IRB ADVISOR

YOUR PRACTICAL GUIDE TO INSTITUTIONAL REVIEW BOARD MANAGEMENT

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INSIDE

AHC Media

New Draft Recommendations and Checklist for Written Policies

Checklist should make IRB paper chase easier

By Gary Evans, Senior Staff Writer

Everyone loves paperwork. Or not. For IRBs facing written documentation demands, help may be at hand.

Two leading federal agencies in human research have issued draft recommendations and a user-friendly checklist to help IRBs ensure they have appropriate written documentation for key procedures and functions.

The Office for Human Research Protections (OHRP) and FDA recently issued the guidance to assist IRBs in preparing and maintaining written policies and procedures.[1]

"This draft guidance, when finalized, will represent the OHRP's and the FDA's current thinking on this topic," according to the agencies. "You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations."

> "THE IRB'S WRITTEN PROCEDURES SHOULD BE REVIEWED ON A REGULAR BASIS AND UPDATED AS NECESSARY TO ENSURE THEY REFLECT THE IRB'S CURRENT PROCESSES."

When finalized, the joint draft guidance will replace the ORHP's 2011 *Guidance on Written IRB Procedures*, and the FDA's 1998 *Appendix H: A Self-Evaluation Checklist for IRBs.*

"The IRB's written procedures should be reviewed on a regular basis and updated as necessary to ensure they reflect the IRB's current processes," the draft recommendations state. "When IRBs develop and follow clear written

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procedures, we believe there is a greater likelihood that the rights and welfare of human subjects are protected."

Though as mentioned the approach is somewhat flexible, the agencies require written documentation for the initial and continuing review of research, reporting findings and actions to the investigator and the institution, and determining which projects require review more often than annually.

Written documentation is also needed to show which projects need verification from sources other than the investigator documenting that no material changes have occurred since previous IRB review. Written policies are also required to ensure prompt reporting to the IRB of proposed changes in a research activity.

In addition, policies must reflect that any changes in approved research — during the period for which IRB approval has already been given — may not be initiated without IRB review and approval. The only noted exception to this is if the changes are necessary to prevent immediate hazards to human subjects, OHRP and FDA report.

Furthermore, the agencies indicate in the draft document that written documentation is needed to ensure prompt reporting to the IRB and other appropriate institutional and regulatory authorities of the following:

- Any unanticipated problems involving risks to human subjects or others.
- Any instance of serious or continuing noncompliance with the applicable HHS and FDA regulations or the requirements or determinations of the IRB.
- Any suspension or termination of IRB approval.

If this all sounds like a winding labyrinth of paperwork, remember the new *IRB Written Procedures Checklist* can be used to navigate the regulatory requirements and recommendations for IRB written procedures. The regulatory requirements are broken down into sections on the checklist, which denotes the various written criteria under each of the major regulatory areas. *(The checklist is available at: http://bit.ly/2b8wxDd.)*

Avoid simply listing the various regulations in favor of describing the IRB operations necessary to meet the requirements. The draft checklist suggests topics to cover in written procedures to make sure your IRB describes its primary oversight functions.

"For example, if an IRB reviews studies involving children as subjects, the IRB should have written procedures that describe how the IRB ensures the review of such research is in accordance with the regulatory requirements for the additional protections for children," the draft guidelines state.

That said, the agencies do not provide prescriptive details and minutia that will vary by the IRB.

"[This] gives IRBs the flexibility to establish procedures best suited to their own operations," the draft states. "Developing robust IRB written procedures involves a comprehensive and critical assessment of the IRB's responsibilities, functions, operations, and organizational structure. IRB written procedures should be sufficiently detailed so that IRB members and administrative staff understand how to carry out their duties consistently and effectively in ways that ensure that the rights and welfare of subjects are protected, and that the IRB operates in compliance with the regulations."

The written procedures should

specify which position title (e.g., IRB Administrator) is responsible for the tasks described, as this is preferred to listing names that will have to be updated with personnel changes.

"IRBs should consider making their written procedures available to investigators to ensure investigators are aware of the IRB requirements, and to facilitate investigator compliance with IRB requirements," OHRP and FDA recommend. "Step-by-step operational details in written procedures also help regulators understand how the IRB operates and fulfills its regulatory responsibilities."

