IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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Legislation, community education on research radar screen for 2004

Senior policy fellow offers projections on big issues in upcoming year

With the changes that have occurred for IRBs and the research industry in recent years, it's a safe bet that the trend will continue in 2004.

For some ideas of the challenges that IRBs may face in coming months, **Felix A. Khin-Maung-Gyi**, PharmD, MBA, CIP, chief executive officer of the Chesapeake Research Review Inc. of Columbia, MD, provides a look at some of the more important issues. Khin-Maung-Gyi is a senior policy fellow with the Center for Drugs and Public Policy at the University of Maryland in Baltimore, and the Chesapeake Research Review, which recently celebrated its 10th anniversary, is one of the nation's largest independent IRBs with a staff of about 50 and an IRB board consisting of 20 members.

Here are some of the issues he believes will be important to follow this year:

• **Recruiting women and minorities:** "The National Institutes of Health [NIH] has long addressed the issue of recruiting women and minorities into research, and both the Food and Drug Administration [FDA] and the NIH have guidelines posed in the 1993-94 *Federal Register* encouraging enrollment of women and minorities in research," says Khin-Maung-Gyi. "But here is the dilemma that we as a society are facing: Overall, fewer than 10% of the eligible population participates in research. When we look at critical issues like cancer, the participation of women and minorities falls drastically to less than 5% and less than 3%."

Research must continue to take a systematic approach to evaluating safety and effectiveness prior to FDA or other regulatory approval, yet there must be some effort made to reach greater numbers of the

populations that will use these drugs and products, Khin-Maung-Gyi says.

"We have to go into the community," he says. By making greater efforts to include minorities in studies, researchers also could help to improve the long-standing lack of trust that exists between some minority communities and the research community.

"If we take a look at minority communities, there is a huge gap in understanding what the research enterprise might be, and this gap is fueled by a lack of trust in the research enterprise," Khin-Maung-Gyi says. "It's a lack of trust that is well founded, by the way."

There have been many examples of government research that has violated basic ethical principles of justice, autonomy, and beneficence, he notes. "But other basic principles, like permission and respect, also were violated, and people remember those things."

Examples include the Tuskegee syphilis study, prisoner research in the 1960s, and radiation experiments of the 1960s and 1970s.

"There is a good reason for them to feel skittish about research," Khin-Maung-Gyi says. "They already are feeling as though they don't have access to good health care and other societal benefits that nonminorities have, and so we can't ignore that."

• **NIH road map and education:** "I have long believed that education is a critical component in identifying and recruiting and retaining subjects for appropriate identification, appropriate inclusion, and appropriate retention," Khin-Maung-Gyi says.

Three sectors of the public need additional education about research, including the public, legislators, and researchers, Khin-Maung-Gyi notes. Although the NIH road map promotes further education, IRBs and the research community cannot hold NIH solely responsible and accountable for education, he says.

"They are entrusted with public funds to forward public agendas, and the industry also has to share in that responsibility," he says. "We have a burden in training and assuming that level of investment."

It also is important to have the right legislation in place, as well as voluntary accreditation. "Things like accreditation are steps in the right direction to help us assure each other that there are minimum standards being met," Khin-Maung-Gyi says. "But it's a costly venture."

• **Health Insurance Portability and Accountability Act (HIPAA):** "Clearly HIPAA has had a huge impact on all of us," Khin-Maung-Gyi says.

"I think we need to remind each other that HIPAA is a regulatory constraint that was implemented to protect clinical issues," he adds. "It wasn't drafted with research in mind as a primary

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focus." However, now that it's implemented, it must be a top priority for IRBs.

"Whenever we get to protecting rights and welfare of subjects in any kind of peripheral way, all eyes turn to the IRB," Khin-Maung-Gyi notes. "Administration, researchers, and regulators all turn to the IRB, and the IRB is woefully understaffed to address all of those issues, and it's not really fair."

• **Potential legislation:** "The IRB community needs to be aware of pending or potential legislation," Khin-Maung-Gyi says. "There are a couple of bills proposed on the Hill that should be reviewed by IRBs and research communities, and they should educate their own legislators in terms of what's going on."

Specifically, the bills are as follows:

— **H.R. 3594:** Protection of Human Subjects; Uniform National Applicability of Common Rule and Provisions Protecting Vulnerable Populations.

