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INSIDE

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Recent Controversy About Conflicts of Interest Highlights Need for Strong Policies

A zero cap on gifts can work

By Melinda Young, Author

A recent report that a top cancer researcher failed to disclose in journal articles millions of dollars in payments from pharmaceutical and other companies has shed a spotlight on the uneven way conflicts of interest are managed at research institutions.

A researcher at Memorial Sloan Kettering Cancer Center in New York City had not ensured his financial ties to drug companies were published in research articles in *The New England Journal of Medicine*, *The Lancet*, and other journals (https://nyti.ms/2OdkypY).

The researcher resigned on Sept. 13, 2018, saying in a resignation letter that he hoped this incident would result in the medical community developing a more standardized system for reporting industry ties (https://nyti.ms/2N4Ohwz).

> "ACADEMIC PUBLICATIONS HAVE BEEN REPORTING ON THIS ISSUE QUITE A BIT IN THE LAST COUPLE OF YEARS. WE KNOW IT'S AN ONGOING CHALLENGE TO HAVE DISCLOSURES MADE IN RESEARCH INSTITUTIONS."

Memorial Sloan Kettering Cancer Center (MSK) senior media strategiest **Nicole H. McNamara** said the organization was unable to speak about the physician. McNamara referred *IRB Advisor,* via email, to information about the steps they have taken to create a task force that will assess the institution's policies and procedures for reporting and managing outside activities and industry-supported clinical trials.

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The task force will review policies, procedures, and training on conflicts of interest (COI) and identify best practices, including monetary and commitment limits. *(More information on the task force can be found at: http://bit.ly/2RdQjxF.)*

The MSK incident has caused some institutions to revisit their own conflicts of interest policies and practices.

"We definitely took a look at our own program after hearing that news," says **Kara Manning Drolet**, PhD, associate vice president in the Oregon Health and Science University (OHSU) research integrity office in Portland. Drolet also is the chair of the conflict of interest in research committee.

"This wasn't a shock," says **June Insco**, outside interests and conflict of interest manager in the office of regulatory affairs at the University of Michigan Medical School in Ann Arbor.

"Academic publications have been reporting on this issue quite a bit in the last couple of years," Insco says. "We know it's an ongoing challenge to have disclosures made in research institutions."

Ensuring researchers adhere to an institution's COI policies might be too challenging for a single IRB office. It is a task that needs dedicated oversight, review, and checking back with investigators to assess whether their information is accurate.

"The whole IRB system is based on the honor system," says **Charlotte Coley**, MACT, CIP, education and training manager in the office of human research ethics at the University of North Carolina at Chapel Hill. "I used to have an IRB chair who said, 'Trust, but verify,'" Coley says. "I tell board members what the red flags are for when something doesn't look right."

The regulations related to conflicts of interest might not change very often, but the guidance is more fluid. New advances in science and technology and societal changes can prompt an institution to reconsider its COI policies, Coley notes.

For example, researchers can patent their discoveries — even when these were funded by the National Institutes of Health (NIH) — to drug companies in exchange for royalties. This was not always the case, she says.

"And sponsors now are far more involved in the design of the study, and they want the data sent to them, and in the past wanted to control publication so if there is a negative result, they wouldn't let the researcher publish it," Coley adds.

These factors make COI rules important for checks and balances and to ensure participant safety. They also have made research institutions come up with stricter COI rules than they had previously. At the University of North Carolina, there is a $0 minimum beyond which researchers must report all funds and gifts. This means that even a pencil or notepad must be reported or not accepted, Coley says.

If researchers are paid to speak, this must be disclosed, she adds. "I remember years ago when drug companies would come in with lunches and give the residents reference books and do educational sessions."

Now, many medical and research institutions understand that even accepting a pen makes a person feel beholden to an institution, Coley says.

"There really is no such thing as a minimum amount that won't make you feel an obligation," she adds. "So I give out pens with our IRB's name, so now researchers have no excuse

not to call us with questions, and they can accept these because we're all part of the same family."

OHSU also prohibits gifts from vendors and pharmaceutical companies. "Researchers have to disclose all of their outside activities," Drolet says.

