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HIPAA and informed consent forms get the comic book treatment

New trend: graphic medical story design

In their search for ways to improve informed consent, IRBs and the research community have used illustrations, different sizes and styles of fonts, simple language, videos, interactive displays, and other innovative methods. Now comic strips can be added to that list. The Mayo Clinic Center for Innovation in Rochester, MN, has designed a consent form with comics.

"Leah Eisenberg and I coordinated on how we might use comics to improve informed consent, and we decided to start with the HIPAA Notice of Privacy Practices because it's more broadly applicable and it's required of every health care institution," says **Rose Anderson**, service designer for the Mayo Clinic.

"My background is in law and medical ethics, and one of my interests is in helping people understand the law and what their rights are," says **Leah R. Eisenberg**, JD, MA, who previously worked for the Mayo Clinic Mitochondrial Disease Biobank and now is an instructor in the division of medical humanities at the University of Arkansas for Medical Sciences in Little Rock. Both Eisenberg and Anderson featured a poster on their HIPAA comic form at the 2013 Advancing Ethical Research Conference, held by Public Responsibility in Medicine and Research (PRIM&R), Nov. 7-9, 2013, in Boston.

"Because of my background in law, I disagree when people say legal documents like HIPAA forms have to be complicated because it's the law," Eisenberg adds. "I believe you can satisfy the law while making things clear and understandable."

The comic consent project was Eisenberg's brainchild. She saw an email with comics at a Graphic Medicine medical conference, and it looked so clear and engaging that she felt certain it would work for HIPAA and informed consent for research, as well.

Eisenberg met with Anderson, and the pair decided to create consent forms that use the comic — also called graphic novel — format. They worked with an illustrator who was able to translate their ideas into a

comic format.

"There has been an increase in the graphic novel world around medical narratives," Anderson says. "There is an emerging genre of medical narratives in graphic novel format; so why not take these text-heavy medical forms and make them more engaging?"

Anderson was interested in the challenge. She wanted to see how an illustrated storyline or narrative might engage participants and compel them to read further while digesting chunks of information.

The main character is a woman with glasses who is pondering whether to bother reading the HIPAA Notice of Privacy Practices. In the first three panels she decides to read the entire form and learns that her private medical information can be shared. In the next few panels she learns about the specific ways the information could be shared. The panels illustrate the information's use for treatment, payment, quality of care, research, to contact the patient, for public health benefit, for worker's compensation, and, when the patient wishes, to inform the patient's family. Less common ways the information might be shared are also mentioned below the panels.[1,2]

Using the HIPAA comics, they conducted a small-scale qualitative investigation to understand this format as a proof of concept, Anderson says.

"We wanted to know if it was possible to translate all of this text into images and to try to understand how people might engage with the information," she explains. "So we had people review the comic version and the regular version of the HIPAA form and then give us feedback about what they thought of each."

Getting patient input

They recruited people from the patient cafeteria and showed them the forms. Among the feedback they received, people said that the regular HIPAA form was fairly dense and intimidating and they might just throw it away, Anderson recalls.

By contrast, the same people found the comic version to be engaging and fun, she adds.

"It drew them in, and they found the information relevant; people said they were more likely to read it," she says.

There was one problem, however. The same people who admitted they did not care for the standard HIPAA form also said that the comic version did not meet their expectation of a medical form.

"They said the comic seemed too simplistic and not sophisticated enough for a hospital like the Mayo Clinic," Anderson says. "There was a contrast between what people expected and what they found useful; some people said they thought the traditional form was best, but they wouldn't read it because they trusted the Mayo Clinic."

This reaction to the comic version seeming too simplistic was repeated when Eisenberg had a comic assent created to use with youths ages 12 to

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17 enrolling in research, Eisenberg says.

"We gave the kids surveys and talked with them in focus groups with their peers, and they would say about the comics: 'That's not what you show to adults, and we're smart enough to look at what you show adults,'" Eisenberg recalls.

The adults surveyed about the comic HIPAA forms said they were concerned some information was left out of the comic version, but their concerns were unfounded, she says.

"I was careful that the comic version followed all HIPAA rules," Eisenberg says. "We left out excess legalese, but it had all of the necessary information and was vetted by several people."

The next step will be to conduct a quantifiable study, she notes.

"We need some data about the efficacy of a comic HIPAA versus a text HIPAA, and we've also been working on comic consent and assent for biobanking," Eisenberg says. "Informed consent for biobanking is new, and we can't tell people in it what kind of study we're doing or how long it will last because we don't have that information."