This bill would require IRBs to review all human subject research, and boards would have to consist of 25% or no fewer than two members who have primary expertise in scientific areas, 20% or no fewer than two members who have an expertise in nonscientific areas, and 20% or no fewer than two members who are not affiliated with the institution served by the IRB and who are not immediate family members of anyone affiliated with the institution and who do not have a significant conflict of interest.

The bill also specifies a list of other requirements for IRBs, including requiring an orientation program and continuing education program for members and the disclosure of significant financial interests.

Sponsored by U.S. Rep. Diana DeGette (D-CO), the bill was referred to the House Energy and Commerce committee as of Nov. 21, 2003.

— **H.R. 1585:** Establishes an office to oversee research compliance and assurance within the Veterans Health Administration of the Department of Veterans Affairs.

The bill establishes an office of research compliance and assurance to promote responsible conduct and ensure ethical treatment and safety of research subjects. The office will investigate allegations of research impropriety and misconduct and suspend, restrict, or modify research as determined appropriate.

Sponsored by U.S. Rep. Steve Buyer (R-IN), the bill has 19 co-sponsors and, in October 2003, was forwarded by the House Subcommittee on Health to the House Committee on Veterans' Affairs in the nature of a substitute by voice vote.

— S. 3060: A bill to amend the Public Health Service Act to provide protections for human participants in research.

The bill, also called the Research Revitalization Act of 2002, amends the Public Health Service Act to require research involving human subjects in America, funded by the U.S. government, to meet specific criteria, including prohibiting investigators from conducting the covered research without IRB approval.

Sponsored by Sen. Edward Kennedy (D-MA, the bill was introduced Oct. 4, 2002, and referred to the Senate Health, Education, Labor, and Pensions committee, where it has remained.

"My position is that legislation that is going to be considered should be pretty inclusive to include not only IRBs, but researchers and institutions and sponsors because human subjects protection issues don't reside only on the IRB level," Khin-Maung-Gyi says. "Other people seeing subjects have to have some shared responsibility for human subjects protection, and it must be fair, inclusive, and consistent." ■

Special Coverage:
2003 PRIM&R/ARENA Conference

NIH roadmap calls for IRBs to clarify role

Key NIH players discuss roadmap's goals

Among the many changes experienced by IRBs and the research industry in recent years is the trend of more clinical studies being conducted in the community and in small clinics, a subtle shift away from major research centers. This trend is one of the many reasons the National Institutes of Health (NIH) unveiled late last year a series of initiatives called the NIH Roadmap for Medical Research.

The roadmap initiative identifies as the three most critical areas for the NIH to address the new pathways of research of discovery, new research teams, and re-engineering clinical research enterprise.

According to NIH's announcement, there has been a scientific revolution that poses complex challenges to transform scientific knowledge into

benefits for people. One way to expedite the research process is to promote the move of clinical trials into the community, where it often is easier to find research subjects. The drawback may be that smaller community IRBs are not as well equipped as IRBs at major academic research centers to handle an increase in complex biomedical or social-behavioral protocols, and this is a hurdle that the NIH will attempt to address in coming years.

IRB Advisor spoke with the principal leaders of the roadmap's Re-Engineering the Clinical Research Enterprise steering committee to learn more about how the roadmap will impact the research industry and IRBs in the coming decade.

"Some of the issues that have to come up are what's the role of central IRBs?" says **Stephen I. Katz**, MD, PhD, director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases in Bethesda, MD. He also is a principal leader of the NIH steering committee on Re-Engineering the Clinical Research Enterprise.

Other questions that the NIH roadmap may address, Katz says, include:

- What is the relationship between the data safety monitoring board and the IRB?
- What are the best practices with regard to consent form developments?
- Are there better ways to educate the research community in terms of preparing investigators for developing protocols for IRBs?

"Those are issues that are important in terms of harmonization of clinical research and regulatory burdens," Katz says.

The NIH roadmap is a commitment to improving the nation's research infrastructure, including enhancing training for investigators so that more diverse practitioners can engage in research, says **Stephen E. Straus**, MD, director of the National Center for Complementary and Alternative Medicine in Bethesda, MD. He also is a principal leader of the NIH steering committee.

"Research is not a hobby," Straus notes. "You need to be in the right environment with the right safeguards for patients' safety and ethical oversight, and you have to be in the hands of people who are skilled and have the right monitoring."

