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As Internet-based research evolves, IRBs and PIs need updated guidance

Data security, collection, IC, recruitment are focus

As Internet use has exploded worldwide, so has Web-based research. Between 2004 and 2009, the number of web-based research studies published in the American Psychological Association's (APA) *Journal of Personality and Social Psychology* rose by more than 500%.[1]

Even within Web-based research, the methods and strategies have been continually and rapidly evolving. This has made it challenging for IRBs when reviewing these studies for issues important to research participants, including privacy and confidentiality, experts say.

"One of the things that's easy to overlook in Internet-based research is this expectation of privacy versus information that is placed online for the public," says **Vern Paxson**, PhD, a member of the social-behavioral research committee at the University of California–Berkeley.

"There's a tendency among researchers to think if they can grab it over the Internet that it's fair game," Paxson adds.

The office for the protection of human subjects at the University of California–Berkeley recently completed new guidance on conducting Internet-based research. The eight-page document, which is available on the office's website, focuses specifically on recruitment, informed consent, data collection, and data security.

"We review many social-behavioral applications here, and we were beginning to see a trend with applications involving Internet-based research. So we saw a need to develop guidance for our investigators," explains **Adrienne Tanner**, CIP, IRB coordinator in the office for the protection of human subjects.

The IRB office spent about one year writing and reviewing the guidance. The development time was long enough that the types of Web-based research reviewed by the IRB evolved and required some updates in the guidance, Tanner notes.

"Internet research is constantly changing, so we'll probably make more revisions in the future," she adds.

The guidance addresses specific issues investigators encounter when planning a study that involves some Web-based research. For example, one part discusses how it's challenging to properly identify and qualify subjects.

"Without face-to-face or voice-to-voice interaction, it's difficult for investigators to be sure that participants are not misrepresenting themselves," the guidance reads. "In certain situations investigators should discuss measures taken to authenticate subjects."

Interactions with subjects via the Web is more complicated from a research ethics perspective, Tanner says.

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"When contacting someone through Facebook, is that an acceptable practice?" she asks. "The person using their social network working site might not feel that way and might have the expectation of privacy."

When developing guidance involving Web-based research, it's important to use the flexibility inherent in human subjects protection regulations, suggests **Rebecca D. Armstrong**, DVM, PhD, director, research subject protection in the office for the protection of human subjects and responsible conduct of research coordinator at the University of California–Berkeley.

"Our IRBs at Berkeley are very good at utilizing the flexibility that is in 45 CFR 46," Armstrong says. "This enables us to alter consent forms or waive documented informed consent to facilitate research without increasing risks to subjects; it's a balancing act."

The new guidance includes seven main points and examples about conducting informed consent online. *(See excerpt from UC-Berkeley guidance on informed consent in Web-based research, p. 63.)*

"I recollect a protocol that came to a full committee review that had a researcher who wanted to download an individual's Facebook page at one point in time," Armstrong recalls. "There was a lot of discussion because of the privacy issues involved."

The purpose of the research was to examine how individuals signal social status and express their individual characteristics through online social networking sites. This particular protocol raised issues of secondary subjects, such as the people whose identifiable information appeared on the main research subject's Facebook page, she said.

"In a Facebook profile you have photos, names and identifying information of yourself and your friends, and your friends have not consented to have this information made available to researchers even if you have consented to it," Paxson explains. "It's a complex determination to decide how to protect those subjects or even to identify whether you have that problem."

The study involved looking at Facebook profiles to analyze pictures, status updates, posted links and "check-ins." The IRB had the investigators remove all identifying information pertaining to secondary subjects before coding the data.

"Our IRBs tend to be creative when coming up with solutions," Armstrong says.

Another common issue with Web-based research involves determining the level of review needed, Tanner says.

"For example, if an investigator wants to use publicly available, existing data for their research, it would not need to go through a review," she says. "But it's difficult to know if data published online is publicly available or not, and it depends on the intention of the person posting that information."

The guidance addresses that issue by focusing on the use of a login or registration: "Data only accessible through special permission or registration/login (with username and password) are generally not considered public. When determining whether or not data are public, the investigator must decide if there exists an expectation of privacy."

This nuance might occur when someone posts online personally identifiable information about someone else without asking the person for permission, Tanner says.

"We wanted to let investigators know these are factors to consider," she adds.

