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Your Practical Guide To Institutional Review Board Management

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Special Report: Streamlining IRB Process

Experts: Saving time while improving review quality is top priority

"Unchecking the box" is a good start

Research programs and IRBs across the nation increasingly are focusing on streamlining their human subjects research programs. One change that has grown over the past decade involves "unchecking the box" on the Federalwide Assurance (FWA).

According to recent data from the Office for Human Research Protection (OHRP), 37% of research organizations uncheck the box on all subparts (A, B, C, D) and another 32% unchecked the box on all but subpart A.[1]

This trend has its own organization, called the Flexibility Coalition, which was started in 2011 by the University of Southern California in Los Angeles. More than 50 research organizations, including the Association for the Accreditation of Human Research Protection Programs (AAHRPP), have joined the coalition. AAHRPP reports that 51% of AAHRPP-accredited organizations had unchecked the FWA box and another 22% checked only the box applying to Subpart A. The trend of institutions unchecking the box has progressed over the past 15 years. In the 1990s, more than three-quarters of institutions checked the box.[1,2]

The Flexibility Coalition's stated goal is to identify ways research institutions can implement flexibility without harming human subject protection. By unchecking the box on Federalwide Assurance for the Protection of Human Subjects, institutions can limit the FWA scope to

Editor's note: The August 2013 issue of IRB Advisor *is focusing on the national trend among IRBs and research institutions to look for ways to improve efficiency and quality, reduce regulatory burden and unnecessary documentation, and, essentially, streamline their human subjects research programs. In this issue, the cover story focuses on the growing trend of "unchecking the box" for Federalwide Assurance. Additional articles focus on ways to improve informed consent, expedited reviews, reducing review turnaround time, and hiring IRB liaisons.*

federally funded research. Unfunded research projects have the same human subjects protection, but the unchecked box gives an institution more flexibility in how it handles these studies.

"We unchecked the box six or seven years ago," says **Susan L. Rose**, executive director of the office for the protection of research subjects at the University of Southern California (USC).

"Unchecking the box had never crossed my mind, and then I heard about it at an AAHRPP meeting," Rose recalls. "We did it here and it has been a life changer."

The change has impacted hundreds of studies at USC, including both biomedical and social-behavioral studies. One priority in making the change has been to emphasize to researchers that the level of human subjects protection for research that is handled through the flexibility changes must be equivalent to protections for all federally funded research, Rose says. *(See excerpt from USC's flexibility policy, page 87.)*

One of the goals of unchecking the box and improving flexibility is to avoid having investigators report trivial issues when they occur in a study that is not federally funded and is of minimal risk. For example, if a participant answering questions through an electronic questionnaire were to have dry eyes from staring at the computer screen, that would have been reported prior to "unchecking the box," Rose explains.

"It takes a huge amount of paperwork to report everything," Rose adds. "This allows flexibility to be applied to those projects that are not federally funded and have no risk."

USC's flexibility policy allows for exceptions and also states that it creates exempt categories 7 and 8 for projects that do not conform to a specific exempt category in the regulations (45 CFR 46), and it allows for two-year approvals for nonexempt unfunded projects that are not FDA-regulated and involve minimal risk.

"We have a huge list of items that may be flexed and items that may not be flexed, and if funding changes during the year and someone receives federal funding, we need to know immediately," Rose says. "No one has violated that."

Streamlining research and unchecking the box are trends that are slowly growing in the IRB world, says **Lori Roesch**, CIM, CIP, manager of the research subject protection program at Aurora Health Care Inc. of Milwaukee.

Roesch recalls first learning about the drive for flexibility in research through AAHRPP.

"I think it is the wave of the future," she says. "As we talk about it more at AAHRPP conferences, more people will get the word out there, and the Flexibility Coalition will help."

"I saw how you could improve your program through that flexibility," Roesch says. "In August 2009, we had a discussion about unchecking the box; I recommended we no longer check the box

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and limit OHRP's jurisdiction to studies that have federal funds."

When Roesch presented this change to the organization's leadership, she talked about how many institutions were moving in that direction and that AAHRPP, which had accredited Aurora Health Care, also supported flexibility.