Since biobanking informed consent is new, it seems like a good time to employ a new IC format, she adds.

Another possible use of a comic consent form is to supplement the traditional form, Eisenberg says.

"That way, the people who feel like the text document has more information are not missing anything," she says. "My only concern is that it adds a lot of length and paperwork and might turn people off."

Whether IRBs begin to approve comic/graphic novel versions of informed consent documents or some other alternative format, the point is to improve research participants' understanding of consent, Anderson notes.

"Overall in health care we're going to see an increase in the need to engage with and collaborate with patients," Anderson says. "We're going to learn a lot about how patients want to engage, and this will inform how we communicate with people."

REFERENCES

1. Eisenberg LR, Pringnitz J, Hasadsri L, et al. Drawing Patients in with HIPAA in Comic Form. Poster presented at the 2013 Advancing Ethical Research Conference, held by the Public Responsibility in Medicine and Research (PRIM&R), Nov. 7-9, 2013, in Boston, MA.

2. Eisenberg L, Anderson R. Picture this: illustrating the future of HIPAA documents. Atrium. Spring 2012:10-12. Available at http://bioethics.northwestern.edu/docs/atrium/atrium-issue10.pdf ■

IRB's core training gives new staff autonomy

Goal is broader program

IRB staff professionals need a greater breadth of knowledge and training now than they might have a decade ago, which is why one HRPP recently created a more comprehensive educational program that also offers greater autonomy to staff.

"We really wanted a broader education program," says **Judith Birk**, JD, director of the IRBs at the University of Michigan Medical School (IRBMED) in Ann Arbor.

The new program provides self-directed study, timelines, and checkpoints, says **S. Joseph Austin**, JD, LLM, senior education and regulatory coordinator at IRBMED.

The result is a new core training curriculum for staff with focus on three general areas: orientation, self-directed education, and continuing education.[1]

"Our previous program relied heavily on peer-to-peer education and training," Austin says. "We took this as an opportunity to expand the program and make it more autonomous for new employees."

The curriculum incorporates a multiplatform approach with a reading and self-directed portion, face-to-face classes, an online module, and peer-to-peer mentorship, he adds.

The new program has been well-received by new IRB staff, and it has continued to improve and evolve based on continuous feedback.[1]

Austin and Birk describe how each of the three general areas works:

• **Orientation:** The first part of the educational program provides an introduction and overview of human subjects research regulations and institutional policies, Birk says.

New staff training includes a meeting with the education coordinator, who goes over human subjects research, Austin says.

New employees will learn more about HIPAA, research ethics, conflicts of interest, and IRB oversight and responsibilities in online modules, which have to be completed within the first week. Occasionally, the new employee will be given two weeks to meet the deadline, he adds.

The last part of the orientation involves a one-on-one meeting with the eResearch coordinator, who provides basic information about the IRB's electronic application process, Austin says.

"We try to give new employees dedicated time to complete these educational components," Birk says. "We want them to have peer-to-peer training and not just have them do videos and self-directed reading."

New staff also can meet with other IRB professionals and attend IRB meetings, she adds.

• **Self-directed education:** Presented as a peer-to-peer education module, this part of new staff education and training includes a core education handbook and online modules, Austin says.

"There are multiple IRBs at the University of Michigan, and our University of Michigan IRB collaborative brings them all to the table to create standardized online materials," he explains. "This sends a consistent message to the UM community and to all IRB members and staff."

New employees will view IRB materials online during this second education segment, and they'll cover broad topics. This part can last several months, Birk says.

"There are close to 30 sessions," she says.

New employees review a core education handbook of 52 pages. It provides a high-level review of all applicable regulations and information related to institutional practices, as well as information on collaborative units. This includes information about conflicts of interest and compliance, Austin says.

"It's an interactive program that is best utilized in an electronic format," Birk notes. "It has links to additional information, so it's a more interactive approach than just reading 52 pages."

There also is a regulatory component where the new employee can watch an OHRP video, she adds.

"The program has action items, usually one or more at the end of the session, and these might direct them to a video, Web guidance, or a University of Michigan resource," Austin says.

The goal is for this multi-platform program to move education away from paper and have it more adapted to the way people are learning today, Birk says.

• **Continuing education:** All IRB employees — new and experienced — participate in the continuing education component of the core training program.

