of Human Research Protection (OHRP) shut down the medical college's IRB, suspending

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all research, Dresch says.

"We had a tremendous amount of resistance at first because people didn't see what was coming," Dresch says. "But when the medical college's research was suspended in December, we had a line at our door for a couple of days."

The instant converts jump-started the new IRB, creating immediate buy-in, he recalls.

"We had the opportunity to see firsthand the edge of the abyss," Dresch says. "We could observe the crippling financial repercussions when the place was shut down and there were articles in the newspaper every week."

This made it easy for the new IRB to establish stricter rules, more oversight, meticulous observations, and many safeguards, Dresch says.

There was no money for the new IRB until the VA decided to put to use the funds collected by the VA's nonprofit corporation, established in 1989 to support VA hospital research, Dresch explains.

The nonprofit corporation, which is the McGuire Research Institute, had gradually grown through grants and involvement in multisite studies where the residual costs could be saved to build net assets. Over time, it had collected and managed a nest egg that could only be spent on peer-reviewed research activities, Dresch says.

"There had been pressures to do this or that with the money, but we always felt we wanted to save it for a rainy day," Dresch says. "That rainy day hit in 1999, and we could throw a half-million dollars at this IRB without batting an eyelash."

The money has been used to develop IRB software from scratch, as well as to build the IRB's infrastructure and pay for making the IRB a professional board. **(See story on MIRB software, right.)**

"So we had a big advantage in starting our IRB — plus we controlled the purse strings," Dresch says. "Without money, people can talk about ethics, but you can't run an IRB without money; and we understood very quickly that good human subjects protection equals good business."

Unfortunately, most IRBs are not as well funded as the McGuire VA's IRB, so the cost of compensating members is a major issue. The way some IRBs have handled this issue is through alternative forms of compensation, Boccanfuso says.

"I'd differentiate between additional compensation vs. credit for the effort the university's faculty expend," he says. "For many faculty, they'd be just as happy not receiving additional compensation, but would like their department to receive credit for their time."

For example, the IRB member's time would be paid by the IRB to the faculty member's college department. In turn, this credit would help the department make more money available for the faculty member to do his or her own research, Boccanfuso says.

"Those individuals want to support their research endeavors, so having the IRB either offset compensation or having a research account set up for them is something they would value more than the extra dollars in their pockets," he explains.

Alternative forms of compensation can be distributed in a variety of ways. For instance, a faculty member could be released from the obligation to teach a course, so instead of teaching three courses, the person would teach two, Boccanfuso says.

In turn, the IRB and department would determine what the cost is to the department for that professor to drop a course, and that amount of money would be credited to the department, Boccanfuso says.

Another form of compensation might be to hire a graduate student to support the faculty member in his or her work, so there would be more time to spend on the IRB.

At the University of South Carolina, the IRB chair is paid a stipend, and departments are asked to provide some sort of quantified recognition for faculty members who serve on the committee, Boccanfuso says. "The chair's stipend can be credited to a research account if he chooses, so there is some flexibility."

The important thing is that that the IRB members' time for serving on the board is measured and compensated in some way, he says.

"The IRB committee is much more professional than it has been historically," Boccanfuso says.

"It's really only been five to seven years where we've really looked hard at IRBs and how they've operated," he adds. "Before that, they were treated in a much more casual manner than was expected by the regulations." ■

IRB software wins best-practice award

Software created along with IRB

Four years ago, when the IRB at McGuire Veterans Affairs (VA) Medical Center in Richmond, VA, needed software to support the IRB's work, there appeared to be very little

commercial software available. So the IRB decided to create its own software.

Since the IRB itself was brand new, it only made sense to allow the IRB's software and database to evolve and grow with the board, says **Bob Dresch**, MSW, executive director of the McGuire Research Institute, which is affiliated with McGuire VA.

The resulting software was MIRB2002, which is used by about 30 VA hospitals, and a non-VA version called MIRBu2003, which is used by Baylor Research Institute in Dallas. Because of MIRB, McGuire VA Medical Center received the 2002 Award for Excellence in Human Research Protection by the Health Improvement Institute of Bethesda, MD.

The research institute had the funds available to develop the software, so everything came together at the right time, Dresch says.