"They agreed to move forward with the recommendation," Roesch says. "We decided to apply this only to studies that don't leave our organization and which will be maintained here."

Aurora Health Care recently joined the Flexibility Coalition, which provides tips on flexibility and streamlining, she says.

"I'm looking forward to hearing other ways we can use flexibility while having protections in place for subjects," Roesch says. "We have to make sure we're applying equivalent protections, but the flexibility of unchecking the box allows you to do it in ways that are not as proscribed as the regulations are."

One flexibility project Aurora Health Care started a year ago involved streamlining residents' medical record retrospective reviews. Before unchecking the box, the organization would have had to handle these studies through the formal expedited review process, Roesch notes.

"What we've done is used flexibility to provide our researchers with a very streamlined application and review process that we call a category 10 for expedited review," she explains. "Studies that meet certain parameters can be expedited and informed consent is waived."

This change has made the submission process simpler and more straightforward for these retrospective studies, and it's helped the IRB turn around requests much more quickly, Roesch adds. *(See story on IRB efficiency measures, page 88.)*

"Researchers are pleased with how quickly we can turn these around and how streamlined the application process is," she says.

Flexibility and streamlining have become such an integral part of Stanford University's research enterprise that the university has named 2013 as the "Year of Streamlining." The institution's research leadership has made streamlining a priority for the entire research enterprise, and the goal is stated clearly on its website. Its intention is to cut back on unnecessary activities, says **Kathy McClelland**, CIP, research compliance director of Stanford University in Stanford, CA.

Stanford University unchecked the box a couple of years ago and has continued to find new ways to streamline its research operations since then, she says.

"We unchecked the box and are streamlining operations so we can concentrate on the higher-risk studies, putting our resources where it's most important," McClelland explains.

For example, Stanford no longer requires annual continuing reviews for around 1,000 active, nonmedical studies, she says.

"Instead of having them fill out the continuing review form annually, we send a communication telling them that if they haven't made any changes or haven't received any new federal funding then they don't have to file anything with us," McClelland adds. "We do this for three years; then after three years if they're still doing their study they will need to renew at that time."

This frees up time for both the IRB and

Special Report: Streamlining IRB Process

USC's flexibility policy has these exclusions

Funding is factor

The University of Southern California in Los Angeles allows flexibility in its research protection program through limiting the scope of its Federalwide Assurance (FWA) to federally funded research that is of minimal or no risk. These studies are given similar protections to funded studies. Nine mandatory exclusions, listed below, apply:

- funding (exceptions may apply for non-federally funded research);
- no-cost extensions;
- projects where a student is paid/supported from a federal training grant or otherwise paid/supported directly from the faculty advisor's federal funds;
- federal sponsorship, including federal training grants;
- studies with FDA-regulated components;
- studies with contractual obligations or restrictions that preclude eligibility in this policy;
- studies with clinical interventions;
- studies using prisoners as subjects;
- studies seeking or obtaining Certificates of Confidentiality. ■

investigators. The dean of research has a goal of helping investigators free up their time so they can do their research as opposed to doing time-consuming paperwork, she says.

"It's a win-win for the IRB and researchers and saves some staff time, as well," McClelland says. "We started this one and a half years ago and it's working very well."

To ensure that investigators remain compliant during this three-year lag, the compliance office randomly audits study sites, asking investigators to send in their last three signed informed consent forms and inquires about their funding sources, she adds.

Another streamlining change was made for retrospective chart reviews. When investigators are not receiving federal funding to look at existing medical records to find trends for improving treatment, they also are eligible for a three-year IRB approval, McClelland says.

"That will save a lot of people's time so they won't have to renew annually," she says. "We've created a new chart review application form, which is very much abbreviated from our regular, 22-page form down to six pages."

The regular form asks questions about investigational drugs and devices, and this information is not pertinent to a chart review, she adds.

Unchecking the box gives research institutions the flexibility of categorizing more research as exempt, Rose notes.

For example, USC has a flex policy that lists these examples of non-funded research that might be exempt: online surveys, in-person focus groups, behavioral games, studies requiring no-risk performance tasks, medical record reviews, data analysis from court records, and studies using eye-tracking technology.