When a researcher is inconsistent with COI disclosures, this could be intentional or just confusion. "In his mind, something may be minimal or small or not important and not what he thinks is a conflict of interest," Coley says. "And when you're working with people, they become friends, and you trust friends."

One way to add consistency to the review of conflicts of interest is to delegate COIs that hit a certain institutional threshold to a conflict management plan.

"When we have someone on a research study that is somewhat related to a financial interest of the investigator, and if that interest is worth $5,000 or more or if they have equity in the company, then we will impose a conflict management plan for the research study," Insco says. "This puts requirements in place, depending on the nature of the conflict and nature of the research."

Consulting fees can be problematic, depending on the amount paid to the investigator. Research institutions should decide what amount is a threshold for what they would allow.

"If someone makes over $20,000 in consulting fees, we would not allow that person to be the principal investigator on a study unless there really are compelling circumstances," Insco says. "If it's $5,000 to $20,000, they could be a principal investigator with a conflict management plan, which allows them to disclose to colleagues they have an outside interest."

All members of the study team are subject to the same disclosure rules and conflict management plan policy, she says. *(See story about managing COIs, below.)*

Faculty members taking on the role of research sponsor for undergraduate students have to complete COI disclosures, Coley says.

"If a conflict of interest has changed, then they have lots of opportunities to update it," she says.

What IRBs and researchers should keep in mind is that even the appearance of a conflict of interest can taint research, suggesting it could be biased, Coley explains.

"Maybe it's excellent research, but anytime there's an IRB situation or where someone calls in to question whether you did something right, it casts a shadow over the research, and people might dismiss it," she says.

Coley reminds the IRB of the importance of following COI rules with regular educational updates on the subject.

"I do a 10-minute education session at the beginning of every IRB meeting, and conflicts of interest show up every now and then," Coley says. "When we were preparing for our AAHRPP renewal, we had our conflicts of interest officer come in and do an hour presentation."

At that time, there were a number of new board members, and the presentation helped them get up to date, she says. ■

Managing Conflicts of Interest Requires Time, Expertise

Check, verify, use Open Payments Data

Research institutions could improve their conflicts of interest (COI) management by devoting staff or departmental resources to the issue. Some larger research organizations place a COI manager within the regulatory affairs department or in a research integrity office. And they make COI review part of the research ethics review process.

"The way our system works is any human subjects application comes to our office before it goes to the IRB," says **June Insco**, outside interests and conflict of interest manager in the office of regulatory affairs at the University of Michigan Medical School in Ann Arbor.

"If we want a disclosure on the informed consent document, we'll ask for that before we send the application forward to the IRB," Insco says. "Our plan gives the IRB discretion to change what subjects see."

Monitoring COI requires help from the institution, says **Kara Manning Drolet**, PhD, associate vice president in the Oregon Health and Science University (OHSU) research integrity office in Portland. Drolet also is the chair of the conflict of interest in research committee.

"We have to make sure COI disclosures are being made to journals," she says. "It's difficult, given limited staff and with all the other things we need to do. We consider some of the higher-level conflicts and monitor people in those categories more than those with lower-level conflicts."

Insco and Drolet provide the following tips on how to improve conflicts of interest management:

• Monitor publications and disclosures. "When we do an annual review of somebody's disclosure form, we monitor publications," Drolet says.

"We do a PubMed search and look at articles where investigators should have made a public disclosure statement, and if it's not there, we talk to the investigator about it and find out why it's not there," Drolet says. "We require a correction to the journal if we find they haven't disclosed."

The University of Michigan also checks on publications each year. "Once a year, we ask them to provide us with copies of publications to see if they did, in fact, disclose as they're required to do," Insco says.

Researchers send letters to journal publishers, outlining their COIs. If the journal fails to publish the disclosure, the investigator will need to show the COI staff a copy of the letter, she explains.

"Then we contact the publication and tell them to put in the disclosure online," she says. "One of the challenges for investigators is that journal-to-journal requirements for disclosure vary; there is no standard practice, and that makes it difficult to get the right disclosures out there."