Editor's note: Comments and suggestions regarding the draft document should be submitted by Oct. 3, 2016. Comments can be submitted electronically at http://www.regulations.gov (Docket Number FDA-2016-D-1605). ■

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How Can Teaching Dull Regulations Evolve into Excitement and Real Learning?

Answer: 'ReguBingo'

People working in human research need to be well-educated about IRBs and federal regulations, but how well are the classes really working if learners appear glassy-eyed and confused?

This is the question that led one IRB to create a novel way to teach regulations: ReguBingo.

Instead of relying on didactic lectures, IRB instructors hand out ReguBingo cards and let the games begin.

"People were folding their arms and didn't want to hear another presentation," says **Armida Ayala,** MHA, PhD, director of the Southern California Kaiser Permanente IRB in Pasadena.

"We were using the didactic method, a teacher-student relationship, to teach the regulations, so we decided to shift toward a more interactive method," Ayala says.

"The didactic method is very important because it creates consistency," she explains. "But it results in little interaction between students and teacher."

Ayala had mentored under Paulo Freire, who had been an education director in Brazil. Freire's education model called for not treating learners as empty accounts to be filled by the teacher, but rather as active partners in learning, Ayala says. "He taught me the participatory impact of education."

It seemed to Ayala that she could use those skills to improve IRB regulatory education.

"I asked people about their glassy eyes and why the lectures were not filling their needs," she recalls. "They said those were very boring and not fun and that regulations are boring."

Taking up the challenge, Ayala came up with Bingo-type game designed with illustrations, regulatory terms, and definitions. *(See how ReguBingo works, page 100.)*

"Gamification is an approach to engaging employees in training activities and to reinforce the value of a company," Ayala says. "Sessions have to be fun and designed to increase awareness of regulations."

After piloting the ReguBingo game with 25 nurses, she found that their knowledge of the regulations covered in the game had increased by 80% between the pre-test and post-test.

"We thought, 'This can't be,'" Ayala says.

The game also was successful, although not by such a large difference, with IRB staff and researchers, she says.

With positive initial results, the IRB made ReguBingo games to cover a variety of topics, including conflict of interest, generalizable knowledge — quality versus research, continuing review, elements of informed consent, and HIPAA.

Each ReguBingo game begins with a teacher whose goals are to be quick, witty, and make it fun, Ayala says.

Attendees have incentives, such as inexpensive water bottles, rain jackets, and healthy food, offered as prizes for winners. Teachers tell knock-knock jokes about HIPAA and do whatever it takes to generate excitement. Participants are encouraged to shout out if they win.

"We have so many funny things around this, and people laugh a lot

because it's silly," Ayala says. "It's a way we can get them excited."

So far, more than 60 people, including nurses, doctors, pharmacists, IRB members, IRB staff, researchers, and others, have taken the ReguBingo class over five different sessions.

ReguBingo instructors also offer case study examples to illustrate any particular regulatory policy.

"We do case discussion and policy guidelines, presenting these along with a game so they relate to conflicts of interest in research," Ayala says.

IRB staff answer questions from the audience and introduce other experts.

For example, the compliance department joined the sessions to talk about how to mitigate conflicts of interest or HIPAA breaches.

"One case we discussed at length involves Andrew Wakefield, the British gastroenterologist who was stripped of his medical license after conducting fraudulent research involving the vaccine for measles, mumps, and rubella," Ayala says.

Wakefield published a paper in 1998 in the *Lancet* that suggested there was a link between the MMR vaccine and autism in children. Later, he was found by the British General Medical Council to have engaged in misconduct, including failure to obtain informed consent, and having conflicts of interest.

"Wakefield was charged with conflicts of interest because he recruited children through his son's birthday party and would draw their blood without parental consent," Ayala notes. "He conducted his study without IRB approval, and he developed a company that he owned and that was in his wife's name."

The study created hysteria over vaccination and misrepresented the results of his research, and he planned to benefit financially from his anti-vaccine claims, Ayala says.