"IRBs are overloaded, so having their attention focused on things that cause risk is a life-changer," Rose says. "We haven't measured how much time is saved, but we know it allows more attention to be paid to [higher-risk] studies."

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Special Report: Streamlining IRB Process

IRBs may improve efficiency with these tips

Improve expedited review process

Research institutions nationwide continue to look for ways to improve quality while eliminating redundancy, regulatory creep, and inefficiencies. The key to success is flexibility and considering changes in any type of process that is not working as efficiently as possible, experts say.

Areas that can be addressed for improvements and greater efficiencies are varied, ranging from revamping the board to improving the way expedited reviews are handled. Here are some ideas:

• **Revamping the IRB board:** For instance, some IRBs have found that adding more ethics boards can help reduce the time from protocol submission to an IRB decision. But one IRB has found that making the opposite change also can improve operations. The office of research compliance and biosafety at Texas A&M University (TAMU) in College Station condensed its IRB from four boards to one board to improve efficiency, says **Catherine L. Higgins**, PhD, IRB manager.

"We also increased the IRB's membership, and that seems to work quite well," she says. "We have 16 IRB members, and we are adding 10 more."

The institution made the change to one board last year with the goal of going back to basics while also engaging more IRB member enthusiasm and commitment, Higgins explains.

"One board makes sense for us; IRB members meet once a month for about five hours," she says. "The IRB meeting discussions are extremely interesting, and the group has become more vibrant and exciting over the past year."

The IRB has close to 2,500 active studies, and the number of submissions per month doubled from 150 to 300 after the consolidation of boards. Also, the IRB's processing time for submissions dropped from 17 days to two days in that same period of time, Higgins says.

• **Using IRB liaisons:** Credit for the improved processing time at TAMU is shared by several initiatives, including the board consolidation. One of the biggest contributors to the improvement is the IRB's adoption of an electronic submission system and the creation of IRB staff liaisons for pre-reviewing studies and working with

researchers. Higgins looked for staff liaisons that would fit in well with particular colleges, and she sought people who were energetic and go-getters, she says.

"I wanted employees who have a lot going on outside of work because if they have a lot going on outside of work, they want to get their work done," Higgins says.

The liaisons meet regularly to discuss problem studies and to reinforce IRB management and processes. They also work directly with investigators and research departments, getting to know one particular department's needs, she adds.

Staff liaisons attribute much of their improved efficiency to the online system, but also to a variety of changes, including these: better meeting and minutes preparation, addressing specific application questions, using a pre-review checklist, easier revision requests online, less time spent finding files and submissions, improved communication with investigators, fewer crises, faster amendments and continue reviews online, and better knowledge of regulations and IRB expectations, Higgins says.

The change to a single IRB also involves board members participating on subcommittees to provide guidance on different topics. Each board meeting features a special topic that has been the focus of a subcommittee. Then subcommittee members discuss these with the full board at meetings.

Also, some IRB members mentor new investigators, helping them with study design and identifying their project's goals. The IRB consists of people from across the university so each can be a representative of his or her department and different types of studies, she adds.

The IRB members enjoy working with fledgling investigators to improve study applications, especially in the colleges of education and sociology and psychology, Higgins notes.

"An IRB member will say, 'I want to partner with investigators and help them fix this,'" she says.

• **Use expedited reviews efficiently:** Aurora Health Care Inc. of Milwaukee created a special process, application, and expedited review category 10 to streamline review of research activities that involve review of public health information. These include specific parameters for retrospective chart reviews, says **Lori Roesch**, manager of the research subject protection program.

The policy specifies how the IRB might grant a waiver of informed consent for the medical record/database request. According to the Aurora Health Care application, the criteria are these:

• The research involves no more than minimal risk and will not adversely affect the rights and welfare of subjects because the clinically indicated intervention or tests were already completed.

• The results would not affect clinical decisions about the individual's care because they are analyzed after the fact.

•The subjects are not deprived of clinical care to which they would normally be entitled.

