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INSIDE

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Respect Tribal Sovereignty in Indigenous Research

'The truth comes from many places'

By Gary Evans, Medical Writer

In what may help overcome a history of well-earned distrust by indigenous people, a research collaborative has developed a curriculum to teach IRB members and others the distinct cultural issues that arise in studying Native Americans.

To cite one example — which tragically updates the traditional petition of Native Americans for the return of stolen lands — the Havasupai Tribe in Arizona successfully sued to get their DNA samples back after finding they were used for purposes other than the diabetes research they agreed to in 1990. *(For more information on the lawsuit and study, see the story in the December 2016 issue of* IRB Advisor.*)*

> EVEN ASSUMING ALL PARTIES COME TO THE TABLE IN GOOD FAITH, THERE ARE CULTURAL BARRIERS THAT MAY CONFOUND WELL-INTENTIONED RESEARCHERS.

Even assuming all parties come to the table in good faith, there are cultural barriers that may confound well-intentioned researchers and IRBs. To address this issue, **Cynthia Pearson**, PhD, a professor in the school of social work at the University of Washington in Seattle, began developing a curriculum to teach people about ethical research with American Indian and Alaska Natives. Working with a network of partners including native tribes and other researchers, Pearson created a training curriculum that explains key aspects of tribal sovereignty and includes a code of ethics that acknowledges past wrongs. *(For more information, see story on code of ethics, page 39.)*

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The curriculum can be accessed online at: http://bit.ly/2FWgvdj. Pearson and colleagues recently published a paper analyzing the methods used to create the training.[1]

Training for those engaged in research is primarily written by and for academic types, but the tribal governments have a right to oversee any research that takes place on their own land.

"We started involving our indigenous community members in research, but the training didn't resonate," Pearson says. "It didn't really speak to the issues that are happening in tribal communities. We decided to write a training curriculum that really speaks to the issues that occur in American Indian and Alaska Native communities."

In doing that, the curriculum can show IRBs how the Common Rule applies to these indigenous communities. For example, one typically thinks of informed consent in terms of a single research subject, but American indigenous people have a tribal identity, a collective that supersedes the individual. Thus, giving individuals anonymity but naming the tribe in a research report can be seen as a grave transgression by native people.

"Some of the specific things are recognizing tribal sovereignty, but also recognizing the history of colonialization and trauma that has happened as the result of research," Pearson says. "When you are dealing with small communities and you are naming those [tribes], then there is the chance that you may harm those communities."

There are 567 federally recognized indigenous tribes in the U.S.

"Those are all sovereign governments," she says. "So just as if you were going to Mozambique or China, you would not pop in and start conducting research without getting appropriate permission," she says. "This is important to understand when you are working with tribal communities. I think most IRB members may be getting that now."

In the curriculum and related materials, Pearson and partners outline these type of issues and different types of tribal approval that could occur.

"You don't necessarily need to go to a tribal council, but there might be other steps along the way that should be considered," she says. "Another real important thing has to do with respect for persons."

Such respect is among the central tenets of the Belmont Report, but again, it extends beyond individuals to the tribe itself.

"You think about the Havasupai study when they started doing research reports that named the tribe," she says. "That case was all about respect for communities as opposed to just respect for a person."

Curriculum Created

The curriculum was created with input from representatives of tribes, academics, and researchers who work with indigenous communities.

"We also pulled together some IRB administrators," she says. "And we had a member of the National Congress of American Indians that sat in on one of our expert panels. One of the first things we did was hold a meeting with the community people. These are leaders in their communities that have reviewed research protocols — very savvy people."

An initial attempt to translate and rewrite existing academic and tribal

research documents was abandoned in favor of a clean slate.

"Originally, the curriculum was developed for American Indians and Alaska Natives and people conducting research within those communities," she says. "As it has gone out, we have heard repeatedly that it is really good for any person, academic or otherwise, to do this training. If they are going to conduct research in Indian country, they should review this curriculum."

The curriculum is now being reviewed for possible inclusion in the ethical research protocols offered by the Collaborative Institutional Training Initiative Program. "This is great for IRB members," Pearson says. "There may be a lot of things they don't know about working with diverse communities. This curriculum can help them get that understanding and exposure to things that they should be considering and questions to ask while reviewing a protocol."