"So the teacher has to be very knowledgeable about cases and things people may not know about," Ayala says.

Plans are to create more ReguBingo games until all of the human research protection regulations are covered, Ayala says.

The IRB started with games related to topics where researchers appeared to have confusion or questions, she says. "Right now, we're covering those things that are very controversial and in-demand." ■

ReguBingo Sample is Focused on Conflicts of Interest

Add cartoon drawings & color

The Southern California Kaiser Permanente IRB of Pasadena has created ReguBingo, a new game for IRBs to use to teach IRB members, staff, researchers and research staff, and others about human research protection regulations.

The following shows how a conflicts of interest (COI) ReguBingo game works:

• The game includes the following items:

- ReguBingo game set of one deck of cards and 11 boards,
- pre- and post-tests related to the regulatory subject,
- chips, pencils or pens,
- resources about the regulations and policies, and
- incentives, such as books, key chains, and other items.

• An IRB instructor gives participants a regulations pre-test, including the following questions:

- The person I call to report a possible financial or non-financial conflict of interest is… Answer: COI officer.
- When I have a conflict of interest, I must do a… Answer: COI Management Plan.
- Financial conflict of interest is anything of monetary value, whether or not the value is readily ascertainable. True or False? Answer: True.
- Arrangements such as when relatives of the same household working together may create an awkward situation is in what section of the Principles of Responsibility? Answer: 8.4.1.
- Kaiser Permanente must train investigators prior to investigators engaging in research, every four years thereafter, and immediately. True or False? Answer: True.

• There are 8.5 x 11-inch ReguBingo cards with 16 boxes that can be filled.

• Each box contains a colorful illustration, such as a graphic, cartoon, or photo, and the words describing that part of the regulations, including these samples:

- the COI,
- the COI officer,
- the conduct,
- the 60 days, and
- the corrective action.

• The instructor has index card-sized cards that are randomly pulled and read, including the following samples:

- "If an investigator has significant financial interests, the investigator must declare this HOW?" The answer: "In writing."

- "Kaiser Permanente must train investigators prior to investigators engaging in research, every how many years thereafter, and immediately?" Answer: "The four years."

- "This person may not accept enrollment bonuses from research payments related to achieving targets or meeting timeframes established by the sponsor." Answer: "The investigator."

- "It is when covered individuals are expected to avoid actual or apparent conflicts of interest and conflicts of commitment. Any such actual or apparent conflicts and any institutional interest of SCPMG are to be disclosed and managed in accordance with R&E policy." Answer: "The disclosure."

- "A significant financial interest that could directly and significantly affect the [WHAT?] of research? Answer: "The conduct."

• The instructor calls out cards, one at a time, and if an attendee knows the answer, he or she can place a chip on the square that lists the correct answer.

• The first person to complete four boxes diagonally shouts out "ReguBingo" and wins a prize.

• All participants take a post-test and answer an evaluation question that reads: "What did you like most about ReguBingo?"

• They receive a summary with the answers for the pre/post tests and card deck. ■

Pre-review Process Can Result in Satisfied Research Staff

Improved collaboration is goal

A research institution has found that a model way to improve collaboration between research protection staff and research staff is through a study initiation program (SIP).

Collaboration between an IRB and research team works better when the research group is well-educated to the IRB's process and human subjects research protections. Trust also enhances collaboration. Both of these aims can be achieved through a study initiation program.

"We're looking at not only what the IRB approves, but how we can support best practices with their study," says **Martha Jones,** MA, CIP, executive director of the human research protection office at Washington University School of Medicine in St. Louis.

The study initiation program resulted in 30 SIPs last year and very positive responses from research staff, she says. A survey that asked if investigators or research coordinators would recommend the SIP to peers showed that 92% said they would make the recommendation.

Also, more than 90% said they agreed or strongly agreed that the human research protection and human research quality assurance staff had answered all questions effectively and with constructive advice, she says. Most researchers and coordinators also agreed that they had learned more as a result of the SIP, according to survey answers.

The IRB uses the SIP to provide helpful tools to research staff and to guide them in beginning the research process, Jones says.

