IRB ADVISOR

YOUR PRACTICAL GUIDE TO INSTITUTIONAL REVIEW BOARD MANAGEMENT

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INSIDE

NIH Designates LGBT Community as Health Disparity Group

Move encourages research across broad area

By Gary Evans, Senior Medical Writer

The National Institutes of Health's recent decision to designate sexual and gender minorities as a "disparity" population for research purposes was welcomed by researchers and advocates for the LGBT community.

"I am excited about this because some of the work that I do is with populations of gay men and transgender women," says **Brandon Brown**, PhD, MPH, a researcher and assistant professor in the Center for Healthy Communities at the University of California, Riverside School of Medicine. "This really opens up the opportunity for researchers like me to submit [research] projects. It also gives credence and credit to this population — at least in the HIV field — as one that faces significant health disparities."

> "WE REALLY NEED RESEARCHERS TO BE UNDERSTANDING THAT SEXUAL AND GENDER MINORITY PARTICIPANTS ARE IN THEIR STUDIES ALREADY AND THEY NEED TO BE COUNTED."

In addition to forging new paths for research, the NIH move will add credence to including LGBT factors in studies in general, says **Kellan Baker**, a senior fellow for the LGBT Research and Communications Project at the Center for American Progress in Washington, D.C.

"If we expect to be able to craft effective solutions for closing these health disparities, we really need researchers to be understanding that sexual and gender minority participants are in their studies already and they need to be counted," he tells *IRB Advisor*. "There needs to be more studies looking specifically at the experiences of sexual

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and gender minority populations."

By regulatory authority, the director of the National Institute on Minority Health and Health Disparities (NIMHD) at the NIH, in consultation with the director of the Agency for Healthcare Research and Quality (AHRQ), can define health disparity populations. According to an NIH statement on the action, the term sexual and gender minority (SGM) includes "lesbian, gay, bisexual, and transgender populations, as well as those whose sexual orientation, gender identity and expressions, or reproductive development varies from traditional, societal, cultural, or physiological norms."

"We currently fund sexual and gender minority research across many of the institutes and centers at NIH," says **Karen L. Parker**, PhD, MSW, director of the SGM office at the NIH. "The NIMHD is one of those institutes. However, they fund a much smaller proportion than some of the other institutes and centers. This designation does not specifically provide additional funding for research, but it does help validate the field of sexual and gender minority research as a relevant and important area for investigators to pursue."

While underscoring that the NIH is committed to increasing research in this area, Parker echoes Baker's point that new disparity designation also signals investigators that it is important to collect and analyze SGM-related data in other types of research, she says.

"We are hoping that investigators who may not have previously considered collecting data in the SGM population, or even asking the questions to know who within their populations are members of a sexual and gender minority community, will begin to ask those questions so that we will have more and better data," Parker tells *IRB Advisor*. "A lot of times people do trials and they ask a lot of demographic information, but they are not asking about sexual orientation or gender identity. Then they are unable to analyze the data by sexual or gender minority populations. So, we are hoping that this encourages people to find out who within their study populations are part of a SGM."

In that regard, IRBs could encourage the inclusion of such data in research under review, she adds.

"If someone is doing a study on 'x' and we don't know if there is a higher burden in sexual and gender minorities, maybe IRBs could encourage researchers to ask who in their population is a sexual or gender minority so that they can include that in the analysis," Parker says. "It's important for IRB members to understand that we do see differences in health outcomes and health-seeking behaviors by SGM versus heterosexual and [non-minority] gender individuals."

Toll of Stigma

The traditional NIH structure finds research focused around specific diseases or conditions, which do not address the breadth of health challenges faced by the SGM population. "For example, things like resiliency or how does family rejection impact health?" she says. "A lot of these types of questions may be related to structural stigma."

Structural stigma in communities with high levels of anti-gay prejudice was shown in one study to shorten life expectancy by 12 years for sexual minorities. "Analysis of specific causes of death revealed that suicide, homicide, violence,

and cardiovascular diseases were substantially elevated among sexual minorities in high-prejudice communities," the researchers found.[1]

HIV and AIDS disproportionately affect black and Latino men who have sex with men and transgender women, she observes. Moreover, emerging data also indicate SGM populations have less access to healthcare in general and suffer a greater disease burden of anxiety, depression, and cancer. However, previous LGBT research may be diluted in the various NIH disease categories, Parker notes.