"Some components are practice and guidance documents, and the practice and guidance committee meets here," Austin says. "The members represent different roles of the IRB, including management and five IRB regulatory teams."

The five regulatory teams support the IRB's activities, Birk says.

The teams document how the most effective and experienced employees do their jobs so new and other staff can learn from their best practices, Birk explains.

Best practices committee

"If you talk to one team, they do a job correctly one way, and another team does it correctly another way, so we created a committee to collect the best practices and document that," Birk says. "We select the best among them and document them, working toward consolidating our practices."

The committee's primary purpose is to provide standardized internal documents about how the board acts as a unit. The group meets every two weeks, Austin says.

"We expect our new staff to review pre-existing documents, such as internal practices and procedures that we've developed within the group and that are finalized," Austin explains. "Everyone in the office has access to them, but our new staff should look at what those practice documents say and how they impact their staff position," he adds. "As the practice documents are completed, we teach them at all staff meetings."

Other aspects of continuing education include conferences, seminars, webinars, in-house classes, and special programs on topics such as informed consent. These subjects are designed for the research community, but IRB staff also must attend, Austin says.

The core training program was designed to rely heavily on autonomous education partly to help conserve the IRB's resources, Birk notes.

"In light of the fact that academic budgets are tight and only getting tighter, we can't just hire three or four people to have education coordinator roles and manage all of it," she says. "So the program is moving toward being more self-sustaining, and we have one full-time education coordinator with small amounts of people to do more planning."

Education sessions are taught by existing staff experts, as well as university experts, she adds.

REFERENCE

1. Austin SJ, Miller D, Birk J. Development of core training for IRB staff: reimagining the education and training program for new members of IRB staff. Poster presented at the 2013 Advancing Ethical Research Conference, held by the Public Responsibility in Medicine and Research (PRIM&R), Nov. 7-9, 2013, in Boston, MA. ■

BEST PRACTICES SPOTLIGHT

IRB improves workflow, eliminates hard stops

Redesign works for PIs

When an IRB redesigns its electronic submission system, it's the right time to consider redesigning the IRB's workflow as well, some experts say.

The key is to identify the hard stops in the IRB submission process and to design process improvements to eliminate them, says **Michael Centola**, MHS, CIP, IRB manager with the University of Massachusetts Medical School in Worcester. Centola was a co-author of a poster about IRB workflow, published at the 2013 Advancing Ethical Research Conference, held by the Public Responsibility in Medicine and Research (PRIM&R) Nov. 7-9, 2013, in Boston.

"The hard stops we were trying to avoid include, for example, having department chairs actively sign applications before they were submitted to the board," Centola says.

Previously, every application was emailed to the department chair, waiting for his or her signature before it could be submitted. This caused lengthy delays, especially when the email was overlooked or the department chair was on vacation, he explains.

With the workflow redesign, the new process is a passive approval approach: When an application is submitted to the IRB, the researcher's department chair receives an email stating that the researcher has submitted an application to the IRB and if the chair is OK with this application, he or she does not have to respond. If there is a question or problem, the chair may choose to call the IRB office immediately, Centola says.

"The idea behind this is that most department chairs have their own systems and a good awareness of what to expect when studies go to the IRB," he adds. "If they don't know about a study or already have similar studies, then they can contact the IRB."

Investigators were pleased with the change because it eliminated one of the frustrating delays in obtaining IRB approval.

"Their time to IRB submission was shortened," Centola says. "We're not collecting metrics, but some investigators say it was shortened by weeks."

But there also was some resistance to the change: Soon after the IRB switched to an electronic submission process and improved its workflow, some users complained that the new electronic system did not work intuitively, Centola says.

"The new system required some learning, and it was difficult for them to attend training sessions," he says.

The system would work easily for users once they had gone through the process once or twice because every step had the same workflow, he explains.

"Regardless of what they were doing — a request for exemption, a modification — they all had the same process," Centola says. "The only divergence was whether it went to expedited or full committee."

Once investigators used the system and grew accustomed to its logic, they were pleased with how it worked, he adds.

Workflow improvements

Here are some additional workflow improvements the IRB made:

• **Passive approval for staff signatures:** The IRB further improved workflow by using the passive approval approach for additional signatures required on IRB submissions. Previously, each person listed on the study staff needed to sign the application to participate in the research study, regardless of their role, Centola says.