"With a research study and waiting for approval, they could work on detailed procedures about how to conduct activities and how things change," she says. "This process allows us to make a personal connection that, hopefully, will help them feel comfortable contacting [the IRB] for help if they run into problems."

Once trust exists, research staff will call with questions before problems arise. For instance, research staff often calls to learn more about data management and recordkeeping, says **Mickey Clarke**, director of human research quality assurance at Washington University.

IRB staff can help research staff with writing protocols and improving flaws.

"People might say they'll do individual consent for a study at some gathering, but then they arrive and there's no place to speak with people privately, so they'll do a mass consent that wasn't approved by the IRB," Clarke explains. "They have difficulty because they haven't thought through how they would

provide informed consent and get it approved."

Another example involves clinical trials with inclusion/exclusion criteria. Investigators might have the criteria written into the application, but they haven't gone through and shown how they might document each criterion to ensure the person is eligible for the study, Jones says.

The SIP helps researchers think about logistics and other obstacles to a successful study.

"We might ask, 'Do you really think the subject can tolerate nine different tests in one day, and could you really get that many scheduled?'" Clarke says. "Changing the protocol might lengthen their timeline for accomplishing things, but that's better than having people drop out or withdraw, and we want people to think through those logistics in advance."

The SIP starts with an email as the protocol is being reviewed. The email notifies a research team that the study has been selected for the study initiation program, which is explained in detail. It also asks the team to schedule about an hour for the meeting with a member of the human research protection office and someone with the human research quality assurance program.

Research staff receive a packet of materials, including a report that walks them through their application, giving examples of best practices and templates.

"We also provide a small gift — a little box of mints — for everyone," Jones says. "It has contact cards in it so they know who to contact after the visit."

Next, SIP reviewers meet with research staff.

"We almost always go to their site because Martha's staff and my staff are a mile apart, so it's best to meet in the middle and it's always courteous to go to the faculty," Clarke says.

"Then the teams spend a lot of time reading the review," Clarke adds. "We've developed a template that covers X points, and they read the submission before discussing it."

Questions the SIP reviewer might ask include the following:

"BY INTERVENING EARLY ON WITH SOMEONE IN THEIR CAREER HERE, WE GIVE THEM A TOTALLY DIFFERENT IMPRESSION OF HOW WE MEAN TO BE HELPFUL AND CAN HELP THEM NAVIGATE THE SYSTEM; IT'S VERY POSITIVE."

- How are you going to recruit and consent subjects?
- How will you carry out your procedures?
- How will you minimize risk?

"We go through key parts and regulatory issues first, and then look at execution and best practices," Jones says. "We look at how to document and how to run a study effectively, including having good communication between study team members and the investigator."

Researchers have been receptive to the program to the point that some call Clarke's office to request a study initiation program visit.

After the meeting, research staff receive a follow-up survey to gauge satisfaction.

"One of the most important things is we're actually forming relationships with researchers," Clarke says.

New investigators welcome the help with their protocol submissions, and as a result, they are less likely to see the IRB as an adversary, Clarke notes. "By intervening early on with someone in their career here, we give them a totally different impression of how we mean to be helpful and can help them navigate the system; it's very positive."

Researchers can learn from IRB and human subjects protection classes, but it's much more helpful if they learn while working on a specific research study, Jones notes.

"They can modify their studies and the minor changes go through our system very quickly," Clarke says.

"A lot of what we do is about logistics and execution, rather than regulatory determination," Clarke adds. "From my perspective, we do a lot of monitoring and review of open studies, where we've seen all kinds of issues and activities."

One goal is to get research staff to think about which parts of their plan are feasible and to consider things that might go wrong. It takes someone with experience to shed light on these issues, Clarke says. "People are willing to engage you around those questions because they're talking with two people from my staff who have a lot of experience."

Another goal is to address special regulatory requirements.

"The staff familiar with those additional requirements can walk through them with the research team to make sure they understand those requirements," Jones says. ■

Educating IRB Members in 10 Hours or More

IRB revamps education program

A common challenge for IRBs is educating board members who come from a variety of backgrounds and levels of experience.