The re-engineering clinical research portion of the NIH roadmap will work to make it easier for research findings in the laboratory to be tried in the clinic, he says.

"It will bring practitioners and patients together in community research to test out these approaches and then to attempt to see whether they work in the community setting," Straus explains.

"The re-engineering clinical research components can only help us in complementary and alternative medicine [CAM] research because so much of what we do is clinical research," Straus adds. "In fact, more of what we do is clinical research than any other institute in NIH."

What's ahead

Katz and Straus offer these ideas for how the NIH road map may impact future research:

- **Harmonization of clinical research regulatory burdens:** "That's the most difficult task because, first of all, that's not something NIH can do alone," Katz says. "In fact, we're not a regulatory agency, and we really can't do that."

Instead, NIH will need to work with other governmental agencies, as well as with nongovernmental organizations, to identify the areas that need harmonization and simplification, he notes.

"We can make the role of the clinical investigator a little bit easier, while at the same time not in any way compromise our commitment to human subjects protection," Katz says.

NIH officials have continued to meet with leaders at other governmental agencies to discuss this issue, he adds.

- **Development of interdisciplinary research:** This is the second major pillar of the roadmap approach, and it recognizes that research is increasingly complex and multifaceted in today's world, Straus says.

"It requires us to bring together individuals to make a research collective that may not have come together previously," Straus says, adding that this approach is particularly important to the goals of the National Center for Complementary and Alternative Medicine.

"This is very relevant to complementary and alternative medicine research," Straus says.

For example, CAM research, needs the input of anthropologists, behavioral scientists, brain imagery technicians, biomechanical engineers, physicists, and physical chemists, he adds.

"So our approach already is a highly integrated, multidisciplinary and interdisciplinary one, but the commitment on the part of the NIH as a whole to expand the creation of interdisciplinary researches into the more robust enterprise will help us," Straus says.

- **Accelerating research:** The roadmap will encourage research projects to move forward in

order to bring medical improvements and therapies to the public more quickly than what currently occurs.

"Everything within the road map is made up of initiatives that no one institute could do on its own," Katz says. "It really serves as an infrastructure to accelerate and to facilitate research in all these areas, whether it's new pathways of discovery, whether it's the development of interdisciplinary research teams for the future, or whether it's re-engineering clinical research."

The road map is expected to make it easier for researchers to gain access to necessary tools and technologies.

"There are certain tools and technologies in certain research communities that are simply not available, and to try to do research when all the tools are not in place is always a slower process," Straus says.

This focus on accelerating research will help smaller institutes, such as the NCCAM, which do not have the financial resources to invest millions into developing new tools whenever a need arises, he notes.

"We have to rely on the growth and maturation of the larger research enterprise to be more successful, so this will accelerate our work without question," Straus says.

The roadmap is intended to help accelerate research along the entire continuum from discovery to application, Katz says. "Even if we're the fastest [in the world], it doesn't mean we couldn't be faster."

• **Moving research into the community:** "In the real world, medicine is not practiced in the hospital wards the way it had been a century ago," Straus says. "It's increasingly practiced in clinics, in offices, and even in the community. We have tools and technology that are widely dispersed."

For example, the imaging technologies available at the NIH campus also are available at 500 other places around the country, he notes. "So the public increasingly has access to new tools and technologies."

As such, researchers no longer can expect research subjects to come to them as they may have in the past when there were fewer options available to patients who wanted to receive the latest treatments, Straus adds.

"We have to come to them, and we can do it in two ways: We can place university hospitals in every major city in the United States, and we do that to a great extent, but there's great costly duplication," Straus says. "But the other way is to put practitioners with some research training in the community so when they are caring for patients in their own practices, they are better attuned to making observations that could flow into research design and conduct, and they can even participate in research studies."

"The roadmap process envisions training thousands of practitioners, dentists, physicians, nurses, chiropractors, and others who, within their own practice, could enroll patients into multicenter trials," Straus says. "We have telemedicine today and electronic technologies, so our ability to community and interact broadly creates a web of opportunity that didn't exist before."

The NIH roadmap's goal is to harness technologies into a virtual research enterprise in which academic investigators, clinical practitioners, and patients all have access to each other and each other's tools and ideas, Straus adds. ■

Special Coverage:
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U.S., international IRBs forming partnerships

International organization offers model

As more research heads for underdeveloped countries, there are greater challenges and opportunities for research institutions and IRBs located in the United States that may be connected to the research done in these countries through sponsorship or multisite clinical trials.