Even if the journal publishes the disclosure solely online, it is sufficient because people reading the article would have access to the disclosure, Insco notes.

Sometimes there are misunderstandings and mistakes that lead to problems with journal disclosures. "Last week, we found a disclosure where the lead author failed to disclose," Insco says.

It turned out the journal used a disclosure form that asked for financial interests of the past 12 months. The University of Michigan's own COI rules did not limit disclosures to the past year, so the researchers should have followed his institution's rules, she says.

"ONE OF THE CHALLENGES FOR INVESTIGATORS IS THAT JOURNAL-TO-JOURNAL REQUIREMENTS FOR DISCLOSURE VARY; THERE IS NO STANDARD PRACTICE, AND THAT MAKES IT DIFFICULT TO GET THE RIGHT DISCLOSURES OUT THERE."

"The author said, 'I haven't worked for this company for a year, so I don't have to report it,'" Insco explains. "But in our minds, the principal investigator had received many payments from this company over the years."

• Include COI disclosures in IRB submission template. "We have a section in our template that asks, 'Who could benefit financially?'" Insco says. "For example, if someone is a consultant to a company, we ask the study team to put in the sentence, 'In interest of transparency, we would like you to know that Dr. Jones is a consultant to the sponsor of this study.'"

If the investigator's consulting relationship is over, then the wording would include the past tense: "We would like you to know that Dr. Jones was a consultant to the sponsor of this study."

• Focus on more significant COIs. "We're looking at what we consider to be those higher-level conflicts, and are we capturing all the ones we want to capture?" Drolet says. "If investigators are doing higher-level consulting, we might start including those in the monitoring requirements we're already using."

Conflict management plans at the University of Michigan can be applied in a variety of conflict of interest circumstances, including significant financial COI and others.

For example, there might be a situation where a co-investigator on a study should not be the person who determines whether a participant's adverse events are directly related to the study drug. "Someone else has to determine the relatedness," Insco says.

"Over the years, the IRB and conflict of interest committee have had a general dialogue about these issues," she adds. "Sometimes, a situation arises where someone is very conflicted and also is a senior faculty member, so we might say, 'You cannot be the principal investigator because you're too conflicted.'"

Then, the senior faculty member might return with a junior staff member and say this person could be the principal investigator and the senior person will be the co-investigator. If the junior person does not have the experience and influence

to carry out that PI role, then the COI office will not agree to the arrangement or will arrange for an ombudsman to work with the junior researcher, she explains.

"That ombudsman would have to reach out to the junior person and talk to them a couple of times a year, to keep a comfort level and make sure they don't feel coerced in any way by that conflicted party," Insco says.

• **Check Open Payments annually.** Open Payments Data is a federal government website with a search tool to find payments made by drug and medical device companies to physicians and teaching hospitals.

Anyone can enter a physician's (or teaching hospital's) name and search for information about the general payments the person has received, research payments, ownership and investment interest, associated research transactions, and disputed payments. The tool also provides context, showing where the person's payments stand on a line graph that lists the national mean and the specialty mean.

"Every year, when Open Payments Data comes out with new information, we download the data and we compare anybody who received $40,000 in payments to what they told us at the institution," Insco says. "This gives us a systematic look at the people who are getting a higher level of payments, including travel."

Journal editors could also check principal investigators' disclosure information against what is listed on Open Payments Data, she notes.

"To rely on someone to write down all their conflicts is not as necessary as it was before Open Payments," Insco says. "They have it at their fingertips to do themselves." ■

Meaningful Informed Consent Tells People What They Want to Know

What is the 'reasonable person' standard?

The new Common Rule puts forth a reasonable person standard for informed consent (IC). IC forms should provide information that a reasonable person would like to have and that would help an informed person make a decision on whether to participate in a study.

The reasonable person standard comes from tort law and criminal law about negligence, says **Rebecca Dresser**, JD, professor of law emerita at Washington University in St. Louis. Dresser also is the author of the book *Silent Partners: Human Subjects and Research Ethics*, published in 2016 by Oxford University Press.