One of the goals for the Web-based research guidance is to prod investigators into thinking about human subjects protection issues that they might otherwise overlook, Armstrong says.

"That's how we frame our guidance, and we give them lots of examples to make it real for them," she explains.

From the IRB's perspective, the guidance is very useful, Paxson says.

"It's easy for investigators to assume that Internet communication is private, but that's not a sound assumption," he says. "While a best effort is made for confidentiality, it is not a guarantee."

The IRB asks investigators to include in their informed consent documents a sentence explaining how there is no way to guarantee confidentiality, Tanner says.

"We want to make sure participants are not under the assumption that their information is 100% secure," she adds.

At UC–Berkeley, investigators can use template language developed by the human subjects protection office. These templates are available online.

"We also have developed an online consent builder that walks investigators through the process by answering questions," Armstrong says.

REFERENCE:

1. Denissen JJA, Neumann L, van Zalk M. How the internet is changing the implementation of traditional research methods, people's daily lives, and the way in which developmental scientists conduct research. *Intl J Behav Dev* 2010; 34(6):564–575. ■

UC–Berkeley's Web-based guidance focuses on IC issues

"I agree" buttons can be used

The University of California–Berkeley's office for the protection of human subjects has developed new guidance for investigators involved in Web-based research. One of the main sections of the guidance involves informed consent issues. The guidance, which is available at the UC–Berkeley website at http://cphs.berkeley.edu/guideline.html, was published in April 2012.

Here are excerpts regarding Internet-based research and informed consent:

- Investigators conducting non-exempt research must follow the CPHS (committee for protection of human subjects) informed consent guidelines and include required elements of informed consent when generating consent documents. When online surveys are employed, the CPHS template for online surveys may be adapted.
- In general, investigators conducting Internet-based research with minors must obtain both child assent and parent permission. Researchers may request a waiver of parent permission provided the study fits the appropriate criteria.
- CPHS generally accepts the use of "I agree" or "I do not agree" buttons (or other electronic methods for indicating affirmative consent) on online pages in lieu of signatures. For surveys sent to and returned by participants through email, investigators should include a consent document and inform participants that submitting the completed survey indicates their consent. This would constitute unsigned consent. In order to utilize this consent procedure, the investigator must request a waiver of documented consent.
- If the CPHS determines that documented consent is required, the consent form may be mailed or emailed to the participant who can then sign the form and return it to investigators via postal mail or fax.
- The process of requesting consent should not disrupt normal group activity. Researchers need to be particularly sensitive of this when entering online communities and chat rooms as the process of requesting consent is often perceived as disruptive. If seeking informed consent will harm the validity of a study or make the research impracticable, it may be possible to obtain a waiver of consent provided the study meets the appropriate criteria. When requesting a waiver of informed consent, issues regarding deception or incomplete disclosure may need to be

addressed in the researcher's eProtocol application.

• Personas, or avatars, are social identities that Internet users establish in online communities. These personas allow individuals to reveal varying levels of personal information and also allow them to navigate the virtual world as a particular character or alter-ego. Names of Internet personas (characters or avatars) or real names may be used in reports and publications only with consent from the participating individual. In these situations, specific language concerning the release of identifiable information must be included in the informed consent document and specific consent must be sought from subjects for this release. If research participants give consent to be identified, data must still be secured properly to avoid any misuse by a third party.

• Collecting data over the Internet can increase potential risks to confidentiality because of the frequent involvement of third-party sites and the risk of third-party interception when transmitting data across a network. For example, when using a third-party website to administer surveys, the website might store collected data on backups or server logs beyond the timeframe of the research project. In addition, third-party sites may have their own security measures that do not match those of the investigators'. Participants should be informed of these potential risks in the informed consent document. For example:

i. "Although every reasonable effort has been taken, confidentiality during actual Internet communication procedures cannot be guaranteed."

ii. "Your confidentiality will be kept to the degree permitted by the technology being used. No guarantees can be made regarding the interception of data sent via the Internet by any third parties." (Penn State)

iii. "Data may exist on backups or server logs beyond the timeframe of this research project." ■

BEST PRACTICES SPOTLIGHT

IRB is leader in developing multisite research tools

IRB is part of consortium

With federal regulators shifting toward policies that would facilitate more central IRBs for multisite research, human subjects research protection offices need to take note and develop guidelines and tools for handling shared IRB responsibilities in multisite trials, an expert says.

