IRB ADVISOR

YOUR PRACTICAL GUIDE TO INSTITUTIONAL REVIEW BOARD MANAGEMENT

MARCH 2015 Vol. 15, No. 3; p. 25-36

INSIDE

AHC Media

Single IRB NIH guidance may leave more questions than answers

IRBs unclear on methods

In December 2014, the National Institutes of Health (NIH) released draft guidance detailing its support and expectations for the use of a single IRB for multisite NIH-funded studies. But for many in the IRB community, the guidance raised more questions than answers.

"I don't think the case has been made that the use of a single IRB is absolutely necessary," says **Erica Heath**, CIP, director of regulatory affairs at Ethical & Independent (E&I) Review Services in Corte Madera, CA. "I think there are good cases for it, but I think other ways to create and achieve consistency and efficiency have not been explored sufficiently."

In its guidance, the NIH stated that the use of a single IRB for its large, multisite studies is more efficient than multiple reviews and could eliminate redundant reviews and slow turnaround times. "In fact, the use of single IRBs may lead to enhanced protections for research participants by eliminating the problem of distributed accountability, minimizing institutional conflicts of interest, and refocusing IRB time and resources toward review of other studies," the document states.[1]

> "THERE'S NO EVIDENCE, EVEN WITH ALL THE MONEY AND EFFORT GOING INTO IT, THAT THE CURRENT IRB STRUCTURE IS ACTUALLY PROTECTING SUBJECTS."

"There's no evidence, even with all the money and effort going into it, that the current IRB structure is actually protecting subjects," says **Mark Schreiner**, MD, vice-chair of the Committees for the Protection of Human Subjects at the Children's Hospital of Philadelphia

Financial Disclosure: Financial Disclosure: Editor **Melinda Young**, Executive Editor **Russ Underwood**, Associate Managing Editor **Jill Drachenberg**, Physician Reviewer **Mark Schreiner**, MD, and Nurse Reviewer **Kay Ball**, RN, PhD, report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

IRB ADVISOR

IRB Advisor,
ISSN 1535-2064, is published monthly by
AHC Media, LLC
One Atlanta Plaza
950 East Paces Ferry Road NE, Suite 2850
Atlanta, GA 30326.

Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.
GST Registration Number: R128870672.

POSTMASTER: Send address changes to:
IRB Advisor
P.O. Box 550669
Atlanta, GA 30355.

SUBSCRIBER INFORMATION:
Customer Service: (800) 688-2421.
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Hours of operation: 8:30 a.m.- 6 p.m. Monday-Thursday; 8:30 a.m.-4:30 p.m. Friday, EST.

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(CHOP), and physician reviewer of *IRB Advisor.* "There's a lot of duplication of efforts, and IRB budgets and staff are tight." Multiple IRB review should be done if the review adds value, he says.

Industry reaction

One issue with the guidance, Heath says, is that it doesn't clearly define terms or what, exactly, the NIH is looking for. "When they say 'a single IRB' in the proposal, they don't say what they want, and it's really quite open," she says. "I think a lot of people are a little bit at sea over what it is they [NIH] really want. It may be a good direction, but a bit hasty."

In a recently released position paper, Public Responsibility in Medicine & Research (PRIM&R) stated that while central IRB usage would be beneficial for some NIH-funded studies, it may not be appropriate for all.

"PRIM&R believes that, before such a policy is implemented, further reliable empirical evidence is needed on the various ways in which a single IRB can be used to provide ethical review of multi-site research, and on whether such review is better, from the perspectives of subject protections, administrative costs, efficiency, and quality of review, than relying on local IRBs," according to the position paper. "In the absence of sufficient evidence, we believe that a policy requiring the use of single IRBs for all domestic sites of multi-site NIH-funded studies is premature and ill advised," the paper states.[2]

But this requirement from the NIH is nothing new, Schreiner says. "We've seen many studies where we've had to agree to have a central IRB as part of the [NIH] grant application. It's not just hypothetical; it's reality."