"When you're thinking about whether somebody harmed somebody else — not intentionally — should they have been aware it was risky?" she explains. "In law, you're supposed to judge that — when should a reasonable person have known that driving in this way was risky and there was a possibility of hurting someone? So a reasonable driver wouldn't have done this."

Traditionally, the judgment is made by the jury, peers of the defendant. In the research world, there are no juries — only IRBs to assess ethical considerations.

"How are we supposed to know what reasonable people should know?" Dresser says. "Most direct comparison comes from law on informed consent in medicine."

Most cases involving lawsuits and medical or research issues do not go to trial. They are settled after lawyers on each side and a judge sit down and decide on a reasonable way to settle the claims, she says.

"They make implicit judgments on whether the standard was met, based on their own intuition," Dresser says.

One way for IRBs and researchers to determine whether informed consent meets the reasonable person standard is to ask themselves these questions of the informed consent document: "What is it you wish you had known, and what is it you didn't really need to know?" she says.

The informed consent should be designed based on those questions, and IRBs can assist.

Another way to improve informed consent according to the reasonable person standard is to seek empirical evidence of what people want to know when they read an informed consent, Dresser says.

"Members of the public can give you some information, but you can get better information from people who have actually been in research," she says. "They can say, 'I went through this cancer study, and this is what I wish I had known.'"

Focus groups and surveys of former research participants can help obtain useful information.

"Don't ask them whether they want to be in a study or not," Dresser says. "Ask them about what they would want to know, every facet of

research, because we need to know about their perspective."

The same strategy of seeking input from research participants also can be used when creating broad consent related to studies using biospecimens.

"Give them background information about the signs and ways and information about how biospecimens can be used in research," Dresser says. "Even if you just say it's for cancer research, there are different variations in that."

For instance, some potential research participants will not want their samples used in reproductive research where they are creating embryos, she says.

"With both general informed consent and broad consent, there is room for more targeted research to survey what we have now and what we don't have a lot of information on — so let's do surveys, interviews, and focus groups," Dresser says.

"Some people say about this new Common Rule provision that maybe this is an opportunity to remind ourselves that this is what we're supposed to be doing," she says. "We're not targeting research to doctors and researchers, we're targeting it to people who don't have that background. So where can we find out more about what kind of data we need to help us get better at this?"

Here are some of the questions non-research people might want to know:

- Will the study's findings be used by a for-profit company or by a not-for-profit organization?
- Will someone tell me if the study changes, and how will they contact me?
- Who could I call if I see something in the study that I do not like?

There is qualitative data. The drawback is that the various research studies about informed consent have not been comprehensively reviewed. "People do these wonderful studies and publish them, and then that's it," Dresser says. "No one is saying, 'OK, let's do a mega study on everything we've found out and put it in digestible form so IRBs and researchers can use it. That's the missing step."

The bottom line is that IRBs might decide under the new Common Rule that they need to do more than what they previously did to apply the reasonable person standard.

"People on the IRB are thinking of what they would want to know or what the people they know want to know," Dresser says.

"IRBs have been trying to use the reasonable person standard, and it's been speculative and informal rather than evidence-based." ■

NIH Reaches Out to Native Americans to Join All of Us Study

Government working to restore trust in research

The National Institutes of Health (NIH) is treading carefully and erring on the side of communication and inclusion in asking American Indian and Alaska Natives to participate in the All of Us precision research initiative.

As part of this ambitious project, the NIH is seeking the DNA of 1 million Americans that reflect a broad diversity of racial and socioeconomic conditions. The precision medicine initiative will use whole genome sequencing and other cutting-edge tools to create, aggregate, and analyze individual health data for years into the future. *(For more information, see the April 2018 issue of* IRB Advisor*.)*

A Native American working group has delivered a report to the NIH about the complex issues to be addressed if tribes are to participate. The report is under review and the NIH currently has a moratorium on soliciting Native Americans to participate in the project until the issues are addressed.

"We are in the very early stages of information gathering and consulting so we can meaningfully engage these important communities," says **Alyssa Cotler**, MPH, director of communications and marketing for the NIH All of Us Research program. "We'd be happy to have a discussion with you at a later time after we've completed our consultation."