• There are no conflicts of interest disclosed by investigators and key personnel.

The new expedited review policy applies to research that is not federally funded and excludes studies that are reviewed by the Food and Drug Administration (FDA) or which require contact with patients for research purposes. The organization was able to institute the policy only after unchecking the box on its Federalwide Assurance (FWA), Roesch notes.

The change, which applies only to research originating at the organization, has improved and streamlined the IRB application process, she adds.

• **Track study timeline data:** Whenever an IRB makes a change to processes, such as creating new policies for expedited reviews and informed consent waivers, it is a good idea to monitor and track outcomes to see what works and what falls short of expectations.

"We track when the study comes in and when we do our review. If there are questions that have to go back to the investigator, we track that as well," Roesch says. "Our average turnaround time is 15 days."

That is a decline from the initial turnaround time of 25 to 35 days as IRB staff and members first piloted the streamlining changes, she notes.

"There is a learning curve, and we've reduced the turnaround time for the most recent four studies to three to nine days," Roesch says. "Once we've completed the streamlining process, trained everyone on it, we're seeing a decrease in the turnaround time."

A next step would be to track the turnaround time after further changes are implemented, such as a possible change from annual continuing reviews to reviews every two years, she says.

"We have not made that change yet," Roesch says. "We take baby steps because you want to make sure as you do these changes and roll these out that you're not missing something." ■

IC information sheet can be used with IC waivers

Waiver used with Internet, some other studies

Informed consent discussions and recommendations are important and time-consuming. IRBs continually seek ways to improve the informed consent process while also finding better and more efficient ways of handling them. One way to streamline the IC process could be to make certain IRBs are not inundated with IC forms unnecessarily.

There are times when a waiver of documentation of informed consent is appropriate and in everyone's best interest. One example would be research that is conducted solely through a website, notes **Catherine L. Higgins**, PhD, manager of the IRB in the office of research compliance and biosafety, division of research, at Texas A&M University in College Station.

"If research is conducted solely online, researchers could have an informed consent information sheet as the first page of the online survey," Higgins says. "Then participants could stop at the end of reading it or they could stop in the survey at any point. If they finish the survey, we view that as their consent."

Texas A&M University uses an informed consent information sheet whenever the IRB determines that a waiver of documentation of informed consent is appropriate, she says.

The informed consent information sheet is three pages, written in a question-and-answer format. It has no place for a study participant's name and signature and is intended only to answer the participant's questions. The template highlights in yellow the words and phrases that could be personalized to a particular study. The sheet meets federal requirements of a consent. *(See table on TAMU IC information sheet, page 91.)*

The informed consent information sheet is a useful tool in the case of studies that are sensitive and the IRB decides it would be better to have no names in study records. In these cases, the only link between the name of the study participants and the study is the consent document, so if the information sheet is used, no signatures and names will be recorded and stored, Higgins says.

"For Internet-based studies the information sheet generally is used because it doesn't make sense in most cases to have a signed informed consent form," she explains. "And there are some international studies where we might learn from a cultural evaluation that signing a consent document would be outside the acceptable cultural practices; then, we would use an information sheet."

In Texas, an open records law called the Texas Public Information Act gives the public access to government records with no exceptions for research. This posed a challenge in informed consent documents, so the IRB sought guidance from the university's general counsel to see what kind of language would be needed in IC documents and on the IC information sheet, Higgins says.

They decided on IC wording that reads: "Information about you and related to this study will be kept confidential to the extent permitted or required by law."

There have been no issues with the TPIA and the institution's research, Higgins says.

Investigators have responded positively to the information sheet, but some have asked to use it when it is not appropriate. The IRB is careful to watch for studies where the information sheet is proposed as a solution but full informed consent is necessary, she adds.

To obtain a waiver of informed consent, investigators must complete a two-page waiver of consent form that asks for protocol-specific explanations and justifications for these criteria:

- The research involves no more than minimal risk to the participants.
- The waiver or alteration will not adversely affect the rights and welfare of the participants.
- The research could not practicably be carried out without the waiver or alteration.
- Whenever appropriate, the participants will be provided with additional pertinent information after participation.