Many IRBs do not have experience in deferring to a single IRB and may not know where to start, NIH officials acknowledged in the guidance. "Despite enthusiasm for central IRBs, there is confusion about the optimal structure for central IRBs as well as how best to meet regulatory requirements," according to an NIH statement. "There are questions about the loci of responsibilities and whether the IRB or institutions will bear the blame if adverse events occur," the guidance states.[1]

NIH should offer more ways to answer these questions and clear up confusion, says **Cynthia Hahn**, vice president of clinical research and regulatory affairs at the Feinstein Institute for Medical Research at North Shore-LIJ Health System in Manhasset, NY. "There really needs to be more guidance," she says. Hahn is also on the steering committee of the Clinical Trials Transformation Initiative (CTTI) and co-authored research and recommendations for using central IRBs that was cited in the NIH draft guidance. "One thing the NIH needs to do is provide feedback to sites with things they should consider."

Topics for consideration when using a single IRB, according to Hahn, include the following:

- What are each participating IRB's bylaws? Do they conflict with the bylaws of other institutions?
- What are the bylaws for the medical staff at each institution? Are they in conflict with other institutions? Do the bylaws state that the medical faculty must use the institutional IRB?
- Contracts, bylaws, policies, and procedures may need to be updated.
- Who does institutional

approval? If you use another IRB, who does approval for your institution?

"At the same time, you don't want to duplicate work," Hahn says. "You don't want to replicate what the IRB already did. I think the NIH would be helpful to provide that kind of guidance."

Drafting authorization agreements could also be a stumbling block for IRBs that don't have experience in that area, Hahn says. "Lots of places don't know how to do this and don't know where to start. Some are comfortable with the one-page OHRP template, but it's not sufficient," she says.

"I feel sorry for IRB administrators because they will be faced with so many different kinds of reliance agreements," Heath adds. "Agreements range from the one-page OHRP template to 20-page contracts. Administrators will have to go through and see the minimum their institution would need — if they need more conditions or fewer. Unless there is some move to get some consistency in their agreements, administrators will go nuts."

Schreiner agrees that there is no guidance as to the qualifications the reviewing IRBs must have. "It's clear to us that not all IRBs have the experience or manpower to play that role [of reviewing IRB]," he says. "The initial guidance should be fleshed out and include criteria for qualifications to be a reviewing IRB."

But there are positives to the use of a single IRB, Hahn says."I think the whole thing [the NIH draft guidance] stems on people knowing that the days of single-site studies are basically over," she says. "More and more studies are becoming multinational and multisite. Studies are increasingly complex, addressing rare diseases and conditions, and experts on those diseases might be across the country from you. I don't think that's a bad thing. [Single IRBs] could produce better quality reviews, not just more efficiencies. Most of the research has been driven by efficiencies and people need to focus more on a quality review."

There are pluses and minuses to multiple IRB review and single review, Schreiner adds. For instance, multiple IRB reviews could catch something that a single IRB may not. "On the other hand, if there's an issue with the trial, a single IRB has much more impact to forcing changes to a trial than 30 sites do," he says. "If one of 30 sites raises objections, they are dropped as a site. There is a lot of leverage that comes with a single IRB review."

"I THINK THE WHOLE THING STEMS ON PEOPLE KNOWING THAT THE DAYS OF SINGLE SITE STUDIES ARE BASICALLY OVER."

Unintended consequences

The single IRB policy could have unintended consequences for smaller regional IRBs that operate in the shadow of a large academic center, says **W. Parker Nolen**, MBA, CCRC, CIP, network manager of the IRB at Community Health Network in Indianapolis.

"My initial reaction is that it's nice that streamlining is occurring, but it's not necessarily in the best interest of those who don't have a lot of NIH funding," he says.

It's a question of access to study participants, Nolen says. If a researcher wants to use the patients at a particular hospital as part of a multisite study, "the inability of the IRB to at least look at the consent form is a bad idea," he says. "It exposes the hospital system to a great degree of liability. They're then faced with the decision to turn over the population to a researcher elsewhere, or to become a subcontractor for the grant."

"Turning it over blindly is never a good idea," he adds. "The IRB may not allow physicians and patients to participate because it's too great a risk."

It's also a question of patient safety and personal liability, Nolen says. "It places hospitals at a large disadvantage if they have to say, 'Wait, we need to get on this as a subcontractor,'" he says. "My gut says it's really bad for the long run — in situations like that, research could start drying up at hospital systems."