"This [new designation] will allow those [research] applications to have a 'home' at the NIH, where before it was a little more difficult to find a more appropriate place where that research was in the mission of a specific institute," Parker says. "In terms of money, NIH can't fund what doesn't come in, so we are hoping that this will encourage people to do research in this area. The more applications we get, the higher the chance of getting applications funded."

Research has shown that there are certainly unique heath challenges, and in the absence of more data there are troubling unknowns afflicting this population.

"There are a lot of unanswered questions related to health disparities because people haven't been identifying this population in their research," she says. "NIH is really committed to research in this area and we're committed to encouraging scholarship in this area. We want science to be a welcoming place for SGM researchers."

It wasn't always that way. Despite few words of encouragement, Baker has long labored to get the NIH to make the designation change.

"I am a researcher myself, and when I entered the world of LGBT health about 10 years ago, it was told to me by many people that I needed to get this LGBT thing out my system because it wasn't going to be a viable career path," Baker says. "It wasn't some place where I could expect to have support, interest or traction with policymakers and researchers [in order to] figure out what disparities were affecting the LGBT community and actually do something about it. There have been many people who have worked on this issue for a long time — issues of LGBT health and health disparities and getting this on the federal agenda."

For example, in the 1990s there was a struggle to deal with HIV health disparities and the incidence of breast cancer in lesbian and bisexual women, he says.

"We really struggled as a community for a number of years to educate and establish the legitimacy of what the facts were showing, which is that the LGBT population does experience significant health disparities," Baker says. "[The NIH action] will provide emphasis and support for younger researchers who are considering entering a field where they are looking at LGBT health disparities, and seeing that this is an area of legitimate scientific inquiry. This is an area where we need to understand that there are problems that are effecting different communities, and we as a country need to be developing the evidence base and figuring out strategies for addressing the problems."

Thinking Beyond the Niche

Demographic niches cannot be parsed into neat categories, as they actually overlap in human research populations.

"Health disparities are not monolithic by any one aspect of their identity," Baker says. "Nobody is just gay or just black or just Latina. There are many people who are living at the intersections of multiple marginalized areas. We are not able to fully address the health disparities, for example, of racial and ethnic minority populations without also taking into account disparities in minority sexual orientation and gender identity."

Two areas that should be high on the agenda are lesbian health and bisexual and transgender people, he says.

"Bisexual and transgender people are sort of the two silent letters in the LGBT population, but they are actually very much front and center," Baker says. "We need to be thinking beyond our traditional understanding of lesbian and gay to an understanding of folks who identify as bisexual and transgender. If you look at the social factors of poverty and discrimination on the basis of race, access to healthcare services intersects with aspects of discrimination related to sexual orientation and to gender identity. [Otherwise], we are not going to be able to get to the roots of why gay and bisexual men and transgender women are the only populations in the U.S. in which rates of HIV continue to increase. We can't understand what's going on there unless we are understanding how such orientation and gender identity interact with all the other aspects that drive HIV in populations." ■

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AAMC Official Discusses Implications of Laws that Target Fetal Tissue Research

Controversial video sets changes in motion

Research involving fetal tissue increasingly could be affected by new state regulations. The changes come in the aftermath of the 2015 Planned Parenthood controversy in which an activist posed as a representative from a biomedical research company to secretly videotape discussions with Planned Parenthood officials about fetal tissue donation.

The videos that were edited to paint fetal tissue research in a negative light have resulted in Congressional investigations, reports, and subpoenas. Soon, the research world will see a final report with possible recommendations that could further affect how such research, which has included the development of Ebola and HIV vaccines, is conducted.

States recently have been passing legislation about fetal tissue research, undoing some of the research ground accomplished since 1993 when Congress passed the National Institutes of Health (NIH) Health Revitalization Act that allowed federal funding for fetal tissue transplantation research and regulated the transfer of human fetal tissues. The act also prohibited anyone from taking payments for human fetal tissue, other than to reimburse for transportation and other costs.

"Because we're in an election year, this has brought some of these conversations of ethics and funding and logistics of fetal tissue research to the forefront," says **Heather H. Pierce**, JD, MPH, senior director, science policy regulatory counsel, scientific affairs at the Association of American Medical Colleges in Washington, DC.