"We do a lot of work in developing countries, and more and more research is heading to those parts of the world," says **David Borasky**, CIP, associate director of the Office of International Research Ethics at the Family Health International (FHI) in Research Triangle Park, NC.

He spoke about building IRB capacity in developing nations at the PRIM&R/ARENA conference, held Dec. 5-7, 2003, in Washington, DC. The annual conference included its strongest focus yet on international research and IRBs, Borasky says.

"A lot of these [third-world trials] require IRB review that follows U.S. standards," he says. "Following the terms of a federal assurance is

easy to sign your name to, but actually implementing it has been a real challenge to a lot of international institutions."

Institutions that work with an international country for particular research may benefit from helping to develop an IRB or research partner in that region, Borasky suggests.

And these types of international IRB relationships likely will increase as global technologies make it easier to communicate and teleconference, he notes. "Even in developing countries, most folks have e-mail, and some have cell phones."

When there is a research connection that may involve multiple studies or long periods of time, it may well be worth the financial resources it would take to mentor the foreign IRB and help IRB members learn the same skills used by their U.S. counterparts, Borasky says.

"It's a little trickier if you have a study here and a study there, because it's tough to find the funding to do capacity building for the IRBs," he adds. "The groups that should look more into this are the sponsors of research; groups like the Office of Human Research Protections will be doing more of this."

FHI has received a National Institutes of Health grant to identify and assist international institutions that need some IRB support. These institutions include the College of Medicine at the University of Malawi in Balntyre, Malawi, and the University of Zambia in Lusaka, Zambia, Borasky reports.

"We identified the institutions and got their verbal commitment to participate in the project, and we'll spend a year trying to get them up to speed for what they agreed to do in their federalwide assurance," he explains. "We'll help them meet the goals of that assurance by going over there, visiting IRBs, spending a week at each site, and looking at their operations from top to bottom."

For U.S. IRBs that often are challenged with finding enough financial and staff resources to meet all regulatory and caseload requirements, it is easy to understand how an IRB at an institution that has far fewer financial resources can struggle meeting U.S. regulatory standards.

"They don't feel like they have the financial capability to do things the Western way," Borasky says. "There is the burden of overhead; they don't have large pots of money sitting around to be spent, so it's tough to make the IRB a financial priority for an institution."

Also, foreign IRBs may find it difficult to figure out how to meet the U.S. federalwide assurance, as there is no instruction or guidebook describing strategies for doing so, he adds.

Through the mentoring program, FHI will observe how the foreign IRBs work and hopefully learn some strategies for assisting these IRBs with improving their processes, Borasky adds.

Here is what the mentoring program will involve:

- FHI staff will visit with the IRB chairs and staff to see how the IRB handles documentation.
- They will examine the IRB roster to see how it is planned and identify areas of improvement.
- They'll provide the IRB with strategies for improving deficiencies.
- IRB chairs from the international institutions will travel to North Carolina to spend a week meeting with IRB staff and chairs at institutions in the Research Triangle Park area. They'll visit both academic and independent IRBs.
- After a year of the mentoring program, FHI staff will return to the international IRBs to see how they've improved and what still is lacking.

"We'll see what barriers they've encountered in trying to achieve their goals, and will look for funds to continue the program," Borasky says. "Both sites are enthusiastic about it, and representatives from both sites attended the PRIM&R conference." ■

Special Coverage:
2003 PRIM&R/ARENA Conference

Subjects often don't understand benefits

Biomed and social-behavioral each pose challenges

While IRBs often pay close attention to a protocol's potential risks and may hold discussions on the risks vs. benefits ratio, the benefits side of the equation often is poorly explained and less well examined, experts say.

"There's a lot of discussion about how to talk about the risks of harm and what kinds of risks you may be undertaking when you join a study," notes **Nancy King**, JD, professor of social medicine

at the school of medicine, University of North Carolina in Chapel Hill.

"Very often, you see consent forms that say you may or may not benefit," she says. "What does this mean in terms of people's expectations of how they might benefit, and what do IRBs, study coordinators, and others think about benefits in addition to risk?"

King spoke about beneficence at a medical sciences panel presented at the PRIM&R and ARENA meeting and conference held Dec. 5-7, 2003, in Washington, DC.

She was involved in a study that looked at research consent forms and conducted interviews of study coordinators and research subjects about risks and benefits.