But having a single IRB review is not an abdication of the relying IRBs' responsibilities, Schreiner says. "There are many things that remain with the relying IRB," he says. "The relying IRB is still responsible for the review of consent forms and for adverse event reporting." The relying IRB can also object to the central IRB's review. "Just because there is central oversight doesn't mean they [relying IRB] have to accept it as-is. Having an IRB of record does not absolve the reliant IRB of its responsibilites of research."

Experts propose alternatives

In its position paper, PRIM&R encouraged the NIH to consider incentives for IRBs to voluntarily adopt the single IRB model, and suggested the following:

1. "Convene an expert panel to host open meetings to develop criteria regarding the types of research that lend themselves to the single IRB model and those that do not;
2. "Sponsor research on existing models of review by a single IRB for multi-site research to gather more evidence about both the quality and cost of review;
3. "Create incentives (e.g., preferential treatment in the award process) that encourage and reward the use of, and require the collection of data on the use of, single IRB review and/or elements of single IRB review processes; and
4. "Develop tools, guidance, and best practices to help facilitate the use of single IRB review mechanisms (e.g., model reliance agreements, standard operating procedures, etc.)."[2]

There are also many different models of collaborative IRB systems, Heath says."If it's mandatory, you forgo other forms and styles," she says. "You get a lot of people working together who may not want to. There are a lot of good things about central review — I do it — but there are better ways of being successful."

Other models include collaborative IRBs, IRB consortia (such as university system consortia), and other reliance models. There are also methods for shared communication, Heath says.

"The first several IRBs could look at something and all their questions and answers could be compiled and given to the next IRBs to forestall their questions," she says.

In a perfect world, Nolen says, the draft guidance would be a good model. "But in reality it's kind of symptomatic of academic myopia — they think that almost everything coming through NIH is through large academic medical centers, and it's not," he says. "I understand the philosophy of it; the NIH has lost a lot of funding from sequestration. They need to be efficient as well."

"There are a lot of things to work on, but it doesn't mean we shouldn't go forward," Schreiner adds. "The biggest issues are how to implement it [the model] and operationalize the IRB."

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Certification testing can be more successful, less stressful with study group method

Managers discover that cross-pollination works

As IRB professionals increasingly invest in their careers and seek certification, they sometimes find that taking the certification test can be stressful and all-consuming.

Although studying for the Certified IRB Professional (CIP) test can be challenging and nerve-wracking, the worry can be mitigated by a cross-institution study group program, suggests **Sarah Marie Huban**, MA, CIP, CHRC, human protections program and research regulatory affairs manager at Children's Healthcare of Atlanta.

"I think taking the test is stressful," says **Sarah Clark-Worley**, MPH, CIP, senior IRB coordination manager of the research compliance office at Stanford University in Palo Alto, CA.

"Depending on the institution where you work, everyone's motivation for becoming certified is different," Clark-Worley notes. "Some do it for professional enrichment; for others, it's a requirement for their job, and others have different pressure."

Clark-Worley and Huban worked to reduce stress and improve CIP passing rates by developing a study group program for taking the CIP test. The new program helped to raise the CIP passing rate among their pilot

groups taking the test.

Study with other institutions

The key to success for the study group program was to include IRB staff from more than one institution. "We saw a big increase from our average passing rate from a study group at a single institution versus a study group with lots of different folks," Huban says.

For instance, the first study group, which had attendees from only one organization, had a passing rate of 67%. The combined study group, including people from three institutions, had a passing rate of 83%.[1]

As IRBs and research institutions increasingly encourage or require staff to obtain CIP certification, pressure builds among IRB staff. Plus, the time and resources invested in certification can make the process very stressful and result in lower than expected passing rates, Huban and Clark-Worley say.

After months of studying, IRB professionals might become burned out by the time they take the exam. Or they might focus on the wrong areas and not pass it the first time around, Huban says.

The CIP program was created in 1999 as part of a grassroots effort by IRB professionals and policymakers. More than 2,000 people have received their CIP certification. Professionals taking the CIP must have a bachelor's degree and two years of relevant human research protection program experience, or three years of HRPP experience. The certification is valid for three years and can be renewed.

