IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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VOICE offers model for thorough, subject–friendly consent process

Health literacy is obstacle to IC

The human subjects protection field continues to search for ways to improve the informed consent (IC) process. IRB professionals often express concern that potential research participants do not understand their rights or the true risks and benefits of a study, although they might sign the IC forms and say they have no questions. Despite a variety of solutions that have been offered and tried, none has been widely used.

So IRBs and researchers continue to struggle with a complex informed consent process and seek new approaches and strategies. One promising new model that has emerged in recent years is the Valid Optimized Informed Consent Education (VOICE) program of Dartmouth College in Hanover, NH. The program addresses concerns about the readability of IC forms and participant comprehension during the IC process.

"I've come to appreciate the fact that consent forms are extremely long, extremely complicated, and a lot of participants struggle with medical terminology and health care terminology," says **Dianne Ferris**, MS, CIP, human research analyst at Dartmouth College. Ferris and colleagues created VOICE several years ago.

"We go to great lengths to make consent forms readable and understandable, but that doesn't address the consent process, and I think the forms and process are equally important," Ferris says.

One way to improve the IC process is by targeting health literacy issues. This became a goal for Ferris a couple of years ago after she attended a local conference on the topic.

"The conference opened my eyes to how much of a challenge health literacy is around the U.S.," she says.

Ferris' colleague **Sandra Knowlton–Soho**, MS, RN, also became passionate about improving the IC process after working in the clinical trial industry for 15 years.

In 2009, Knowlton–Soho and colleagues obtained seed money to start a quality improvement (QI) project involving informed consent. The QI initiative evolved into VOICE, says Knowlton–Soho, who was the

lead on VOICE and now is the practice manager of palliative care and critical care at Dartmouth Hitchcock Medical Center in Lebanon, NH.

"Each of us had another full-time job, but we felt so passionate about VOICE that we made the time and pushed ourselves to keep going with it," Knowlton–Soho says.

The Dartmouth VOICE project launched with a pilot study that had one VOICE education session, as well as new tools to improve IC forms and address health literacy issues.

Also, the VOICE educational session has been incorporated into introductory explanations about VOICE during Dartmouth Hitchcock's Clinical Trials Office (CTO) training programs for research staff.

"We have yet to conduct another full, two–hour education session with members of the research community," Ferris notes. "Our VOICE program is very young at this point; the pilot study was conducted last fall, and the first CTO introduction was in March 2012."

The goal is to have the institution offer the full VOICE education session as a required or voluntary session several times a year, she adds.

Also, they plan to provide VOICE sessions to neighboring research institutions and medical centers.

Dartmouth IRB relies on several key strategies for improving informed consent, including these:

• **Address health literacy issues:** Researchers and IRBs should not expect potential study participants to speak up if they do not understand what the informed consent form says. The typical reaction would be to nod their heads or say nothing. So it's important for IRBs to assist investigators with making the forms more readable, Ferris and Knowlton–Soho say.

Ferris sometimes finds that IC forms use words that no lay person will understand when a much simpler word is readily available.

"A term I saw recently was 'pyrexia' instead of fever," Ferris says. "Pyrexia means fever, so why not just say 'fever'— it's ridiculous."

Addressing health literacy problems could also mean educating potential subjects about their disease, or at least assessing how much they know, she says.

"What do they understand about medicine and health care?" Ferris asks. "You should incorporate these questions in the discussion early on, and then the research coordinator can tailor the discussion, accordingly."

• **Design an informed consent template:** A year ago, the Dartmouth IRB developed a 13–page IC template that could be adapted for any type of research informed consent, or it could be a model for other IRBs. These are its general sections:

– Introduction;
– Background Information;
– What is the purpose of this study?
– Will you benefit from taking part in this study?

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Editors: **Suzanne Koziatek** and **Melinda Young**.
Associate Managing Editor: **Jill Drachenberg**, (404) 262-5508 (jill.drachenberg@ahcmedia.com).
Production Editor: **Kristen Ramsey.**
Senior Vice President/Group Publisher: **Donald R. Johnston**.

Editorial Questions

Questions or comments?
Call Jill Drachenberg at (404) 262-5508.