"We are in the process of analyzing data, but one [finding] we think is really important is that it's a lot harder to talk about benefits of research in the early stage than it is to talk about risks, and people aren't experienced doing it," King says.

For example, the classic phase one drug research study is conceived to test for safety in healthy volunteers, who because they do not have the disease for which the study is being conducted do not stand to personally benefit from any positive effects of the drug. On the other hand, some phase one drug studies use volunteers who have the disease that is being investigated; and with these individuals, there is a potential for a medical benefit from their participation, she says.

"So does that mean if a benefit is possible that you can talk about it with the volunteer?" King asks. "There's a lot of disagreement about the answer to that question."

Lowered expectations?

On the one side, the IRB and investigator may decide not to raise volunteers' hopes by mentioning a potential benefit, and then if there is a benefit, it will be a surprise and bonus, she says.

"But one of the problems with that approach is that people who have a disease or condition go into a study in the first place because they want to benefit," King says. "So you may give rise to under-the-table conversations where investigators say, 'We have to say that in the consent form, but really we think you might benefit.'"

In the study about consent forms, she and colleagues found that the consent forms tend to be vague in their discussion of benefits, and this makes it difficult for participants to understand. Investigators tend to be vague about benefits because they don't fully understand the issue themselves, King notes. "A more thorough discussion of what can and cannot be expected from a study would be very helpful to volunteers," she adds.

Improving the way investigators and IRBs look at potential benefits is one challenge that may require additional education and training. "Let's see if there aren't ways we can be more helpful to IRBs and investigators and talk to them about what potential benefits might be more realistically expected in a given study," King says. "That's the focus of my colleagues and my research."

If benefits to subjects involved in biomedical science are little understood, then the problem may be even more pronounced when it comes to explaining the individual and societal benefits to participation in social-behavioral research.

"There are lots of challenges facing social scientists when it comes to appreciating research they do," says **Moira Keane**, MA, CIP, director, Research Subjects Protection Programs of the University of Minnesota in Minneapolis. She participated in a social and behavioral sciences panel on beneficence at the PRIM&R conference.

"We hear far more frequently about breakthroughs in medicine and challenges in medicine that are overcome by research," Keane says. "It's difficult for social and behavioral sciences to garner the same kind of exposure for advances they are making, because sometimes they are subtle and sometimes they are based on broad population trends, things like crime prevention, risky adolescent behavior."

Likewise, it the potential benefits to an individual research subject are more difficult to pinpoint and communicate, she notes. "In medical science, it's much easier to say we fixed this broken leg due to a new procedure; but on the social-behavioral side, it's more difficult to link the benefits to society," Keane says.

One solution to the obstacles social-behavioral research poses to understanding benefits would be to present what is known to participants in a straightforward manner, she suggests.

"We have to be honest with our research subjects and participants and tell them what we know and think we can predict and often say what we don't know," Keane says. "There are unseen risks, and we don't know what your experience will be."

Benefits in such cases may be experiences that

are difficult to identify and explain. For instance, an investigator who has worked extensively with a particular population may find that some subjects experience relief when they discuss a part of their past with investigators, and this could be a type of individual benefit, she explains.

"But we can't generalize that to the entire population because there may be people who don't want to talk about it," Keane says. "We often have to be honest with people and say, 'We really don't expect that you will benefit, but it's possible other people will benefit in the future.'"

Adult research participants have the choice to make altruistic choices, including giving their time and experience to research for the greater good, although they might not receive a personal benefit from participation, Keane adds.

The challenge to IRBs is to weigh research participants' decision to forgo a potential personal benefit and see if there is a potential benefit to the greater society for which it would be worth asking individuals to make a sacrifice, Keane says. "IRBs are somewhat conservative to their approach to risks and benefits." ■

Supply and demand: Volumes are going up

Increases have resulted in efficiencies

A few years back, the Office of the Inspector General (OIG) released a report that referred to the IRB process as "A System in Jeopardy." Among the problems and challenges described were "conflicts that threaten independence," "lack of training for investigators and board members," and the fact that "IRBs review too much, too quickly, with too little expertise."

Over the years, there has been a focus on recognizing and eliminating conflicts of interests among those who are conducting or overseeing research involving human subjects.

There also has been a big education push with programs springing up locally and on the web that are designed to present ethical concepts related to human subject research, as well as an overview of federal regulations that govern research activities.