"We worked together on the programs as colleagues from Emory University IRB in Atlanta," Clark-Worley says. "We overlapped for three years, and then Sarah went to the Children's Healthcare center and we still worked together."

The collaboration ended when Clark-Worley moved to Stanford University, but she's continued to hold CIP study groups at her new institution.

> "WE SAW A BIG INCREASE FROM OUR AVERAGE PASSING RATE FROM A STUDY GROUP AT A SINGLE INSTITUTION VERSUS A STUDY GROUP WITH LOTS OF DIFFERENT FOLKS."

It proved to be an enormous advantage to have people from different institutions studying together, because IRB members can challenge each other on the perceived regulations, she says.

"When you're working at a particular institution, you get so focused on institutional policy and how that institution interprets regulations," Clark-Worley explains. "But when you work with someone from another institution, you remove the institutional goggles and think about it in the broader sense and apply the regulation to how it applies to everyone without getting bogged down in the details."

Huban saw the institutional bias effect occur when she started her first certification study group with a few people from the same institution.

"I realized that if you're teaching to one institution's policies and procedures, then those might go beyond what the regulations require," she says.

For example, if an IRB's quorum requires 10 attending members, the IRB professional might not realize that 45CFR, Part 46 regulations require IRBs to have at least five members, Huban explains.

"There are lots of little nuances where you think your policies and your institution's requirements are the answer, when those are not the regulations but just the way your institution has interpreted it," Huban says. "Having the perspective of another institution was huge for us."

The following are some multi-institutional certification study group strategies:

- **Build camaraderie.** The first session introduces the various IRB professionals and talks about why it's important to incorporate multiple institutions. Generally, the IRB staff were excited to meet colleagues from other human research protection programs, Huban notes.

"Then we went over the schedule, talking about which chapters we'd cover each week and what we expect them to do," she adds. "We say, 'Here's what it will take to be successful when you take the exam.'"

- **Build incentives.** The multi-institution study group met on Friday mornings. Clark-Worley and Huban would bring in bagels or some kind of breakfast.

"We also had one or two celebratory lunches," Clark-Worley says.

- **Provide structure and**

handouts. The group met for 11 weeks, and the meetings lasted about an hour, with the expectation that attendees would spend additional time studying and preparing each week. The group leaders shared supplemental documents and created slideshow presentations. There also were case studies.

They gave attendees only enough materials to complement that week's assignment.

"We could have given them the handout right at the beginning, but we chose to wait and hand them out each week, thinking it would be overwhelming to receive a giant binder of regulations," Huban says. "We'd say, 'You need to read these chapters,' and they were typically two chapters a week."

At the end of each session, they suggest what participants can read and do to prepare for the next session, and they give them a chapter quiz. *(See program outline, below.)*

• **Make it fun.** They used online toolkits to create interesting games for studying. One is a *Jeopardy!*-type game. Another uses 102 flash cards to make studying more interesting.

For example, on one side of a card would be the words "social harm," and the opposite side would read: "Decreases in quality of life that result from information being created or used in a way that is damaging to the individual in question — a result of the creation or transfer of information in a way that may negatively affect the research subject."

• **Instruct with case studies.** They created a cooperative learning environment with less focus on teaching and more of an emphasis on an open dialogue, sharing information. The case studies helped to facilitate discussions, Clark-Worley says.

"We created case studies and worked through them together," she adds. "We found it was tremendously helpful in the exam as it helped them think critically and work through issues."

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Here's what a certification study group program looks like

10 weeks to a passing score, creators say

The only thing better than forming an in-house IRB certification study group is forming a multi-institutional IRB certification group, according to a pair of IRB managers who found good results with their three-institution CIP study group.

Sarah Marie Huban, MA, CIP, CHRC, human protections program and research regulatory affairs manager at Children's Healthcare of Atlanta, and **Sarah Clark-Worley**, MPH, CIP, senior IRB coordination manager, research compliance office, Stanford University in Palo Alto, CA, designed the 10-week study group program to cover the following topics:

• **Intro.** Overview, handouts, reference materials.

• **Week 1.** Overview and office organization: covering minimal risk, Belmont Report principles, IRB history and oversight, IRB administration, IRB audits, IRB fees.