And investigators seeking waiver of documented informed consent must provide protocol-specific reasons and justification on how at least one of these criteria is met:

- The only record linking the participant and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern, and/or
- That the research presents no more than

(Continued on p. 92.)

Texas A&M IC information sheet template

Sheet addresses purpose, privacy, etc.

The Texas A&M University human subjects protection program uses an informed consent information sheet whenever full documentation of informed consent is waived by the IRB. The information sheet template provides investigators with a simple way to ensure participants are knowledgeable about the research project. It uses bold-faced questions, with answers in regular font. Investigators can adjust the template with the study's information in the areas that are highlighted in yellow or capitalized.

Included in the information sheet's questions are these:

• **Why is this study being done?**

The purpose of this study is to….

• **Why am I being asked to be in this study?**

You are being asked to be in this study because [inclusion/exclusion criteria].

• **What are the alternatives to being in this study?**

If this is not a treatment study: The alternative to being in the study is to not participate. Another activity will be given if you choose not to participate.

For studies that give course credit: The alternative is to sign up for another study or to choose to complete another assignment as described in your syllabus.

If this is a treatment study: The following therapies for treatment of [condition] are available: [treatments]. You should talk to your personal doctor (or study doctor if appropriate) to discuss what would be right for you.

• **What will I be asked to do in this study?**

You will be asked to [describe task]. Your participation in this study will last up to [length in hours/weeks/months/years] and includes [number] visits.

• **Are there any risks to me?**

The things that you will be doing are no more/greater than risks that you would come across in everyday life. [Describe risks, including physical, criminal, social, financial, economic, psychological risk as well as risks associated with breach of privacy or confidentiality.]

Suggested wording if applicable: Although the researchers have tried to avoid risks, you may feel that some questions/procedures that are asked of you will be stressful or upsetting. You do not have to answer anything you do not want to. If applicable, add: Information about individuals who may be able to help you with these problems will be given to you.

• **Will there be any costs to me?**

Aside from your time, there are some/no costs for taking part in the study.

• **Will information from this study be kept private?**

[If applicable] The records of this study will be kept private. No identifiers linking you to this study will be included in any sort of report that might be published. Research records will be stored securely and only [insert names of individuals who will have access to this data] will have access to the records.

Information about you will be stored in locked file cabinet; computer files protected with a password.

Information about you will be kept confidential to the extent permitted or required by law. People who have access to your information include the Principal Investigator and research study personnel. Representatives of regulatory agencies such as the Office of Human Research Protections (OHRP) or [if FDA regulated] the Food and Drug Administration (FDA) and entities such as the Texas A&M University Human Subjects Protection Program may access your records to make sure the study is being run correctly and that information is collected properly.

[If applicable] The funding agency for this study, [insert sponsor name], and the institution(s) where study procedures are being performed [insert school, hospital, clinic, institution] may also see your information. However, any information that is sent to them will be coded with a number so that they cannot tell who you are. Representatives from these entities can see information that has your name on it if they come to the study site to view records. If there are any reports about this study, your name will not be in them.

Information about you and related to this study will be kept confidential to the extent permitted or required by law. ■

(Continued from p. 90.)

minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide participants with a written statement regarding the research. ■

Experts call to restore abandoned trial data

RIAT may lead to better understanding of data

Not every clinical trial report sees the light of day. Some are abandoned when trial sponsors no longer actively seek publication, or when a study is misreported and no efforts are made to correct it.

A group of researchers put out a call to pharmaceutical companies and medical journals to get those studies published. **Peter Doshi**, PhD, postdoctoral fellow at Johns Hopkins University in Baltimore, is the lead author of an article published in the June issue of the *British Medical Journal (BMJ)* in which Doshi and colleagues described the process of Restoring Invisible and Abandoned Trials (RIAT).

The RIAT idea was born when Doshi's co-author S. Swaroop Vedula was preparing for his PhD defense. Vedula looked into 20 trials of epilepsy drug gabapentin (Neurontin), eight of which had gone unpublished. The data were released by Pfizer in the course of litigation over off-label marketing of the drug. The documents on the unpublished trials, Doshi says, were "rich in details." "Why is it that all these years later, we're still referring to these trials as unpublished? We're looking at the results, but no one else really can," he says. "If Pfizer isn't going to publish this, then why don't we?"