"Had we started the IRB six years earlier, maybe we wouldn't have found the need to develop a database program," he says.

More government, public scrutiny

But as the 21st century dawned, the role of IRBs had changed to one that was more closely scrutinized by governmental agencies and the public, Dresch notes.

Now with IRB accreditation systems, there's a lot of emphasis put on IRBs' correspondence systems, documentation of data, and continuing reviews, he adds.

Plus, the new IRB decided to demand a great deal of documentation from investigators, including 10 page-long initial review submission forms, Dresch says.

"It became evident in the first four to five months that it was way more work than we anticipated," he reports.

"You've got to have a database to do all of that," Dresch says. "It was all a matter of timing, and it happened to hit at the same time the IRB world was changing."

The IRB meets weekly and sends out correspondence within one week, which at least has eliminated the need for expedited reviews, he notes.

"We aren't under pressure from investigators," Dresch says. "With monthly meetings, the lag time is long, but with weekly meetings there's no pressure there."

But the challenge was to develop a software system that could handle the IRB's fast correspondence and turnaround time.

In January 2000, Dresch met with N-CORE Systems Inc., also in Richmond, a software company that was hired to help develop the IRB software. "We learned what was required by running an IRB, and that's how we developed the program for the past three years — with constant improvements," Dresch says.

Old data were uploaded, and the IRB staff spent many hours reviewing 200 ongoing projects, Dresch says. "It was a very busy time, and a lot of people went to great lengths and worked many hours to pull this off."

But the effort paid off. The resulting software provides a user-friendly database that allows IRB staff and members to retrieve and constantly re-evaluate every continuous review report, every new serious adverse event report, new amendments, all correspondence, and changes in principal investigators, he says.

"I wanted the IRB to be able to see every previous action and the IRB's history, and I didn't want them to look at some item out of context," Dresch says. "For example, how can you evaluate the amendment without seeing everything about the protocol for the past 16 months?"

All of the IRB data are arranged by date, and the software tracks all voting IRB members and their potential conflicts of interest.

"We had to build in a fail-safe system to not let somebody vote on something they had a conflict of interest with, and that was one of the first key basic things," Dresch says.

"It'll give you a prompt saying that the sub-investigator is on the IRB committee, and it won't let him vote on that protocol," Dresch explains.

The software also tracks items and titles to be reviewed, including investigational drug forms and dates, initial review submissions, conflicts of financial interest disclosures, summaries on the agenda, Dresch says.

N-CORE and McGuire VA are moving into a new phase of the software development in which it will be available via the World Wide Web, says **Jeff Hooper**, MIRB senior developer.

"As the database exists, it is only accessible by research administrators, like Bob and his staff," Hooper says. "But the idea of web interface is that it allows administrators to give access to that data to all of the investigators and research coordinators inside the hospital, via the Internet."

Soon, the new software, called MIRB.net, will allow investigators and coordinators to submit all documents on-line. Then Dresch and his staff will be notified that a new submission is taking place, and they can push a button to grant the investigator

access into the database, Hooper explains.

The result will be a reduction in paper flow and more efficiency for the IRB staff.

Investigators quickly will be able to obtain information that otherwise would have required them to call the IRB office and request that reports be sent to them, Hooper says.

MIRB.net will be secured through a process that requires users to log on with a password, and Dresch will have control over its access and the extent of a specific person's access, he says.

"If you're an investigator, you will be able to see your own studies, and a research coordinator might be able to see one or more studies," Hooper adds. "But they can't make changes at all, and all they can do is make new submissions."

Before any new submissions enter the database, they must be viewed and approved by Dresch, Hooper says. ■

Informed consent must be viewed as a process

Consent should be ongoing endeavor

In the summer of 1971, **Philip Zimbardo**, PhD, was lead investigator on The Stanford Prison Experiment, a study designed to measure the psychological effects that imprisonment and authority would have on participants. Eighteen subjects were selected, nine were assigned the role of prisoner, the other nine the role of guard. For six days — eight shy of the planned 14 days — investigators watched as normal (according to results of psychological testing done on all potential volunteers), middle-class, young men, became subservient, depressed, withdrawn, dictatorial or even sadistic, depending on the role assigned. Two subjects were released from the study — one after suffering a near breakdown and the other after breaking out in a rash that covered his body after he was denied mock parole.