– What does this study involve?
– What are the options if you do not want to take part in this study?
– If you take part in this study, what activities will be done only for research purposes?
– What are the risks involved with taking part in this study?
– Other important items you should know;
– How will your privacy be protected?
– Who may use or see your health information?
– What if you decide not to give permission to use and share your health information?
– Whom should you call about this study?
– What about the costs of this study?
– Will you be paid to take part in this study?
– What happens if you get sick or hurt from taking part in this study?
– Your responsibilities as a person taking part in this study;
– Consent signatures.

• **Train clinical trial (CT) staff on using the teach–back method with participants:** "The teach–back method is a large part of our education program," Ferris says. "We incorporated a discussion about teach–back, how to use it, the types of questions one could use, and our education program explained what it is and provide some guidance about what sections of consent discussion would be apropos and confirm comprehension."

The initial pilot training session used volunteers to act the part of study participants. Research staff practiced using teach–back with the volunteers, and they're offered guidance as they perform the teach–back techniques. *(See story on teach–back strategies on this page.)*

Another technique might be to incorporate teach–back questions in a study coordinator's copy of the informed consent form, Knowlton–Soho suggests.

"One of the people in our group had a 'teacher's copy' of their consent form; it had questions embedded in the form so when they went through the informed consent process they had notices to themselves to ask questions here and tips on what to ask," she says. "This is very helpful when starting a new study."

It's every IRB administrator and member's goal to make the informed consent process as strong and fair as possible, Ferris says.

"Obtaining true informed consent, like Dr. Henry Beecher said, may not be entirely possible in the truest sense, but it's a goal to which we all strive," Ferris says. A prominent investigator, Henry Beecher shed light in the 1960s on how 20 major research studies did not obtain informed consent from subjects despite significant risks. His findings were published in 1966 in the *New England Journal of Medicine*. ■

Tips on using teach-back in the IC process

Site uses simulations in training

Research institutions that plan to use the teach-back method as part of their informed consent process should make certain there is adequate training for clinical trial professionals. One research site has found that simulations work best for this purpose.

The Dartmouth Hitchcock Medical Center in Lebanon, NH, developed an informed consent process that uses the teach-back method as a way for research professionals to make sure potential study participants fully understand what volunteering entails.

"A fundamental aspect of using the teach-back method is avoiding yes-or-no questions or asking the question, 'Do you understand?' because most of the time people will say 'yes' or nod their head," says **Dianne Ferris**, MS, CIP, human research analyst at Dartmouth College.

"The teach-back approach is recognition of the fact that human nature is such that if people are struggling to understand something or if they are struggling with literacy in general or health literacy, they may not admit they are struggling to understand you," Ferris says.

The Dartmouth Hitchcock Medical Center has a simulation center where research professionals can practice and learn teach-back methods.

"This is a patient safety training center that can handle any type of clinical situation and teach people how to react in those situations," explains **Sandra Knowlton-Soho**, MS, RN, practice manager of palliative care and critical care at Dartmouth Hitchcock Medical Center.

"We can have conversations, set up rooms such as clinic rooms, operating rooms, and exam rooms," Knowlton-Soho says. "Also, the simulation center provides us with a standardized patient, which is someone from the community who enjoys acting and comes into the center to pretend to be a patient."

In testing the teach-back method as part of the Dartmouth IRB's Valid Optimizing Informed

Consent Education Program (VOICE), the trainers could videotape research professionals as they performed a mock informed consent process with one of the actors.

When members of the VOICE team initially discussed using the teach-back method in the context of VOICE, they decided it would be a great technique, Ferris says.

"It's a relatively straightforward and simple technique," Ferris says. "It takes a little time getting used to it, and training would help people learn how to implement it and use it well."

The first step was to pilot-test the teach-back method and see if it made a difference in how researchers handled the informed consent process.

"Our project was not just creating the education but seeing if VOICE made any difference," Knowlton-Soho says. "So we had people doing an informed consent discussion before they had training, and then we gave them a two-hour training session and immediately had them do another session in the simulation center."

After two months, the trainees returned to do another informed consent session, and the videotaped sessions were compared, she adds.

"We could see the difference in how people asked more questions that were not just 'yes' or 'no' questions, and they started having more conversations with [mock subjects]," she says.

For example, the study coordinator who is trained in the teach-back approach would first discuss with the potential participant what they'd have to do at their first study visit, Knowlton-Soho says.