Doshi and colleagues created a process for submission of such studies to peer-reviewed journals that are on board with the concept, including *BMJ*, *PLOS Medicine*, *PLOS One*, and *Headache*.

The steps for RIAT submission and publication include:

- obtain clinical study reports and any other study data;
- collect documentation of trial abandonment;
- issue a "call to action" by publicly registering possession of data sufficient for publication;
- collect documentation of the need for restoration;
- presubmission inquiry to RIAT-friendly journal;
- prepare and submit manuscript according to RIAT procedures.[1]

RIAT publishing will become possible, in part, by documents entering the public domain through litigation or through new freedom of information rules in Europe. And pharmaceutical company GlaxoSmithKline (GSK) announced earlier this year that it is planning to make its clinical study reports available to researchers. *(For more details on the RIAT publishing guidelines, see box on 93.)*

Doshi's *BMJ* article puts out a call to action for trial sponsors: Publish, or be published. A copy of the article has been sent to trial sponsors and investigators, calling on them for formal correction of studies. If those who signal intent to publish do not do so within a year, the studies should be considered "public access data" and should be published by others, RIAT authors say. So far, pharmaceutical company GSK has expressed "they'd have no problems with RIAT authors writing up their unpublished studies," Doshi says.

The intention of RIAT isn't just to bring unpublished studies to light, Doshi stresses — it's also about restoring those that have been abandoned and correcting the record on misreported trials. "Because abandonment can lead to false conclusions about effectiveness and safety, we believe that it should be tackled through independent publication and republication of trials," Doshi and colleagues write in the *BMJ* article.[1]

Trials can become abandoned when they are misreported and not corrected due to lack of time, budget, interest, or an investigator not agreeing that it's misreported. Some may languish unpublished also because of little time or budget, or lack of statistical significance. Studies can also go unpublished if the results

are not favorable to a sponsor — which can result in publication bias.

"Some reasons [for not publishing studies] are understandable, while some are not so excusable," Doshi says. "Whatever the reasons, there really is a need to have the scientific record be accurate and complete. That's what RIAT is all about making happen."

Many of the abandoned studies include well-known and widely used drugs. "Read it and weep: On the list are clinical trials for drugs used by millions of people, including zanamivir, atorvastatin, gabapentin, and paroxetine. The number and variety of drugs on the list show clearly that incomplete reporting of clinical trial results is not an isolated occurrence, confined to a few drugs. Rather, it is an entrenched and widespread problem. Secrecy and selective reporting were an integral part of the system," according to *BMJ* research papers editor **Elizabeth Loder**, MD, and colleagues in an editorial response to the RIAT article.[2]

IRBs should have interest in these studies, Doshi says, to ensure that the studies they approve and monitor can benefit the public beyond just the study participants. "Unpublished and misreported studies put other patients in harm's way by exposing other patients to risks that are recorded but not reported," he says. "How are IRBs ensuring that publications are accurately reporting studies they're signing off on? That's part of

A guide to the RIAT process

Here are the steps Doshi and colleagues outlined for the Restoring Invisible and Abandoned Trials publishing process:

Proposal for restoring invisible and abandoned trials (RIAT)

1. Obtain clinical study reports and any other study data

2. Collect documentation of trial abandonment

For unpublished trials: No primary publication detected by systematic search of the literature and/or confirmation from original trial sponsor or current responsible party that no publication exists.

For misreported trials: Evidence of misreporting (ideally, published letters or other articles in the scientific literature or documentation of communication with the original trial publication author[s] detailing the misreporting) and a failure to correct the scientific record.

3. Issue a "call to action" by publicly registering your possession of data sufficient for publication

At least initially, this should be by an electronic response to this article and should include, as a minimum, trial identifiers, number of participants, date completed, publication status, pages in your holding, and level of access to trial data. This declaration offers original sponsors and trialists an opportunity to publish or formally correct their studies within the next 365 days. Send a copy of the rapid response by email to trial sponsors (and authors, for published trials), requesting confirmation of receipt.