The experiment followed the guidelines of the Human Subjects Review Board, Zimbardo explained in a 1973 chapter, "Reflections on the Stanford Prison Experiment: Genesis, Transformations, Consequences."[1]

"There was no deception," he wrote. "All participants were told in advance that, if they became prisoners, many of their usual rights would be suspended and they would have only minimally adequate diet and health care during the study."

What they weren't told is the possible risks and benefits and that they had the right to withdraw from the study at any time. In fact, the informed consent document offered to study volunteers specifically stated, "I will be expected to participate for the full duration of the study, that I will only be released from participation for reasons of health deemed adequate by the medical advisers to the research project or for other reasons deemed appropriate by Dr. Philip Zimbardo."

Zimbardo has written extensively about the study, from the ethics of the execution to the findings yielded during its six-day duration. "Clearly, I would not have been able to conduct such a study today," he tells *IRB Advisor*. "In hindsight, the situation was more powerful than anyone imagined." When asked what he would do differently, he says, "I would have someone from the IRB available at random times to check the progress of the study and have the power to terminate it."

The Stanford Prison Experiment is not only a case study in the psychology of imprisonment, but it also can serve as a case study for IRBs and the issue of informed consent.

A misstep when dealing with informed consent can result in administrative sanctions and possible civil liability, says **LaDale George**, JD, senior counsel, health law department/health care business counseling practicing group at Foley & Lardner in Chicago. "IRBs should consider risks and benefits, route of administration, dosage amount, disclosure of alternative treatments, etc., when evaluating an informed consent document to determine whether there is adequate information being conveyed to protect the rights of human subjects," he says.

The Office for Human Research Protections (OHRP) recently cited National Heart, Lung, and Blood Institute investigators and the IRBs that reviewed their protocols for deficiencies, which included a failure to disclose risks associated with the studies.

"If OHRP finds that the IRB has not been following statutory requirements for approving informed consent documents, they may halt the study and suspend the authority of the IRB to review trials," says George. "Similarly, the FDA [Food and Drug Administration] may refuse to accept data from trials that were approved by an IRB that is found to have approved studies with inadequate informed consent documents."

Informed consent problems also can result in civil liability. Trial subjects have filed lawsuits against IRBs and named individual members in

suits, George points out, particularly when a protocol has been approved and it is determined that full disclosure of risks and benefits was lacking. "Each consent form should stand alone, and IRBs should take the time to really examine the form. Informed consent forms should be tailored to the specific trial to ensure that it meets the needs of informing the patient," he says.

"We like to see the risks described in a meaningful way — that is to have descriptors such as 'more likely or less likely' or to have percentages," says **Marcia Weese**, MHA, IRB director at Emory University in Atlanta. "The risks section should include risks of all procedures that are related to the study. The benefits section is usually not as detailed because you don't want to make it sound too promising."

Documents should not only disclose risks but also disclose any alternative treatments, says **Margaret T. Feeney**, MBA, RAC, Committee on Clinical Investigations Liaison for Quality Assurance and Audit, Beth Israel Deaconess Medical Center in Boston. "Investigators must respect the subject and recognize that if there are alternatives to a certain treatment that they are disclosed."

She points out that not only must known or potential risks be disclosed, if new risks are discovered during the course of the study, that information should be conveyed to participants.

"Principal investigators should first inform the IRB and then provide the research subject with any information that may affect their willingness to continue to participate," Feeney says.

More than just a signature

"There are two goals involved in obtaining informed consent for research: complying with government regulations and meeting the ethical mandate to ensure that people provide authorization to participate," says **Jeremy Sugarman**, MD, MPH, MA, Director of the Center for the study of Medical Ethics and Humanities, Duke University Medical Center in Durham, NC. "The regulations tend to emphasize what needs to be included in informed consent documents, but in order to meet the ethical goal of informed consent, you have to first make sure that the potential research participant has adequate decision making capacity and that they are able to make a voluntary choice." **(See story on obtaining consent from the mentally challenged, p. 91.)**

"Our committee looks at how subjects' understanding is assessed and what happens if the subject is unable to give informed consent — whether they are excluded from a study or whether consent is obtained from a legally authorized representative," says Weese. "The committee also looks at when and where consent will be discussed and documentation obtained to ensure that potential subjects have had time to consider their participation."