As part of the study, the curriculum was tested and validated among a national sample of American Indians and Alaska Natives, with 244 using the new material and 246 using traditional online training.

"Using an 80% correct item cutoff at first attempt as passing criterion, the tailored curriculum achieved a 59.3% passing rate versus 28.1% in the standard curriculum," the researchers reported. "Participants took less time to complete the training and reported significantly higher acceptability, satisfaction, and understandability of the … tailored curriculum." ■

REFERENCE

1. Pearson CR, Parker M, Zhou C, et al. A culturally tailored research ethics training curriculum for American Indian and Alaska Native communities: A randomized comparison trial. *Critical Public Health* 2018; DOI: 10.1080/09581596.2018.1434482.

Code of Ethics for IRBs Working With Indigenous Tribes

IRBs and researchers must recognize that "the truth comes from many places" if they want to work in good faith with Native American tribes.

So says a code of research ethics and integrity developed by the National Congress of American Indians and the Indigenous Wellness Research Institute at the University of Washington.[1] The full document and the rest of the curriculum is available for download at: http://bit.ly/2FWgvdj. Some of the ethics code key points are cited and summarized as follows.

Make Research Culturally Relevant

"This Code of Ethics and Integrity recognizes that the tribe has the right of self-determination and, in exercising that right, must be recognized as the exclusive owner of indigenous traditional and cultural knowledge," the document states. "Research should be beneficial, community-based, culturally relevant, and consistent with tribe health priorities and concerns, and the risks associated with the research should be less significant than the benefits to be gained."

To avoid misunderstanding and harm, the tribe participating in research must:

- understand why the study is being carried out;
- understand objectives, methods, and potential results of the research;
- understand how the research will benefit their partnership and the field more broadly;
- understand if and how the research could potentially harm their partnership;
- understand that participation in the research is voluntary;
- know that they can refuse to participate in the research and still be entitled to benefit from tribe and research-related activities;
- be given the opportunity to be involved in all aspects of the research process;
- know that the research will respect the Code of Ethics and Integrity;
- have the ability to ask the researchers questions about the research at any time;
- contact the overall principal investigator if they have any concerns about an aspect of the research project.

Collaboration:

- our voices will influence work to promote our continued collaboration;
- increasing capacity of our partnership within and outside our tribal community;
- research analyses, interpretations, and results must be presented to and discussed by all partners to ensure accuracy and avoid misunderstanding; mutual

commitment to excellence and rigorous science;

• integrity of indigenous knowledge and wisdom in all communities;

• research must ensure confidentiality and anonymity of individuals, organizations, and communities unless these parties choose to be named in the results ■

REFERENCE

1. University of Washington. Research Ethics Training for Health in Indigenous Communities. Available at: http://bit.ly/2FWgvdj.

Try These Strategies for Improving Review Consistency

Toyota lean methodology shows the way

Inconsistent reviews cause problems for IRBs and investigators. They can elicit complaints of unfairness. They might lead to workflow inefficiencies. Worse, they could be detrimental to human research protection quality.

One IRB office created simple rules and a process to improve workflow efficiency. Using Toyota lean methodology, the office standardized interpretation of regulations and institutional policies. *(For more information on lean methodology, visit: http://bit.ly/2FgAYJy.)*

The Seattle Children's Research Institute has used lean methodology to improve its organizational processes since the early 2000s. The IRB employs the same strategy to increase consistency, improve workflow and efficiency, and to ensure high-quality study reviews.

"We try to follow a system of daily improvement," says **Tia Mynes**, MS, CIP, human subjects protection analyst at Seattle Children's Research Institute.

The IRB used reliable methods as a path to standardize work, says **Nicholas Lew**, JD, CIP, human subjects protection analyst at Seattle Children's Research Institute.

"It's the most effective way of doing something over time," Lew says. "It boils down to figuring out what is the most effective, efficient method, and that's how you implement it."

For example, in the continuing review process, an IRB will check whether the study's enrollment is accurate and whether it matches up with previous years' enrollment, Lew says.

"If the current year's report says the study is enrolling subjects, but the last year's report said the study had completed enrollment, then you go back to the study team and ask them about it," he explains. "The reliable method is to check out discrepancies."