The coordinator might say: "This is your first appointment, and it involves coming into the medical center within three hours of having a migraine headache. Once you're here, you have to sit for four hours and answer some questions from us every hour," she explains. "We also need for you to identify someone who will bring you home after the appointment."

Then at breaks in the conversation with the subject, the coordinator might say, "Let me hear from you when you go home and talk to your husband tonight about what you will tell him about the first visit," she adds.

If the potential participant says, "I don't know, something about coming in early, but what was it?" then the coordinator can repeat the instructions and continue to ask questions that will make certain the person recalls the important information.

Ferris and Knowlton-Soho offer these additional suggestions for questions to ask as part of the teach-back method for informed consent:

- **Purpose of the study:** "If you were going home tonight to talk to your husband or wife about being approached to be in this study, what would you say about what the study is all about? Or if your sister called you later, what would you explain to her?"
- **Study's risks:** "Tell me what are some of the side effects we talked about? And explain to me what you might do if you are concerned about something that's happening;" or "If you were given study drug X, what are some symptoms that you would be looking for? What are some side effects that you would want to keep an eye out for and report to your doctor?"
- **Voluntary participation:** "Tell me what would happen if you decide volunteering for this study is not working for you? What are your options and what would you do? Do you feel you need to be in this study? Explain to me what you would do if you wanted to change your mind about this study at any point."
- **What is required of participants:** "How many times would you have to come to the clinic if you were to take part in this study? How often would you have to come to the clinic? What are some of the major tasks you will have to do if you participate in this study?" ■

BEST PRACTICES SPOTLIGHT

Do the minutes reflect well-run meetings?

Better organization, details are needed

It's important that IRB meetings are run efficiently, keeping discussions brisk and on the important human subjects protection issues. But it's also important that these discussions are well-documented in the IRB meeting minutes. If a discussion takes place and there is no mention of it in the minutes, then the IRB could run into problems during an accreditation review or regulatory survey visit.

As one IRB director notes, the Association for the Accreditation of Human Research Protection Programs (AAHRPP) is paying particular attention to what is recorded in IRB minutes.

"We thought we were doing fairly well in

that department, and then we were surveyed [by AAHRPP] and we were told we needed further monitoring of the IRB," says **Stephanie Gaudreau**, CIP, IRB administrator for the Ochsner Institutional Review Board of Ochsner Health Systems in New Orleans.

So the Ochsner IRB began a review process in which two quality assurance staff members review all IRB meeting minutes every six months. They also review a sample of approval letters, checking to make certain all letters match information in the IRB's electronic database, including the IRB meeting minutes.

"Then I meet with the IRB chair once a month and we go over the set of minutes approved by the panel for the previous month," Gaudreau says. "We make sure we've captured all required elements; if there are any problems, we go back and fix them."

The IRB's process of a thorough, biannual review of meeting minutes will be re-evaluated in January, she adds.

"We might change it to a spot check or just pick one month and three sets of minutes to review," she says.

There were three areas in the IRB minutes that AAHRPP plays close attention to, Gaudreau says. They are as follows:

- Make sure the vulnerable populations are documented correctly in the minutes.
- Ensure that privacy and confidentiality issues are discussed at the IRB meeting and documented in the minutes.
- Make certain all unanticipated problems involving risks to subjects and others and any noncompliance issues are properly documented in the minutes.

"We revised our policies and procedures and created a new checklist that differentiates correctly between a review of unanticipated problems and potential noncompliance and whether these are serious and continuing," Gaudreau says.

Previously, both unanticipated problems and instances of noncompliance were grouped together with the term "protocol event," she says.

The AAHRPP surveyor said these should be separate categories in the minutes documentation, she adds.

The IRB created several IRB minutes templates to assist staff with improving documentation of meeting discussions. *(See sample items from the new study minutes template, p. 115.)*

Gaudreau networked with other IRB professionals and looked at the templates they used before creating the meeting minutes templates. She also worked with the IRB staff and the IRB chair to select the best template language and to make the information consistent between similar studies.

"What we found in looking at the minutes was the language was slightly different each time we made the determination," Gaudreau says. "It wasn't consistent, but the intent was the same."

The goal was to make it simple: The person writing the minutes could cut and paste template language into the minutes, keeping these consistent.

"We tried to do that for all vulnerable populations, for informed consents, waiver of consents, and all the elements required to approve a study," Gaudreau says.