No such national campaigns for managing volume have sprung up. In fact, securing resources and developing efficiencies has become the responsibility of individual IRBs, and if data collected for the *IRB Advisor* Salary Survey report, appearing in the November 2003 issue, is any indication, it's a big job. For example, in October 2003, there were more than 7,000 trials listed on the National Institutes of Health's web site, ClinicalTrials.gov. In 2000, there were 4,000 clinical trials listed.

"There has been a significant increase over the last five years, attributable to the increased and improved educations of researchers. There has also been a corresponding increase in the ancillary requests — e.g., amendments, adverse events, review of IND [investigational new drug] safety reports, deviations, etc.," says **Margaret T. Feeney**, MBA, RAC, Committee on Clinical Investigations Liaison for Quality Assurance and Audit, Beth Israel Deaconess Medical Center in Boston. Improved education has increased awareness among investigators of the need for IRB review, she explains. "For example, a principal investigator now understands that they can't simply go and advertise for study participants, but must first bring that advertisement to the IRB for review."

Growth at St. Joseph's Hospital of Atlanta has been exponential, says **W. Parker Nolen**, MBA, IRB administrator for the hospital. According to Nolen, the full board reviewed 30 protocols in 1999, as many as 54 in 2000, 60 in 2002, and 90 in 2003. Recently, the hospital formed St. Joseph's Research Institute and has seen even more growth. "There has been an 11% increase in one month alone. In January, we expect 17 new protocols alone, so 2004 looks to be a watershed year," says Nolen.

With growth has come some challenges, the most obvious being staffing. The simple solution is to simply hire more people, which is what St. Joseph's — and a lot of other IRBs — did. "In the mid-90s, there was one administrative person, a medical secretary whose role was more clerical," Nolen says. Currently, there are two full-time staff members, and the hospital is looking for a third. "It's difficult to find and hire the most qualified people," he reports, "particularly since St. Joseph's now requires professional certification [CIM or CIP], or a willingness to be certified within six months after hiring, before consideration for any position in the IRB."

It's not always as easy to hire more staff as it was at St. Joseph's, whose management, Nolen says, recognized the need to provide the resources.

One Boston organization's IRB administrative

staff solved their staffing problem by doing a little research of their own, says **Lynette M. Schenkel**, administrative director of research and academic affairs at Beth Israel.

"We collected data on our own volumes, the number of staff compared to the number of active protocols, and compared them to benchmarked data from six of the Boston-area medical center-based IRBs and other medical center-based IRBs throughout the country," she says. "The data were presented to medical center management, which responded very favorably to the documented needs."

What's worked

Whether the challenge is staffing or workflow, IRBs have buckled down or just gotten creative to meet do the jobs they've been charged to do. Here are a few tips on how to efficiently and effectively manage IRB volume:

• **Evaluate workflow.** Beth Israel created an IRB executive committee, made up of senior medical center management, administrative staff, legal counsel, and the chair and vice chairs of the IRB. "The group examines policy, procedure, and process, and has recently sponsored two important retreats, one resulting in the revision of our informed consent template and the second resulting in an updated IRB manual," says Schenkel.

• **Educate IRB members.** In addition to basic ethics and regulatory training, St. Joseph's provides monthly updates of standard operating procedures (SOPs) to board members.

"It may not sound like it increases efficiency, but it does," says Nolen**.** "The members are not involved in the day-to-day operations of the department — in the trenches, so to speak. Educating the IRB on the SOPs helps them understand the administrator's role better and what is expected from the investigators. Ultimately, it leads to more focused reviews, more germane comments, and a better IRB experience for everybody."

• **Fast-track expedited and exempt studies.** Nolen says St. Joseph's is being more diligent about expedited and exempt protocols.

"Any protocol is likely to have several changes during the approval period which do not impact the risk/benefit ratio of the study subject," he says. "For example, suppose a sponsor wishes to advertise. An advertisement usually does not require a full board review and should not take up valuable agenda time."

In some cases, the IRB administrator has been given authority to review materials. "If an institution has a large volume relative to its staff and IRB frequency, they might want to consider relegating some of the expedited and exempt items to the IRB staff — provided the IRB staff are experienced. 21 CFR 56.110 states 'Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers . . . ,'" Nolen explains.