Simple and Reliable

Mynes and Lew offer the following strategies to improving IRB review consistency:

• **Establish simple rules.** The IRB refers to simple rules as strategy to document how its IRB makes decisions about each study so these thought processes could inform the next study with similar issues.

"The simple rules are for regulatory issues where there could be different interpretations, depending on how you read the regulations," Mynes says.

"It's nice to go back and find a written record, a centralized area where you know you can find documents instead of caucusing with people about what happened a year or two ago," Lew says.

"One topic that came up recently involved the secondary use of data and specimens initially collected for research purposes and how do we handle that as an institution," Mynes says. "Do we want to see consent forms to see that subjects consented to their samples being used in research? Or do we let the investigators request waivers to use those samples without really checking to see if the subjects said they could be used for secondary research?"

This is a topic that comes up at times, and IRBs struggle with it, she notes.

"We documented how we want to handle that in our simple rules," Mynes says. "Our simple rules are basically a Word document where we have different categories of things, including an index, table of contents, and we make a regulatory interpretation."

Then the IRB notes the decision about this issue, the background on the dilemma, and provides an example.

When a similar situation occurs,

the IRB can go to these notes to see how it was handled previously.

"We try to be consistent in our language so it can be easily searched," Mynes says. "We try to have a table of contents that's descriptive so you can do a word search."

Another topic documented through simple rules involves recording conversations, Lew notes.

"In simple rules, we've outlined what the law requires and we documented specific examples of what has been permissible with recording conversations in studies," he says. "We reference a study with an audio recording, so when we see another study with a recording, we can see what has been allowed previously and compare it to the current study."

• **Use reliable methods.** Reliable methods can be very detailed steps or more of an outline. They cover many different topics related to what IRBs do daily, Lew says.

"Reliable methods has helped new analysts by giving them a written reference point about information they are looking for, and it tells them how to review items that come into our office," Lew says.

"Previously, we had standard operating procedures," he adds. "Those give a general idea of what to look for, but they don't get into much of the details, and having the reliable method gives us the details."

Before using simple rules and reliable methods, new IRB staff would ask experienced staff with help in every new situation, he notes.

"Having this helps them find a central spot for answers, and we have more focused information on what to do," Lew says.

It's a way to impart institutional knowledge without relying on longtime staff members' recollections, he says.

Improve Review Consistency

The IRB holds reliable methods meetings each week. This also is an institutionwide process.

> "IN SIMPLE RULES, WE'VE OUTLINED WHAT THE LAW REQUIRES AND WE DOCUMENTED SPECIFIC EXAMPLES OF WHAT HAS BEEN PERMISSIBLE WITH RECORDING CONVERSATIONS IN STUDIES."

"It's a chance for people to bring questions about the process," Mynes says. "On top of that, every morning, we get together as an IRB office, huddle, and use a whiteboard to show progress."

The meetings focus on how much existing and new work is being handled in the IRB office. People can troubleshoot problems that arise. They also help each other with consistency issues.

"We discuss different topics, like processing continuing review," Mynes says. "It helps us make sure we're all doing things the same way."

IRB staff and members follow the simple rules strategy to ensure consistency. Then they'll bring questions about these to the reliable methods meetings, she adds.

Here is an outline of the steps they take to improve consistency of reviews:

• **Step 1: IRB professionals use reliable methods when reviewing each new submission.**

They ensure the study has funding and all conflicts of interest documentation. They check the submission for the following items:

- Does the protocol have all of the necessary sections?

- Does it meet criteria for full board review, expedited review, or is it exempt? If necessary, compare the study to the checklist for expedited reviews.

- Does the study have an unusual issue, and has that issue been handled by the IRB previously?

- If this issue was handled in a previous case, what does that previous study's simple rules document say was discussed, and how was it resolved?

• **Step 2: The IRB staff is in charge of pre-reviews, working on protocols, and getting them to the point where they can be reviewed and approved by the board.**

"Then we make a decision about the study — and, since I brought up the issue, I document it in the simple rules," Mynes says.

For example, Mynes might document the case with: "This was the situation for this type of study, and this is how we came to the conclusion."

If the study needs to be reviewed and expedited, Mynes can handle it. But if it must go to the full board, she will provide background about why this study doesn't fit the expedited category.