Now, they can provide their approval to being listed by not responding: "If an investigator names me as the coordinator or research nurse, I will receive an email saying, 'Dr. Smith has added you to this application with the following role. Please log in and see if it's OK. If it's not OK, then you do nothing, but if you are not comfortable with what is listed, please contact the principal investigator immediately,'" he explains.

Previously, investigators had to bring the application all over the hospital to obtain signatures from as many as 20-30 people, Centola says.

"Now they don't have to spend time going around getting signatures," he adds.

The system appears to be working. Centola has been contacted by people who read the email and said they were unaware of the study. Then after they contacted the investigator at Centola's sugges-

tion, they agreed to be listed, he says.

• **Modifications to IRB applications:** "Every time you add or remove someone from your IRB application, there is a modification sent to the IRB and they have to review and approve it," Centola says. "The modification to add someone to the study would be in our office for a couple of days."

The investigator would need to show that the person added to the study had completed all required training, and this might take additional time, he says.

The IRB eliminated this delay by checking with federal regulators and clarifying requirements, Centola says.

"They told us that if the roles of each staff member were listed in the body of the application, then taking an individual off the application and replacing that person with someone who matches that same role would not be a study modification," he explains.

"So now we have investigators describe the role, and if the staff person leaves and someone else comes in with the same certification and training, then it's not a modification to the research because that role was approved," Centola adds.

At continuing review, the IRB checks the study staff and applications to make sure all of the roles are filled appropriately.

"To date, we have not had any issues," Centola says. "Support staff and investigators find it such a huge benefit that they are not taking chances [with being out of compliance] by putting in people who have not done their training."

The IRB's workload also has greatly improved. Before, there would be 30-40 revisions or modifications a day to remove study staff, and now they can focus on more substantive work, he says.

"We have auditors who do routine audits, and there was only one situation where someone was added who did not do their CITI refresher course, and that person was working on it, so this change seems to be working," Centola adds.

• **Eliminating duplication:** The new electronic system eliminated duplication and redundancy. Once an investigator completed a form, he or she would not have to repeat that information in another form, Centola says.

The old process required the IRB to review a form, ask questions, and then have investigators complete another form to address all issues raised in the review, he explains.

"We'd return the form to them and it could take months," he says. "Now, we have one process for everything no matter what they're doing."

Investigators answer all required electronic fields, providing details, and the IRB can make decisions more quickly, and investigators have fewer forms to complete, he adds.

"We're now thinking about looking for more ways to improve the system," Centola says. ■

Research Standards manual updated

No U.S. changes, but many elsewhere

The Office for Human Research Protections' 2014 Edition of International Compilation of Human Research Standards is available with hundreds of updates and three additional nations, including Cameroon, Mozambique, and Zambia.

The 129-page electronic PDF is available online at http://www.hhs.gov/ohrp/international/index.html.

The changes between the 2013 edition and the 2014 edition include hundreds of new bills, regulations, and guidelines internationally. There were no legislative or guideline updates or changes in the United States information.

The compilation features listings of more than 1,000 laws, regulations, and guidelines on human subject protections in 107 countries. It also includes standards, such as issues of informed consent, research ethics committee review, reporting requirements, and vulnerable populations issued by a number of international and regional organizations.

The listings are organized into seven categories: general research, drugs and devices, research injury, privacy/data protection, human biological materials, genetics, embryos, stem cells, and cloning.

Many listings feature a hyperlink that leads directly to the law, regulation, or guideline of interest. The compilation is available in both PDF and Word versions.

The compilation is designed for use by IRBs, researchers, sponsors, and others involved in human subjects research around the world, and it was first published in 2005 with annual updates.

Among the changes from the 2013 edition are:

• The general international guidelines now list this reference: 3. Ethical issues in Patient Safety Research: Interpreting Existing Guid-

ance (2013): http://apps.who.int/iris/bitstream/10665/85371/1/9789241505475_eng.pdf.

• Croatia, Denmark, and Bulgaria have new laws on medicinal products; Germany and Iceland updated their Medicinal Products Act from 2009.

• Finland has new regulations on consent for biobanks.

• France has a new law on embryos, stem cells, and cloning, and new Civil Code Articles on genetic research.

• Switzerland has a new Federal Act on Research Involving Human Beings, as well as three new ordinances:

- Ordinance on Clinical Trial (2014);

- Ordinance on Research Involving Human Beings, with the Exception of Clinical Trials (2014);

- Ordinance on the Organization of the Federal Act on Research Involving Human Beings (2014).