The health sciences institutional review boards office at the University of Wisconsin–Madison is ahead of the curve with a long list of multi-site research tools and the development of the Wisconsin IRB Consortium.

"We developed a lot of these tools in part because we were told there is more of a push from the feds for collaborative research, and this relates to the community-based research we see," says **Carol Pech**, PhD, associate director, health sciences institutional review boards office.

"There is a push on the national level for increased cooperation, and we're kind of on the leading edge of that," she adds.

Regulators and research institutions also have been interested in how they can make the IRB review process more efficient for multisite studies. The answer is to have a single IRB of record for some multisite research, Pech notes.

With these goals in mind, the institutional review board's office added a long list of links and tools about multisite research and IRB review on its website.

"We are clear in our message to researchers that we're aware of the increase in collaborative research, so we'll make it easier for them," Pech explains.

"Many researchers are not familiar with the federal requirements for IRB oversight and research rules," Pech says. "So some of this is to raise awareness among researchers that if you are working with someone outside the institution they need to be named on the study."

The IRB office's Web pages include a variety of links and pages related to multisite research. Examples of these are as follows:

• Overview of IRB Requirements for Multisite and Collaborative Research;

• IRB of Record Request;

• Deferral of IRB Oversight;

• IRB Requirements for Multisite and Collaborative Research;

• Frequently Asked Questions about Exemptions, Not Human Subjects Research Projects, and Multisite Research Requirements;

• UW-Madison HRPP Policy on Multisite Research;

• Completing the IRB Application for Multisite/ Collaborative Research Studies;

• Checklist for Investigator-Initiated Multisite Studies *(See story about checklist, page 65.);*

• How to Submit a Request to Defer IRB Review to Another IRB.

The institution spent close to two years putting together a consortium, for the purpose of facilitating multisite research and using an IRB of record, with the

Medical College of Wisconsin, Aurora Health Care in Milwaukee, and Marshfield Clinic in Marshfield, Pech says.

"Including us, our consortium has the four largest institutions in the state," Pech says.

When any of the four members of the consortium are involved in a multisite study they can name a single IRB of record between them. So if one IRB encounters a multisite study that includes another member of the consortium, the IRB will send the other member or members a letter and ask if they would like to defer to that IRB as the IRB of record for the study, Pech says.

Right now, the IRB-of-record process has involved minimal risk and non-clinical research, such as retrospective chart reviews, but the IRB is trying to expand this to include some standard clinical trials as well, Pech adds.

"We have general guidelines on when we can serve as an IRB of record and how to apply for it," she says.

UW-Madison has created a decision tree for determining the IRB's requirements for studies involving collaborators and others outside of the institution.

"We often send the decision tree out to researchers after an IRB consultation, saying, 'Here is information you might find helpful,'" Pech says.

"This is one of the sections of the website we highlight," she says. "We want investigators to know we are interested in being the IRB of record, so we try to be as proactive as we can."

Excerpts from the decision tree are as follows:

1. Will personnel not affiliated with the UW/UWHC/Madison VA be engaged in research for this study?

2. If no, then external personnel do not need to be listed on the study team in the IRB application, but activities of the external personnel must be described in the IRB application and protocol, and a letter of support from an external site not engaged in research may be required (for example, if the site will be used to recruit subjects).

3. If yes, then are you asking that the HS-IRBs serve as IRB of record for the external personnel or site?

4. If yes, then external personnel must be listed on the study team in the IRB application and external personnel must complete human subjects training; also, activities of the external personnel must be described in the IRB application and protocol and a request for the HS-IRBs to serve as IRB of record must be included in the initial review application.

5. Are the external personnel affiliated with an organization or entity with an IRB?

6. If yes, then an IRB authorization agreement (IAA) will be needed for studies not involving Wisconsin IRB Consortium Members or Meriter; the IRB office will facilitate the completion of the IAA.

Since the decision tree and other multisite study tools were created there has been an increase in studies listing outside personnel, Pech notes.

"We receive more questions: 'I saw this on your website; how does it work?'" Pech says.

Also, the development of the consortium and availability of online multisite study tools has led to a huge jump in collaborative research, she says.

"We measure volume by the number of agreements we have for multisite trials and IRB of record reviews," Pech explains. "It's a proxy for how much we're seeing of this collaborative research."