In other words, it's not enough to hand subjects a form and ask them to sign. "The act of obtaining informed consent is an ongoing process," says Feeney, involving not only communicating the particulars of the study but also ensuring that

Informed Consent Form Contents

- **Introduction/Purpose:** An explanation of the purpose of the research, why the subject is being asked to participate, and how long the subject may be involved in the study.
- **Procedure:** A detailed description of what procedures will be performed on the subject and a detailed description of what the subject is expected to do during the study.
- **Risks:** A description of any foreseeable risks to or discomforts that may be experienced by the subject.
- **Benefits:** A description of possible benefits, including disclosure that the subject my not experience any benefits during the study.
- **Alternatives:** A listing of alternative procedures or courses of treatment that are available.
- **Confidentiality:** A description of how records will be maintained to ensure that subjects' privacy is protected.
- **Compensation/Costs:** A description of how much or what kind of compensation, if any, subjects will receive for participating in the study, as well as a description of costs that may be incurred by participants.
- **Voluntary Participation/Withdrawal:** An explanation that participation is voluntary and that subjects may withdraw at any time. Also include an explanation of medical consequences of withdrawal, if any; circumstances under which investigator may discontinue participation of a subject; and procedures for possible data collection or follow up once a participant has withdrawn.
- **Contact persons:** Names and addresses and/or telephone numbers of persons who can be contacted with questions.
- **New findings:** How and if results of the study will be communicated.

Source: Emory University IRB, Atlanta.

participants understand their rights.

The process begins with communicating to participants the following:

- Participating is voluntary.
- The study may or may not benefit the participant, though knowledge gained through the study may benefit others.
- Participants may withdraw from the study at any time.
- Participation or withdrawal will not affect care.

The rest of the form contains information regarding the specifics of the study, and responsibility and rights of participants. **(See list, p. 90.)**

"We want the subject to be able to make a rational choice, and this can only be done if information is provided in a clear, understandable manner," explains Feeney.

What's clear and understandable?

Clear and understandable seems to be a challenge when it comes to how medical information is communicated. Readability expert Mark Hochhauser, PhD, completed an analysis of more than 30 Health Insurance Portability and Accountability Act privacy notices and found that most were written at first- or second-year college level. Complexity is not just a problem with privacy notices, it's a problem that Weese sees when evaluating consent documents submitted to her IRB. "The most common problem encountered is that the consent is written at too high a level," she says.

Hochhauser recommends that you keep it simple by employing the following:

- Sentence length — 15 to 20 words
- Word choice — use everyday words
- Sentence complexity — short with short words, short with a few long words, or medium with a few long words.

"We're looking for an eighth-grade reading level. Some principal investigators write a consent document that would be challenging for a nonmedical person to understand," says Feeney.

"Our committee makes sure that all procedures described in the protocol are reflected in the consent and that it is written in language that is nonscientific and nontechnical. It's not just a matter of going down a checklist — each consent has to be evaluated," says Weese.

Reference

1. Blass T, ed. *Obedience to Authority: Current Perspectives on the Milgram Paradigm.* Mahwah, NJ: Lawrence Erlbaum Associates; 2000. ■

Consent process honed for mentally challenged

OHRP recognizes and honors the program

In an ideal world, researchers working with mentally ill subjects would be able to present information about their studies in such clear, comprehensive, and organized ways that IRBs could be assured that participants know exactly what to expect. The ideal world has been achieved, or at least as nearly as it has anywhere, at the National Institute of Mental Health (NIMH) in Bethesda, MD.

NIMH created in 1999 a best practices program called CORE (Central Office for Recruitment and Evaluation). CORE was initiated after problems had occurred at several other psychiatric research programs, and NIMH officials wanted to make certain that there would be no similar problems in the NIMH intramural program, says **Catherine Roca**, MD, deputy clinical director.

Although NIMH primarily administers grants, CORE is part of the intramural, hospital-based program that has ongoing research with patients. There are about 100 protocols that are run at the NIMH clinical center site, and there are both inpatient and outpatient clinics in which all patients are admitted as part of a research protocol, Roca explains.