• Turkey created 2013 updates for its Guideline for Good Clinical Practice, Guidance on the Ethics of Pediatric Clinical Research, Drug Observational Studies Guide, and created these new guidelines:

- Guideline for Independent Data Review Committees;

- Guidance on Education Programs Related to GCP and Clinical Trials;

- Guidance on Archiving in Clinical Research;

- Guidance on Ethical Committee Submission;

- Guidance on Submission to the Turkey Pharmaceuticals and Medical Devices Agency in Clinical Trials;

- Guidance on Adverse Event Reaction Reporting in Clinical Trials.

• Australia updated its National Statement on Ethical Conduct in Human Research (previously 2009).

• Japan updated the Ethics Guidelines for Epidemiological Research (previously 2008), Good Clinical Practice Guidelines for Medical Devices (previously 2009), Guidelines for Clinical Research Using Human Stem Cells (previously 2010), Ethical Guidelines for Research on Assisted Reproductive Technology to Develop Human Fertilized Embryos (previously 2010), and Ethics Guidelines for Human Genome/Gene Analysis Research (previously 2008). Japan also passed a new Pharmaceutical Affairs Law (previously 2011) and created new Guidelines on Research on Producing Germ Cells from Human Induced Pluripotent Stem Cells or Human Tissue Stem Cells.

• South Korea's Food and Drug Administration is now named the Ministry of Food and Drug Safety. South Korea also passed a new Pharmaceutical Affairs Act and Bioethics and Safety Act and updated its Korean Good Clinical Practice (previously 2009) and the Enforcement Rule of the Protection of Personal Information Maintained by Public Agencies (previously 2008).

• Mexico passed a new General Health Law, Title V and enacted a new rule on Establishing Criteria for the Conduct of Health Research Projects (2012). ■

Tool helps demystify central IRB process

Considerations Document defines roles

The Office of Human Research Protections (OHRP) and the Food and Drug Administration (FDA) encourage the use of the central IRB model to increase the efficiency and quality of multisite trials. However, many research institution IRBs are reluctant to use a single IRB of record. The Clinical Trials Transformation Initiative (CTTI) conducted a study to identify barriers to central IRB use and developed a guide IRBs can follow to adopt the model. CTTI is a public-private partnership established by Duke University and the FDA that comprises more than 60 member organizations to improve the quality and efficiency of clinical research.

"One of the goals [of CTTI] is to improve the efficiency of the clinical trials process in the US and identify areas where there are opportunities to improve," says **Cynthia Hahn**, vice president, Clinical Research and Regulatory Affairs, The Feinstein Institute for Medical Research at North Shore-LIJ Health System in Manhasset, NY. "We started looking more at the central IRB question and what the barriers are to the adoption of central IRB review," she says.

Finding barriers

To identify barriers to central IRB use, CTTI researchers conducted a literature review and interviewed IRB representatives from institutional IRBs, federal IRBs, commercial IRBs, and industry and regulatory agencies. The project ran from December 2010-January 2013. A follow-on project is currently underway.

"One of the immediate challenges we found was that no one had the same definition of what it means to be a central IRB," says Hahn, who

is a team lead for the CTTI Use of Central IRBs follow-on project. "They would think, 'I'll contract with a commercial IRB and they'll do all our IRB review.' That's not a central IRB — that's outsourcing."

During the interviews, CTTI researchers provided interviewees these definitions of a central IRB: "a single IRB of record for a multicenter clinical trial," and a longer definition, "a properly constituted IRB to which sites cede all regulatory responsibility for scientific oversight and integrity of the protocol from initial review to termination of the research, including review of informed consent."[1]

Another concern, Hahn says, was that interviewees confused institutional responsibilities with ethical review responsibilities. For example, some participants did not realize that reporting of serious or continuing noncompliance is an institutional responsibility, and not one that is just left to the outside IRB to handle. "You have an obligation to report noncompliance, regardless of the IRB that is utilized," she says. "That concept was a little confusing to people."

What also became clear is that many groups simply don't have a strong track record of using an outside IRB, Hahn says. "What came out of the conversations is that it's very unknown — 'Can I trust the review? Is it as good as what we would do?'"