In 2004 there were no studies referred to other institutions and only two where UW-Madison was the IRB of record. In 2010, there were 38 studies deferred to another institution and 37 where the university's IRB agreed to serve as the IRB of record, she says.

"So it's a significant increase," Pech adds. ■

Sample items from UW-Madison's checklist

Eliminates needless submissions

IRBs and investigators sometimes waste time on unnecessary IRB submissions. A simple initial review triage checklist can eliminate this problem, one IRB has discovered.

"We have a high volume of research we see," says **Carol Pech**, PhD, associate director, health sciences institutional review boards office of the University of Wisconsin–Madison.

So what the IRB doesn't need are needless submissions.

"We don't want someone to go to through the effort of doing an IRB application so we can tell them they didn't need to come to us," Pech says.

The solution is an initial review application triage checklist that can quickly let an investigator know whether the IRB review is required.

For example, the IRB does not require researchers to submit an IRB application for a single case report that will be published or if they are doing research with secondary analysis of available data, Pech explains.

"Also, there may be residents who are doing a quick project, so let them know of research they can do without having to come to the IRB," she adds. "We have groups where we see a number of exemption applications, and we'll target those groups, who are

often pharmacy and nursing students."

Here are some sample items from the UW-Madison IRB initial review application triage checklist:

1. Is the project limited to preparing for publication a single case report involving up to three (3) patients?

— If the answer is yes, then: Case reports involving three or fewer patients do not require IRB review, but the HIPAA Privacy Rule may still apply.

— If the answer is no, then an IRB review may be required.

2. Is the proposed research study limited to secondary analysis of data from a publicly available dataset found at the institution's website?

— If yes, then research involving only analysis of data from a listed publicly available dataset is not considered "human subjects research" and does not require IRB approval.

— If no, then an IRB review may be required.

3. Is the proposed research study limited to the inclusion of deceased individuals?

— If yes, then research involving information or samples from deceased individuals only does not constitute human subjects research and therefore does not require IRB oversight.

— If no: If your project involves data or samples from deceased and living individuals, or all living individuals, your study involves human subjects research and IRB review is required. ■

Neurology research network starts IRB review

Sites can choose to participate or not

As IRBs continue to contemplate various models of centralized review for multisite studies, projects have begun to pop up, trying out these models.

One recent example, NeuroNEXT, is coordinating IRB reviews for dozens of institutions across the country in order to conduct trials of neurological therapies. The network was created by the National Institute of Neurological Disorders and Strokes (NINDS) to increase the efficiency of these types of clinical trials.

Massachusetts General Hospital and Partners Healthcare System in Boston won an NINDS grant to serve as the clinical coordinating center and central IRB for the network.

Pearl O'Rourke, MD, director of human research affairs for Partners, has had the task of coordinating the infrastructure to support the central IRB (CIRB) model NINDS has asked for.

She says that process has proved much larger than she originally had anticipated. Although there are 25 primary sites within the network, many have several sub-sites where research may be carried out. For example, she says, the State University of New York is a single primary site but has multiple campuses that may serve as research sites. The network made a decision early on that every site that had a Federalwide Assurance (FWA) required its own separate reliance agreement with the CIRB.

"So we are actually now in excess of 60 sites that we have reliance agreements with," O'Rourke says. "Setting this up has been rather interesting and an unbelievable amount of work."

In order to participate in NeuroNEXT trials, the sites must use the central IRB — NINDS has not provided an option for separate reviews, says **Elizabeth Hohmann**, MD, chair and director of the Partners Human Research Committee. She leads the Massachusetts General IRB panel that will serve as the network's CIRB.

However, she says a site can look at the central IRB's review and decide that it doesn't want to participate in a particular study.

Hohmann says that once the network's protocol steering committee develops a protocol, it will submit it to the CIRB, which will do an initial assessment, making recommended changes to the protocol group.

"Once we say it's IRB-ready, we will send it to the multiple sites who've expressed an interest in the project," she says. "We'll give them two weeks to review it at their local sites, however they wish to — by an IRB chair, an IRB administrator or by the investigators. We hope to get some input from all these folks and to see what issues they may have."

To assist in this pre-review, O'Rourke has spent the last year communicating with all of the sites in order to tease out institutional issues and local requirements that may come into play during a protocol.

She says the CIRB needs to know about relevant state laws, such as those regarding pediatric research or research with decisionally impaired adults, as well as how the site handles issues such as surrogate consent, HIPAA and conflict of interest.