In some cases, IRB staff will need to contact the IRB chair about a logistics issue in a study. For instance,

there might be a statement in the protocol that indicates someone will approach patients at bedside to ask them about enrollment, Mynes says.

"We'd ask the chair if there were any concerns about how they were doing this," she explains. "Our IRB chair works at the hospital and could say whether it could work the way they're describing it."

These strategies of simple rules, reliable methods, and taking steps to ensure review consistency will work only as long as the IRB regularly audits and updates its documents, Mynes and Lew say.

"In simple rules and reliable methods, we have a place where we can look up information to see what we allowed before," Lew says. "It helps to keep the institutional knowledge as much as you can, but it has to be documented and an organizational practice to do it." ■

Smart Checklists Keep IRB on Track With Study Reviews

Tailored lists help with consistency, quality of reviews

As an IRB office prepared for accreditation, staff looked for methods to increase compliance. An answer quickly formed: use the IRB's electronic system to develop smart checklists.

"Our system has the capability of having smart checklists, which are checklists that show only the things relative to the submission, and they have the ability to link to the submission," says **Fanny Ennever**, PhD, CIP, manager of regulatory policy development for the human subjects protection program at Boston Medical Center, Boston University Medical Campus.

IRB staff completed hundreds of smart checklists in 2017, including separate checklists for initial approvals, initial exemptions, amendments, and continuing reviews. The checklists are designed to help reviewers remember all of the details they need to check and to document regulatory and institutional requirements.[1]

One of the chief benefits is that it frees up the board's time in reviewing studies.

"We want to make sure the issues that result from inattention by the submitter are taken care of," she explains. "So when the board does the review, IRB members don't have to waste their time handling petty errors."

Using a checklist for these pre-reviews is one way of ensuring consistency and compliance.

For example, one overarching issue on a checklist has to do with whether the study is internally consistent. So if the study protocol lists inclusion/exclusion criteria, the submission's list of inclusion/exclusion criteria should be identical, Ennever says.

Making this checklist electronic can be complicated.

There are separate checklists for new study submissions, continuing review, etc. Plus, each person viewing the same checklist will see different things because of where their answers lead, says **Khaled Khattar**, BBA, IRB application administrator and website editor at Boston Medical Center and Boston University Medical Campus.

When the IRB created the checklists, the challenge was to communicate the rules to Khattar, who spent several weeks working continuously on the checklist.

"I think we have more than 1,000 rules in the electronic checklist," Khattar says. "It was simple except when you come to the rules."

The checklists also vary according to which box is checked. One answer leads one way; another goes in a different direction. For instance, a checklist for an amendment will look different if there is a consent form versus an amendment without a consent form, Ennever says.

"The checklist only shows things that are relevant," says **Matthew Ogrodnik**, CIP, IRB administrator at Boston Medical Center and Boston University Medical Campus. "It depends on which information is provided in the application, and this drives the questions that appear. So you are only focusing on things that should be in that application."

If the study will enroll minors, then the checklist will pull up all possible regulatory categories for minors, and the study must fit into one of those categories and meet criteria within those categories, he adds.

"It's best practice to record the protocol justifications, using the example of enrolling children, so if you need to go back and look for the justification, you'll know where it is," Ennever says.

The checklist's workflow allows for stops and starts. If IRB staff cannot complete each item the first time going through the study and checklist, the system will generate a red incomplete.

"You can send it to the principal investigator to go through and adjust items that are still incomplete, and you don't have to restart the checklist," Ogrodnik explains. "It's a visual cue that lets you see exactly what was left incomplete — you go directly to the items in red."

The electronic checklist also has room for comments. IRB staff can write, "This section is missing," or "This doesn't match up with the protocol," he says.

If a comment notes that the investigator did not complete the funding section correctly, IRB staff can provide a link that takes the investigator to the funding section.

"All of the back-and-forth mostly happens through the list of stipulations we send back," Ogrodnik says.

The following is an example of how the checklist works:

• 17.2 Verbal consent/assent – waiver of documentation of informed consent

"Will this research include an informed consent process, but require a waiver of documentation of consent?

- No

- Yes, because the research presents no more than minimal risk of harm to the participants and involves no procedures for which written consent would normally be required outside of the research.