Interviewees identified other barriers to central IRB review, including the following:

- the feasibility of working with multiple outside IRBs, each having its own protocol submission process;
- loss of revenue generated from fees for review of commercial-sponsored studies;
- concern for noncompliance and regulatory liability;
- concern for legal liability in the event of litigation secondary to errors, omissions, or negligence of an IRB not directly affiliated with the IRB conducting research;
- quality of review;
- potential loss of local context (for example, unique patient populations, local knowledge of investigators, or a center's resources for conducting the research).[1]

Defining responsibilities

CTTI held an expert meeting following these interviews, and developed its Considerations Document for central IRB model implementation. The document helps demystify the process of creating centralized review, and lays out the responsibilities of the institution's human research protections program and the IRB of record, and shared responsibilities. For example, one shared responsibility between the institution and a central IRB is to execute an IRB authorization agreement.

The document names responsibilities of the central IRB, including the following:

- Maintain program for education and training in human subjects research for IRB personnel.
- Register with the Food and Drug Administration and the Office of Human Research Protections.
- Ensure clinical trial meets generally accepted ethical standards of human subjects protections and complies with applicable regulations.
- Collect, review, and take into account site-specific information provided by the individual sites.
- Review and approve the informed consent form and any other research-related documents or media.

Some of the institutional responsibilities include the following:

- Maintain policies and procedures for the conduct of human subjects research as appropriate for the particular institution.
- Designate the IRB of record for the protocol.
- Ensure that the investigator/researcher is conducting research and recruiting potential research participants in accordance with IRB-approved protocol, procedures, and documents.
- Notify the IRB promptly in writing of serious or continuing non-compliance or unanticipated problems involving risks to subjects or others.

The full Considerations Document can be found on the CTTI website at http://www.ctti-clinicaltrials.org/files/documents/CentralIRBConsiderationsDocument.pdf.

Since publication of the study results and the Considerations Document in January 2013, Hahn has seen much more interest in the central IRB model. "We [NS-LIJHS] used to get only one request a month about using a central IRB — now we're fielding multiple requests every week, asking if they [institutions] can rely on us," she says. "Institutions have told us that they're developing standard operating procedures around the model."

Addressing concerns

A major concern of IRBs around central IRB use is whether it will affect jobs in the individual institutions. "One of the biggest questions we get is, 'If we consolidate, will I still have a job?' I be-

lieve very strongly that IRB professionals will still have a job — the job changes, and we're protecting subjects better," Hahn says.

Instead of having employees dedicated to review and processing of the protocol submission to a committee, the resources can be directed to other areas, such as informed consent monitoring or meeting with investigators for help in protocol design, understanding regulations, etc. "They can be more active in the implementation of the study. They can take those resources and get out there where the rubber hits the road and be side by side with investigators. It's a better use of resources than sitting in an office and processing applications," Hahn says.

Hahn and researchers also address the issue of recouping IRB fees. "People were concerned that by removing local IRB review, you'd be removing that revenue source for the IRB office," she says. "As the grant budget gets tighter, it has a dramatic impact."

To offset this, Hahn suggests institutions could develop a fee for the human research protections program. "Just because you are not doing IRB review doesn't mean you're not doing human subjects protections," she says. "Authorization agreements, reporting, monitoring, making sure investigators are qualified — none of those things go away."

The fees are comparable to IRB fees, and can still allow for IRBs to send staff to conferences and other educational and outreach opportunities. "A couple of institutions I worked with have tried this," Hahn says. "I haven't seen one company say no to a fee. I think a lot of people don't realize they can do this; it's the one thing everyone scribbles down [at seminars]."

CTTI is currently following up with the Central IRB Advancement Project, which will take the findings a step further by giving institutions more tools for adopting the central IRB model. The team is also working to develop a standard reliance agreement template. "There is an enormous amount of variability in adopting a central IRB," Hahn says. "Some authorization agreements are two pages, and some are 20 pages. This [template] will give people a foundation in which to start."

REFERENCE

1. Flynn KE, Hahn CL, Kramer JM, Check DK, Dombeck CB, et al. (2013) Using Central IRBs for Multicenter Clinical Trials in the United States. *PLoS ONE* 8(1): e54999. doi:10.1371/journal.pone.0054999. ■

Microbiome research poses ethical issues

"Do-it-yourself" raises ethical concerns

Just as companies are offering whole genome sequencing to individuals, companies are offering to sequence their microbiomes and determine how they compare to others.

There has been a lot of controversy recently about direct-to-consumer genetic testing, notes **Amy L. McGuire**, JD, PhD, Leon Jaworski Professor of Biomedical Ethics and director of the Center for Medical Ethics and Health Policy at Baylor College of Medicine in Houston.