O'Rourke says that while there are a lot of similarities across the network, there are small but important differences that must be dealt with.

For example, she says, institutions handle research-related injuries in different ways, and use different language to describe it in informed consent documents.

"It's been fascinating to see how different people

do it, as well as the language they use in the consent forms," she says.

She says the CIRB will draw sites' attention to particular issues in pre-review based on this information.

"We'll say, 'This is a pediatric protocol, please look at this in terms of your pediatric state and local laws and regulations,'" O'Rourke says. "We're going to give them leading questions so we can get the information that we need regarding local context."

Once the sites have weighed in with their responses, Hohmann's CIRB will conduct the official review. Sites have the option of accepting this review or declining to participate in the study.

She says the sites will all use a NeuroNEXT template consent form, which will contain certain areas in which they can insert customized language such as contact information, HIPAA language or subject injury information.

"There will be fields where you can insert your own customized language but that will have to come back to us for final review," Hohmann says.

The NeuroNEXT model — where various sites have input into the central IRB's decision but the central IRB carries out all the regulatory requirements — is one of several different approaches currently being used or considered across the country for centralized review.

O'Rourke says one of the strengths of the NeuroNEXT approach has been the strong support of NINDS for her group's decisions.

"The program staff at NINDS has been spectacular in terms of saying, 'We respect the decisions you've made, and we will support this to all of the sites.' If we didn't have that, I think this wouldn't be doable," she says.

She's interested in seeing what issues arise when the network takes on an actual protocol in the next few months. "Have we identified the problematic areas appropriately or not?"

O'Rourke says the group has funding to hold a conference of network members after about a year of operation, to see how the review process is working.

Eventually, she hopes that the experience of setting up the IRB component of this network can add to the national conversation about the best ways of carrying out centralized review.

"I personally see this as experiment — we're an experiment within an experiment," she says. "What I'm hoping is that this experience will allow us to maybe put more information on the table to say, going forward, if this is going to be a model, this is what you're going to need for infrastructure."

The proposed revision of the Common Rule (advance notice of proposed rule-making or ANPRM) released last year by the Department of Health and Human Services asks whether central IRB review should be mandated for multi-site studies.

George Gasparis, CIP, is executive director for the Human Subjects Protection Program/IRB at Columbia University in New York City, one of the NeuroNEXT sites. He says regardless of the decision HHS eventually makes, the field is moving in the direction of central IRBs.

"Regardless of whether the ANPRM develops into a new regulation, there's going to be a push for more central IRBs," says Gasparis. "I think you're going to see more and more NIH institutes push for central IRB models that work well." ■

Report shows challenges of international research

Protection of participants requires extra care

As institutions seek to expand their international research portfolios, IRBs face increasing challenges — differing regulations in different countries, cultural distinctions that may lead to unexpected risks and the difficulties of oversight at such a distance.

The University of Michigan in Ann Arbor is an example of a global research player, with human subjects research projects — ranging from minimal-risk social-behavioral studies to biomedical research — going on in more than 80 countries.

"Here at the University of Michigan and I think at many of our peer institutions as well, there's been a big uptick in interest in international research and international scientific partnerships," says **Ron Maio**, DO, MS, director of UM's Office of Human Research Compliance Review (OHRCR).

With a new push to expand research relationships with China, Maio says UM officials decided to take a closer look at international research — what the university is doing now, what risks are involved and what the expectations are of researchers and IRBs.

The resulting report lays out a series of recommendations to aid the university in enhancing human subjects protections overseas in areas ranging from informed consent and IRB procedures to possible technological aids to investigators *(see accompanying story, page 69)*.

In developing the report, **Terry VandenBosch**, PhD, RN, senior research compliance associate with

the OHRCR, first set out to catalog the current international research being conducted on behalf of UM. She says that process revealed some surprising facts.

"I had thought that there would be more studies being overseen by the IRB than there were," she says. "I especially thought there would be fuller committee reviews. In working with people from [UM's] behavioral science IRB and Center for Global Health I found that, in fact, a number of the international studies aren't subject to IRB oversight. A large number of them are low-risk or exempt or they're in areas other than human subjects research."

Dealing with range of regulations

VandenBosch says that the vast majority of international human subjects research being conducted by the university is minimal risk, with its behavioral science IRB handling 62% of the studies.