"By nature, they're a mix of individuals on the committee of varying expertise and all that is by design," says **Jonathan M. Green**, MD, professor of medicine Washington University (WU) in St. Louis. Green is an executive chair of the Washington University IRB at and an associate dean for human studies.

"Sometimes it's a challenge to provide sufficient education to all members and to help them to fully understand the criteria for approval and how to apply them to studies," Green says. "IRBs strive for consistency in their decisions, but there is a lot of subjectivity."

To find new IRB members, the IRB reaches out to community organizations, churches, disease-related groups, and others.

"We have a waiting list," Green says. "We're setting up a new member training and have at least 30 people that want to be on the board, and we don't have a lot of turnover."

To help improve consistency, the WU IRB revamped its education training system to provide 10 hours of up-front education for each IRB member. There is face-to-face instruction prior to becoming full committee members, in addition to required online CITI modules.

The 10 hours of instruction are tiered with some parts specific to nonscientific IRB members, including an Introduction to Research module, Green says.

Nonscientific members also can learn more about how research is conducted, different study designs, interventional studies, and what controls are about.

"Everyone goes through a two-hour 101 course about the basic criteria for approval and what the Belmont Report is," Green says. "Then for our scientific members, we have a separate session where we get into more advanced topics in IRB review: the subparts, FDA regulations, and those sorts of things."

IRB education sessions are scheduled in two-hour blocks with each session repeated once to help people find a time that works with their schedule. There usually is one week between each new session, and new members typically complete the training within a month and a half, Green says.

The program includes a mock IRB session in which new members can have a trial experience at reviewing and presenting, and there's a buddy system that pairs experienced members with new members for ongoing support, Green says.

"A lot of times people are thrown into the frying pan, and we've found the buddy system helps a lot," he says. "It gives everyone a baseline level of knowledge."

WU IRB has six meetings per week, each with one chair who leads discussions of cases and provides guidance. Since the committee has seven members with 160 alternates, no one has to attend all of the weekly meetings, and they can commit to any particular meeting through online scheduling, Green says.

Ongoing education also includes a 10-minute module at the beginning of every meeting. These educational short sessions include a PowerPoint narration on a broad range of topics, including the following from 2015 and 2014:

- therapeutic misconception;
- keeping focused on the criteria for approval;
- AAHRPP,
- IRB oversight modules,
- study initiation program,
- conflict of interest and IRB review,
- documenting risk findings,
- myIRB tips and tricks,
- changing the human subjects regulations,
- reviewing data and safety monitoring plans,
- keeping focused on the criteria for approval,
- research and the cognitively impaired,
- IRB evaluation of placebo controlled trials,
- HIPAA & research,
- research with healthy volunteers,
- changes to the HRPO reviewer sheet, and
- informed consent documents and health literacy.

"We've developed the curriculum in house, and it's evolved over time — pulled from experience," Green says.

Each year, IRB members have an evaluation accompanied by a survey that asks them about their experience serving on the board. "Generally, feedback is positive," Green says.

"People want to learn and stay engaged in the process, and we have member outreach — particularly for unaffiliated members," he adds. "We stay in close contact with them so they don't feel like we're just using them for warm bodies in the meeting." ■

Governor Signs Off on State Law Requiring Oversight of UM Psych Drug Research

State ombudsman given broad powers in wake of research suicide

Culminating a turbulent saga that began with the suicide of a research subject more than a decade ago, Minnesota Gov. Mark Dayton has signed into law a bill that gives the state unprecedented control and oversight of psychiatric drug research at the University of Minnesota.

The new law grants broad powers to the state Office of the Ombudsman for Mental Health and Developmental Disabilities to monitor the treatment of research subjects participating in drug trials at the university's department of psychiatry.

"The ombudsman shall monitor the treatment of individuals participating in a University of Minnesota Department of Psychiatry clinical drug trial and ensure that all protections for human subjects required by federal law and the institutional review board are provided," the law states.

According to the law, matters appropriate for review include unusual deaths or injuries of a research subject, reports of emergency use of manual restraint, and situations which may be unreasonable and unfair. It also empowers the ombudsman office to check into situations that are "unclear or inadequately explained, when reasons should have been revealed."