• **Week 2.** Organizing the IRB committee: defining the roles of the IRB chair, IRB committee, and IRB meetings.

• **Week 3.** Review categories: going over exempt categories, expedited categories, research, human subjects, compassionate use, emergency use, and waiver of consent in emergency medicine.

• **Week 4.** Initial review and committee meetings: covering initial submission review, including study design and quality, study populations, recruitment, etc.; community consultation, privacy, confidentiality, meeting preparation, and meeting procedures.

• **Week 5.** Informed consent: explaining witness signature, deception, waiver of consent, waiver of documentation, beneficence, and informed consent evaluation feedback tool.

• **Week 6.** Continuing review: defining amendments, adverse event reporting, unanticipated events, related or possibly related events, serious events, data safety monitoring board, non-serious and non-continuing noncompliance, serious

or continuing noncompliance, and study closure.

• **Week 7.** Administrative and regulatory issues: going over HIPAA, private health information, de-identified data, Federalwide Assurance, investigational new drugs, and a variety of other terms and concepts.

• **Week 8.** Study populations: focusing on vulnerable persons, criteria for waivers of consent, subpart D exemption limits, fetus research, exceptions to father signature requirement for fetus research, pregnancy, parent assent, Subpart C, prisoners, and minimal risks.

• **Week 9.** Issues based on study design or category: covering component analysis, ethnographic research, definition of medical device, humanitarian use device, investigational device exemption, non-significant and significant risk determinations, anonymous, anonymized, and Phase 1 trials.

• **Week 10.** Review/practice exam: reviewing the foundations and concepts of IRB practice, organizational and personnel knowledge, IRB functions and operations, and records and reports. ■

Study: Clinical trial site violations not reported in peer-reviewed literature

FDA findings left out of final publication

A study published in *JAMA Internal Medicine* in February found that serious violations of good clinical practice discovered by the Food and Drug Administration (FDA) at clinical trial sites are not mentioned in peer-reviewed publications in which the trial results are published.

Author Charles Seife, MS, professor at the Arthur L. Carter Institute of Journalism at New York University, and graduate student assistants searched an FDA database of inspection results to find investigators and clinical trial sites that received "official action indicated" (OAI), the most severe classification. The researchers put in a Freedom of Information Act (FOIA) request for details on the inspections, and received heavily redacted documents of 20 related investigations. They also searched the FDA database and used official notifications of regulatory actions against investigators.[1]

"This investigation has found numerous studies for which the FDA determined there was significant evidence of fraudulent or otherwise problematic data. Such issues raise questions about the integrity of a clinical trial, and mention of these problems is missing from the relevant peer-reviewed literature," Seife wrote.[1]

"No corrections, retractions"

In all, Seife and researchers found 57 published clinical trials between 1998 and 2013 that found evidence of one or more problems, including: "falsification or submission of false information, 22 trials (39%); problems with adverse events reporting, 14 trials (25%); protocol violations, 42 trials (74%); inadequate or inaccurate recordkeeping, 35 trials (61%); failure to protect the safety of patients and/or issues with oversight or informed consent, 30 trials (53%); and violations not otherwise categorized, 20 trials (35%)," according to the study.[1]

Of the 78 publications from the trials in which FDA violations were found, only three mentioned the violations. "No corrections, retractions, expressions of concern, or other comments acknowledging the key issues identified by the inspection were subsequently published," Seife wrote.[1]

Seife gave examples of unreported violations, including the following:

• In a clinical trial of anticoagulant drug rivaroxaban, eight of 16 site inspections received OAI for infractions such as falsification, unauthorized unblinding, and "concerns regarding improprieties in randomization." The FDA deemed the entire study unreliable — a determination that was not mentioned in articles related to the study results or trial.[1]

• Clinical trial records for a chemotherapy study were falsified by a researcher, partly because already-falsified patient records led to the death of a research subject with impaired kidney and liver function. The subject's condition was hidden, and the

subject died after the first dose was administered. The researcher was sentenced to prison after pleading guilty to criminally negligent homicide and fraud. The same researcher also falsified records in other studies. The falsifications and patient death were not reported in subsequent journal articles on the studies.[1]