"We've also used our minutes as a running timeline of what happened at the meeting, so we've divided them up with one template for continuing review, one for amendments, and one for new studies," she explains. "They're specific for one study, so one new study will have one set of minutes, and if we review two new studies at a panel meeting then all are combined in one set of minutes for that date."

The IRB office keeps a signed paper and electronic copy of the full minutes, which are sent to the whole IRB committee.

The IRB monitors reviewing the meeting minutes have already seen evidence the templates are being successfully used, she notes.

"They say the minutes are much easier to review now," Gaudreau says. "It's easier to find the information they are looking for related to a specific study." ■

IRBs ease conflicts with investigators

Survey shows policies are only part of the equation

Most IRB directors or chairs can recount stories about their tensions with investigators. All boards must balance the institution's need to protect subjects with investigators' concerns about unduly hampering their research.

But not every IRB goes about that balancing act

Here's a sample Ochsner IRB meeting minute template

It's used for new study reviews

The Ochsner Institutional Review Board of Ochsner Health Systems in New Orleans has created templates for use in writing minutes at the IRB's meetings. These help the IRB keep documentation of meeting discussions consistent and accurate.

Here are some of the items included in the IRB's new study meeting minutes template:

- meeting date;
- members present;
- guest presenters;
- guest observers;
- staff present;
- name of IRB members who did not participate in the review [due to financial conflict of interest, a conflict of interest because of (name) and was not present for the final discussion or vote];
- new protocol study title;
- sponsor;
- principal investigator;
- RB # and ERSA Pro #;
- scientific reviewer;
- CF reviewer;
- Each reviewer received a packet of pertinent information which included a copy of the ERSAS Basic Study Information application (date), protocol, proposed consent form. Packets also included information about each new study, protocol revision, and continuing review listed on the agenda for the (date) panel meeting;
- Dr. (name) was invited and did attend the meeting to present this study. (Name) gave an overview of the goal of this study. The study is designed to determine (narrative);
- When asked by a board member about the (study item), Dr. (name) explained that or Dr. (name) responded to board members about the (study item);
- With no further questions, Dr. (name) exited the meeting room prior to board discussion and voting;
- The board found that the risks to the subjects are minimized and are reasonable in relation to the anticipated benefits. The selection of subjects is equitable and adequate provisions are made to protect the privacy of subjects and to maintain the confidentiality of data. The research plan makes adequate provisions for monitoring the data collected to ensure safety of subjects. There is or is not a DSMB available … but the normal safety monitoring plans in the protocol are acceptable;
- The board found that subjects are not likely to be vulnerable to coercion or undue influence based on disease. A motion was made and seconded that this study population is not vulnerable; Vote: For (#), Opposed (#), Abstained (#);
- A motion was made and seconded to approve this study with the investigators listed and all other study related materials for one year; Vote: For (#), Opposed (#), Abstained (#);
- Consent form is approved as submitted: The consent process was reviewed and is acceptable. The PI submitted [insert number] consent forms. The eight required elements are present and the optional elements were considered. A motion was made and seconded to approve the consent form as submitted;
- Approved with changes: The consent process was reviewed and is acceptable. The PI submitted [insert number] consent forms. The eight required elements are present and the optional elements were considered. The board requires revisions to the consent form. The revisions will be provided to the PI on a red-lined version and an approved copy of the consent form. A motion was made and seconded to approve the consent form with the modifications indicated;
- Tabled: The consent form was reviewed and is/is not acceptable. The PI submitted [insert number] consent forms. The eight required elements are/are not present and the optional elements were considered. The board requires revisions to the consent form. These changes will be sent to the PI on a red-lined copy of the consent form. A motion was made and seconded to table the consent form; Vote: For (#), Opposed: (#), Abstained (#). ■

the same way. A recent qualitative survey of IRB chairs, directors and members showed a variety of approaches to dealing with conflicts with investigators.

Some of those approaches involved formal structures, such as open-door policies and invitations to investigators to attend IRB meetings. Others involved more of a matter of tone, says **Robert Klitzman**, MD, an associate professor of clinical psychiatry and director of the masters in bioethics program at Columbia University in New York City.