But there are risks associated with social and behavioral studies, risks that can be complicated by the different cultures and governments in which research is being conducted, according to Maio and VandenBosch.

"Looking at the bucket of low-risk studies, they aren't all the same," VandenBosch says. "It could be that there may be political consequences for the subjects if the data are known. If confidentiality protections aren't put in place as they should be, it could bring more risk to the subjects or to the students who are conducting some of the studies and aren't covered in the regulations."

She says students conduct a number of low-risk studies, although only 20% are international research, often in the countries of their origin. The report notes that only 50% of UM student investigators stated that their departments had an effective mentoring program that helped them to understand the ethical obligations of conducting human subjects research. Seventy-five percent reported that their faculty advisors helped them in this area.

Investigators and IRBs also must cope with an array of levels of regulation at research sites.

The country with the greatest number of UM research studies was Michigan's northern neighbor Canada, where there is strong regulatory oversight.

In what VandenBosch calls "middle-resource developing countries" — China, for example, or Brazil or India — governments are creating regulations, but she says they haven't been tested in the way that the United States' regulatory system has.

"We don't always know exactly how to interpret the regulations because they're written broadly, to fit many different kinds of situations," she says. "But that means that agencies put out guidance frequently, as to what the regulations mean, as issues occur."

In "low-resource developing countries" such as some African countries, there may not be research regulations and guidance, or the information may not be available in English on a website, VandenBosch says. She does note that the Office of Human Research Protection's (OHRP's) International Compilation of Human Research Standards guidance is helpful.

In addition to that, "you have to rely on your collaborative relationships," VandenBosch says. "And I think one of the things we're looking at is what does a collaborative relationship look like, so that we know we can rely on the information that we're getting?

"Investigators are the ones that have those relationships, so the burden will probably be on them in terms of what information they're getting," she says. "And they need help."

IRB relationships

VandenBosch says it's also important for IRBs to find out what they can about the regulations and oversight in the countries in which U.S. investigators are carrying out projects. Because IRBs can't be experts on regulatory oversight in 80-plus countries, that process requires some care and thought, not a one-size-fits-all approach. Particularly in behavioral science, investigators are working in some areas with no IRBs whatsoever.

She says the university may base a decision about whether to cede to a foreign IRB on whether it had a Federalwide Assurance (FWA), whether it was accredited by the Association for Accreditation of Human Research Protection Programs (AAHRPP) and whether OHRP has determined that the foreign institution has equivalent human research protections in place.

Meanwhile, university officials are seeking more long-term relationships with IRBs in places where they plan to conduct many studies. Maio notes that UM has begun a research collaboration with Peking University in Beijing, one that has involved the two universities' IRB officials.

"Right from the start, the regulatory component of that relationship was something everybody wanted to make sure we understood and got straight," he says. "We have actually met with their people face to face, as well as through some teleconferencing to talk to their IRB people and to figure out how to do

things that will be efficient and will maximize human subjects protection."

VandenBosch would like to see some mechanism for U.S. institutions that have these types of international collaborations to network with each other to help facilitate research. For example, she notes that UM is doing a great deal of research in Ghana, and has strong relationships with IRBs there.

"It would be useful, if another school of public health is sending students to Ghana, for them to contact our IRB and get some information about it," she says.

Other institutions have similar strengths in various areas of the world, but currently, VandenBosch says, it's very difficult to find out where they are.

"There's no place where IRBs can get that information, other than to put a post on the IRB Forum and hope that someone there has worked in that country," she says. "We need some kind of international perspective to help IRBs work with each other, more than just how to do an international study with your IRB."

To read the UM report, "International Human Subjects Research Risks, visit http://ohrcr.umich.edu/reports/. ■

Improving oversight of international studies

Report advises IRBs to get creative

The report prepared for the University of Michigan about international research conducted there lays out a series of recommendations that can aid other institutions' investigators and IRBs.

Author **Terry VandenBosch**, PhD, senior research compliance associate with the university's Office of Human Research Compliance Review, says that among the most important steps an institution can take to help improve human subjects protections international research is in its informed consent process.

She says the U.S. model of consent — requiring a written form and a subject's signature — is cumbersome and ill-adapted to many cultures. She'd like to see IRBs show some flexibility in encouraging innovative techniques to better educate subjects around the world.

"We should think more creatively about how to get information across," she says, pointing to an example of research conducted in Guatemala, where investigators use newsprint with pictures to go through the informed consent process.