• A patient had a foot amputated two weeks after receiving stem cell treatment in a trial involving patients with ischemic limbs. Despite this, the article on the study stated that "all patients recognized and were aware of major clinical improvements in the treated (more ischemic) leg, despite no significant clinical changes in the control (less ischemic) leg."[1]

The FDA does not notify peer-reviewed journals about an OAI determination for a clinical trial that the journals may have published, nor does the agency inform the public, Seife noted. FDA site inspection documents received through the FOIA request were heavily redacted, making it impossible to match many of the documents to published clinical trial information. "The FDA has legal as well as ethical responsibilities regarding the scientific misconduct it finds during its inspections. When the agency withholds the identity of a clinical trial affected by scientific misconduct, it does so because it considers the identity to be confidential commercial information, which it feels bound to protect," Seife stated. "However, failing to notify the medical or scientific communities about allegations of serious research misconduct in clinical trials is incompatible with the FDA's mission to protect the public health."[1]

Implications for research

The implications can be felt in the research community and the public, according to Seife. "For the research community, it means that you cannot trust that findings of research misconduct are reflected in the peer-reviewed literature — that in the majority of cases, even when the FDA has documentation of fraud, there is no indication in the peer-reviewed literature that this has gone on at all," Seife said in an audio interview with *JAMA Internal Medicine*. "For the public, you have to be aware that the FDA is finding problems but isn't always telling the public about it. So you have to be aware that the peer-reviewed literature is not fully reflective of the problems that are found with the scientific trials." *(The interview can be found at http://archinte.jamanetwork.com/article.aspx?articleid=2109855.)*

One possible remedy, Seife noted in the study, is that the FDA could make unredacted information on clinical trial site misconduct available to the public and to the scientific community, either through ClinicalTrials.gov or through a separate database. "[H]owever, most of the burden for ensuring the integrity of the research in the peer-reviewed literature falls to the authors of the articles submitted to peer-reviewed journals," Seife wrote. "Currently, there is no formal requirement for authors seeking to publish clinical trial data to disclose any adverse findings noted during FDA inspections. Journals should require that any such findings be disclosed."

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How do IRBs or PIs rate risk of ordinary life experiences?

Researcher has tool that may help

IRBs often find it challenging to determine whether risk is minimal in many social-behavioral studies. What might bring emotional distress to one person could be a shoulder-shrug to another.

Now a researcher has devised research and a tool to better define minimal risk. Called the Ordinary Life Experiences Rating Scale (OLERS), the instrument measures minimal risk in the context of federal regulatory terminology. Items on the tool include such

distress-causing situations as social embarrassment, environmental nuisances, and loss.[1]

There's a great deal of variability in how IRB members evaluate research for greater than minimal risk, says **Evan Harrington**, PhD, associate professor of the department of clinical-forensic psychology at The Chicago School of Professional Psychology in Chicago. Harrington is a member of two IRBs and had served as chair previously.

Harrington observed that what is minimal risk to one person is not necessarily minimal risk to another. While the Office for Human Research Protections (OHRP) provides guidance, there is no uniformity in how IRB members assess such risk.

Even a simple blood draw could be distressing to some individuals, while for others it is not. Thinking about this variability in how people perceive risk and experience distress in ordinary life experiences is what led Harrington to create the tool.

"My intention was to create a very easy-to-use scale that could be tacked onto the end of any experiment so participants could answer how distressing they find a variety of ordinary life stressors and, having taken the study, how distressful they find the study to be," Harrington says. "Then, the researcher can find that question to compare to ordinary life stressors."

The scale has gone through preliminary psychometric testing, and a manuscript for publication is being prepared, he says.

The benefit to having a minimal risk tool like this is that it can answer long-standing research questions about the emotional risk for research participants when asked about past trauma or abuse, Harrington says.

"In this field, there's a big controversy that IRBs are weighing these types of studies too heavily in risk, estimating it to be too high," he explains. "IRB members tend to think there are all sorts of risks in studies of this nature, that participants might become suicidal."

Although IRBs take a conservative stance on surveys covering sexuality or past traumatic experiences, their caution is based on assumptions, not facts, as some previous research has demonstrated, Harrington says.[2]

"IF WE USE A STANDARD WITH ITS GENESIS IN BIOMEDICAL RESEARCH AND APPLY IT TO SOCIO-BEHAVIORAL RESEARCH, IT'S COMPARING APPLES TO ORANGES."