Investigations and inquiries can be triggered by confidential complaints from any source about a research subject or a clinical drug trial.

"The university shall not retaliate or take adverse action against any person who in good faith makes a complaint or assists in an investigation," the law states.

If an investigation finds lax compliance with federal protections of human subjects or with the requirements of the university IRB, the ombudsman may recommend corrective action be taken by the university and the state Board of Regents.

It is not clear whether there is another such arrangement in the country, and in responding to *IRB Advisor* the university called it "new and quite novel." Having unsuccessfully fought the law, the university issued the following statement in response to our request for comment:

"The University of Minnesota is committed to upholding the highest ethical standards in research practices involving human participants. We continue to report monthly to the legislature on the progress in implementing our work plan to improve research with human participants across the entire university. An early review of our progress by the Office of the Legislative Auditor issued in May [2016][1] said our reform plan is 'ambitious and far reaching,' and that 'we think it will significantly strengthen protections for human subjects research' if fully implemented and sustained. We look forward to sharing our progress with the Ombudsman for Mental Health and will provide them with the information they may request on pharmaceutical trials in the Department of Psychiatry. Although the arrangement under the law is new and quite novel, we have no reason to anticipate disruption to ongoing or future research projects."

The state ombudsman office had no comment on the development, but **Carl Elliott**, PhD, a professor in the Center for Bioethics at the university, welcomed the news after having previously testified in state hearings that the oversight was needed.

"It's happening and I'm glad it is," he tells *IRB Advisor*. "I went over there and testified and pushed as hard as I could to get it passed."

Arguing that the university was reluctant to enact reforms, Elliot and other university critics called for oversight by an outside agency to finally resolve continuing questions about the safety of research in the psychiatry program.

To that end, the resulting language of the law indicates the oversight will be far from cursory, with the onus on the university to report the death of a research subject to the ombudsman office within 24 hours.

We will never know if having the full provisions of this new law in place in May 2004 could have prevented the suicide of Dan Markingson, a 27-year-old aspiring screenwriter who had a mental breakdown and was enrolled in a University of Minnesota psychiatric drug trial under somewhat dubious circumstances. He faced commitment to a state psychiatric facility if he declined to participate in the drug trial, according to a state auditor's report.[2] In 2009, the Minnesota legislature passed a law restricting the

enrollment into drug trials of persons under a stay of commitment.

Markingson was extremely vulnerable when recruited into the study, his mother expressed strong concerns about it, and later warned after he was enrolled that he was not improving, according to the report. His subsequent suicide occurred in the bathroom of a state-licensed group home for people with mental illness. A spate of lawsuits, investigations, and reports of university progress or lack thereof took on a life of their own in the aftermath, as the suicide metastasized into an indictment of leadership at the university and the state Board of Regents.

Will this new oversight arrangement finally free the university from the long shadow of the Markingson incident? One thing is clear: The powers now granted to the state suggest that no research incident of any significance could be shielded from full scrutiny for very long.

Within the scope of the law's intention, the ombudsman office has the power to gather records related to psychiatric clinical drug trials at the university and issue subpoenas to move investigations forward.

"If the records are private and the client is capable of providing consent, the ombudsman shall first obtain the client's consent," the law states. "The ombudsman is not required to obtain consent for access to private data on clients with developmental disabilities. The ombudsman is not required to obtain consent for access to private data on decedents who were receiving services for mental illness, developmental disabilities, or emotional disturbance."

The subpoena power means in the wake of an adverse incident, ombudsman investigators can demand the appearance and compel testimony by those involved in psychiatric drug research.

However, with appropriate political acumen, the law secures a potential loose cannon securely to the deck by requiring the ombudsman to report all findings to the governor before any release of information.

The law also calls for a "Medical Review Subcommittee" — which already exists at the ombudsman office, but may be appointed separately as described in this law — to determine whether the death of a research subject is "unusual" and warrants investigation.