"Many of the IRB chairs and members said, 'We realize that researchers don't like us,' and a lot of them tried to respond to that," Klitzman says. "I was struck again and again by the number of IRB chairs

who said, 'Therefore, I try to be charming, I try to engage them. It's not just what you say to researchers, but how you say it.'"

Klitzman says his survey originally set out to ask IRBs about issues of research integrity, but he quickly found that as chairs and directors talked about their roles, they continually brought up the problems involved in working with investigators.

Results from the survey of 46 IRB chairs, members and staff were published in a recent issue of the journal *BioMed Central Research Notes*.[1] Klitzman says that while many surveys have looked at the complaints that investigators have about their interactions with IRBs, there's been little research into how IRBs manage these relationships.

He says the conflicts between IRBs and investigators are invariably about power.

"When I've interviewed researchers, they say IRBs have tremendous power," Klitzman says. "IRBs tend to say, 'No, we don't have power, we're just following the regulations,' but there's a perception that IRBs have power. And I think that's at the root of a lot of the tension."

Open doors and board rooms

He says many IRBs are actively fighting the perception that they are a "faceless bureaucracy," by taking steps toward transparency.

"The more there can be a sense of open doors and transparency and the notion that we're not the enemy and the notion to explain the reasons for what the IRB is doing, I think that can help both IRBs and researchers," he says. "It can help improve relationships and hopefully improve compliance and research integrity."

Some of those Klitzman surveyed were attempting to do this in both formal and informal ways. Formal structures such as having "open door" policies and inviting investigators to meetings were not universally employed, he says.

"I was surprised at the range," Klitzman says. "Some IRB chairs or administrators would say, 'I try to have an open door. I tell researchers whenever you want, just come by, email me, call me.'

"Others would say 'No, we don't allow researchers to contact individual IRB staff.' Investigators send emails to 'IRBinfo@(institution name). Generic. There's no name, there's no person; it's just a bureaucracy."

Similarly, some IRBs would invite investigators to meetings to hear the discussion about their protocols, while others didn't want them there. Some IRBs would allow the reviewing member to talk directly to the investigator, while others discouraged such interactions.

Klitzman noted that there are legitimate concerns about an investigator knowing who's reviewing his protocol.

"Should reviewers be anonymous? That's a worthwhile discussion," he says, noting one example where a reviewer was advised not to seek out the investigator to discuss problems with a protocol because the reviewer had a relatively low position in the investigator's department and could face difficulties because of it.

"There are issues that aren't easily corrected, but I think we need to realize that some flexibility is important."

Klitzman says he was surprised by the number of IRB chairs and directors who brought up the tone of their communications with investigators, rather than just the content of a yes-or-no decision about a protocol.

"They talked about charm and tone and style and saying no with a smile," he says. "They said, 'I have staff who are really good at this, and some staff who frankly aren't that good at it, at having the right charm and style.'"

Often, he says, the survey respondents who most often leaned in the direction of transparency and using a pleasant tone were women.

Klitzman acknowledges that some of the methods used by IRBs to promote a sense of openness can take their toll on staff. But he says they probably require fewer resources than a chair or IRB administrator might think.

"Having an open door, meaning people are welcome to come by — not that many people actually come by," he says. "A lot these are symbolic gestures. You don't want to be saying, 'Call me in the middle of the night at home.' But between 'faceless bureaucracy' and 'call me at home at night,' there's a wide spectrum of things you can do."

And he notes that many of these steps don't just improve the perception of the IRB; they also improve the quality of review. For example, when one IRB chair surveyed encountered a new research methodology, he invited the investigator to come explain it to the board. The IRB chair noted that this gesture helped from a public relations standpoint: "Investigators feel we're willing to be taught, and to reach out."

But in the process, the board also learns more about a new methodology.

"Some IRBs said we do a lot of PR work, and I think yes, that's PR work, but there's also substance there," Klitzman says.

Another important factor in gaining investigator buy-in is explaining the ethical reasoning behind the IRB's decisions, Klitzman says.

"It gets back to the issue of power," he says. "Studies of power show that people resent authority and power when they perceive that it's illegitimate. The more legitimate and transparent it is, if there's an explanation of the underlying reason for the power, people accept it, rather than thinking it's just being arbitrary or abusive."

Klitzman says he hopes that IRBs are willing to look at these ideas to help bridge the gaps that can occur with investigators.