"With this as the political context of what's happening right now, there have been a significant number of states that have moved to introduce or pass new laws that could have some impact on the ability of a researcher to conduct research with fetal tissue," Pierce says.

"WITH THIS AS THE POLITICAL CONTEXT OF WHAT'S HAPPENING RIGHT NOW, THERE HAVE BEEN A SIGNIFICANT NUMBER OF STATES THAT HAVE MOVED TO INTRODUCE OR PASS NEW LAWS THAT COULD HAVE SOME IMPACT ON THE ABILITY OF A RESEARCHER TO CONDUCT RESEARCH WITH FETAL TISSUE."

According to the Guttmacher Institute, 38 states and the District of Columbia have Uniform Anatomical Gift Act regulations that treat fetal tissue the same way as other human tissue. Five states ban research using fetal tissue obtained from abortions.

"IRBs need to be thinking about this quickly moving process in certain states, ensuring that the institution's research or collection of tissue is in line with current state law," she adds.

For instance, some states have introduced laws that prohibit donation and research with fetal tissue. Some prohibit the sale of the tissue or making a profit. Other states have introduced legislation about the disposition of fetal remains and what must be done with the remains of a spontaneous or induced abortion, Pierce explains.

Such laws could make fetal tissue unavailable, making sure there is no fetal tissue available for such research, she says.

"Some states have a law requiring consent from a woman before the donation takes place, specific to fetal tissue research, and this is of interest to IRBs," Pierce says.

Even though the women had already given consent for the abortion and donation, they might not have been asked to consent for the fetal tissue to be used in specific research, and now they are required to obtain that specific consent, she adds.

"Most state laws apply primarily to fetal tissue from miscarriage, stillbirth, or abortion," Pierce says. "In some cases, the difference may

well be in the definition of fetus versus embryo."

No one can say what the long-term effect of the changes will be. What is known is that fetal tissue research has been recognized as an important direction for researchers involved in vaccine development, as well as in research involving Alzheimer's disease, Parkinson's disease, and other incurable conditions, Pierce says.

"Many researchers have pointed out the importance of studying developing fetuses in order to make advances," she says.

"Most of the new laws and much of the discussions have really focused on the ethics of doing the research at all, and I'm not suggesting the IRBs debate that," Pierce adds. "But most of the regulations and proposed state laws are really at the tissue acquisition and collection side of things and not about the research itself unless fetal tissue is banned as a whole in the state."

But when researchers begin to acquire fetal tissue, they could be affected by new laws, and it's important for the IRB to be aware of these sorts of questions, Pierce says. ■

Research Institution Works With Native American Tribes to Streamline IRB Review

Tribes set up their own ethics reviews

The Havasupai Tribe's 1994 lawsuit against Arizona State University (ASU) researchers and the institution illustrated some of the particular problems and challenges related to research involving Native American tribes.

The long legal battle raised questions about researchers using tissue samples without complete informed consent and without permission from the tribe. It also highlights how difficult it is to obtain and retain trust when research studies clash with cultural traditions.

"Historically, for decades now, there has been a mistrust [among native tribes] for western research and researchers, in general, because of unethical practices done in the past," says **Jyoti Angal**, MPH, CIP, director of community-based research for Sanford Research in Sioux Falls, SD.

In the Havasupai case, the tribe claimed researchers failed to provide adequate informed consent for how blood samples would be used. The study began as a diabetes project, but evolved into studies of schizophrenia, migration, and inbreeding — all of which the Havasupai consider taboo topics and for which investigators had not obtained informed consent, according to the American Indian & Alaska Native Genetics Resource Center. *(For more information on the study, visit http://bit.ly/1LP01ML.)*

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The lawsuit also claimed that ASU researchers violated civil rights through mishandling of blood samples, unapproved use of data, and violation of medical confidentiality because the tribe was named and could lead to a risk of identification of individuals.

After 16 years of court battles, ASU settled with the tribe in 2010. The tribe received $700,000 for tribal members, funds for a clinic and school, and return of DNA samples.

