IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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Risk-benefit assessment: One size doesn't fit all

IRB's review worksheet is useful tool

Assessing risks and benefits is an evolving process in the human research protection world — especially for IRBs that handle social-behavioral, as well as biomedical, studies. One size in risk-benefit assessment definitely does not fit all. For instance, IRBs sometimes over-emphasize risks in studies involving social-behavioral topics without considering protections that researchers have put in place, IRB experts say.

At Baruch College in New York City, the IRBs previously would send automatically any study involving sexual content or deception to the full board, notes **Keisha Peterson**, coordinator of the Baruch College human research protection program office. Baruch College is part of the City University of New York (CUNY) organization.

"In the past four to five years, the mindset has changed regarding these risks in research," Peterson says.

Now, the IRB office assesses whether identifiers are collected and whether researchers have communicated clearly that answering any of these types of sensitive questions is entirely voluntary, she explains.

"If investigators are providing an [opt-out] to subjects and are decreasing and minimizing the risk, protecting data, and making sure subjects are fully informed of the research purposes, then the risk level is lowered," Peterson adds.

IRBs have moved further away from the locked cabinet mentality of previous generations. The way they envision confidentiality risk now involves encryption software, more complex questions about how confidentiality and privacy are protected, and how electronic systems are protected from breaches, says **Jean Larson**, MBA, human research protection program education and community outreach manager at Yale University in New Haven, CT.

The key question from an IRB standpoint is: "Are the risks to subjects minimized?" As IRBs adjust their risks and benefits assessments, they should start with the elements of informed consent and then broaden their consideration of what might be achieved, Larson suggests.

For instance, studies might have variable risks depending on which population is enrolled in a study, she notes.

"A good example would be split findings for children's studies, where the risk to one group may be different from the risk to another group," Larson explains. "You might have a protocol where there is one group of children with a condition and one group without the condition, so the children's risk findings would be different from one group to another."

In the biomedical field, some researchers are questioning conventional wisdom about risks and benefits involving some vulnerable populations. For example, one researcher asks how IRBs might arrive at a decision about risks and benefits involving pregnant women, as technology and cutting-edge research provide opportunities for greater benefits to fetuses or the women.

"We have recognized that research potentially beneficial to pregnant women has not been carried out because of concern about injuring the fetus. There now seems to be increased interest in testing medications during pregnancy to benefit either the pregnant woman or fetus," says **Carson Strong,** PhD, a retired professor of bioethics in the department of internal medicine at the University of Tennessee Health Science Center in Memphis. Strong also is an IRB member at the university.

"This increases the importance of having discussions about how to balance risks and benefits between the pregnant woman and fetus, given that the federal regulations leave a number of questions in this area unanswered," Strong says.

"In my view, IRBs generally do a good job of protecting vulnerable subjects," Strong says. "However, there are exceptions, which can occur in situations in which the assessment of risks is controversial or the regulations do not provide sufficient guidance."

The Yale University HRPP's protocol review worksheet includes questions that help the IRB assess whether risks are minimized adequately. Larson developed the worksheet in consultation with the IRB chairs and IRB manager. They created it to provide IRB members with a handy tool to use when conducting a protocol review, she explains.

"We also included it with the protocol minutes, further supporting the fact that the committee has looked at these issues," Larson says. "We were looking for a way to support our members in their approach to reading a protocol or thinking about the review criteria or informed consent criteria as it applies to the individual study they were looking at."

The protocol review worksheet is completed before the IRB discussion of a study. The reviewer who used the worksheet can use it as a guide during his or her oral presentation, Larson says. *(See story about Yale reviewer worksheet, page 99.)*

IRBs primarily are concerned that studies' risks

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and benefits are clearly stated to participants in the consent form, and sometimes there are issues with investigators not clearly stating their risks and benefits, or with consent forms and IRB review applications not matching, Peterson says.

But there often are other issues involving risks and benefits. For instance, IRBs in the CUNY system often assessed risks based on their individual campus' culture, Peterson says.