Another impetus for CORE was the National Bioethics Advisory Commission report on decision-making impairments. The report recommended that for people with mental illness participating in greater than minimal risk protocols there should be a provision for independent capacity assessment, she adds.

"We were trying to figure out how we could best address some of these issues with our subjects," Roca says. "We wanted something protective of patients to make sure they understood what they were signing up for when volunteering for research."

Since CORE was implemented, the NIMH IRB has been more comfortable with approving the most difficult protocols, he says.

"They know there's somebody objectively monitoring the protocol, and if there are problems, they

come back to the clinical director and to the IRB much more quickly," Roca says. "In the past, the IRB may not have heard about problems until they became a huge issue."

Also, CORE staff give feedback to the IRB chair and the clinical director on a regular basis, and the CORE team attends various unit meetings, providing feedback on participants, she says.

"From the standpoint of the IRB, we have been able to find out if there are any protocol violations or to intervene before protocol violations occur, because we have someone who sits in on the IRB and who looks at protocols," Roca says. "It gives the IRB a sense of comfort that there is a number of protections for patients."

Award-winning process

As a result of CORE, the informed consent process now is considered among the best in the nation for dealing with mentally ill subjects, and NIMH received from the Health Improvement Institute of Bethesda, MD, the 2002 Award for Excellence in Human Research Protection last fall because of the CORE program.

Here's how the CORE program works:

• **Set up a recruitment team.** Through CORE, trained staff have a number of sessions with subjects, and they remain available to answer telephone inquiries from both participants and people interested in volunteering for a study, Roca says.

"We did this because we felt informed consent begins right when the person first calls," she says. "And we try to explain what the study involves."

Optimally, the person who first had contact with the participant via telephone will be the same staff person who sits down with the volunteer at the time the informed consent document is explained and signed, Roca adds.

"We try, and we can't always do it with staffing, but we try to have the person who sat in on the informed consent be the same person who touches base with the participant as he or she proceeds through the protocol," Roca says.

There are six full-time CORE representatives, who answer the phone and assist with all inpatient and the outpatient protocols in cases where the IRB has directed consent monitoring. Their caseloads average seven to 10 patients/subjects.

"Not all protocols are monitored because some involve high-functioning folks, and the protocols are low risk," she says.

CORE representatives are clinically competent in psychiatry and have experience in caring for psychiatric patients. They also have backgrounds in research, she says.

"We've tried to not have them specialized within any particular branch so they are aware of what's going on with all different groups and are not affiliated with any one research group," Roca says. "It is really difficult if you are close within a group and you take an unpopular stance."

The representatives receive bioethics training at the NIMH Clinical Center's bioethics center and through a course taught by the IRB chairman, who has co-authored articles on psychiatric ethics, she says.

Although CORE is labor-intensive, it can easily be reproduced at other hospitals through the use of hospital social workers, Roca suggests.

It would probably be easier for social workers to remain independent, yet knowledgeable about research protocols, she says.

"If you're a nurse on a particular unit, it can be difficult to buck the system you're living in," Roca explains. "The social worker goes to the unit but doesn't live and work there; so if you had a central social work area and had staff trained in bioethics and performing capacity assessments and doing consent monitoring, then you could really implement this anywhere."

• **Assess subject's capacity for decision making in the informed consent process.** CORE representatives perform capacity assessments.

NIMH researchers developed a capacity assessment tool based on the MCAT-CR clinical research capacity assessment tool, Roca says. "They took the MCAT-CR tool and used it for capacity assessment for a schizophrenia population, and modified it depending on the protocol."

Typically, a social worker will modify the capacity assessment tool and show it to the principal investigator (PI) and to make certain the PI has hard data with regard to risks and benefits, she says.

"Then we have the IRB chair look at the instrument, as well, to make certain it covers all bases and is administered by the representative who knows the patient best," Roca says. "Two representatives sit in on the dialogue and rate the patient according to the patient's ability to give informed consent, and they come to a consensus of the patient's capacity for understanding, and they tell that to the PI."

If the CORE representatives agree that the patient understood the consent process, then the investigator can proceed with the study, she says. "If the consensus is that the patient didn't understand what he

or she was getting into, then the PI cannot proceed with the research."