"The FDA [Food and Drug Administration] recently sent a stern warning letter to 23andMe, one of the most well-known direct-to-consumer genetic testing companies," she says. The letter reiterated that the test kit is a medical device under the jurisdiction of the FDA to regulate, expressed concerns with the clinical validity and safety of the test, and reminded the company that it must comply with FDA requirements for regulatory oversight. (To view the letter, go to http://1.usa.gov/1crGLGd.)

In addition, a class action lawsuit filed against 23andMe alleges that the company has made false and misleading claims about the clinical validity of the test.

The direct-to-consumer sale of human microbiome analyses faces the same risk of being classified as a medical device subject to FDA regulation, especially as evidence of its health implications grows, says McGuire.

"There is a 'do-it-yourself' community that's developed around this. People with certain diseases see a lot of potential for benefit from the science, and are understandably desperate for treatment," says **Jean E. McEwen**, JD, PhD, program director of the Ethical, Legal and Social Implications Research Program at the National Institutes of Health (NIH)'s National Human Genome Research Institute.

Explain limitations of science

A related development is an attempt to "crowdfund" microbiome research projects over the Internet. "In some ways, it's an interesting new model, but it also raises all sort of potential ethical issues," says McEwen.

A key concern involves uncertainty about what

the science means, and the likelihood that some people will misinterpret information about their microbiomes.

"It is very, very early. One of the risks is that people will attach more certainty to the science than is warranted," says McEwen. "Bioethicists can play a role in explaining the limitations of the science."

There are also ethical issues related to probiotic treatments making claims based on microbiome research, says McGuire, especially the regulation of probiotics like yogurts being marketed as providing benefits for digestive health.

It is important that the public is educated about the current state of microbiome research; what it can and cannot tell us about the role of bacteria on health and disease at this point; and the risks and benefits of different pharmaceuticals, probiotic foods, and supplements, she says.

"This area of research is relatively new. Although there have been some exciting advances, we still have a lot to learn," says McGuire.

Unique ethical issues

The NIH program has received funding specifically to look at ethical issues of microbiome research. "Some of these are pretty similar to the issues we've all been hearing about for a long time with genetics more generally, but some are unique to microbiome research," says McEwen.

Privacy is a major ethical concern with microbiome research, in terms of how to ensure the information generated in the research can't be tied to a particular person. "It's hard to get a sample that doesn't also include some human DNA," says McEwen. In addition, some preliminary research suggests that individuals may actually have unique microbiome signatures.

"This raises a whole new set of possible ways that somebody could be tied back to a particular sample," says McEwen. There are potentially some forensic applications, such as law enforcement using microbiomes to track someone's whereabouts. "Some of that, at this point, may seem a little bit farfetched — but maybe not," says McEwen.

There is also a concern that people might be stigmatized somehow based on their microbiomes, either at the individual or group level. For example, research may suggest that particular patterns are found more frequently in some racial or ethnic groups than others.

"We don't know where the research is heading, but some researchers are already suggesting that there may be certain differences among populations," says McEwen.

People may make negative associations about certain individuals or groups, whether they are warranted or not. "Given the historical association between microbes and contamination, there is the potential of negative reactions in people's minds that don't exist as much with other types of research," says McEwen.

Concerns about informed consent are mainly due to safety risks being largely unknown at this point. "It's hard to consent people in a way that is informed when we don't even know what the potential risks are, because the science is so new," says McEwen. ■

Study: Trial subjects conceal health info

Concealment can jeopardize subject safety

Concealment and fabrication of prior health information is a real and growing concern for researchers, suggests a study published in the December 2013 issue of *Clinical Trials*.

Researchers from Boston University School of Medicine and Fairleigh Dickenson University in Florham, NJ, surveyed 100 subjects who had participated in at least two studies in the past year. The survey asked participants to self-report any deception used to gain entry into clinical trials.