The report says many tribal nations are reluctant to participate in biomedical research due to "historical transgressions by both the federal government and researchers. The history of the government's mistreatment of tribal nations includes forcible removal of tribes from their lands and attempts to eliminate their way of life, their social structure, and their culture."[1]

Among the various examples cited about researchers, tribes report being misled about a study's aims, publication of negative health information like use of alcohol, and subsequent use of biospecimens by later researchers that did not consult the native Americans.

"Tribes have also reported that researchers who have conducted studies on tribal lands failed to report to the tribe on their results," the report states. "This has left tribal members feeling that they were used for the researcher's own professional advancement and that they received no benefits in return."

However, Native Americans have incentives to participate. They have a history of health problems brought on by poverty and social disparity, including a shorter life expectancy, high rates of liver disease and cirrhosis, diabetes, and suicide. In another striking example cited in the report, the infant mortality rate in American Indians and Alaska Natives is 60% higher than in whites.

Cynthia Pearson, PhD, a professor in the school of social work at the University of Washington in Seattle, is developing a curriculum to teach people about ethical research with American Indian and Alaska Natives.

"This is an excellent report, well thought out, and put together by a very astute group of individuals," says Pearson, who is not on the NIH panel. "It clearly and succinctly covers some of the most important issues to consider when conducting research with American Indian and Alaska Native communities."

The report[1] by Tribal Relations Working Group outlines a series of themes and conditions that must be addressed by the NIH if native Americans are to participate in All of Us. These include:

- showing respect for tribal sovereignty;
- acknowledging that tribes — not genetics — establish an individual's membership;
- acknowledging the history that American Indians and Alaska Native individuals and communities have had with the government;
- remaining responsive to the indigenous community as the program continues.

In addition, the plan for the All of Us Research to use a single IRB of record for the program may run afoul of tribal communities.

"While a single IRB may be sufficient for other populations, because of tribal sovereignty, NIH's single IRB requirement does not apply to tribal nations," the working group reported. "Therefore, All of Us must also obtain approval from a tribal and/or Indian Health Service (IHS) IRB, as applicable, when recruiting on tribal lands or at a tribal facility. When a tribe has an IRB, they have jurisdiction first, before the IHS IRB. When recruitment for research takes place on tribal lands, the tribe and the tribal IRB have jurisdiction."

The program should seek to build trust through frequent contacts and provide cultural sensitivity training to address the ethical and cultural issues of Native Americans, the panel advised.

Spero M. Manson, PhD, director of the Centers for American Indian and Alaska Native Health at the University of Colorado Anschutz Medical Campus, is co-chairman of the tribal working group. He spoke to *IRB Advisor* about the obstacles and opportunities to Native American involvement in All of US in the following interview.

IRB Advisor: The report cites several historical examples of indigenous people being misled or misused in the context of human research. How did we get to the point now where you are trying to facilitate a way to join the All of Us project?

Manson: Under Dr. Francis Collins' leadership, work proceeded — now 20 years ago — to map the human genome. American Indian and Alaska Native communities did not participate to the extent that was desired by the NIH. It was largely because of the lack of attention to all the sensibilities that surround research in native communities. There is a long historical set of circumstances that we recapitulate in the report. To Dr. Collins' credit, when that work on the human genome translated into the precision medicine initiative, and now the All of Us research program, he realized that he needed to encourage outreach and education to American Indian and Alaska Native communities.

We knew this could enable us to examine the interaction of our genomic, lifestyle, and behavioral factors that contribute to risk, and ultimately may help us target therapeutics more effectively in addressing a wide spectrum of various kinds of diseases and disorders.

IRB Advisor: So, your committee was formed in part to guide and facilitate this NIH outreach.

Manson: The NIH began soliciting tribal communities' input about concerns, and the types of recommendations that might follow from those concerns, to ensure appropriate and full engagement in the All of Us Research program. That's the history behind the formation of the tribal working group. Our membership represents tribal communities, providers, family advocates, etc. We met beginning in October 2017 by phone repeatedly — and then ultimately face to face in March 2018 — to identify the major

areas of emphasis that a guidance document of this type should have.