In recent years, tribal nations begun forming their own ethics review boards, enabling tribes to have an active voice and role in research. This trend suggests the need for IRBs to work with tribal boards to create tools and resources that will educate and inform tribal IRB members.[1]

Sanford Research in Sioux Falls, SD, which is part of the Collaborative Research Center for American Indian Health, is working to bring together tribal communities and researchers in the Dakotas and Minnesota, Angal says.

The Collaborative Research Center was funded by a National Institutes of Health (NIH) National Institute of Minority Health and Health

Disparities grant in 2012, she says.

"We're building capacity for tribes to conduct and govern their own research," Angal says. "Our role is to help tribal communities that are interested in creating their review process and building their capacity to review their own research and also to streamline their research process."

The current trend is to do more than just participate in research. Tribes want to review and authorize research conducted on their land, so this raises their interest in creating IRBs. "They don't want a large IRB process," she notes. "It could be a smaller, alternative community advisory board model."

The Collaborative Research Center's role is to work with tribes to decide what type of research review they want.

"We have six tribes we're working with right now and four of them have IRBs; the other two are still in the process of building a process," she says.

"We put together a tribal IRB toolkit that is available online at our website as a free download for anyone who wants to use it," Angal says. "This toolkit was put together in response to requests by our tribal partners."

The toolkit addresses what an organization will need to start a tribal IRB and includes answers to questions about obtaining approval from the tribal council. *(For more information on the tribal IRB toolkit, see related article on page 139.)*

The following is how the toolkit's Tribal IRB Review Submission and Review Process works, according to one of the sample flow charts:

- Principal investigator submits required material to Tribal IRB by submission deadline.
- Tribal IRB coordinator pre-reviews material.
- Tribal IRB coordinator includes the research project on the IRB meeting agenda.
- Tribal IRB reviews proposed project and makes a determination.
- Research project may begin after approval is received.

The toolkit even addresses the most basic of questions that a new IRB might ask, such as, "What do I call my IRB?"

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Angal researched this question and found that federal regulatory agencies do not provide guidance on the IRB's name. "We came to the conclusion that you can call it whatever you want," Angal says. "But when it's registered, it's registered as an IRB, and that was new learning for us."

One of the goals in developing the toolkit was to provide details about processes according to what the tribes wanted to include. For instance, the approving authorities of tribes made suggestions and reviewed drafts. This gives tribes a voice they usually lack, Angal notes.

"One of the biggest differences between academics and tribal dissemination is that, typically, publications from scientific studies do not go back to the IRB for review," she says. "However, tribal research requires publications to come back to the tribe IRB."

The reason for this is to prevent community harm. For example, a tribe that participated in a study involving prenatal alcoholic exposure may not want to be named in the study because of stigma, she explains.

Tribal IRBs can help make the research design stronger, and it improves community engagement in research, Angal says.

For example, when research involves the collection of biospecimens, a tribal IRB will know how biospecimens are sacred in some cultures, she says.

"You need to look at what it means culturally to them," Angal says.

When researchers wish to collect specimens for a study, they can talk about how members of the tribe do not have to consent to future uses of those specimens if that particular study is approved. This might be a more comfortable approach for a particular tribe, she adds.

"The toolkit was created in response to a tribal request," Angal says. "It goes back to the thought that you don't tell people; you work with people and give them respect and help them and ask them to tell us what their needs are." ■

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Sample Checklist from Tribal IRB Toolkit

Checklist for tribal IRB pre-review

The Collaborative Research Center for American Indian Health Tribal IRB Toolkit contains 101 pages, covering all aspects of initiating and running an IRB. Included is the Tribal IRB Pre-Review Checklist:

• Type of Submission

- Application for initial review
- Application for continuation
- Amendment
- Final report/closure
- Response to IRB request
- Other

• Initial Review — New Protocols Only

1. Determine if the activity is research. Refer to 'Determine if Research' flowchart.

2. Determine if activity involves human subjects. Refer to 'Determine if Activity Involves Human Subjects' flowchart.

3. Determine if the research is within the jurisdiction of the tribe, i.e. on reservation land.

4. Identify relevant tribal, state, federal, or international law that may apply to the research. Reference federal and international research protection laws in these resources:

- Human Research Protections Standards & Regulations, and
- Application of Research Protections Standards & Regulations.