"When you have a scale like this, showing evidence of participants' reactions that are not that negative, then IRBs could use those findings as empirically based assessment for future studies," he adds.

So far, the standards available for assessing risk come from biomedical fields and are not a comfortable fit with socio-behavioral research, Harrington notes.

"If we use a standard with its genesis in biomedical research and apply it to socio-behavioral research, it's comparing apples to oranges," he says.

"For example, you may have risk from a blood draw or a poor administration of the technique itself; things can go wrong with a blood draw, and that's what people are thinking when they say there's a risk involved," he explains. "But when you think about the psychological distress a blood draw can cause, it's a different standard."

The Ordinary Life Experiences Ranking Scale has 15 questions related to common life events, such as the following examples:

- getting lost in a neighborhood where you are afraid for your personal safety;
- having a mosquito buzz in your ear;
- carelessly saying something that hurts a friend's feelings;
- going to the dentist for major work, such as a root canal or crown, that takes over two hours.[1]

Study participants rank each event according to whether it is not at all distressing, which is a ranking of one, to moderately distressing, a 6, to intensely distressing, which is 11.

The benchmark standard for the OLERS is the question, which is among the 15, how stressful someone finds "having blood drawn by a nurse with a syringe for a routine medical test," Harrington says.

"With my scale, what I try to do is come up with a variety of different, ordinary life stressors," he says. "If you're going to ask if something is minimal risk, and the definition OHRP provides us is 'ordinary life standards,' then a stress in a quality of life study has to be in comparison to ordinary life stressors."

Another benefit to using the OLERS is that researchers and IRBs

will have a better idea of what types of socio-behavioral research causes greater than minimal stress among study participants, he says. The last question on the scale asks, "Now that you are done, how distressing were the surveys that you completed today?"

"A scale like this could be tacked onto any socio-behavioral study to evaluate and give researchers the ability to demonstrate the safety of the protocol," Harrington says. "Or, if you do have a large number of people reporting that the study is more distressful than benchmark standards, then perhaps the IRB would need to take a closer look at the risks involved and improve safety measures."

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Comic assent/informed consent for biobanking is accessible

Riding the graphic novel trend

As IRBs continue to evaluate informed consent (IC) and youth assent forms according to regulatory guidelines and readability, researchers have come up with a format that engages, informs, and even entertains people being asked to participate in biobanking: comic assent.

The comic strip-style format is particularly appealing in an age when the graphic novel market has resurged in popularity among both children and adults.

"Research has shown that people do not understand informed consent forms, in general, and biobanking is a new type of technology that makes research enrollment more complicated than it was in the past," says **Leah R. Eisenberg**, JD, MA, assistant professor in the division of medical humanities at the University of Arkansas for Medical Sciences (UAMS) in Little Rock.

"We're asking for biological specimens that will be used for undetermined purposes for future, undetermined times," Eisenberg says.

Eisenberg and a colleague at the Mayo Clinic Center for Innovation in Little Rock had already been working on projects involving informing research participants through illustrated panels when Eisenberg realized that children who were being asked for assent in biobanking were not given the kind of information they needed to decide whether this was something they wanted to do.

> "MY BACKGROUND IS IN ETHICS AND LAW, SO I WANT PEOPLE TO HAVE INFORMATION ON WHICH TO MAKE ACTIONABLE DECISIONS..."

"My background is in ethics and law, so I want people to have information on which to make actionable decisions — even if these are not required by the letter of the law," Eisenberg explains.

"We were going through the letter of the law, not the spirit of the law, when we were asking children for assent," Eisenberg says. "So I thought it would be a good time to do innovative assent work."

The popularity of graphic novels suggested that illustrated assent might work well for this purpose, she adds.

"I thought comic assent might work for adolescents and children for biobanking involving mitochondrial disease," she says. "This would give them a more engaging form."