IRB Advisor: While you do include recommendations, the report also raises a lot of issues that the NIH needs to be aware of in involving indigenous people in research.

Manson: It was clear that the document needed to perform several different functions. One is, we were constantly impressed by the lack of remembrance or just simple ignorance surrounding these issues in tribal communities. We thought it was really important to highlight some of the key factors regarding tribal sovereignty and matters of historical traumatic circumstances in terms of research with native communities. There was careful attention to that.

It has also been our experience that many people — not just at NIH, but throughout the federal government — are not aware of the structure, process, and organization in tribal communities. We saw a major role of this document of being one of education — placing the research experience of tribal communities within that historical context. There are a series of recommendations in there that are meant to encourage inclusion of American Indian and Alaska Native representation in domains around governance, protections, and review.

IRB Advisor: You note that the report has gone through a government-tribal reconciliation process. Why is that important?

Manson: Federally recognized tribes represent domestic sovereignties and thus constitute a form of government that our federal government needs to acknowledge and work with as co-equals.

IRB Advisor: What stage are you at now with this process?

Manson: Letters are being drafted to tribal leaders across the country about this particular guidance document. This is a strategy for engaging tribal leadership and other representatives of tribal communities to make sure that they are aware of it, that they have access to it, and that they have an opportunity to provide comment. That will take the next three to four months, and at that time, we anticipate it will be largely adopted in its current form.

"IT HAS ALSO BEEN OUR EXPERIENCE THAT MANY PEOPLE — NOT JUST AT NIH, BUT THROUGHOUT THE FEDERAL GOVERNMENT — ARE NOT AWARE OF THE STRUCTURE, PROCESS, AND ORGANIZATION IN TRIBAL COMMUNITIES."

Then it will return to NIH, and assuming that they concur and adopt it, the current moratorium on the outreach recruitment of engagement of American and Alaska Native people in the All of Us research program will be lifted. It's important to note that the NIH felt so strongly about the importance of this kind of guidance and critical nature of the relationship with tribal communities that they put a moratorium on the recruitment of all American Natives until this guidance document has been fully vetted by tribal leadership.

IRB Advisor: So you took that as a show of good faith?

Manson: I think the NIH moratorium on recruitment of American and Alaska Natives in the All of Use program is a very clear indication of the nature of their commitment to doing it right. We are taking time and making sure that it is very adequately presented to tribal leadership in a meaningful and authentic way.

IRB Advisor: Can the historical atrocities be overcome? Can enough trust be restored that you will get good participation from these indigenous communities?

Manson: Absolutely, we are already seeing some indications of that emerge. It is not across the board yet because I think there were some communities violated more fully and aggressively than others. We see different levels of trust being established across the county. This is another move to attempt to do that more broadly and nationally. I think that the attention the NIH has given to this matter in the context of this precision medicine All of Us research program is being well received by the tribal communities.

IRB Advisor: The report notes that tribes may have individual IRBs that need to be respected and brought into the process.

Manson: As part of the outreach program, there will be discussion on mutual collaborations between tribal IRBs and community boards and the All of Us program. One of the recommendations in the report is that there actually be an American Indian or Alaska Native appointed to the All of Us research IRB. So that presence is there at the highest level of review. I think there are a variety of different options that are available, none of which are likely to be a panacea. We just have to navigate our way through these matters.

IRB Advisor: It may surprise some not familiar with tribes and indigenous ways that membership to a certain tribe is not necessarily dependent on a DNA test from some of the popular swab kits on the market.

Manson: Yes, people use these and say suddenly 'I've realized I'm 30% Native American. How do I go about acting on that and become a tribal member?' There is a misconception about how American Indian and Alaska Native tribal membership is defined and implemented. As a part of their sovereignty, each tribe is authorized to development their own criteria for membership.