4. Collect documentation of the need for restoration

Save time-stamped copies of all rapid responses to this article (or other relevant websites) to document the time elapsed and consequent need for third party restoration.

5. Presubmission inquiry to RIAT friendly journal

Present editors with documentation from steps 1-4 and seek confirmation of editors' interest.

6. Prepare and submit manuscript according to RIAT procedures

- Include explanation (with references) in the Introduction of why this trial is being restored.
- Provide auditable record of decisions (use RIATAR template), documenting which parts of the clinical study report (page number and paragraph) were used.
- Report analyses specified in protocol.
- Denote any analyses that were not prespecified.
- Make all underlying data available electronically.[1]

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1. Doshi P, Dickersin K, et al. Restoring invisible and abandoned trials: a call for people to publish the findings. *BMJ* 2013;346:f2865. ■

the ethical responsibilities of the researchers to the subjects."

IRBs can also become involved in the RIAT process. "In trials where there may have been ethical questions, it would make sense to consult an IRB in the publication of that trial," Doshi says. "That should not mean that IRBs should be preventing us from learning from studies because the context of the studies was problematic. Learning from studies that have already been done is crucial to preventing unnecessary harm by unnecessarily repeating those studies."

Doshi says that linking the data with the republished trials will move clinical trials publishing to a new level of credibility. "One of the key elements of RIAT is that it will set a new standard by linking publications of trials with data and audit records so that the full data set will be available to anyone who wants to see it and explore it," he says.

REFERENCES

1. Doshi P, Dickersin K, et al. Restoring invisible and abandoned trials: a call for people to publish the findings. *BMJ* 2013;346:f2865.
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University explores transnational IRB

Bridging culture, compliance gaps is key

For about 30 years, the Indiana University School of Medicine in Indianapolis has had a research partnership with Moi University's Teaching and Referral Hospital in Eldoret, Kenya, including an exchange program for medical students. As the clinical collaboration grew, IU researchers partnered with researchers at Moi to conduct studies in Kenya and other parts of Africa.

But when researchers from either institution sought approval, they had to go through two processes: the IU IRB and the Moi University Institutional Research and Ethics Committee (IREC). The IU IRB might have changes that the Moi IREC didn't have, and vice versa. "Researchers were frustrated," says **Shelley Bizila**, MS, CIP, clinical research compliance officer for Indiana University. "We talk and communicate issues well with IREC, but for an investigator it's frustrating. The timelines would never match up."

In order to streamline the approval process, IU looked into forming a joint IRB with Moi University. IU received a federal research grant from September 2010-September 2011. "What we were hoping to do was create a joint IRB process," says **Edye Taylor**, JD, MA, CIP, senior compliance project manager with the IU Clinical Research Compliance Office. "Even if it didn't come to fruition, we would learn a lot to make the process better."

First, the IU grantees looked into whether such an international partnership would be possible from a regulatory standpoint. When searching the U.S. IRB regulations, Bizila and Taylor discovered there was nothing in the literature pertaining to international IRB partnerships of this nature.

"We looked at the regulations — there were none prohibiting such a partnership, but there was nothing to govern how to do this," Taylor says. "It wasn't really on anyone's radar." They put forth the question to the U.S. regulatory and accrediting bodies as well as to the governing bodies in Kenya. "Once we determined there were no regulatory issues to prevent us going forward, we began the process."

The IU IRB members sat down to hash out the joint IRB process and make it more compatible with Moi University. They studied the IREC process at Moi and compared how each board handles things. They also had to determine when and how often to have meetings, what technology would need to be used, who would chair the meetings, etc. "We had to harmonize all the details," Taylor says.

One of the key things learned, Taylor says, is the value of interpersonal relationships and how they differ across cultures. "Anyone who has worked in any part of Africa knows that personal relationships have a very different role. In the U.S., we have very much become a society where we don't have as much face-to-face time," she says. "We would have to take a different approach there. The agencies also work a little differently in Kenya."