When CUNY reorganized in 2011, the multi-campus institution eliminated local IRBs and moved to a centralized IRB structure. Instead of having 19 IRBs, the institution has four full boards. This has affected how risks and benefits are handled, Peterson says.

"We used to assess risks based on campus culture," she adds.

Since moving to a centralized IRB system, CUNY increasingly has used non-research and exempt determinations, which previously were rarely used, Peterson says.

"When we had 19 IRBs, every IRB was run differently; everyone had their own rules," she explains.

The centralized review system ensures quality and that every review is conducted according to the institution's policies and procedures, she adds.

As a result, the number of studies taken to the full board because of their perceived risks has declined by an estimated 75%, Peterson says.

Instead of sending all studies with sexual content or deception automatically to the board, the HRPP office conducts pre-reviews to determine whether a study qualifies for a review exemption or whether the study can be expedited, Peterson says.

"We have a separate board solely tasked with expedited protocols," she says.

Studies with risks that are not mitigated still might be sent to the full board, but these full board reviews are much rarer than they were before the centralized IRB process was created, she adds.

"Now, more attention is paid to the federal definition of research; does the study meet that definition? Does the project meet exemption criteria?" Peterson says.

This change has resulted in a more streamlined and fair review process that gives researchers more options than they had previously, she says.

"I've seen a shift where people are starting to trust the IRB more, and more research is being done," she adds.

Strong has called for new federal guidelines for handling risks and benefits in studies involving pregnant women to clarify risk and benefit assessment.

"There have been minor modifications in the regulatory guidance for research involving pregnant women and fetuses, but there still is a need for specific guidance in a number of areas," Strong says. "There have been risk-benefit discussions in the literature, mostly focusing on how to interpret the regulatory concept of minimal risk. We need more discussion concerning how to understand minimal risk in research involving pregnant women and fetuses." ■

Yale reviewer worksheet helps with risk assessment

A "cheat sheet" for reviewers

IRBs might help board members improve their protocol review process through the use of a tool that guides them through questions to ask about each study.

One such tool, created at Yale University in New Haven, CT, is four pages and comprehensively covers a protocol.

"This is almost a cheat sheet," says **Jean Larson**, MBA, human research protection program education and community outreach manager.

"It's the document that helps reviewers ensure they have considered all the things we need to consider and that they've outlined and identified any specific items that need significant discussion," Larson says.

The worksheet explains that the presentation of a new protocol begins with a description of the research study. "In reviewing the protocol, the following criteria should include information necessary for the committee to make an informed decision regarding approval of the protocol, a critique that describes any pertinent deficiencies and criticisms of the protocol and consent documentation and a recommendation regarding approval," the worksheet states.

There are 15 points on the worksheet, and after each point, the reviewer has space for comments.

Here are a few examples of the points in the Yale University human investigation committee's protocol review worksheet that help assess risk:

- **Additional safeguards are in place for**

vulnerable populations.

• **Subject privacy and confidentiality are maximized.** "The risk of a breach of confidentiality is always a concern," Larson says. "So what we're looking for are measures the investigator has taken to provide the best privacy and confidentiality, like are they having an informed consent conversation in the waiting room, or are they talking in a private area with the potential participants?"

• **Informed consent process is appropriate.** "Informed consent documents must have all of the elements of informed consent, and it must match the protocol that the IRB is reviewing," Larson says.

• **Risks to subjects are minimized.**

• **Subject selection is equitable.** "One of the things we look for in the exclusion and inclusion criteria is whether there is a reason people with a particular lab result or condition are being excluded," Larson explains. "We look at whether recruitment methods or materials are appropriate so people are not using recruitment materials that are misleading or don't make it clear that it's research."

• **Subject safety is maximized.**

• **Benefits are stated appropriately.** "They should describe the fact that the study may or may not benefit participants, and they should include information about how the study is designed to help people in the future with this disease or condition and to improve knowledge about the disease or condition," Larson says.