The PI may ask the CORE representatives to reassess the volunteer after the person is given more information, Roca notes. "They can have them perform a capacity assessment one more time."

Since the program has begun, PIs have gained a better understanding of what constitutes capacity for making informed decisions, and as a result they most often will screen out the volunteers who would not pass the capacity assessment process, she says.

• **Monitor study and ongoing informed consent.** After the lengthy informed consent and capacity assessment process, the CORE representatives answer participants' questions and will meet with volunteers about once a week to see how they're doing and whether they are experiencing any conflicts, Roca says.

For example, a CORE representative might say to a participant, "I heard you have an MRI scheduled for tomorrow. Do you understand what an MRI involves?" she says.

CORE representatives attend team meetings to hear how the participants are doing, and if they hear that someone is not doing as well as hoped they will talk to the PI and express their concerns, she adds. "There may be a point when someone has a lot of symptoms and is very uncomfortable, and so the CORE representative will bring that to the PI's attention," Roca says.

CORE representatives will check the PI's plan for intervening in the case of a subject's difficulty. For instance, maybe the PI will shorten the placebo washout period and get the patient back on active medications, he reports.

"We've had very good luck with our PIs," Roca says. "Usually all it takes is talking with somebody about it, but if ever there is a situation where somebody is not being responsive, then we'll talk with the clinical director because he has the ability to take someone out of the protocol." ■

Should infectious disease research be fast-tracked?

National IRB could expedite approvals

Current federal research regulations in the United States limit efforts to study emerging infectious diseases, and an alternative model is needed to allow a rapid response to immediate threats to public safety, a top U.S. researcher claims.

The recent experience of Canada, Hong Kong, and China during the severe acute respiratory syndrome (SARS) epidemic provides a perfect example of how a completely new disease can rapidly and mysteriously decimate large populations, says **Richard Whitley**, MD, professor of pediatrics, medicine, and neurosurgery at the University of Alabama-Birmingham. He also is the project director for the Collaborative Antiviral Study Group, a multi-institutional collaborative network funded by grant from the National Institute of Allergy and Infectious Diseases (NIAID).

Although the SARS outbreak appears to be under control, there is every indication the illness will re-emerge in the future. And researchers still do not fully understand where the virus came from and why it is so deadly, Whitley wrote in an editorial in the June 19 edition of *The Wall Street Journal*.[1]

"We still don't understand, for instance, whether there are any genetic variations in the virus that might account for differences in mortality or whether genetic differences in people play a role in who gets sick and who dies," he stated. "Moreover, we don't know where the virus came from — birds or pigs or some other animal — and how it got into humans."

SARS is just the latest in a new outcrop of emerging infectious diseases that threaten large numbers of people here and around the globe. And as human populations continue to grow, have more contact with one another, and encroach on previously untouched habitats, more diseases will emerge, Whitley tells *IRB Advisor*.

"What our problem as a research community is, we can neither predict where an emerging infection is going to appear nor when it is going to appear," he states. "Because of that, we cannot put in place a clinical trial network the same way you would for cancer or the way you would to study herpes simplex encephalitis, for example."

This lack of predictability for emerging infectious disease threats, coupled with the need to test new therapies in an ethical, acceptable way, means that new information, therapies or vaccines are going to be slow to emerge, he says.

The local institutional review board at each site enrolling participants in a study must carefully vet research protocols involving human subjects. If a new disease outbreak occurs in a region without a study already in place, the long, cumbersome process must be initiated in the midst of a public health crisis.

"If West Nile breaks out in Des Moines and I don't have a clinical trial site there, yet all of a sudden there are 10 cases, we end up denying the opportunity of those 10 patients to receive a potential therapeutic drug this summer," Whitley explains. "The local IRB might say, we will grant you one compassionate plea patient, but it would not be good practice for the chair of the IRB to say, 'I'm going to let you study 10 patients on a compassionate plea protocol.' It is just bad form. It violates public trust in the institutional review board process because it appears as though someone is coming around to the backdoor to get approval in an easy fashion."

The solution, Whitley argues, is to have a single national IRB devoted to reviewing and approved research protocols that study new and emerging infectious diseases. "What I've proposed is to have some sort of omnipresent, universal institutional review board that would be just for emerging infections — not to circumvent all of the cancer protocols that need to go through or the cardiology protocols — but to provide rapid, public health response for the U.S. people," he explains.