5. Review application form and/or documents submitted. Check for missing material.

6. If missing material is found, send letter to the investigator requesting this information. If application is complete, schedule the project on the next IRB meeting agenda. Send a letter to the investigator, notifying them of scheduled date. See 'Letter Templates.'

7. Check to see if the investigator is already listed in the IRB records (for conducting research on the reservation previously). If not, enter contact information, CV, and human research protections certifications into IRB records.

THE COLLABORATIVE RESEARCH CENTER FOR AMERICAN INDIAN HEALTH TRIBAL IRB TOOLKIT CONTAINS 101 PAGES, COVERING ALL ASPECTS OF INITIATING AND RUNNING AN IRB.

8. Determine the board member expertise that is most relevant for review of this research project. Identify what special determinations the IRB needs to make in order to approve the submission (e.g., risk to vulnerable populations). If board member expertise is not sufficient, a consultant may be needed.

- Notes

• Continuing Review Protocols Only

1. Look for changes in the submission from the most recent approval.

2. If applicable, check whether the consent forms and scripts being used are the most recently approved versions.

3. If needed, communicate with the investigator regarding missing material or to resolve any questions about the material submitted for 'continuation review.'

4. If application is complete, schedule the submission for continuation on the next IRB meeting agenda. Send a letter to the investigator, notifying them of scheduled date. Refer to 'Letter Templates.'

5. Send the Continuation Review Checklist together with the submission materials for review, at least two weeks prior to the scheduled board meeting.

• Responses to IRB Requests

1. Review relevant minutes and determine if the investigator responded to the request appropriately (e.g., made required modifications or provided additional information). Communicate IRB response to investigator. Refer to 'letter templates.'

- Notes

• Project Termination/Close Out

1. Ensure that the investigator has submitted a complete 'Project Termination/Close Out' Report form. Check for missing information.

2. Determine if any new information about the research project has been provided (e.g., new risk to participants or the Tribe).

3. If applicable, ensure that the investigator has submitted a completed 'Data Return Form' and accompanying materials.

4. If needed, communicate with

the investigator regarding missing material or to resolve any questions. If determined that project close-out will be on an IRB agenda, send investigator communication regarding this. Refer to 'Letter Templates.'

5. Once verified that all material has been received, send a letter to investigator acknowledging receipt. Refer to 'Letter Templates.'

6. Ensure files of project information contain all research submissions from the investigator and all records of correspondence between the IRB and the investigator.

7. If applicable, ensure that data returned by the investigator is filed correctly.

- Notes

• Other Submissions

1. Review application form and/or documents submitted for missing material.

2. If missing material is found, send letter to the investigator requesting this information.

3. If all submitted material is complete, choose the relevant form of written communication to the investigator. (e.g., send letter to investigator confirming submission, or schedule item on the next meeting agenda and send letter with the date). Refer to 'Letter Templates.'

4. If the submission requires board review, identify what special determinations the IRB needs to make in order to approve the submission (e.g., risk to vulnerable populations) and prepare appropriate checklists and supplemental reference material for the board.

5. If applicable, identify relevant Tribal, state, federal, or international law that may apply to the research. Reference federal and international research protection laws in these resources:

- Human Research Protections Standards & Regulations, and
- Application of Research Protections Standards & Regulations.
- Notes ■

When IRBs Take a Walk on the Wild Side: The Dark Web

There are legitimate reasons to go there

Recent presidential politics put electronic communications and hacking of information into sharp focus, particularly with the underground WikiLeaks making the headlines every other week. But what many IRBs might not know is that researchers increasingly are turning to the "dark web" for data.

"We think all of the data from the dark web is bad and suspicious, and if you're working in the dark web then you're looking at child pornography, but that's not what this is all about," says **Elizabeth A. Buchanan**, PhD, an endowed chair in ethics and acting director of the office of research and sponsored programs at the University of Wisconsin-Stout in Menomonie.

"The dark web enables privacy and anonymity, and we value anonymity in the social-behavioral realm," she says. "It's a good time for researchers to be active using data on the dark web."

What's good for researchers can be a major challenge for IRBs. "The challenge for IRBs is when we look at where we're getting data, what are the risks to researchers and the risk to institutions?" Buchanan says.

"Then we think about the whole WikiLeaks concept, and we see risks to individuals," she adds. "We don't want to be on the front page of the paper, saying we used leaked data or that our researchers are scrubbing data, because it sounds bad."