• **Alternatives to participation are stated.**

• **Economic considerations are equitable.** Larson suggests researchers consider these questions: "How does the compensation of the group with the condition compare with compensation of the group that is the control? If there are differences, are those differences reasonable? If the study is able to offer a significant payment to the subject, is that payment appropriate in relation to the activity?"

• **In case of injury, plans are clear.**

The Yale University IRB reviewers are expected to use their personal and professional expertise to assess whether certain study risks are reasonable for a particular population, Larson says.

Also, reviewers look for studies to describe accurately the potential benefits from participation, she says.

"Our pre-review process looks at that, and the committee looks at that, as well," Larson adds. ■

Try "InfoShorts" for quick education strategy

Topics keep IRB up-to-date

*[**Jean Larson**, MBA, HRPP education and community outreach manager for Yale University in New Haven, CT, recently rolled out a quick and effective education program for the IRB. Called "InfoShorts," the program keeps IRB members up to date on regulatory changes and other topics at meetings.]*

IRB Advisor: What are InfoShorts and what gave you the idea for this educational program?

Larson: We wanted to give our IRB members a very brief educational moment at the beginning of each meeting on a topic of interest to them. We started InfoShorts with the topic of conflict of interest because the NIH [National Institutes of Health] conflict of interest regulations had changed, and we wanted to make sure our members were aware of that. For our newer members, InfoShorts also provide a brief review and additional information on a topic that is chosen every month. InfoShorts are short, but there is time for people to ask questions or have a discussion about the topic. They've been successful.

IRB Advisor: Who presents the InfoShorts, and what kinds of topics do you cover?

Larson: Presenters are whoever is available and interested. The chair has presented several of them; our IRB analysts have presented some, and I've done a couple. We want the monthly topics to be areas that we know will impart something valuable and of interest to our members. After conflict of interest, we had InfoShorts on compliance and children's research, congruency, protocol approval criteria and informed consent requirements. We've also presented information about presenting a protocol and expedited review because that's a high percentage of what we do as an HRPP. Next we are doing an InfoShort on our review and revision to policies and procedures. After the InfoShorts are presented, we post them on the website in

a PowerPoint presentation. We keep these to eight or nine slides. The InfoShorts last five to 10 minutes. They are tickler education — not our only education, but a nice addition to the agenda. ■

Be prepared for what's up next: E-consent

Better informed consent tips

Technology now is driving the way informed consent documents are formatted and presented, according to an expert.

"People keep trying different strategies and approaches, and there is a whole array of options," says **Elizabeth A. Buchanan**, PhD, endowed chair in ethics, director of the Center for Applied Ethics at the University of Wisconsin-Stout in Menomonie. Buchanan speaks at national IRB conferences about technology, privacy, and informed consent, including the Office of Human Research Protection (OHRP) Research Community Forum, held May 2, 2013, at Oakland University in Rochester, MI.

"Now, we're trying to think about how — especially in today's world — most of us are used to looking at a screen and reading a little bit here and there," Buchanan says. "The days of reading a whole page and 15 pages in a row are really gone."

This means IRBs and human research protection programs increasingly are trying to map innovative strategies for improving informed consent documents, she adds.

"We're letting the technology drive the way we format these documents," Buchanan explains. "With information overload all around us, we need to find better strategies for showing people information."

One of these changes involves e-consent, including electronic signatures and digital stamps.

"Those conversations are happening across the IRB and research world," Buchanan says.

Research into how people read and comprehend information shows that bulleted lists, boxes, and bold-faced text improve reading and comprehension, she says.

In an e-consent document, each section stands alone visually, making it less daunting than picking up a 15-page narrative, she explains.

For instance, some studies have used electronic slides and other visuals and technology for delivering informed consent, Buchanan says.

IC information can be put on a scrolling Web page in the way online user agreements appear, but it is a less interesting way to present the information, she notes.

"We want to get away from that model of taking a 20-page form and putting it online," Buchanan says.