• **Create checklists.** St. Joseph's considers checklists "tools that allow for clearer tracking and clearer evaluation of steps," says Nolen. St. Joseph's checklist is taken directly from federal regulations. "Our tools provide a way to document the review, recommendation, and action."

• **Create subcommittees.** After a routine U.S. Food and Drug Administration audit, First Dynamic Health Care Services Inc., an independent IRB headquartered in Waco, TX, reevaluated some of the IRB processes and decided to create subcommittees to handle increased request demands.

The subcommittees included an ethics committee, a site review committee, and a committee charged with evaluating consent forms and all proposed advertisements, explains **Robert Allison**, PhD, president and CEO of First Dynamic. "All activity of the IRB is reviewed by physician members," he says.

Beth Israel created a continuing review committee in 2002. "The process for notifying the clinical researchers regarding need for continuing review was evaluated, refined, and implemented, and committee members and the IRB staff created comprehensive continuing review report forms that undergo review and revision on a regular basis," says Schenkel.

• **Automate.** A number of programs exist to reduce the paperwork associated with submitting protocols and permit on-line tracking. Baylor College of Medicine created its own proprietary system — BRAAN (www.api.md) — two years ago in an attempt to increase efficiency without increasing staff, and St. Joseph's is doing the same. "It's a proprietary productivity tool designed to take away the clerical aspect of the job," says Nolen.

"Not only is our tracking system designed to eliminate a large part of the clerical aspects of the job, it is also designed to be a productivity enhancement for the investigator — no longer will they have to resubmit the same information to us, such as site address, license number, etc.," he explains.

"Most importantly," Nolen points out, "it is a compliance tool for the institution. At the touch of a button, we will literally be able to have a snapshot of a protocol, trending on its SAE [serious adverse event] profile, medications, amendments, and anything else an auditor may wish to see. A quality tracking system not only enhances staff productivity by automating repetitive tasks, it also helps the institution remain compliant with federal regulation and guidelines." ■

SPOTLIGHT ON COMPLIANCE

Compliance, integrity issues focus of reports

Recent OIG reports cover research issues

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It is difficult for those receiving federal dollars for research to avoid continuing interest by the Office of the Inspector General (OIG) in compliance efforts. In the last few months, two federal reports have included discussions of human subject protections.

The Department of Health and Human Services/OIG Fiscal Year 2004 Work Plan, which can be found at http://OIG.hhs.gov, acknowledges a U.S. Food and Drug Administration (FDA) request to review the effectiveness of FDA's own corrective actions designed to provide better control and oversights of FDA's clinical trials. Integrity issues with FDA's trials have led FDA itself to initiate an inventory of clinical trials, and a mandatory educational and certification program, which will include ethical issues, for all FDA clinical investigators. The OIG will take steps to determine whether the FDA's program is sufficient to avoid the unnamed integrity issues.

A second effort responsive to FDA's request will determine whether a specific FDA trial followed procedures on safeguarding participant records and other confidential information and documents. The trial involved a nutritional supplement designed to increase bone density. Reports on both projects are anticipated in 2004.

OIG also will review the National Institutes of Health's (NIH) research grants to ascertain the extent to which awards are made for noncompeting continuation grants and whether NIH closes out grants on time. While this effort will likely lead to greater diligence by NIH, its impact on providers only is indirect.

More direct will be the OIG effort to evaluate whether selected NIH grantees have themselves followed all the applicable rules. That effort, which is anticipated to be completed in FY 2005, will assess performance against not only the specific laws and regulation, but also more particularly whether actual expenditures were in line with and consistent with achievement of the grant objectives. The key focus group identified is grantees of the Human Genome Research Institute.

This latter effort could raise a series of interesting questions not usually subject to intense review, starting with: Were the objectives and structures desired by the grant achieved, as opposed to whether the expenditures were within budget and met broad general category requirements?

More specifically, the following types of questions could be asked: 1) If structures such as an advisory group were envisioned, was it actually created; did it meet regularly, and make recommendations; or 2) Was the knowledge envisioned to be developed through the grant actually reviewed and the subject of publications or educations programs?

The OIG also will review NIH practices with respect to ensuring compliance with adverse event reporting and processing, and the use of data safety monitoring boards. This activity could provide guidelines, or even regulations, about the definitions and processes surrounding adverse events. Currently, there are concerns over not reporting every potential adverse event and questions over whether trial participants are well served in large multicenter trial efforts when essentially every event can be perceived as adverse and, thereby, should be reported to the IRB.