"A lot of these things are easy to do," he says. "I would hope that this opens up a dialogue. I think people can at least think about these issues and see if there are things they can do to improve the tone and style of their interactions."

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IRB officials share ideas for bridging the gap with PIs

Robert Klitzman's survey of IRB chairs, members and administrators revealed a number of ideas that can be adopted by other institutions that want to improve relations with their investigators.

Klitzman, MD, an associate professor of clinical psychiatry and director of the masters in bioethics program at Columbia University in New York City, says most of these ideas are inexpensive to implement, but require changing attitudes about dealing with investigators.

• **Opening the door** — Several IRBs spoke of "open door" policies, making administrators, staff, and even chairs easily available to investigators via phone or email. Some also open the doors to the IRB board room itself, inviting investigators to come to meetings. However, at some institutions, interviewees complained that investigators wouldn't attend when invited.

• **Rethinking anonymity** — IRB officials interviewed showed nuances in the ways they deal with the difficult issue of whether an investigator should know who reviewed his or her study. An IRB may allow a reviewer to remain anonymous in specific situations, but encourage reviewers to reach out to investigators more generally when they see an opportunity to help.

One IRB director asked several members of the IRB to leave the board because they were adamantly opposed to communicating with investigators prior to meetings.

• **Reaching out to educate** — Many IRBs use newsletters and workshops to address continuing problems with studies that they see. Many note that their institutional human subjects protection training isn't extensive and may only consist of short online courses.

• **Hauling out the charm offensive** — IRB officials say they try to use tone, language, even humor, to ease the bite of an unpopular decision or request. One chair describes taking the blame for losing paperwork that she knows the investigator didn't turn in, in order to ask him to submit it "again."

The goal, they say, is to be seen as facilitators and allies. They try to impress this on staff as well.

• **Choosing where to put the effort** — However, even the most helpful IRB officials have their limits. Some officials note that they work with principal investigators who frequently turn in poorly written proposals or complain about changes. With these PIs, they say, they are less likely to put in extra effort.

• **Showing the basis for decisions** — Not just the regulations, but the ethical principles that underlie them. If PIs understand how institutional rules tie back to ethics, they may be less resistant to them. ■

More active consent for newborn screenings?

Ethicist argues that newer screenings are research

Nearly every baby born in the United States undergoes a simple heel-stick in the first few days of life that has potentially profound health implications for his or her life.

Through this blood test, babies are screened for a variety of rare metabolic, endocrine and other conditions that, left undiagnosed, could lead to disability or even death. The advent of new technologies has made it possible to test this small amount of blood for a growing array of conditions.

Among the common conditions screened for

are phenylketonuria (PKU), which can lead to brain damage if untreated, and sickle cell anemia, where early treatment with antibiotics can be extremely beneficial.

At the U.S. Department of Health and Human Services, the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children has developed a uniform screening panel of recommended conditions that should be included in state screenings.

However, some ethicists are concerned that the mandatory newborn screening (parents have limited opt-out exceptions in a few states) is expanding in some states to include conditions that are not as well understood and for which treatment options aren't necessarily clear cut.

In the case of these newer conditions, the screening program is in essence more like research, and should be treated as research — complete with informed consent and IRB oversight, they say.

Lainie Friedman Ross, MD, PhD, a professor of clinical ethics and pediatrics at the University of Chicago, points to the example of Krabbe disease, a rare genetic disorder whose infantile-onset form can be fatal. Bone marrow transplantation can sometimes slow the progress of the condition if done early enough.

However, Ross says that when the state of New York added Krabbe disease to its roster of newborn screening conditions, it became clear that doctors don't know as much as they thought about how the condition progresses and when treatment is advisable.

"When they started, they expected that 90% of the children who they diagnosed as high-risk would go on to develop Krabbe's within one year of life," Ross says. "It turns out the answer is closer to 5% are early onset and 95%, we don't know. We don't know if they'll present as adults, we don't know if they'll ever present."

In the meantime, she says, a positive result for a condition raises concerns for parents and requires that children be tracked to see how they progress.

"It's really hard to say to parents, 'We did this [screening] without your permission and now we want to follow your children,'" Ross says. "That's research, and the idea of doing it without parental permission is conscripting children into research. And we don't do that for any other group of research subjects."