During planning, it was clear that the venture would be a strictly equal partnership, with no one side dominating or taking charge over the whole process, Taylor says. Each side also had to learn cultural and procedural differences,

and find a middle ground. For example, she says, the Kenyan researchers at Moi tend to be more softspoken and less likely to interject with questions during discussions, and Americans are perceived as more dominant personalities. "We had to get the dynamics of the team right and get people who have no problem jumping into the conversation to ask more questions and press for more answers," she says.

There are also differences in how each institution approaches protocol review. "We are more systematic and process driven, while the Kenyan IREC has a more personal approach," Taylor says. "Their process in Kenya is far more formal in how they review each protocol — they feel strongly that every board member should know every detail of what is being approved. Not that Indiana doesn't take the necessary steps for protocol review; it's just a different approach." In the end, Taylor says, "Moi found processes from us that they wanted to incorporate, and vice versa."

The IU grantees went to the Office of Human Research Protections (OHRP) with the proposal of an international IRB with staff consisting of equal parts IU and Moi members. "[OHRP] were supportive and in their eyes there were no barriers," Bizila says. "They were very excited to see us attempt [the partnership]."

In Kenya, nothing was found in the regulations to prevent the joint IRB from happening. However, the country's National Bioethics Commission was skeptical. "Kenya has been a research performance site in the past, and [the commission] felt that the Kenyan people had been taken advantage of in the past," Taylor says. "They were concerned that the time wasn't right, if was there a genuine need to flesh this out, and if it would create more work for the agencies — there were a lot of great concerns in general."

So while the joint IRB plan is now on hold, the two universities are continuing the long-standing research partnership. There is also hope that the plan will someday be approved. "The politics are starting to change at the regulatory level in Kenya, and we're positive there will be renewed interest in the next couple of years," Taylor says. "At the institutional level, the folks at Moi thought it was a really good idea. They clearly understood how much this would mean for them and their Kenyan counterparts. On both sides, there was complete institutional buy-in."

While researchers still need to go through both institutions for research approval, the process of planning the joint IRB helped to smooth communication and make the dual review process a little easier. "Even though researchers have to do the dual review, it's more harmonized and the communication is better," Taylor says. "If there is a question about something that has already been approved, there's more of a group conversation that takes place." ■

CNE/CME OBJECTIVES & INSTRUCTIONS

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

- establish clinical trial programs using accepted ethical principles for human subject protection;
- apply the mandated regulatory safeguards for patient recruitment, follow-up and reporting of findings for human subject research;
- comply with the necessary educational requirements regarding informed consent and human subject research.

Physicians and nurses participate in this continuing education program and earn credit for this activity by following these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. ■

COMING IN FUTURE MONTHS

- eConsent and other solutions for IC offered
- Central review acceptance growing in IRB world
- ANPRM update — what is happening?
- Trends in IRB staffing demands

CNE/CME QUESTIONS

1. Which of the following is a criteria for research institutions that want to "uncheck the box" on the Federalwide Assurance?
   A. Research subject to the unchecked box must not receive any federal funding
   B. The research project must provide equivalent human subject protection
   C. The research project must involve no more than minimal risk
   D. All of the above apply

2. Aurora Health Care Inc. of Milwaukee created an expedited review category 10 to streamline review of research activities involving public health information. Which of the following is not one of the new policy's specific parameters for retrospective chart reviews?
   A. The results would not affect clinical decisions about the individual's care because they are analyzed after the fact
   B. The research involves only state, local, or pharmaceutical company sponsor funding
   C. The subjects are not deprived of clinical care to which they would normally be entitled
   D. There are no conflicts of interest disclosed by investigators and key personnel

3. When might it be useful and appropriate to use an informed consent information sheet in the place of a signed informed consent document?
   A. When a study is sensitive and the IRB decides it would be better to have no names in study records
   B. Internet-based studies
   C. International studies where a cultural evaluation indicates that signing an informed consent document would be outside the acceptable cultural practices
   D. All of the above

4. According to Peter Doshi, PhD, a clinical trial can become abandoned when the trial is misreported and not corrected.
   A. True
   B. False