"At our IRB council, we said, let's post examples of creative uses of the informed consent process for other investigators," VandenBosch says. "We did a search of the literature to see if we could find something on informed consent other than [relying on] the written document or verbal script, and we found what we think is the same Guatemalan study. That's it."

She says guidances and templates don't promote creativity in the process, "so investigators don't even realize that it would be supported by the IRB for them to do that."

The report recommends that investigators make use of more visual materials, especially with low-literacy populations; that IRBs provide them with examples of fresh approaches; and that UM consider a demonstration project of alternative methods to written signatures to document informed consent.

"It's possible that to ask for a signature could be offensive to someone, because their culture relies on verbal contracts," VandenBosch says.

Training, collaborating key

Other recommendations from the UM report include:

• **Cross cultural training:** The report recommends providing human subjects protection training in a number of languages for international co-investigators, study staff and students conducting research overseas. In addition, U.S. and international investigators should know applicable human subjects laws and guidance in the study countries, using resources such as the Office for Human Research Protections and the International Compilation of Human Research Standards. Investigators should maintain close and open relationships with international collaborators.

IRBs should promote the use of the Collaborative Institutional Training Initiative (CITI) human subjects courses, which are available online in several languages.

• **IRB collaboration:** When working with an IRB in another country on a sensitive ethical issue, a U.S. IRB should educate itself about the other IRB's membership and processes. They can use faculty members to serve as consultants about various areas of the world in which studies are being conducted.

Consider investing in capacity building for international investigators and IRBs where the university has ongoing collaborative relationships.

• **Enlisting technology:** The report notes several areas where technology may make it easier for

investigators and IRBs to communicate across borders and oceans.

It recommends that IRBs dealing with difficult ethical issues consider using tools such as Skype to talk to each other "face to face." The university could create a web portal that can guide investigators to necessary documents and guidance. VandenBosch says there's been discussion of creating mobile applications for IRB submissions.

"It also would be possible, if our collaboration was with an English-speaking country, that we could actually open up our submissions system and with a different set of confidentiality protections, we could actually help run the electronic submission system for an IRB in another university in another country," she says. "I don't know at what point or if there will be a sharing of that electronic capability across countries, but it would be possible."

She says it's also important for IRBs and investigators to recognize the potential for them to be working at cross-purposes because of lack of information. VandenBosch says she became aware of this problem when interviewing both investigators and IRB officials for her report.

She says investigators she interviewed told her that IRBs often ask about unimportant issues and don't ask about important ones. IRBs told her they didn't have enough information from investigators to determine the risks of research in another country.

"How can an IRB be up to date on the cultural aspects of 86 different countries? No wonder they ask questions, and they're going to ask questions that flow from our culture. The PI is going to have more general information about the [study] culture. That chasm needs to have more examination." ■

Plan helps certify dbGaP studies for NIH

UW creates process for certification

When the National Institutes of Health (NIH) released its policy regarding data sharing for NIH-supported genome-wide association studies (GWAS) in 2007, officials at the University of Washington in Seattle knew it would have an effect on their operations.

"We have a lot of active genetic and genomic researchers here, so we realized this was really going to affect us," says **Shannon Sewards**, MA, CIP, assistant director for operations for the university's human subjects division. "We knew we were going to have to get something up and running soon."

The policy requires that any studies submitted to the NIH's GWAS repository, the database of Genotypes and Phenotypes (dbGaP), be certified by institutional officials, assuring that:

- data was properly collected;
- data submission follows state and federal laws;
- appropriate informed consent was obtained;
- data has been properly deidentified;
- and the institution has considered any risks to individuals and groups posed by the submission.

The NIH created the dbGaP in order to encourage more rapid advancement of genomic research, but in its policy noted that the personal and sensitive information generated by such studies, particularly as technology evolves, make human subjects protections critically important.

Sewards says that initially, UW handled these dbGaP certifications on a case-by-case basis, going through the NIH guidance and checking whether the requirements were met.

From that trial run, the university has developed a certification process that does the job more efficiently. Sewards discussed that process at PRIM&R's recent Advancing Ethical Research Conference.

When her department took on this project in 2008, Sewards says she couldn't find other institutional policies on which to model it. She says UW was able to craft a successful dbGaP certification process by adapting its existing study review process.