Ross wrote about this topic in a recent issue of *The Journal of Pediatrics*.[1]

Dealing with uncertainty

Krabbe disease is one of a number of lysosomal storage diseases (LSDs) that affect the body's ability to rid cells of waste material. Despite the uncertainty around many of these diseases — how they progress, whether they will present with symptoms in infancy or later and what treatments are most effective — groups are lobbying to add them to the newborn screening programs in more states.

In Ross' home state of Illinois, advocates, many of them parents of children with LSDs, successfully lobbied the state legislature to add seven LSDs to the screening list, sidestepping an expert advisory committee which generally makes those decisions.

Ross, who is a member of that committee but does not speak for it, says one of the LSD conditions added through legislation is Niemann-Pick disease, "for which we don't even have a screening test that's verifiable and valid."

She proposes that instead of adding these types of conditions to mandatory screenings, states should offer two tiers of screenings:

– one tier that includes conditions where there are established treatments and a strong consensus about when patients should be treated, such as PKU and sickle cell anemia. Ross says this array of tests could be mandatory, although she would prefer a strong recommendation in favor of screening with the right of parents to opt-out.

– a second tier would include lesser-understood conditions that lack consensus about when and how to treat. They would be offered to parents through an IRB-approved protocol with an informed consent that would explain the potential benefits and risks of screening, including the possibility of anxiety caused by false positives or risks of treatments.

"Many of the treatments we're using are experimental — they may represent the current standard of care, but they're often not yet fully evidence-based because we don't really have a lot of experience — these are very rare conditions," Ross says. "It is possible that we're going to treat some people who may have remained asymptomatic for months to years. And some of the treatments are pretty aggressive."

This second tier of screening would require a more active consent from parents, she says.

IRB review

State public health department IRBs would be the

logical boards to handle these protocols, weighing the risks of inclusion on the list with the potential benefits to children. Ross notes that it may be necessary for IRBs at individual birthing hospitals to review them as well.

"If you have a state where everyone's going to require their own review, it's going to be very time-consuming," she says. "There are a lot of hospitals where babies are born."

However, she argues, it's important to gain consent from parents and to inform them about the screenings being performed, as well as what would happen in the event of a positive result.

She notes that many mothers don't even realize that there are newborn screenings being conducted on their children.

"I adamantly encourage parents to have their children screened for conditions that are part of the uniform panel," Ross says. "And I think there's really valuable information that we can get for these expanded conditions.

"But I don't think we can say, 'You must agree to experimental expanded screening; we're not going to even tell you about it.' We must inform parents what we're doing."

She says that in the case of positive results, a research protocol would lay out how to give parents information about it.

"We would have people who are educated about these seven lysosomal storage diseases, who can explain to families that most likely this is going to be a false positive, that we still need to check it and most of all, that we're not going to abandon you," she says. "That's what parents really need to hear.

"They need that first phone call to be someone who can actually answer some questions."

Ross says she does not envision the standard multi-page boilerplate informed consent document for newborn screening research, and would favor instead having parents sign the back of the card on which the newborn blood spot is collected. Parents could be given an informational booklet to take home.

"That would minimize the impact on hospitals but still require parents to be involved," Ross says.

She acknowledges that conducting the expanded screenings as part of a research protocol would require more resources. "But ethically, it needs to be appropriately resourced, so that when a child is identified, parents understand what it means."

REFERENCE

1. Ross LF, Waggoner DJ. Parents: Critical stakeholders in expanding newborn screening. *J Pediatr* 2012 Sep;161(3):385-9. ■

Trials don't ask cancer subjects about tobacco use

Tobacco can hamper cancer treatments

Despite evidence suggesting that tobacco use can hamper cancer treatments, patients with cancer who enter clinical trials are rarely asked about their use of tobacco, according to a recent study.

The study, published in the *Journal of Clinical Oncology*[1], looked at more than 150 national cooperative-group trials that were actively enrolling participants. Investigators found that less than a third of the trials assessed any form of tobacco use when subjects enrolled, and less than 5% asked about tobacco use during follow-up visits. None of the trials provided cessation support for participants who wanted to quit using tobacco.

Graham Warren, MD, PhD, assistant professor in the department of radiation medicine at Roswell Park Cancer Institute in Buffalo, NY, says these findings are significant because of research that shows tobacco use can erode the effectiveness of cancer treatments, decrease survival, increase risk of recurrence and increase the risk of mortality from heart disease, stroke and pulmonary disease.