The national IRB would approve one protocol that would be followed at each site nationwide studying a particular new disease, vaccine, medication or other treatment. It would eliminate the need for local IRB approval at each participating site.

"In that way, we can guarantee that: 1) an IRB has looked at the protocol and does think that it should be performed; and 2) that the protocol gets the buy-in of the U.S. Food and Drug Administration and the Office of Human Research Protection [OHRP]," Whitley continues. "So, then, we would not be putting ourselves in the position of having an investigator fighting at each institution to get approval in the next 24 hours, so the protocol can be done."

Establishing such a national body, of course, will require new legislation. So, Whitley is now making the rounds, explaining his proposal to representatives with the Infectious Diseases Society of America (IDSA) and the American Association of Medical Colleges (AAMC), as well as select lawmakers.

Once he has input and buy-in from the professional organizations and policy community, he hopes get sponsorship from both the NIAID and IDSA to hold a national meeting in Washington, convening medical, legal, and policy experts to draft a proposal.

Whitley acknowledges his plan might be a tough pill for local IRBs to swallow. "This represents a serious paradigm shift for people who like power — and those are the local institutional review boards. I think we will see challenges possibly from OHRP and from the local institutions," he notes. "Particularly, the legal representatives who serve on local IRBs may not be very receptive. They may not necessarily care as much about what his happening overall with the emerging infection, but about the potential liability of the individual institution for any adverse events."

To those who might think his approach is overkill, he points out that other countries, such as the United Kingdom, are considering similar plans, and that new, infectious diseases are an increasing threat. Each missed opportunity to study a case might be an opportunity for a cure lost forever, he adds.

"Delay in review of research in the face of emergencies may mean missing the emergency and forsaking research opportunities necessary to make advances that may not recur," Whitley states. "The Great Influenza Pandemic of 1918-19 came and went in less than 12 months. To this day, we don't know what caused it and how to prevent it. Who knows when the next pandemic, terrorist incident, or natural disaster will occur?"

Reference

1. Whitley R. We need to "fast-track" research. *The Wall Street Journal.* June 19, 2003. ■

You've got questions? We've got answers

IRB launching new column

In this issue of *IRB Advisor*, we are starting a new column designed to answer reader questions. If you have questions regarding IRB responsibilities, federal regulations, adverse event reporting, day-to-day functions, anything related to clarifying the duties and responsibilities of your IRB, we'd like to know. Please forward questions to alison.allen@ahcpub.com, and each issue we'll ask an expert in the field to provide an answer.

Question: What is the role of a local IRB when a trial is conducted in several locations (i.e., is part of a multicenter trial)?

Answer: John Isidor, JD, CEO, Schulman Associates IRB, Cincinnati — I believe the intent of the question is to distinguish between the role of a local IRB in a multicenter trial and in a trial being conducted only at its institution.

The role of an IRB in reviewing biomedical research is defined by the applicable Code of Federal Regulations, 21 CFR 56 (for FDA regulated research), and 45 CFR 46 (for federally funded research), as well as the standard operating procedures of the IRB. Nothing in the federal regulations distinguishes between obligations of an IRB in a single site study vs. a multicenter trial. The same should be true for IRB standard operating procedures, unless the local IRB has agreed to transfer its obligations to a central IRB.

Accordingly, the local IRB must review a multicenter trial with the same level of responsibility and oversight as it would a trial being conducted only at its institution. The local IRB should establish a period for approval of the research, consistent with the degree of risk, not to exceed one year.

Additionally, the local IRB must have in place procedures for reviewing safety information it receives during a trial. In multicenter trials, a local IRB will receive both adverse event reports and IND safety reports. The local IRB will receive only investigator-generated adverse event reports about events that occur at its institution. If the multicenter trial is being conducted under an IND, the local IRB could receive sponsor-generated IND safety reports about adverse events that occur at other sites.

The local IRB should have a process for reviewing both adverse event reports and IND safety reports that arise from the trial. Additionally, if the study has a data safety monitoring board (DSMB) in place, I would recommend that the local IRB find out when the DSMB meets and request copies of any reports that the DSMB issues.