- Yes, because the only record linking the participant to the research would be the consent document and the main risk in the research would be the potential harm because of a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

Reviewer Comments Editor:

17.2: They have not requested a waiver of documentation of consent in 17.2, but there are no signature lines in the consent form. Do they intend to obtain signed consent or waive documentation? This needs to be clarified."[1]

Smart checklists use reviewers' time more efficiently by eliminating duplicate entries and making it easy to see what is incomplete. But they were labor-intensive to create, Ennever says.

"It was a lot of work, and we're very fortunate we had a computer expert, Khaled, who was able to make a change when needed," she says.

One of its chief benefits is that it serves as a good training tool for IRB staff, Ogrodnik notes.

"You catch everything on the first review," he says. "I wouldn't want to go back to the old system." ■

REFERENCE

1. Ennever F, Ogrodnik M, Khattar K. Smart checklists in the Boston Medical Center and Boston University Medical Campus electronic system. Poster presented at the Public Responsibility in Medicine and Research (PRIM&R) Advancing Ethical Research Conference, held Nov. 5-8, 2017, in San Antonio. Abstract: 33.

Preparation, Communication Key to Establishing IRB of Record

Nail down reliance agreement

The first time the Vanderbilt University and Medical Center IRB served as an IRB of record was 15 years ago — a decade before the concept began to catch on with multisite clinical trials and large IRBs.

The IRB also participated in an early-concept single IRB project in which five IRBs jointly developed standard operating procedures and took turns serving as the IRB of record. But this didn't work. It was very premature, says **Julie Ozier**, MHL, CIP, director of the human research protection program at Vanderbilt University and Medical Center in Nashville, TN.

Clearly, the concept had potential, and once the National Institutes of Health (NIH) supported it, the Vanderbilt IRB prepared for the change. *(For more information on the NIH single IRB policy, visit: http://bit.ly/2GQ1DdF.)*

When the recent Common Rule changes were announced, "in it was this mandate for a single IRB for all multicenter studies, and that's when we thought about what we could do to answer that call," Ozier says. "Our single IRB team was formed in late 2016."

Vanderbilt's IRB now has reliance

agreements with about 50 medical research sites, says **Kari Campbell**, PhD, CIP, regulatory compliance analyst in human research protection at Vanderbilt University and Medical Center.

There are 21 analysts that perform pre-reviews for the IRB, says **Jenni Beadles**, MEd, single IRB operations manager in human research protection at Vanderbilt University and Medical Center.

"We've taken those with a certain number of years of IRB experience and moved them into the role of the single IRB team," Beadles says. "It's been very beneficial overall to know you have point people who are well-versed with single IRBs."

The following are some of the steps the IRB of record takes to facilitate successful reliance:

• Garner institutional support. Some IRBs will not choose to be the IRB of record because they lack the necessary manpower to make it work well, Beadles says.

"We are very well-supported by our institution," she adds. "The decision depends on the resources available to you."

The NIH has published guidelines on how an IRB can charge for the single IRB review, so there is a possibility of some direct cost recovery, Ozier notes.

The NIH guidance, published June 21, 2016, states, "The additional costs associated with sIRB [single IRB] review may be charged to grants or contracts as direct costs, provided that such costs are well-justified and consistently treated as either direct or indirect costs according to applicable cost principles in the NIH Grants Policy Statement and the FAR 31.202 (Direct Costs) and FAR 31.203 (Indirect Costs)." *(The Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research can be viewed at: http://bit.ly/2F22cjQ.)*

• Establish IRB of record agreements. The IRB of record needs to reach agreements with institutions that will be relying upon it even before the first study.

"The first step is to reach out to other IRBs participating on a study or in a network to negotiate a reliance agreement," Ozier says. "The reliance agreement outlines who is responsible for what pieces."

> "WE MAKE SURE LOCAL TRAINING OF KEY PERSONNEL IS ACCURATE AND COMPLETE. ONCE WE NEGOTIATE A RELIANCE AGREEMENT, WE KNOW ABOUT THE INSTITUTION AND THE INSTITUTION'S TRAINING."

Once an agreement is ironed out for a group of research institutions, renegotiating isn't needed when new studies begin, Campbell notes.