The goal of e-consent should be to use technology in a way that helps facilitate better informed consent and comprehension while maintaining confidentiality. *(See story on electronic IC confidentiality issues, page 102.)*

"We want to make sure everything we need to know is in the document, but that the information is moving in a way that makes things easier to digest," Buchanan says. "We have to move towards a language that explains to people the possibilities and not only the realities of how an investigator expects to use data."

"I think many investigators and IRBs still are using the language of the locked file cabinet and paper documents when most of us are using electronic documents, and our language needs to shift," Buchanan notes.

As IRBs and researchers adjust the IC process to accommodate new technology and better data on how people digest and retain complicated information, they should make certain the e-consent meets all ethical and regulatory requirements for informed consent, she adds.

"We still have to remind people of the basic elements of consent," Buchanan says.

"Another piece is consent via mobile devices," she says. "More research is taking place with mobile devices, and so we should call attention to how you provide consent information to someone on their cell phone and make sure researchers follow regulations."

IRBs and researchers also should be aware of the limitations to informed consent in use with social media studies, she notes.

If a study is monitoring dialogue in a chat room, how might a participant opt out of being included in the study?

"If you are looking at a chat room, the speed and flux makes it difficult to consent people in the room, so some venues present more challenges than others," Buchanan says. "Think about best practices, identifying language, and the venue."

Also, in a chat room or other social media research, investigators might use screen shots in the informed consent process to show potential participants what they might see if they take part in the study, she suggests.

Another issue in this type of research involves

terms of service agreements on social media websites where researchers are collecting data.

"For example, if one is a member of a Facebook group or has a Facebook page, and a researcher is using that for recruitment, data collection, or dissemination, the researcher is subject to the terms of agreement for Facebook," Buchanan says. "Sometimes that might be a conflict between the terms of service and what the researcher says in the informed consent document."

In the electronic era, information sharing between research participants is both easy and fast, and this also can be a problem, Buchanan says.

"In a study on how individuals were communicating about their research study, participants were sharing information," she explains. "They were unblinding the study by virtue of the information they shared."

Researchers and IRBs can prevent this problem by informing study participants that while they are free to discuss the study with their families, they should not discuss it in online public sites because of the potential of harming the study, Buchanan says. ■

Recommendations for confidentiality language

Be upfront about confidentiality

As e-consent and informed consent for technology-driven studies increase, investigators and IRBs should take steps to ensure confidentiality and privacy are accurately described and adequately protected.

Informed consent should be upfront and let participants know about the possibility of data being shared with other researchers. This will help avoid conflicts that arise when an investigator is prohibited from sharing data with other studies because participants were not told the data would be shared, says **Elizabeth A. Buchanan**, PhD, endowed chair in ethics, director of the Center for Applied Ethics at the University of Wisconsin-Stout in Menomonie.

For example, an informed consent document might state, "Confidentiality will be kept to the degree permitted, regarding the technology used," Buchanan suggests.

"Address the uncertainty in data longevity, telling participants that data might be used beyond the timeframe of this research project," she adds. "We don't want to scare anyone off by saying we don't know what will happen to the data, but we should present the statement in a more open fashion."

A better way to word this would be to say, "We're collecting these data and another research team might come along and use these data for great discoveries. That's the intention behind data sharing: to further knowledge and research," Buchanan says.

Informed consent documents now must avoid guarantees of individual privacy and instead educate participants about what data might be used for and what is protected and not protected, she adds. ■

COMPLIANCE CORNER

Ensure compliance with new PHS rules on COIs

COI transparency is new model

As often happens in research, new rules, policies, and guidelines often follow media reports of research integrity and ethical breaches.

The federal government's revised financial conflict of interest (COI) policy is one example of this, says **Linda Darga**, PhD, grant development specialist in the office of research administration at Oakland University in Rochester, MI.

The Public Health Service (PHS) finalized its revised policy on research conflict of interest in August 2012. One change was the requirement that investigators disclose to their institution any significant financial interests, including those of their spouses and dependent children, and that institutions have a disclosure form for this purpose.[1]

"Before, it was up to the researcher to disclose any kind of financial conflict of interest," Darga says. "Under the new rules it is up to the institution to have a disclosure form."