In the vast majority of tribes, it is something called "blood quantum," which is a percentage of hereditability or heritage that can be documented through descent in birth records. The Bureau of Indian Affairs is the central archive for all of that information. So in some tribes you have to be able to demonstrate a 25% blood quantum, and in other tribes, it is 50%. There are also tribes that don't have a blood quantum criteria. For example, the Cherokee Nation of Oklahoma. Their criteria is that you are able to demonstrate descent from one of the original signatories to the Dawes Act in the late 1800s, which was the federal action that actually defined the relationship between the federal government and the Cherokee Nation. So, you can see then that estimates of ancestry as reflected in these DNA assessments don't align with tribal definitions.

IRB Advisor: How do you view this process as an individual Native American?

Manson: I and my family are from the Turtle Mountain reservation in North Dakota. We are from the Pembina Chippewa tribe. It is very much a part of one's identity, but I am also a father, a grandfather.

We talk these days about identify in terms of intersectionality. That means there are different aspects of who we are that come together in a variety of different ways to understand our place in the world culturally and otherwise. Identity is very important, but it is identity in context: understanding how that identity can pose risk or serve to protect one from the contemporary pressures that modern day life poses for Indian people. ■

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Reporting Individual Results to Research Participants

An idea whose time has apparently come

Noting that IRBs historically have "actively discouraged the disclosure of research results to individual participants," a recently published consensus report[1] calls for a paradigm shift toward transparency and disclosure of findings to research subjects.

"Our push toward more disclosure, we believe, is part and parcel of the larger cultural transition toward more engagement, collaboration, and transparency between investigators and research participants," states the report by the National Academies of Sciences, Engineering, and Medicine.

This will not be done overnight, as the report calls for sweeping changes that include establishing a system to ensure accurate lab results are being reported to participants in studies and clinical trials.

In the interim, IRBs and researchers should start discussing ways individual results could be fed back to participants. If the Common Rule is finalized next year as currently proposed, the informed consent process would include information to participants about whether their individual results will be returned.

The report cites a "longstanding tension" in biomedical research between divulging or withholding results that may be poorly validated. Thus, investigators and IRBs often have asked research subjects to participate for the common good without expecting an individual breakdown of the findings.

"Investigators drop into communities or people's lives, engage with them in often very personal ways, and then take off, never to be heard from again," the report states. "Yet, people are curious about themselves, particularly about their health and their family's health, leaving a sense of frustration and loss

when investigators take but do not share."

The rise of genetic research has driven this trend, as individual data heretofore unimagined is available to researchers. There have been longstanding exceptions to the general rule of nondisclosure, such as "duty to warn" if some important health concern is identified in a research subject. A more general argument is emerging that subjects should have access to their genetic data if they participate in such a study.

To gain more insight into this ambitious initiative, *IRB Advisor* talked to **Jeffrey R. Botkin**, MD, chairman of the National Academies panel and the associate vice president for research and professor of pediatrics at the University of Utah School of Medicine.

IRB Advisor: The report cites the need for a paradigm shift, which implies this is a beginning point that will take some time for full adoption.

Botkin: As the report emphasizes, we hope we're going to see a gradual transition of more return of results over time. There are a variety of different pieces that will have to come together to make it more appropriate and more feasible. But right now, it is still possible in a lot of circumstances. Investigator sponsors certainly ought to be asking the question on a regular basis. Maybe, the answer is we are not ready yet, but I think it is appropriate to begin thinking in those terms.

IRB Advisor: Your report argues that full disclosure to human subjects will make research stronger.

Botkin: We think it is an opportunity to expand the relationships with research participants in a way we know participants appreciate. They often will want results and expect results even when investigators have advised they are not going to get them. It is something that is valued by people, and we think it is going to strengthen the relationship between investigators and participants, and that is going to have a lot of positive impact on the research process.

IRB Advisor: Favoring a case-by-case approach, the report recommends moving beyond firm rules (e.g., those in the Clinical Laboratory Improvement Amendments [CLIA]) that stipulate when results may be disclosed by clinical labs. However, noting that no such alternative exists for research labs, the report recommends that the NIH develop a "quality management system" for research labs.