Of those surveyed, 75% reported some form of fabrication or concealment to avoid exclusion from a study. Concealed or fabricated health information included:

- health problems or medical conditions (32%);
- use of prescription medications (28%);
- recreational drug use (20%);
- exaggerated health symptoms (25%);
- pretended to have a health condition (14%).[1]

"The fact that 75% of respondents reported some element of concealment is worrisome, as is the appreciable frequency of fabrication of health information (33% overall)," Neal W. Dickert, MD, PhD, assistant professor of medicine, cardiology, Emory University School of Medicine, Atlanta, wrote in an editorial accompanying the study. "Fabrication is obviously concerning, because false data involving important outcomes — whether subjects identify them as such or not — may directly affect the nature and impact of the findings generated."[2]

Another area of concern are the methods with which experienced clinical trial subjects avoid exclusion criteria and enroll in multiple trials. "The problem of simultaneous enrollment is well known, and many investigators are likely aware that experienced subjects know common exclusion criteria," Dickert wrote. "However, the existence of 'research kingpins' and networks for sharing screening tips is eye-opening. This report does not identify how common these practices are, but the presence of organized efforts to skirt exclusion criteria raises the level of concern."[2]

The results of this study, Dickert said, shine a light on a shift toward protecting studies rather than the protection of human subjects. "The principal shift is toward greater emphasis on protection of scientific integrity as opposed to protection of subjects," he said. "Regardless of one's view of who bears ethical responsibility for harm to subjects that result from deception, these practices are indisputably problematic if they occur with significant frequency due to their scientific implications and their potential to jeopardize the research enterprise."[2]

There are limitations to the study. The authors point out that the study did not address the frequency and context of the deception. And, Dickert added, it does not address magnitude or impact of deceptive practices, or the types of deception used. "Embellishing seasonal allergy symptoms, for example, is entirely different from reporting fictitious suicidal ideation, though both could be categorized similarly in this study," he wrote.[2]

"Understanding the context and frequency of deception will inform the extent to which it jeopardizes study integrity and safety," the authors said.[1]

Though the study does have limitations, it also highlights a need for further investigation into clinical trial subject deception. "Deception may be fueled in part by undue inducements, overly restrictive criteria for entry, and increased demand for healthy controls," the study authors wrote. "Screening measures designed to detect deception among study subjects would aid in both protecting subjects and ensuring the quality of research findings."[1]

REFERENCES

1. Devine EG, et al. Concealment and fabrication by experienced research subjects. *Clin Trials* December 2013 vol. 10 no. 6 935-948. Epub ahead of print, 18 July 2013.
2. Dickert NW. Concealment and fabrication: The hidden price of payment for research participation? *Clin Trials* December 2013 vol. 10 no. 6 840-841. ■

Hospital Report blog

For further analysis and discussion of topics important to hospital professionals, check out **Hospital Report**, AHC Media's free blog at http://hospitalreport.blogs.ahcmedia.com/. *IRB Advisor*'s executive editor Russ Underwood and associate managing editor Jill Drachenberg both contribute. ■

CNE/CME OBJECTIVES & INSTRUCTIONS

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

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

Physicians and nurses participate in this continuing education program and earn credit for this activity by following these instructions.

1. Read and study the activity, using the provided references for further research.
2. Scan the QR code below or log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. ■

COMING IN FUTURE MONTHS

■ A model for handling QI projects

■ IRB has 30-second solution to better documented informed consent

■ Want better research compliance? Consider this site's auditing method

■ Tips for HIPAA Omnibus Rule compliance

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CNE/CME QUESTIONS

1. According to Rose Anderson of the Mayo Clinic, patients found comic HIPAA forms to be engaging and fun, but too simplistic for the hospital.
A. True
B. False

2. According to experts at the University of Michigan Medical School IRB, self-directed IRB staff education can provide which of the following benefits to a human research protection program?
A. If the program is electronic and interactive, it can provide links to additional information, including explanatory videos and federal regulations.
B. A self-directed program could be self-sustaining and less costly than hiring additional education coordinators.
C. The program could include having employees review an education handbook, which also provides consistency and standardization in the education and training process.
D. All of the above

3. Which of the following is the most efficient and timely strategy for obtaining approval of a research project pre-submission to the IRB, according to Michael Centola, MHS, CIP?
A. Have a researcher or research coordinator obtain signatures from everyone involved in the research, as well as from the head of the research department.
B. Send an IRB application out by email to all involved to seek their approval, giving them a one-week deadline.
C. Use a passive approval approach where the people who need to review a research project can provide assent by not responding, and those who have questions or changes can contact the investigator.
D. All of the above

4. Which of the following does the Clinical Trials Transformation Initiative list as a barrier to institutions adopting the central IRB review model?
A. Quality of review.
B. Lack of time for generating an authorization agreement.
C. Loss of revenue from commercial-sponsored study fees.
D. Both A and C