Buchanan speaks about the dark web and research ethics at national conferences, often beginning with giving people definitions, since the term evokes images without offering an understanding of what it really means.

"There are locations on the internet that are not indexed and findable through Google," Buchanan explains. "They are off the grid, like Silk Road, which is a good example from a few years ago."

The Silk Road website was an online marketplace for illegal drugs and other items that people could buy using the internet-based currency bitcoin.

"It was amazingly lucrative, resulting in millions of dollars in profits until it was shut down because it involved drug trafficking, illegal banking, and cybercrimes," Buchanan says. "You could have these truly anonymous purchases and order something that would be packaged to look like a video or game."

This pushed the limits of the internet and societal norms around privacy and anonymity and safety,

she says.

People's intentions for using the dark web are not all bad, however. "Sometimes it gets conflated with both the dark web and WikiLeaks," Buchanan says. "Just because you want to be anonymous automatically means you are guilty of something, and that's just not true."

Some legitimate reasons people might use the dark web include research and social justice or civil disobedience, for example.

By going to the dark web, social-behavioral researchers can reach populations that are otherwise extremely difficult to find.

"If you want to study illegal behaviors and if you want to study ugly things like child pornography, there are reasons to study these on the dark web," Buchanan says.

And there are other reasons for using the dark web in research. For instance, one researcher was pregnant and wanted to experience her pregnancy anonymously online, she says.

"It was neat the way she talked about what experiences people can have in a nonpublic internet environment," Buchanan says. "Also, if you don't want your identity as a researcher known, or if you're doing gang research and for your own safety, using [the dark web] is an option."

One way researchers access the dark web is through a browser called Tor. It is downloaded like any major web browser, but pings from different servers and IP addresses aren't logged. It's the way to browse the Internet without being tracked, she explains.

Naturally, IRBs would have a number of questions and concerns about research that involves the dark web, including the following:

• **Looking at the population or topic being investigated, what is the researcher doing?** "Just like we would do with any other protocol, if the protocol involves something that looks at pockets of opioid use in a particular environment, it could have real risks both for the investigator as well as participants who could be identified," Buchanan says.

"So we'd want to assess it, look at risks and benefits, and make sure the investigator has the qualifications to be engaging in research that could be potentially risky," she says. "You don't want to find yourself as a researcher in a space that's a sting operation, and the FBI is in there while you're in there."

> "THE DARK WEB ENABLES PRIVACY AND ANONYMITY, AND WE VALUE ANONYMITY IN THE SOCIAL-BEHAVIORAL REALM. IT'S A GOOD TIME FOR RESEARCHERS TO BE ACTIVE USING DATA ON THE DARK WEB."

It's a good strategy for researchers or IRBs to get in touch with their local FBI field office before starting a dark web study that involves observing illicit behavior, she suggests.

"The worst thing is if your researchers are messing around and talking with an FBI officer, and neither knows what the other one is doing," Buchanan says. "There are simple practices you can take to help you into these research studies in a safe way."

• **How will a researcher protect himself or herself?** IRBs, as well as investigators, need to fully grasp all of the risks of navigating the dark web. They should be fully aware of which risks are individually based, technologically based, and which are related to the research itself, she says.

• **What are the social benefits of the research?** There are a variety of social benefits to research on the dark web, including studies that involve dissidents and civil disobedience.

"Think of political science research these days," Buchanan says. "It's very important to look at all of these things."

• **Is it research or public health information?** Suppose a researcher proposed conducting real-time surveillance of opioid users, Buchanan says.

"Is this research or public health information?" she asks. "Is it even human subjects research if it's in a completely anonymous setting?"

In big data studies, studies like these probably are not human subjects research because the object is to collect data about people who can never be identified. "There's a line between human subjects and data subjects, and what does that do to our current regulations?" Buchanan says.

Whether IRBs explore the issues revolving around research in the dark web, it is a topic that likely will not disappear, Buchanan notes.

"It's becoming more common as people hear about it more because of WikiLeaks," she explains. "The more we hear about things in the popular press, the more researchers will keep digging and see where this takes them — the dark web is not new." ■

Vandy-Duke Research Partnership to Put Clinical Trials on Fast Track

IRB review centralized, but protections in place

Two venerable research institutions are collaborating in a far-reaching partnership that aims to safely speed research, translating trial results to patient interventions in more expedited fashion.