If so, the medical review panel can review the causes of the death and request an autopsy. They would then submit a report regarding the death to the ombudsman, the client's next of kin, the facility where the death occurred and, if appropriate, make recommendations to prevent recurrence of similar deaths to all appropriate parties. ■

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Report: Socioeconomic Factors Undercut Participation in Internet Studies

Study does not bode well for the Precision Medicine Initiative

Launched by the federal government last year, the Precision Medicine Initiative (PMI) is a disease prevention and treatment model that is envisioned as linking unprecedented access to genetic information with the expanding reach of the internet to form research "cohorts" of racially and socially diverse subjects.[1]

"The idea is create a database and develop precision medicine where [researchers] will get samples and genotypes and they will link this data to medical records," says **Sarah M. Hartz**, MD, PhD, assistant professor of psychiatry at the Washington University School of Medicine in St. Louis.

A major thrust of the program is to overcome the longstanding lack of inclusion of African-Americans and people on the socioeconomic margins in medical research. The hope is that PMI will recruit enough of these underserved groups to generate meaningful data on their risk factors and health challenges. One of the suggested incentives for participation is that research subjects

will have access to their genetic data that is collected by PMI investigators. Information could be gathered and exchanged over the internet and via email and text, a PMI working group suggested.

However, Hartz had a question, and was ultimately surprised by the answer: Will internet-based approaches effectively engage participants from diverse racial and socioeconomic backgrounds? The answer is an unequivocal "no" based on a study by Hartz and colleagues, which found that participants' initial enthusiasm to go online to get personalized genetic results faded into apparent disinterest by the time their saliva swabs had been decoded.

"I think [the findings] are directly relevant as we are talking about recruiting people for the PMI, with emphasis on recruiting underserved populations," Hartz tells *IRB Advisor*. "They want to engage these people through the internet, so what can we do within those constraints to maximize engagement? This is when that has to happen or we are going to miss the boat."

Hartz and colleagues recruited subjects into a genetic study of smoking, which was approved by the Washington University IRB. Participants were interviewed briefly about basic demographics and history and asked if they wanted to see their ancestral genetics as compiled by 23andMe. The research subjects were assisted in setting up an account on the website and 83% reported an existing email address. The remainder were assisted in setting up an email account and given a written copy of needed login information to see their genetic analysis results.

A total of 967 participants were recruited and offered genetic ancestry results. Of the participants, almost two-thirds told the researchers they were "very" or "extremely interested" in their genetic tests results. Yet for reasons not completely understood, when the genetic testing was available four to six weeks later, many participants did not follow through and view the results. Even after follow-up reminders that the results were available, it appeared that the subjects lacked the means or interest level to retrieve their genetic data.

"We [examined] the group of participants who said they were 'very' or 'extremely' interested in receiving their genetic ancestry results," the researchers reported. "Surprisingly, even of these participants who expressed high interest, only 16% actually viewed their results."

Among interested participants, 19% with a high school diploma viewed their results compared to only 4% without a diploma. Moreover, 22% of participants with household incomes above the federal poverty level viewed their results, compared to only 10% of those living in poverty.

"Despite high levels of initial expressed interest in their genetic ancestry results, we observed challenges with engaging participants from typically underrepresented groups, including individuals without a high school degree, individuals living below the federal poverty level, and African-Americans," Hartz and colleagues concluded. "In addition, it is important to note that, even after adjusting for education and living below the poverty level, African-Americans were less likely to engage in our study than European-Americans."

The researchers cited data estimating that 84% of American adults use the internet and 68% own a smartphone. However, the study did not ask the participants if they had convenient — or, for that matter, any — access to the internet.

"They needed to go online to view the results," she says. "They could come back into our offices to access it there if they didn't have a computer at home or didn't want to go to a library. It surprised us, so we are now doing additional studies and asking more questions about how they use the internet to get a better sense of that. There were questions that we didn't ask [in this study] that would have helped clarify this, but there certainly was the option to come back to our offices and log on there."

Another possibility is that those with little education may not have understood the explanations on how to access the genetic information.

"We're not sure what the barrier was — whether it was access or knowledge, or perhaps both," Hartz says. "We were really surprised by the results, and had we come into it knowing what was going to happen, we would have definitely asked different questions to get a better sense of what the real barriers are. So that is what we are doing with the follow-up studies now."