Also, the financial trigger is lower. Instead of $10,000 as a threshold, it's now $5,000, including stock, ownership shares, payments for consulting, etc., Darga says.

"This includes any payment that would conflict with their position at their institution, which

usually would be a university," she adds. "Anything a researcher does for a university, whether it's teaching, meeting, sitting on an IRB, or conducting research, if there is a significant financial interest over $5,000 with an entity that might conflict with their position at the university, then they must report those interests to the university."

It's up to the research institution to write guidance consistent with the federal regulations and to create and send a disclosure form to all researchers. These forms must be completed annually, and researchers receiving PHS grants must complete COI training, Darga says.

"Now that this is taken care of separately, the IRB will know whether a person is applying to an agency that requires a disclosure form," she says. "If there is a financial conflict of interest, the institution has to manage the COI so it would not bias the research."

Oakland University has had very few significant financial COIs so far, she adds.

While the new policy might be inconvenient for some institutions, it provides uniformity across the field. Before the changes, reporting conflicts of interest was handled on a trust basis: Either investigators made the report or they didn't, and institutions might not know whether the omission of a report meant there were no conflicts of interest or whether the investigator simply did not file a report, Darga notes.

"Over a couple of decades looking at submitted IRB forms, I don't ever remember having to answer a question about financial conflicts of interest," Darga says. "It was not on people's radars at that point."

Now every institution that applies for these grants has to comply with the regulations on conflicts of interest, no matter how large or small the organization is, she adds.

The Oakland University significant financial interest (SFI) disclosure form is four pages and includes four questions for which the available answers are as follows:

- I personally have no SFI to disclose in this category.
- My immediate family members have no SFI to disclose in this category.
- I personally have SFI to disclose in this category.
- My immediate family members have SFI to disclose in this category.

The chief questions on the form include:

- With regard to publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000.
- Remuneration that includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value.
- With regard to non-publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or when the investigator (or the investigator's spouse and/or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest).
- Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income that exceeds $5,000 related to such rights and interests.

The form also lists exclusions, reports of sponsored travel, and has a page with a chart for reporting the range of SFI in categories of $5,000-$9,000; $10,000-$19,999; $20,000-$100,000, and greater than $100,000.

When researchers complete these forms, the information becomes public and can be obtained by research participants and others, Darga says.

"Research participants can call the IRB number or principal investigator number on the consent form and they have to answer their questions about the conflicts of interest," she adds.

Some organizations might even put the information online.

"A lot of this is becoming more transparent, and I think that's a good thing," Darga says. "Research is based on truth and honesty."

REFERENCE

1. Implementing the final rule on financial conflicts of interest in Public Health Service funded research. Association of American Medical Colleges. Published March 2012. https://www.aamc.org/download/277644/data/coi-rule.pdf. ■

For international consent, clarity is key

Conversational tone is more engaging, expert says

Creating clear, truly understandable informed consent documentation can sometimes be a challenge for IRB members and researchers, particularly in the area of international research. Making

sure that details are not lost in translation and that the documentation meets U.S. federal and international regulations can also present some difficulty.

"It's particularly challenging with international research because each country has different rules that govern research," says **Jacob Stoddard**, BA, CIP, senior IRB protocol analyst at The Ohio State University's Office of Responsible Research Practices. "We make sure researchers go through that country's approval process as well, as it's a precursor to our IRB offering final research approval."

OSU is conducting more research in China, India, and Brazil, and is establishing gateways in those countries by forming partnerships with universities and research entities. The university is also seeing a growing amount of research in Africa, particularly in Kenya and South Africa. OSU's study abroad program sees many undergraduate students developing research projects in these and other countries.

Expanding research overseas

"At The Ohio State University, we see a growing amount of international research, especially in social and behavioral sciences," Stoddard says. "As researchers went overseas to conduct more and more projects, one of the challenges they faced was developing an informed consent process that respected the culture and the social norms while maintaining and being in line with federal regulations in the U.S. One of the practices we focus on is putting processes in place to help the researchers develop a consent process to best explain the research."