The newly minted Trial Innovation Center will be run by Duke Clinical Research Institute and Vanderbilt University Medical Center. The center is funded by a seven-year, $26.5 million grant from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health.

According to the project website, the goal of the center is "to create innovative methods to accelerate the implementation of multisite clinical research studies, especially those done within the national Clinical and Translational Science Award consortium."

The collaboration will focus on the following four core tenets:

- A Study Design Core will work with investigators to develop protocols and feasible study budgets.
- A Study Start-up Core will create Master Clinical Trial Agreements and oversee a central IRB to get trials underway as quickly as possible.
- A Study Conduct Core will provide support to investigators from trial design to research results.
- An Innovations Core will create solutions to streamline and expedite interactions with the clinical trial sites.

Two principals in the project recently talked to *IRB Advisor* about the implications for research advancement and improved patient outcomes. **Gordon Bernard**, MD, is director of the Vanderbilt Institute for Clinical and Translational Research. **Phillip Brian Smith**, MD, is chief of the Division of Quantitative Sciences in the department of pediatrics at Duke University Medical Center.

IRB Advisor: As outlined, the project will study how multisite clinical trials of new drugs and therapies in children and adults can be conducted more rapidly and efficiently. Can you comment on some of the historical background on this issue, particularly the aspect of prolonged or multilayered IRB review?

> INSTEAD OF HAVING TO UNDERGO 30 INDEPENDENT REVIEWS, WE WOULD BE BEING DOING THE SAME LEVEL OF REVIEW, BUT THERE WOULD BE JUST ONE.

Smith: There are lots of barriers to clinical trials — procedural things that have to be done, guidelines to be followed, institutional and FDA [requirements] — and one of the things is IRB review.

For most studies, traditionally, every site has to review the site and give approval. It's a really cumbersome activity and it gets even more cumbersome the more sites that you have. So, you can imagine if you have, say, 30 IRBs, a handful of IRBs are going to have something they have questions about. If it's a protocol item — what if it has already been approved by 25 sites but you need to change it for five sites?

Individual IRBs may also insert their own language in an informed consent template form that may be at odds with other sites. All of this takes a large amount of effort for questionable benefit. The central IRB models are designed to avoid that, so you have an IRB that serves as the central board and the others defer review to that central IRB.

IRB Advisor: In that regard, you call for the creation of a "Study Start-up Core to establish Master Clinical Trial Agreements and oversee a central IRB to get the trials underway as quickly as possible." Can you explain a little more how this would work?

Bernard: Under current approaches, every site's IRB has to review the project and every site has to negotiate a contract either with a commercial sponsor, with the NIH, or a lead investigative site. The nature of the beast is that those contract negotiations can really slow the process down. Our notion on the contract part of this is that I will oversee the contract process here at Vanderbilt for the clinical trials.

[Investigators] usually already have an agreement designed to suit them. We then need to go through the components and see what doesn't suit us. Then we negotiate that for a period of several weeks and several

months, and then meet in the middle. We say OK, and we sign it and we are good to go, but as I say sometimes that can take months.

What we are trying to do with the Accelerated Clinical Trial (ACT) agreement is write a contract that is very similar to one we end up with — in the middle. So instead of starting off at one end and meeting in the middle, we will see if we can just meet in the middle and shave off some time and have a contract that people can agree with on day one.

IRB Advisor: Of course, the other side of the coin is that some may perceive a bid to speed up trials and drug development as increasing the risk to human research subjects and, ultimately, patients. How will researchers balance the need to expedite research but proceed with caution in terms of subject/patient safety?

Smith: It's not that the protocol and consent form wouldn't undergo IRB review. They absolutely would. It's just that instead of having to undergo 30 independent reviews, we would be being doing the same level of review, but there would be just one. No one has ever shown that [a multiple review process] has been more protective of study participants. The protocols we take care of and manage will look at the science and also look at the risk and benefits of the study procedures. There are additional levels of people deciding whether the research should go forward. All of the issues around conflict of interest and informed consent would still have to be managed around the central IRB.