"Adapting a new process to one that's existing is less change and less worry, on behalf of staff and researchers," Sewards says.

Handling non-human subjects research

The dbGaP request process is used not just for studies undergoing IRB review, but for research activities that don't meet the federal definition of human subjects research, such as use of deidentified data.

"For IRBs themselves, it's been difficult from a conceptual point of view, because this isn't human subjects research," she says. "We're being asked to certify something that we normally wouldn't see. For example, within the past couple of months, we've been grappling with whether children who were assented at the time of the study should be consented once they reach the age of 18 for their data to remain in the dbGaP. IRBs sort of get confused with that because it's not identifiable, it doesn't meet the definition of a human subject, but they're asked to make that decision within the same lens."

To address this issue, UW created a form that investigators can use for the use of non-identifiable biological specimens and data. The investigator fills out the form and can request a dbGaP certification to accompany it.

"Because [dbGaP certification] is not an IRB action, we have to have some sort of action for it to accompany," Sewards says. "That's how we've made it work in our office, so it goes through the proper channels, it gets a number and we can track it in our database."

When a dbGaP certification request is made, the human subjects division determines whether the proposed project requires IRB review. If so, the certification request accompanies the IRB review. Projects that involve minimal risk, are exempt or are not found to be human subjects research are handled by a "minimal risk team" — staff who are also IRB members and can approve research activities.

"We're in a large IRB office, so we are fortunate in that we have two staff — we call them roving administrators," she says. "I and these two administrators have become the experts in the office, and we help guide the other staff.

"We'll attend the IRB meetings when a dbGaP certification is taking place. If there's a dbGaP certification that occurs with an expedited application or a not-human-subjects [application], we work together as a team to check each other's work. I think by keeping it more centralized, we didn't have to put forth such a huge education effort."

Local considerations

When making a determination about whether to grant a request for dbGaP certification, the UW staff must consider not just NIH's guidelines, but Washington state law.

For example, Sewards says, federal regulations do not consider a deceased person to be a human subject, but Washington state does. Because it would not be possible to obtain consent from these individuals for research use of residual clinical specimens, "it was determined that these types of specimens could not be certified," she says.

The university has created a set of documents to carry out this process, including guidance documents for investigators, IRB members and humans subjects division staff; a dbGaP form; and a checklist that staff can use to determine whether the project has all of the NIH-required elements. Sewards' office also has created consent language investigators can use to meet the NIH requirements.

She's shared these documents and the UW process with other IRBs, noting that one problem that has arisen in UW's certifications is working with other IRBs because of a lack of consistency in their processes.

"We say these are our forms, this is our guidance, please feel free to duplicate it, because in the end, it's going to make more of a consistent process, and it's going to make it easier for everybody."

But in using these resources, Sewards recommends that institutions still start with their own organizational structure and adapt this new process to it.

"Feel free to look around at what other IRBs are doing," she says. "Feel free to use our forms, and see if it works. I think it's really helpful so you're not just starting from scratch."

For more information about the University of Washington's dbGaP certification process

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. ■

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or to see the documents developed for it, visit http://www.washington.edu/research/hsd/topics/GWAS+dbGaP+Studies/. ■

CNE/CME QUESTIONS

1. Collecting data over the Internet can increase potential risks to confidentiality. Why does this occur?
   A. Third-party sites may have their own security measures that do not match those of the investigators.
   B. There is frequent involvement of third-party sites and the risk of third-party interception when transmitting data across a network.
   C. The website might store data on backup or server logs beyond the time frame of the research project.
   D. All of the above

2. Which of the following is a good strategy for facilitating multisite studies that have a single IRB of record?
   A. Send word out to neighboring institutions to let them know your IRB will serve as IRB of record on all multisite studies with which it is involved.
   B. Put together a consortium for the purpose of facilitating multisite research and using an IRB of record.
   C. Send all work to an independent IRB.
   D. All of the above

3. True or False: The NeuroNEXT research network requires that participating institutions accept the review of its central IRB in order to carry out a particular protocol at their sites.
   A. True
   B. False

4. Which of the following is not a requirement in the National Institutes of Health policy regarding certification of studies submitted to the database of Genotypes and Phenotypes (dbGaP)?
   A. that data be collected and deidentified properly;
   B. that data submission follows state and federal laws;
   C. that there is a policy for informing participants of incidental findings;
   D. that the institution has considered risks to individuals and groups posed by the submission.