"If tobacco decreases the effectiveness of chemotherapy, biologic therapy, radiation therapy or if it increases the risk of recurrence after surgery, then tobacco can alter the treatment outcomes used in clinical trials," Warren says.

Measuring the magnitude

Warren says that while many people understand that tobacco use can increase the risk of developing cancer, its role in decreasing the effectiveness of cancer treatment is less well known.

Failing to assess tobacco use in subjects means that clinical trials will be unable to measure the magnitude of these effects, Warren says. At the same time, it poses potential risks to the subjects themselves.

"If you're looking at risk from toxicity of treatment, there are several studies that show that toxicity of treatment is elevated by tobacco," he says. "If you're looking at risk of recurrence, then yes, the risk of recurrence is increased with the use of tobacco. If you're interested in the risk of heart

disease or pulmonary problems or wound infections or pneumonia, tobacco use increases the risk for those as well.

"I think the biggest conclusion is yes, these are all risks," Warren says. "In reality, many of these things probably occur and are amplified by tobacco, but unfortunately right now, we have no randomized data that has looked at it well."

He says the first step toward changing that is for researchers to agree on guidelines to measure tobacco use — past use, current use and any use of tobacco cessation products. Asking those questions of participants would provide important data about how tobacco use can affect outcomes.

"I think that assessment not only at diagnosis but also during follow-up is an important parameter to try and include in clinical trials design," Warren says.

Warren says there is interest in developing these questions and in providing a formal structure for assessing tobacco use in clinical trials.

Considering protocols

In the meantime, Warren says, IRBs should consider this issue when reviewing cancer treatment protocols, asking whether a past or current use of tobacco has been considered in the design of the trial.

"We know that about 30% of cancer patients use tobacco at time of diagnosis," he says. "That means there is a reasonably substantial portion of the population who is at risk for tobacco use and could therefore be at risk for having changes in treatment response, diagnosis and outcomes that most clinical trials look at."

He believes that informed consent documents should also address this issue.

"I believe that there should be an awareness of the fact that tobacco can increase the risk of treatment failure, toxicity, as well as decreased overall health," Warren says. "It should be something that patients should be made aware of because there is a good likelihood that continued tobacco use will substantially alter their long-term outcomes whether they're related to the clinical trial or not."

And Warren says IRBs should ask investigators in clinical trials whether they plan to offer tobacco cessation programs for participants who currently use tobacco. He believes that cancer patients — including trial participants — should be offered tobacco cessation support as a standard of care.

"A lot of times, clinical trials may or may not benefit the patient, but this is one area where tobacco cessation would benefit the patient directly," Warren says. "It's not a theoretical benefit — it would be something that would improve the health of the patient."

REFERENCE

1. Peters EN, Torres E, Toll BA, Warren GW et al. Tobacco assessment in actively accruing national cancer institute cooperative group program clinical trials. *J Clin Oncol* 2012 Aug 10;30(23):2869-75. ■

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

- An update on revisions to Common Rule
- Improve IRB handling of complaints
- Update on privacy after GINA and HIPAA
- Ethical considerations: Internet research with minors
- AAHRPP's top 10 findings revealed

CNE/CME QUESTIONS

1. Which of the following questions would not be suitable to use in a teach-back informed consent session about voluntary participation in a clinical trial?
   A. Tell me, what would happen if you decide volunteering for this study is not working for you?
   B. Do you feel you need to be in this study?
   C. Do you understand what it means to volunteer to participate in this study?
   D. Explain to me what you would do if you wanted to change your mind about this study at any point?

2. Which of the following is an important area that IRB minutes should pay close attention to in the documented record of the IRB meeting?
   A. Make sure the vulnerable populations are documented correctly in the minutes.
   B. Ensure that privacy and confidentiality issues were discussed at the IRB meeting and documented in the minutes.
   C. Make certain all unanticipated problems involving risks to subjects and others and any noncompliance issues are properly documented in the minutes.
   D. All of the above are important areas to include.

3. Scientists know a great deal about how lysosomal storage diseases such as Krabbe disease progress, which treatments are best, and when treatment is advisable.
   A. True
   B. False

4. What percentage of cancer patients are believed to use tobacco at the time of their diagnosis?
   A. 20%
   B. 30%
   C. 70%
   D. 90%