Botkin: We are very sensitive to the concerns in this domain, which are that investigators are going to be returning results that are by their very nature uncertain because it's research. The downside to returning results are that people may make important decisions based on information that proves to be wrong. One way to minimize that is to make sure that the laboratory quality standards are high. At this point, we've got CLIA, which is excellent for clinical laboratories and for some research laboratories. But it is not necessarily the right thing for all research laboratories. We think a better way to go would be to develop an independent quality standard system specially for research laboratories so that everybody can have a higher level of confidence in the results.

IRB Advisor: Have you had some pushback on this lab recommendation?

Botkin: One of the things in the report is to have the IRBs become more familiar and have access to expertise to help guide them on laboratory quality issues. We did a webinar last week, and one of the questioners sort of got the impression that we are asking the IRBs to judge the quality standards of laboratories in their institutions — to become sort of regulators of laboratory standards. That's really not what we are looking for. We are looking for IRBs to become familiar with quality standards — to have that experience on the panel or available to the panel to provide input on quality issues related to a particular laboratory result. So, it is an expansion of responsibilities for the IRBs to have input and more

knowledge and expertise in that laboratory quality domain.

IRB Advisor: Are you advocating that IRBs generally take a broader view of when individual results could be given to participants?

Botkin: Yes, very much so. I think that is a question that ought to be asked in the context of each project that comes to an IRB. Hopefully, folks have asked that question before it gets to the IRB. If you think results can be returned, then you ought to put that in your protocol and have the process and timing outlined there so the IRB can take a look at that. Conversely, if you don't think it is appropriate to return results for whatever reason, then you should outline why you think that is the case, and the IRB can look at that as well.

IRB Advisor: You mention this question is now in the latest iteration of the Common Rule. If the default position is to inform participants, would the Common Rule or other regulations have to be changed?

Botkin: I don't think we need regulatory changes at that level in order to accomplish this. I will say that the regulations don't require anybody to return results, so it is not a matter of conforming with any regulatory requirements in that regard. In order to comply with regulations, IRBs don't have to develop policies and procedures related to this issue. But we think it is advantageous and IRBs ought to play a role in this.

IRB Advisor: What about the old rationale that research subjects participate in studies to benefit future generations? Does this focus on individual results undermine that to some extent?

Botkin: I don't think so because we see the return of results in some circumstances as something that is appreciated by participants. We don't really see that as compensation, if you will, for the time, effort, and risks that people are willing to put into research. They are still contributing quite a bit out of their own goodwill. That situation won't change even if you get some results back. So, it is not a contractual sort of thing. We still think it is important to maintain the altruism that is part of the people's decision to participate in research. ■

REFERENCE

1. Botkin JR, Mancher M, Busta ER, et al. Committee on the Return of Individual-Specific Research Results Generated in Research Laboratories. Returning Individual Research Results to Participants: Guidance for a New Research Paradigm. National Academies of Sciences, Engineering, and Medicine, 2018. Available at: https://bit.ly/2EbA9m9.

CME/CE QUESTIONS

1. **Which of the following is a useful way to independently verify conflicts of interest disclosures by researchers?**
   a. Ask department heads to sign off on researchers' disclosure forms
   b. Have investigators report any financial COI twice a year
   c. Check Open Payments Data, a government website to compare with disclosures
   d. None of the above

2. **Which of the following would *not* be a common question that research participants would like to have answered in informed consent, according to Rebecca Dresser, JD?**
   a. Where do I collect my monthly check for participating in the study?
   b. Will the study's findings be used by a for-profit company or by a not-for-profit organization?
   c. Will someone tell me if the study changes, and how will they contact me?
   d. Who could I call if I see something in the study that I don't like?

3. **To stay abreast of science, American Indians and Alaska Natives agreed that tribal membership will be determined by DNA in the All of Us initiative.**
   a. True
   b. False

4. **According to a National Academies report, IRBs historically have done which of the following regarding return of individual results to research subjects?**
   a. Actively discouraged it
   b. Required it to be in compliance with the Common Rule
   c. Encouraged it as a form of compensation for participating
   d. Left it up to individual researchers

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