"It's a lot easier to negotiate moving forward because you're already a member of that group," Campbell says.

The preparation work includes gathering information about each institution's local context, paving the way for the IRB of record to begin a study review, Ozier says.

Establishing a single IRB can take time, but preparation makes everything that follows much simpler.

"The way we designed the process is we can review an entire study for the lead site first, and then, once that's approved, it gives us the master study, and we can add on the other sites as children to the master," Ozier explains. "So each site can be added quickly that way, as you already know the study is approvable."

The additional sites bring their local context and questions.

"We've had one study that had an excess of a dozen to two dozen amendments to add, and it does create some fatigue for the committee," says **Heather Phillips**, MBA, CIP, regulatory compliance analyst in human research protection at Vanderbilt University and Medical Center.

But it helped having the study approved for the lead site first. This gave the IRB of record time to focus on the local context of the additional site, and it facilitated a more efficient review process, she adds.

• Survey relying IRBs to collect data about their local context. "We've used two surveys through an IT platform here at Vanderbilt, and we've sent that one to the IRB and to the relying investigator, who helps collect that information," Beadles says.

Survey questions include:

- Is there specific HIPAA language you have to use at your site?
- Is there a specific template you use?
- What subject injury language is used at your site?

For instance, the Vanderbilt IRB works with the ECHO network. ECHO is a research program launched by the NIH (http://echochildren.org/). It's designed to learn about early environmental influences on child health and development. A lot of questions for IRBs reviewing those studies involve

local laws and policies regarding children in research, Campbell says.

The goal is for the IRB of record to look at the overall risks of a study, while local IRBs assess the study according to their community's concerns.

• Assess training quality of relying IRBs. "We make sure local training of key personnel is accurate and complete," Campbell says. "Once we negotiate a reliance agreement, we know about the institution and the institution's training."

Each IRB and institution must be up-to-date on all required human subjects protection education and their individual organization's policies and procedures.

• Make learning a two-way street. "We actively learn from each other," Beadles says. "One way we are sharing information is through work with the Trial Innovation Network."

The Trial Innovation Network brings several institutions together to facilitate training and share best practice models. It's a collaborative national network that leverages resources from the Clinical & Translational Science Awards program (https://trialinnovationnetwork.org/).

"We hope to develop multiple models that other organizations can use," Beadles says. "They can come to our network and say, 'Here's what works for us.'" ■

The Search for Justice in the Human Genome

All things are possible, but will they be possible for all?

With sequencing of the human genome completed at the turn of this century, there was the heady expectation that the summit to great cures was about to be climbed like the iconic spiral staircase of DNA.

"Having the essentially complete sequence of the human genome is similar to having all the pages of a manual needed to make the human body," the NIH's Human Genome Research Institute explains on its website. "[Genome-based] research will eventually enable medical science to develop highly effective diagnostic tools, to better understand the health needs of people based on their individual genetic make-ups, and to design new and highly effective treatments for disease." *(For more information, visit: https://www.genome.gov/.)*

But what if this new frontier disproportionately benefits the haves over the have-nots, leading to exceptionally expensive drugs and treatments in an era when many Americans are struggling for access to basic healthcare?

That, warns **Jenny Reardon**, PhD, is exactly what is happening. The founder of the Science and Justice Research Center at the University of California in Santa Cruz, Reardon compares the current state of genome research to the blind that preceded the 2008 financial collapse.

"Are we sitting on top of a biomedical bubble that is about to burst?" she says. "People are going to lose trust in this system because no one understands how it works. A lot of people are making a lot of money off of it, but on the other end of the spectrum it is really aggravating the inequalities in the healthcare system."

To meet this research inequity in genome research, Reardon urges IRBs to return to the cardinal principle of "justice." This was one of the original core tenets in the Belmont Report outlining the ethics of human research.

In her new book, *The Postgenomic Condition: Ethics, Justice, and Knowledge After the Genome*, Reardon argues that issues like informed consent have overshadowed the human research principle of justice. One aspect of justice in medical research is that the gains will be realized by humanity in general, not solely to those with the wealth and healthcare access to benefit, she says.