That said, 45% of participants who had a high school education, lived above the poverty line, and were either white or female accessed their genetic results, she says.

"That isn't low for this kind of a study," she says. "It still doesn't align perfectly with all the people that said they were interested [in the genetic results], but it's not uncommon for follow-up to be in that range for this kind of study."

There is also the suggestion of a kind of quasi-Hawthorne Effect, wherein human behavior changes when it is observed. "They could have been saying they were more interested than they were because

they were asked these questions in person," she says. ■

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2. Hartz SM, Quan T, Ibiebele A, et al. The significant impact of education, poverty, and race on Internet-based research participant engagement. *Genet Med* 2016;Jul 28. doi:10.1038/gim.2016.91. [Epub ahead of print]

Another Call for Transparency in Clinical Trials

'Study results may influence the willingness to share data'

The demand for clinical trial transparency and research results continues to gain momentum, as it was recently reported that almost half of the data from randomized clinical trials (RCTs) from four sponsors registered at ClinicalTrials.gov were not available to researchers.[1]

The glass-half-full take on this is that 53% of the RCT data from the four sponsors were accessible on the Clinical Study Data Request (CSDR) website, where companies can voluntarily list data that has been requested.

The researchers targeted studies on 61 drugs from four sponsors registered at ClinicalTrials.gov. A total of 521 RCTs (53% of total reviewed) were listed on CDSR. The availability of various documents and findings in the RCTs varied from 83% to 99% on many studies, but 385 trials (40%) had all documents listed. Again, 47% of the clinical trials from the four sponsors were not listed on CSDR.

Lead study author **Isabelle Boutron**, MD, PhD, of Paris Descartes University, replied to questions from *IRB Advisor* via email.

IRB Advisor: Can you comment on disincentives for companies to release all data?

Boutron: First, I think it is important to be careful when interpreting these results. The listing of trials on CSDR is a recent and an ongoing process and the number of studies listed is increasing. It is important to acknowledge that it may take some time and effort to give access to these data. Further, we considered all the trials registered and we did not take into account the policy of the sponsor.

However, our results showed that a substantial number of trials were missing and we could imagine that the study results may influence the willingness to share data. Nevertheless, our study did not explore this hypothesis.

IRB Advisor: How might full release of research data aid other researchers and, ultimately, patients?

Boutron: The full release of research data is very important to improve evidence-based medicine as it will allow access to unpublished data and the conduct of individual patient data meta-analyses. This would increase our understanding of the efficacy and safety of treatments and improve the care provided to patients. It could also allow improving clinical research as we could explore factors associated with better research.

IRB Advisor: Can you comment on why you undertook this study and whether you support calls for data transparency for all RCTs by groups like the AllTrials campaign?

Boutron: We undertook this study because we felt the initiative of pharmaceutical companies to share their data is a very important initiative. We definitely support calls for data transparency for all RCTs by groups like the AllTrials campaign. We are members of the EQUATOR network, Cochrane, and the REWARD Alliance, and we call for more transparency and reduced waste in research. ■

REFERENCE

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COMING IN FUTURE MONTHS

- Ethics of continuing treatment post-trial
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IRB ADVISOR

CME/CE INSTRUCTIONS

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CME/CE QUESTIONS

1. Draft federal guidance for IRB written documentation of regulatory requirements recommends identifying by name those responsible for the various tasks, and then updating the document within one month of a personnel change.

A. True
B. False

2. Which of the following is a chief problem with instructors only using a didactic method of teaching human subject research protection regulations and standards?

A. The didactic method results in less consistency.
B. The didactic method is less efficient.
C. The didactic method results in little interaction between students and the teacher.
D. None of the above.

3. What is a chief benefit of starting a study initiation program (SIP) with researchers and their staffs?

A. Research staff learn directly in real time about how to handle issues that arise with their study protocols.
B. IRBs can easily divert staff time to performing SIPs.
C. An SIP can replace a formal IRB review.
D. All of the above.

4. A new state law grants which of the following powers in order to oversee psychiatric drug research at the University of Minnesota?

A. Subpoena
B. Access to documents
C. Investigations prompted by confidential reports
D. All of the above