For example, one page of the Mayo Clinic comic assent panel, relating to biobanking for mitochondrial diseases, begins with teens sitting at a table discussing their participation in a biobank. One boy says, "Okay, so we're all participating in this biobank thing, right? Why exactly is it important? What does it mean?" The characters

express some embarrassment about not knowing the answer, and one boy says he did some reading and can help out. Other teens say they know a little too, and they begin to talk about it, with one athletic character saying, "Well, I know this particular biobank is run by a group of researchers who are studying mitochondrial diseases. Their research might help them learn more about how medicines work, how our bodies work…"

While the adult comic for informed consent follows the Common Rule requirements for informed consent, including risks and benefits, alternatives, etc., the pediatric assent comic doesn't contain quite as much information, Eisenberg says.

"Adults need to know possible implications, privacy rights, and things like that," she explains. "Children need information to assent, but they don't need all the information the informed consent requires."

Getting broad consent

Comic assent and IC provides a narrative flow that progresses from someone thinking about participation to talking about what a biobank does and then to what the participant needs to give to the biobank, what the pros and cons are, and how they can withdraw from the study, Eisenberg says.

"It's true that with biobanking you cannot tell everyone all the ways your information may be used because we just don't know that," she says. "Research I've done shows that patients generally don't want to be contacted each time their information is being used in a biobank."

Plus contacting biobank participants each time a new study wants to use their sample is cumbersome and challenging, she adds.

"So I do believe a broad consent is appropriate," Eisenberg says. "We need to tell people we're going to use this information, although we can't say how, and we may come back to you if we have information that is actionable. Then they can decide."

The comic assent illustrator made the panels more engaging to teens, using different styles. They purposely chose to have a group of teens talking about participation on their own so it wouldn't appear that a scientist is feeding kids information, she says.

The comic assent and informed consent panels still are in research prototype use, but Eisenberg says she hopes they'll be ready to use in studies soon. "It's definitely my goal," she says.

"I'd definitely like to send participants a PDF of the comic assent so they can read it by email," she adds. "It's my idea to give this to them instead of a text-based consent."

Each comic assent and informed consent can be made disease-specific, targeting people at their appointments with physicians. Some participants also might be recruited through social media and other marketing efforts or through disease advocacy groups.

"I think this has broad application for biobanking or research," Eisenberg says. "If we can put together data showing this is helping people to understand better, then I think we would need to use it more broadly."

Some IRBs might never be comfortable with an IC that is entirely in comic format, so the comic version also could be a supplement to the traditional informed consent, she says.

"Each institution has its own comfort level with using nontraditional consent, but the comic was made to stand alone; it contains all the information the text form contains," Eisenberg says. ■

COMING IN FUTURE MONTHS

- Best practices in training IRB administrators
- Learning strategies for responding to participant complaints, concerns
- Improving electronic IRB efficiencies in large health data systems
- Improve training, communication with research coordinators

IRB ADVISOR

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CNE/CME QUESTIONS

1. Which of the following is not in the list of topics for consideration when using a single IRB, according to Cynthia Hahn?

A. Do the IRB's bylaws conflict with those of other institutions?
B. Who conducts institutional approval?
C. Will the IRB's electronic systems need to be updated?
D. Do contracts, policies, and procedures need to be updated?

2. According to Sarah Marie Huban, which of the following is a good reason for having IRB staff study for a certification exam with peers from other research institutions?

A. Since they will be competing for certification passing scores, the competition will sharpen their studying skills.
B. They can learn from each other which study items are related directly to regulations and which are more likely a requirement of a particular institution.
C. Asking for and charging study participants from additional institutions is a way to help pay for the study course.
D. All of the above

3. According to Evan Harrington, PhD, what's the advantage to using a tool that has research participants rate their level of distress on ordinary life experiences?

A. A minimal risk scale can help investigators with designing socio-behavioral studies.
B. The tool can be used in screening research participants to see who would be better suited for a particular trial.
C. As a minimal risk tool, this scale can answer questions about the emotional risk for research participants when they're asked questions that IRBs typically believe pose above minimal risk, such as past trauma or abuse.
D. None of the above

4. Which of the following would be a benefit of providing juvenile assent and adult IC for biobanking in comic format, according to Leah Eisenberg, JD, MA?

A. It can be more engaging than traditional consent/assent text documents.
B. It can contain all of the required elements of consent.
C. It can explain the biobanking process in a way that most youths and adults can understand.
D. All of the above