"We've been really good at focusing on some of the other Belmont principles, especially looking at informed consent," she says. "But justice has not gotten nearly enough attention, and I'm not the only person to point this out. What made me begin to think about this in the context of IRBs is the legal scholar **Patricia King**, who sat on the presidential blue ribbon committee that wrote the Belmont Report. In the context of Tuskegee, that seemed like a real win. They were kind of elated about that and didn't do as much with justice, and she said later, 'It is my major disappointment.'"[2]

Now a professor of law, medicine, ethics, and public policy at Georgetown, King said in a 2004 oral history of the Belmont Report that, "In my view, though we stated a principle of justice, it's the forgotten principle."[2]

Now, with the level of research

underway with the human genome, Reardon argues that justice needs to be the guiding principle for IRBs and researchers.

"Who is going to access the end results of this research?" she says. "That is a core issue. In genomic medicine, we are producing these drugs that are inching toward the million-dollar-a-year category. Of course, people without health insurance won't get access."

Indeed, those with health insurance that have prohibitive copays and large deductibles could well be shut out from some new genomic breakthrough.

"They are just going to be priced out of their reach," says Reardon, observing the irony of political leaders who pour billions into medical research while showing near disdain for expenditures to ensure basic healthcare.[3]

"You might be benefiting now from all the investment and high-end genomic research, but if no one gets access to any of this then it's not sustainable," she says. "I think it is a train wreck waiting to happen unless we address the underlying structural problems with the system. To me, people turn to justice when they feel the dominant institutions don't serve them. They say this system is unjust."

Reardon's book calls for human genome data from more diverse populations, raising issues of informed consent, trust, and use of biological samples. Human research is certainly scarred by unethical actions toward vulnerable populations, some of whom will be reluctant to participate in research that will not benefit them.

"It's interesting the we are living in a moment where for decades nobody cared about sickle cell," she says. "Now, because it happens to turn out to be an ideal disease for CRISPR [Cas9 genome editing] technology because it affects a single organ — the blood — people suddenly want to pour money into sickle cell and do a clinical trial. Are they going to get enough people to participate in that trial?"

It's a fair question, as African-Americans predisposed to the disease will be asked to participate in research even as they struggle to keep basic healthcare. Past unethical research in this community needs no introduction. Did Tuskegee poison the well?

"For too long, this field has ignored the vast majority of people who are not high-end users and are not the ones purchasing designer drugs and fancy pharmaceuticals," Reardon says. "The elephant's in the room — I'm just naming it." ■

REFERENCES

1. Reardon, J. *The Postgenomic Condition: Ethics, Justice, and Knowledge After the Genome.* University of Chicago Press, 2017.
2. HHS. Oral History of the Belmont Report and the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Interview with Patricia King, JD, Sept. 9, 2004. Available at: http://bit.ly/2pdWs0t.
3. Pear, R. Medical Research? Congress Cheers. Medical Care? Congress Brawls. *The New York Times* Jan. 6, 2018. Available at: http://nyti.ms/2FhcugG.

Five Years in the Making, FDA Issues Final Rule on Data and Devices

The FDA issued a final rule, effective Feb. 21, 2019, to revise regulations about accepting data from clinical studies involving medical devices.[1]

The rule, titled, "Human Subject Protection; Acceptance of Data from Clinical Investigations for Medical Devices," updates FDA's standards for accepting clinical data from investigations in the United States and internationally.

Comments about the proposed rule suggested the rule should not be finalized until there are established harmonized international good clinical practice (GCP) guidelines for medical devices. The FDA's response was there already is a GCP standard for medical devices, called the "Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice."

Sponsors and applicants under the new rule must provide information about how their investigations conform with GCP. These include clinical data, supporting investigational device exemptions, premarket notifications, requests for De Novo classification, premarket approvals, product development protocols, and humanitarian device exemptions.

According to the published final rule, "FDA believes the requirements outlined in the rule allow the flexibility needed to accommodate the laws and regulations of other

countries. We also believe that conducting a clinical investigation according to a standard that meets the definition of GCP as provided in the rule will help to ensure the integrity and quality of the data and the protection of subjects."

The rule also allows sponsors and applicants to explain why GCP was not followed and to describe the steps they took to ensure that the data and results are credible and accurate and that the rights, safety, and well-being of human subjects have been adequately protected.