When considering language for an international consent form, Stoddard has these recommendations:

- Do your homework on the country in which the research will take place, and especially look at the literacy levels of the study population.
- Create a list of cultural consultants. These can be members of the university staff or community who are knowledgeable with cultures in the studies.
- Have the consultants look over the consent language and make sure there are no confusing translations or terms with which participants may be uncomfortable.
- Create sample consent templates that researchers and student investigators can tailor to the population being studied.
- Create checklists or other IRB review tools to ensure that IRBs consider a population's social and cultural norms when reviewing international study protocols.

When reviewing international research consent forms, the OSU IRB focused on several key factors, including studying the population and making sure IRB members and researchers are knowledgeable about the culture. Some consent forms are written more conversationally instead of as a long speech. OSU also uses cultural consultants, who are volunteers from the university or global research community who are knowledgeable about certain cultures. The IRB attempts as much as possible to use consultants within the country to be studied. "The consultants take a look at the consent script to determine any translation issues, that the language will be easily understood by the participants, and give us feedback on the culture as a whole," Stoddard says. "For instance, researchers may be studying a culture where a researcher would need to get the approval of a patriarch or chieftain before going out and talking to individual members of the family or community. The consultants support the IRB in making informed decisions. We gather as much information as possible in advance so the IRB can inform the researchers of any concerns during the review process."

Don't become lost in translation

Cultural consultants make sure that elements of the informed consent translate well and that examples used in the language will make sense to international participants. For example, a researcher in South America tried to explain that participants would be part of random groups. The difficulty lay in trying to explain the word "random" — the researcher equated the term with flipping a coin, though the translation said, "Random is like throwing money in the air," a nonsensical phrase. "What also comes up is that the idea of flipping a coin is something we're familiar with, but that doesn't mean it symbolizes chance all over the world," Stoddard says. And with a tribal culture, "All information collected will be anonymous" may be a confusing idea; a better statement is, "We will not write your name down." "That's more in line with the language of that particular group," Stoddard says.

Creating verbal consent

For the behavioral and social research and other minimal risk studies at OSU, researchers

University's verbal consent script template

Keep the dialogue conversational, informal

The IRB office at The Ohio State University helped develop a template for verbal consent for international studies. The template was created as a starting point for researchers, and can be edited as needed for clarity in the language:

Hello, my name is [student's name]. I am a graduate student in [department name] at The Ohio State University, and I am here in [country name] undertaking research that will be used in my [dissertation, thesis, etc.].

I am studying [project description].

The information you share with me will benefit others by [explain].

This interview will take about [approximate amount] of your time. There is a small risk of a breach of confidentiality, but all efforts will be made to keep everything you tell me in the strictest confidentiality. I will not link your name to anything you say, either in the transcript of this interview or in the text of my dissertation or any other publications.

Participation is voluntary. If you decide not to participate, there will be no penalty or loss of benefits to which you are otherwise entitled. You can, of course, decline to participate, as well as to stop participating at any time, without any penalty or loss of benefits to which you are otherwise entitled.

If you have any additional questions concerning this research or your participation in it, please feel free to contact me, my thesis supervisor, or our university research office at any time.

I would like to make a tape recording of our discussion, so that I can have an accurate record of the information that you provide to me. I will transcribe that recording by hand, and will keep the transcripts confidential and securely in my possession. I will erase the tape after I transcribe it.

Do you have any questions about this research? Do you agree to participate, and may I record our discussion? If so, let's begin… ■

will often get a waiver of consent documentation and use verbal consent instead. In some cultures, participants may be intimidated by signing documents that appear to be legal and official, and verbal consent scripts can be written more conversational or informal in tone. "We're seeing this more and more in international research, especially in developing countries which do not have a prevailing Western influence," Stoddard says.