Bernard: From the contracting perspective, I see no reason for increased risk. From the IRB side, you could conceivably have increased risk, but there is a formal IRB review. It's not rushed — it's just one [IRB]. It doesn't have 29 more reviews that are unlikely to change the project significantly. So, I'm not really worried about that and each of the IRBs that are relying on the reviewing IRB get all of the documents and the minutes — the "thinking" of that IRB that they can then review.

What we're seeing with some of the pilot work in this area is that IRBs enjoy reading about how other IRBs operate because up till now they have been very siloed. They don't talk to each other much at the clinical, individual study level. They talk to each other about rules and regulations and working with federal authorities and that kind of thing, but when it comes down to John Smith's protocol for congestive heart failure, they virtually never talk to each other. They don't have a feeling for where they are on the continuum of conservative or liberal, and then in some cases they may not have a full understanding of the regulatory component of things like device trials, which can be very complicated.

IRB Advisor: This sounds like an ambitious and sweeping project that has the potential for major research transformation. Can you comment on the scope of this project and the kind of breakthroughs it could potentially lead to?

Bernard: Well, just imagine there was another outbreak of Ebola in the United States — more so than what we saw previously — and there was a treatment of possible benefit, a treatment that woud work. You would want to get that into patients as quickly as possible. With a central IRB process, you could have an IRB that says, "We're ready to go and we will review it tomorrow." They would be the central IRB for the project, and any other sites simply need to receive that paperwork and agree that they are applying the next day. Likewise, we would have a standard contract, a budget: "Here's what we think it should be." In theory, a site could sign up and be in IRB compliance in a day and enrolling patients. Right now, if you tried to do that I estimate conservatively that it would take six months for all the sites to be up and running, and maybe even a year.

Smith: There hundreds, if not thousands, of really bright investigators with great ideas that are developing things that could really have an impact on patient health. One of the barriers to getting those things to the bedside, getting the trials done that show these things are safe and effective [is the protracted and laborious current system]. Really, these trial innovation centers will be set up to help facilitate those trials and get them done in the most efficient manner.

There are a finite number of healthcare dollars that are going to get spent on research. We have to make the best use of those dollars, so our goal is to get these trials done, to make sure they don't fail from an enrollment standpoint, and make sure that we don't waste time and money on steps in the research process that don't benefit the patients. ■

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CME/CE INSTRUCTIONS

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CME/CE QUESTIONS

1. While underscoring that the NIH is committed to increasing research in the sexual and gender minority (SGM) area, Karen L. Parker, PhD, says the new disparity population designation also signals investigators that it is important to collect and analyze SGM-related data in other types of research.

A. True
B. False

2. States recently have addressed new legislation governing the handling and use of fetal tissue in distribution for research. Congress also has held hearings on this matter. What was the impetus to the new legislative and Congressional focus?

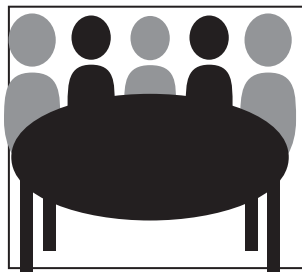
A. The 1993 NIH Health Revitalization Act is up for renewal.
B. The FDA did an undercover investigation into allegedly illegal fetal tissue handling practices.
C. An anti-abortion activist clandestinely videotaped Planned Parenthood employees discussing how fetal tissue is handled and edited the video to portray the organization in a bad light.
D. All of the above.

3. In a checklist for a tribal IRB's project termination/close out process, which of the following is not one of the steps to take, as listed on a checklist created by the Collaborative Research Center for American Indian Health?

A. Recheck investigator's conflicts of interest and credentialing to see if there were any recent changes.
B. Ensure the investigator has submitted a complete 'Project Termination/Close Out' Report. Check for missing information.
C. Determine if any new information about the research project has been provided.
D. If applicable, ensure the investigator has submitted a completed 'Data Return Form' and accompanying materials.

4. In a hypothetical example of fast-tracking a drug for Ebola, Gordon Bernard, MD, said the Duke-Vanderbilt research consortium could lead to a process where a central IRB and participating institutions could get a clinical trial up and running in a matter of days. How long did he estimate it would take under current review and oversight conditions?

A. Six weeks to three months
B. Two to four months
C. Eight months
D. Six months to a year



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