In general, the FDA agrees that data from clinical investigations that were not conducted in conformity with GCP may still provide useful information — even information that is relied upon to make regulatory decisions, the rule states.

"The intent of the rule is not to disallow the use of data from certain investigations, but rather to ensure FDA's decisions are based on scientifically valid and ethically derived data," according to the rule. "Conformance with GCP is one way to help ensure clinical data are credible, accurate, and ethically procured."

For more information, contact the Division of Industry and Consumer Education in the Center for Devices and Radiological Health at 1-800-638-2014, 301-796-7100, or dice@fda.hhs.gov. ■

REFERENCE

1. Human subject protection; Acceptance of data from clinical investigations for medical devices. *Fed Reg*. Feb. 21, 2018. Available at: http://bit.ly/2t1KhIC.

Into the Gray: Local IRBs Must Define Research

It's only fitting, with the revised Common Rule in limbo, that there should remain some uncertainty about what constitutes human research — and what doesn't.

"For IRBs, one issue that they should think about is how do they see their own purview," says **Carl H. Coleman**, JD, a professor of law at Seton Hall University in Orange, NJ. "Do they want to be reviewing things in this sort of borderline area? What is their constituency and how do they see their IRB's purview? The bottom line is that there are some gray areas. Whether they require IRB review, whether it is research — it's really going to depend on a judgment call."

The Common Rule defines research, in part, as an effort to create "generalizable knowledge," he notes, adding that it leaves ambiguity in discerning research from a hospital quality improvement effort or public health surveillance of disease.

"It's often hard to know where to draw that line between something that is just feeding back information into a quality program so it can be used to improve the program, versus developing new knowledge," he says.

A broad and indiscriminate definition of research for regulatory purposes could "sweep in many benign activities for which the costs and burdens of IRB review are not justifiable," Coleman warned in a recent paper.[1]

There was discussion of creating an "exemption tool," in the early iterations of the Common Rule, but the current version proposed for finalization jettisoned the idea.

"Based on the response and the comments, it seemed like they decided there just wasn't enough buy-in at this point," Coleman says. "I think it would be a good idea. It doesn't have to happen now, but one of the concerns with exemptions is that the process of applying for one [is laborious]. It's not as burdensome as going through the whole review process, but it almost defeats the purpose of having an exemption."

In any case, the generalizable knowledge definition remains an "imperfect proxy" by which to separate research from other activities, he notes.

"The idea is that there is something special when the use of [data] is for the development of generalizable knowledge," he says. "As if that is the only situation where you might be interacting with people or using their private data for reasons other than their own benefit. I think that is a false idea. It is not a perfect standard." ■

REFERENCE

1. Coleman, CH. Reining in IRB Review in the Revised Common Rule. *IRB: Ethics & Human Research*. November-December 2017;(39):6. Available at: http://bit.ly/2FEjQ1A.

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CME/CE QUESTIONS

1. **Which native American tribe successfully sued for return of their DNA after being subjected to unethical research?**

   a. Lakota
   b. Apache
   c. Havasupai
   d. Nez Perce

2. **In using Toyota lean methodology, the Seattle Children's Research Institute IRB has established "simple rules." What are these?**

   a. Simple rules are policies and procedures that are written in plain language.
   b. These are steps to follow to ensure an IRB follows all institutional policies when reviewing a protocol.
   c. Simple rules are a strategy to document how the IRB makes decisions about each study.
   d. None of the above

3. **When an IRB becomes an IRB of record, which of the following survey questions would help the IRB of record collect useful data on the relying IRBs?**

   a. Do you have specific HIPAA language you have to use at your site?
   b. Is there a specific template you use?
   c. What subject injury language do you use at your site?
   d. All of the above

4. **According to Jenny Reardon, PhD, which of the following core ethical principles must be emphasized in human genome research?**

   a. Justice
   b. Beneficence
   c. Cultural respect for people
   d. Informed consent

CME/CE OBJECTIVES

The CME/CE objectives for IRB Advisor are to help physicians and nurses be able to:

1. establish clinical trial programs using accepted ethical principles for human subject protection;
2. apply the mandated regulatory safeguards for patient recruitment, follow-up and reporting of findings for human subject research;
3. comply with the necessary educational requirements regarding informed consent and human subject research.