The IRB office at OSU worked with research professor Dr. Richard Gunther from the OSU Political Science Department to develop a sample verbal consent template for researchers to use. The university does not require the use of that particular template, but employs it as a starting point for developing verbal consent. "We look over the form to make sure certain regulatory information is there, and we use the consultant for the international form. We have them look over the study protocol and consent to help the IRB understand before the review if there are any risks or cultural norms that we need to be aware of to help conduct a project that will be beneficial to the research."

The biomedical studies, Stoddard says, sometimes use consent forms with more visual elements, such as pictures and graphics, to better explain the consent process to subjects in other cultures. For instance, a researcher from another institution described four vials of blood as "small glass bottles," which frightened participants into not signing up, as they envisioned glass soda bottles. A new visual form showed the actual size and shape of the vials. "The forms may explain a blood draw with a picture of what that means and how much blood will be taken," he says. "They figured out ways to make the process more visual."

Instead of being written as a speech that some participants could find intimidating, the verbal consent template is more conversational and can encourage participants to ask more questions and engage in discussion about the study. The sample template starts off with the researcher introducing him- or herself and explaining the research project. The participant is told that the study is voluntary, and that the participant's name will not be linked to anything he or she says or does. *(For more on the verbal consent template, see the above box.)*

"We do see in countries where the majority of the population does not speak English, researchers will utilize a verbal consent for behavioral research," Stoddard says. "If the fear is that a signed document is a legal concept — in that culture, it just makes a lot more sense to do a verbal consent that's more in line with the cultural expectations and to not intimidate potential participants." ■

University tests model for six-week protocol approval

Ad hoc IRB speeds approval process

When attempting to activate a clinical trial, one of the biggest concerns an institution faces is turnaround time. At Cedars-Sinai Medical Center in Los Angeles, activation of a new clinical trial could sometimes take 118 days, including IRB review, study team response time, and non-IRB required reviews such as contract negotiations. But for some protocols, including early-stage oncology or therapeutic studies, the institution looked for other ways to bring those new therapies to patients as efficiently and safely as possible.

The Samuel Oschin Comprehensive Cancer Institute at Cedars-Sinai led an effort to respond to the institution's challenge to develop a way to activate early-phase oncology clinical trials within six weeks. This meant completing all phases of review, from confidential disclosure agreements, IRB and non-IRB reviews, and trial site activation and enrollment, in just 42 days.

"The Cedars-Sinai cancer institute established a new mandate for Phase 1 clinical trials in oncology. Those clinical trials, sponsors and investigators expect very fast turnaround time," says **Eifaang Li**, DVM, MPH, CIP, director of research compliance at Cedars-Sinai. "However, we found that the six-week time frame is very difficult to achieve because many delays are coming from the sponsors' response to IRB questions, not from the IRB or the institution."

Cedars-Sinai developed the Rapid Activation Process (RAP) in an effort to speed these protocols to approval within the new six-week time frame. Other eligible protocols include compassionate use requests, therapeutic trials with urgent need, early phase protocols with a limited activation window, and those dealing with unanticipated problems or serious noncompliance issues.

To identify the key issues and deadlines involved in getting protocols on the fast track to approval, the leadership at Cedars-Sinai formed a working group consisting of IRB administrative personnel, researchers, patient care personnel from the cancer institute, and representatives from the medical center's Office of Sponsored Research and Funds Administration, Office of Research Compliance, and ancillary committees such as Radiation Safety.

"The team worked together and studied the overall process and each entity involved in that process," Li says. "They identified delays, errors, and how we can work together to meet the turnaround times, including engaging sponsors from the beginning to coordinate the tough issues."

Setting milestones

In order to get RAP moving, the group developed a protocol study calendar. The calendar consists of milestones that occur in the life of each protocol, the deadline by which each milestone must be met to achieve activation within 42 days, and the personnel responsible for the task. The study calendar encourages flexibility in the milestone dates if a responsible party is having trouble meeting the goals.