A final issue is the dilemma of a local IRB requesting changes to the protocol in a multicenter study. The local IRB must decide whether the protocol is approvable based on a risk benefit evaluation and whether it is appropriate to be conducted at its institution. This charge cannot be modified based on whether the research is being conducted at one institution or 400 institutions. If the local IRB decides that the protocol needs modification to be approvable, it must notify its investigator who in turn will notify the sponsor. The sponsor has one of three possible responses to such a request: it could agree to modify the protocol for all sites; it could agree to a site-specific modification, or it could refuse to amend the protocol. If the sponsor will not agree to what the IRB considers to be a modification necessary to make the benefits of the study outweighs the risks, the local IRB should not approve the research. ■

Regional conference looks at ethics, HIPAA

Schulman Associates Institutional Review Board Inc., the University of Cincinnati, and the University of Kentucky will host a one-day conference, "IRBs: The Times They Are A Changing," Sept. 19, 2003, at the Northern Kentucky Convention Center in Covington.

Topics to be covered include "The Past, Present and Future of Human Experimentation," "Compliance and Quality Improvement in Human Subject Protection," and "HIPAA and Research: Where Do We Stand Now?"

The cost to attend the conference is $100. For more information, contact Lori Levesque at (513) 761-4100, ext. 121, or via e-mail at LLevesque@sairb.com.

Other upcoming conferences include:

- **Respect for All Involved: A National Research Integrity and Human Subjects Protection Workshop,** New York City, Sept. 8-9, 2003. For more information visit http://columbiacme.org/OHR-03/SAVE_THE_DATE_Final.pdf.
- **Responsible Conduct of Research (RCR) Expo**, Pittsburgh, Oct. 18-22, 2003. For more information, visit http://ori.hhs.gov/html/programs/October_18-22_2003.asp.
- **Enhancing Integrity in Clinical Research**, Los Angeles, Nov. 15, 2003. For more information, visit http://ori.hhs.gov/html/programs/November_2003.asp. ■

COMING IN FUTURE MONTHS

■ Custom software developed out of necessity goes on to win best practice award

■ Model education program gives new IRB members quick expertise

■ Accreditation update: Here's how some IRBs made the grade

■ More IRB trouble: Recent OHRP actions criticize IRBs for lax monitoring of informed consent

CE/CME objectives

For more information on this program, contact customer service at (800) 688-2421; e-mail: customerservice@ahcpub.com.

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

- **establish** clinical trial programs using accepted ethical principles for human subject protection;
- **describe** 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;
- **explain** the potential for conflict of financial interests involving human subject research;
- **discuss** reporting adverse events during research. ■

CE/CME*questions*

5. Which of the following is not a way in which some hospitals or universities have compensated IRB members?
A. Provide a salary that fairly compensates IRB members for their time spent on the IRB.
B. Provide IRB members at universities with a graduate assistant.
C. Provide IRB members with local cultural and restaurant gift certificates.
D. Provide IRB members at universities with time and salary credit to a department research account.

6. Key elements of the informed consent process include conveying which of the following:
A. Participation is voluntary.
B. Risks and benefits.
C. Participants may withdraw from the study at any time.
D. All of the above

7. Which of the following best describes the informed consent process that garnered NIMH an award?
A. Representatives read the informed consent document to subjects, answering all questions. If a subject seems unable to remember or repeat the important elements of the informed consent, the investigator is asked to provide special assistance to that subject before the study begins.
B. Representatives give subjects a capacity assessment for decision-making test and make a decision that the principal investigator must follow about whether a subject is capable of making informed consent. The same trained and experienced representatives continue to follow subjects' progress as the study proceeds.
C. Representatives serve as a go-between for investigators and the IRB, modifying the informed consent document at the IRB's request, and answering all questions potential subjects may have.
D. None of the above

8. According to the article, a national IRB would:
A. Be able to approve study protocols rapidly, obviating the need for multiple IRBs to examine the same protocol.
B. Consider only study proposals related to emerging infectious diseases.
C. Be established by national legislation with input from the National Institute for Allergy and Infectious Diseases, the American Academy of Medical Colleges, and the Infectious Diseases Society of America.
D. All of the above

Answers: 5-C; 6-D; 7-B; 8-D.