Finally, OIG will evaluate compliance with federal regulations on reporting inventions and to what extent NIH monitors this process. As part of this effort, OIG will investigate whether NIH has received the required royalty-free licenses to inventions. A third element in this area will be an

assessment of the extent to which NIH receives royalty income on all products to which it is entitled. This series of efforts, to be the product of reports in FY 2005, signal a desire to examine and tighten up the commercial side of research development.

Grantees should see this as a signal to review their own processes and procedures ahead of government audits, and subsequent claims. Indeed, one can envision sizable where years of grants lending to products and royalties are at issue and books and records have not reflected appropriate notifications, accounting, and payment.

A second area reflecting OIG interest is an effort that began in September 2003 (68 *Fed Reg* 52,783) to develop compliance program guidance (CPG) for recipients of extramural research and cooperative agreement awards from NIH. Noting that the primary recipients of such grant funds are nonprofit and university entities that have initiated their own sponsored research compliance programs, OIG, nevertheless, seeks to create its own model.

As has been the case with other CPG efforts, the OIG notes that the resulting guidance will include the standard seven elements for such plans (which should be a part of any provider's compliance plan):

1. Written policies and procedures with respect to compliance.
2. A designated compliance officer and compliance committee.
3. Effective training and education.
4. Effective lines of communication.
5. Internal monitoring and auditing.
6. Disciplinary guidelines.
7. Prompt responses to problems, including corrective action and reporting.

OIG indicates it also is considering an eighth element — "Defining roles and responsibilities and assigning oversight responsibility." This element would "include a discussion of the importance of effectively delegating oversight authority."

There is a concern that this will, in effect, create an entire new set of regulatory requirements under the guise of guidance, with attendant new costs not likely to be included in any reimbursement or grant system of payment.

The notice of this effort also identifies specific areas of concern based upon the OIG's fraud investigations. In listing these areas, the OIG is alerting grantees to exposure areas for review:

- proper charge allocations;
- accurate time and effort reporting;
- appropriate use of program income.

Those seeking to avoid problems should review each of these areas to check their own processes and their underlying results. ■

Sociobehavioral issues focus of new branch

The National Human Genome Research Institute in December formed a new branch — the Social and Behavioral Research Branch (SBRB) — within its Division of Intramural Research.

The SBRB will concentrate on:

- testing communications strategies aimed at relaying an individual's risk for developing a genetic condition;
- developing and evaluating interventions aimed at reducing genetically susceptible individuals' risk of acquiring a disease;
- translating genomic discoveries to clinical practice;
- understanding the social, ethical, and policy implications of genomic research.

Research groups within the SBRB will include a behavioral genetics unit; a health communications unit; a genetic counseling service unit; a health promotion research section that includes a unit for disseminating counseling research methods; a community genetics research unit; and an ethics and social policy unit that includes research ethics. ■

COMING IN FUTURE MONTHS

- ■ Longitudinal research requires a different look at respect for people
- ■ A guide to selecting research educational materials and textbooks
- ■ Embryonic stem cell and related research pose ethical challenges to IRBs
- ■ IRB organization guidelines offered by expert

CE/CME objectives

The 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;
- 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

Physicians and nurses participate in this continuing medical education program by reading the article 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. You must complete the evaluation form provided in the June and December issues and return in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

1. Why do IRBs and investigators often fail to provide detailed discussion of a clinical trial's potential benefits?

A. In some cases, such as phase one studies, there may be no potential personal benefits to subjects.
B. When a social-behavioral study is conducted, the potential benefits to either an individual or society may be poorly understood by those conducting and reviewing the protocol.
C. The potential benefits are of far less importance than the potential risks.
D. A & B are correct.

2. Which are the three most critical areas to address, according to the National Institutes of Health's road map for research in 2003?

A. Revamping IRB process, including minorities into more research, expediting research projects.
B. New pathways of research of discovery, new research teams, and re-engineering clinical research enterprise.
C. Regulatory reform, improving IRB funding, enhancing biomedical research initiatives
D. None of the above

3. Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers.

A. True
B. False

4. Which of the following should be part of an IRB's compliance plan?

A. Written policies and procedures with respect to compliance.
B. Effective training and education.
C. Internal monitoring and auditing.
D. All of the above

Answers: 1-D; 2-B; 3-A; 4-B.