"We look at milestone date, and if there's a player who says there's something getting in the way of meeting the date, we look and see if anyone can get their milestones done a couple of days earlier, allowing us to shift extra days to the party who needs more time," says **Rebecca Flores Stella**, CIP, manager, IRB Operations and Education. "One of our biggest accomplishments was seeing overall study activation as our goal, rather than focusing on issuing IRB approval versus finalizing the budget versus having the contract signed and circulated. We worked together as one unit to help our team members meet their goals. That was a very helpful process. We accomplished that by meeting regularly and tracking our milestones and identify any potential barriers. As we did this more, we got used to doing that and would do it automatically and we didn't have to meet so much."

Ad hoc IRB

In developing the study calendar, the Cedars-Sinai IRB recognized that meeting the target dates for each RAP protocol would be difficult with the current meeting schedule. For instance, if a protocol involved research-related radiation treatments, the radiation committee would have to give approval

after reviewing the IRB-approved consent form, but its next meeting may occur before the next available IRB meeting. To avoid such approval delays, a special board was formed that consists of members who could meet quickly if needed. "We developed the ad hoc IRB to give us an alternative when waiting for the next scheduled IRB meeting would add more days to the turnaround time," Flores Stella says. "We wanted to develop this flexibility without overtaxing our available resources, and without appointing and training new members."

Meetings for the ad hoc IRB can be called quickly when everyone concurs they have had enough time to review study materials, generally within 48 hours of receiving the materials. Membership consists of five seats: three clinicians, one bioethicist, and one community member to comment from a patient's perspective. Clinician members are chosen based on expertise; for example, a cancer protocol would call for an oncologist to be on the board. The meetings can be conducted in-person or via teleconference, and meeting minutes are distributed and approved by electronic vote for greater scheduling flexibility. The ad hoc IRB meetings can be convened quickly — a protocol can be received on a Friday and the meeting held on Tuesday, Flores Stella says.

So far, the Rapid Activation Process has been used in the review of seven protocols. "These were high priority because they were high enrollment, or a therapeutic trial with patients waiting," Flores Stella says. The first four protocols were managed primarily by senior and management staff. "For tests five through seven, we were able to transfer activities to those who were highly trained but may not be in a management role. We want to be able to transfer the responsibilities from management to other staff while maintaining the same kind of turnaround time."

Constant communication is key

Li says two key practices helped the success of the program: regular RAP group meetings and frequent communication. "It's a very comprehensive collaborative process," she says. "We also learned that the earlier we could review the protocol, the better it is for everybody. During initial assessment, the radiation safety committee, for example, provides feedback and says maybe the facility doesn't want us to conduct this kind of protocol, then we can decide we don't need to continue the review process. It's very helpful. We don't want to spend a long period of time on processing the protocol and not have it initiated. I think this process helps to address this kind of issue."

Investigator response has been very positive, Li and Flores Stella say. And while the ad hoc IRB and RAP program are in the early stages, there is hope of having the process extend to more protocols. "Based on the experiences so far, the model should be transferable to process more protocols," Li says.

"I think the biggest benefit is having the opportunity and the institutional mandate to sit down and identify issues and change the perception of the process — we're one team with one goal of activation by day 42," Flores Stella says. "It really results in forward thinking." ■

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%.
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CNE/CME QUESTIONS

1. Which of the following would not be an appropriate element on a study reviewer guide and checklist?
   A. Additional safeguards are in place for vulnerable populations
   B. Subject privacy and confidentiality are maximized
   C. Informed consent process is appropriate
   D. All of the above are appropriate elements

2. What might be an appropriate goal when using e-consent for research studies?
   A. The goal of e-consent is to create a faster and more efficient informed consent process for participants of all research studies
   B. The goal of e-consent should be to use technology in a way that helps facilitate better informed consent and comprehension while maintaining confidentiality
   C. The goal of e-consent should be to provide visual and pictorial consent information to an illiterate participant population
   D. All of the above

3. The Public Health Service (PHS) finalized its revised policy on research conflict of interest in August, 2012. Which of the following is the compensation threshold for reporting significant financial interest related to a particular research project?
   A. $5,000
   B. $7,500
   C. $10,000
   D. $15,000

4. For international research, the verbal consent script is more engaging and understandable if written as a long speech.
   A. True
   B. False

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