

IRBs and data sharing

Research oversight will have to change to accommodate new requirements for studies using biorepository materials



Ellen W. Clayton

As funding agencies such as the National Institutes of Health (NIH) begin requiring researchers to share data, IRBs will be required to change the way they examine studies involving human subjects, according to Ellen W. Clayton of Vanderbilt University.

Director of the Center for Biomedical Ethics and Society at Vanderbilt, Clayton said researchers will also have to change the way they handle information.

“Scientists typically are not inclined to share data, especially investigators in genetics,” she said during a presentation at the Advancing Ethical Research Conference in Nashville.

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Central DOE IRB is up and running -

Includes Former Worker Medical Screening and multisite research involving health/productivity of workers at DOE facilities

The Central DOE IRB (CBeIRB) is officially up and running. The IRB has evolved over the years and had its origins as the Central Beryllium IRB.

The IRB’s history and purpose were described by Elizabeth White, DOE’s Program Manager for Protection of Human Research Subjects, during the first meeting of the expanded CDOEIRB, in April 2010.

In 2001, she said, DOE established the CBeIRB jointly funded by DOE’s Office of Health, Safety, and Security and the Office of Science to bring “vision, expertise and consistency to the review of all DOE-funded or conducted beryllium-related human subjects research.

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Elizabeth White

Ethics in research

Belmont Report may not address all current issues

The Belmont Report, viewed as a founding document of the research ethics field since its publication in 1979, is still useful, but it may not adequately address some of the issues in current research.

That is one of the positions that emerged during a wide-ranging discussion of the report’s applicability to 21st century human subjects protection at the Advancing Ethical Research Conference in Nashville.

Revisions were expected

Albert Jonsen, who was a member of the Commission that wrote the Report, explained that the Commissioners aimed at a succinct statement of very general principles that would have to be interpreted in light of particular cases.

“That interpretation would come, they believed, as IRB members became more adept at reviewing protocols in light of the principles,” Jonsen said.

“More importantly, the Commissioners expected that a formal structure (called the Ethical Advisory Board), would be established to provide on-going revisions and modifications as circumstances required.”

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Albert Jonsen



Lynnette Neufeld

What works? How can they be most useful to communities and to research?

The importance of community members -

These days, IRBs everywhere incorporate community voices in their deliberations about human research studies. But each IRB includes community representatives in its membership in different ways.



William Nebo



Susan Rose



Tim Ledbetter



Ann-Maria Dake

scientific particulars, and to watch for ethical discrepancies.

“As such, the community member role requires atten-

tiveness, diligence, preparation, and initiative in order to contribute to the overall integrity of the research and the respectful cooperation with the essential participants (subjects). The IRB Chair and committee members can help by regularly inviting and valuing input from the community member along these lines.”

Some use a single member, some more; some use people from the local scientific community, others avoid that, finding people far removed from science. Some IRBs provide extensive training for community members, some do not.

DOE provides special resources for community IRB members within and outside of DOE. This includes a Web site, which has an area where community IRB members can post messages, ask questions, and read various materials distributed to the community about research ethics.

The Web site is at
<http://www.ornl.gov/communityirb/>

DOE sought other ideas from IRBs connected to national laboratories and universities, with the goal of hearing from community IRB members and others involved in the process what works and how community representatives' participation could be enhanced. Here is what they had to say:

Tim Ledbetter, community member, Pacific Northwest National Laboratory IRB

“I’ve been an IRB community member for a decade or so. When joining an IRB, it is helpful to have a clear statement made to the committee about the unique roles and responsibilities of the community member.

“These include the obligation to think and speak on behalf of the local community and greater society, to ask what difference the research hopes to make, to ensure the research documents make common sense to a 6th grader, to keep the larger social-cultural perspective in balance with the

Susan Rose, University of Southern California program manager for the Office for the Protection of Research Subjects

“At USC, actively listening to our IRB community members has resulted in some wonderful products and events.

“Among these are a nationally recognized community member resource booklet, a community member CITI module, an annual lunch for local community members, a community member listserv, funding for travel to PRIM&R meetings, and more.

“Community members join the IRB for various reasons: prior illness, the honorarium, feeling a need to “give back,” learning something new, and finding about research going on in their community—all noble reasons.

“Community members represent a diverse population—some are wonderful and lead, some contribute minimally, some sleep during meetings, and some are domineering. But all must be heard in the IRB context.

“USC has endeavored to respect all of its community members by including them in retreats, education sessions, being speakers at IRB and national meetings, and listening to their requests and needs.

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Describe precisely how the institution is involved with human subjects research, being very honest about the pressures of the work.

The importance of community members -

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“Below are some resources that community members inspired us to create at USC:”

- You Want to be an IRB Community Member . . . Now What?
http://www.usc.edu/admin/provost/oprs/private/docs/oprs/brochures/community_member_web.pdf
- Informed Consent in Human Subjects Research
http://www.usc.edu/admin/provost/oprs/private/docs/oprs/brochures/IFC_Booklet.pdf
- The IRB Member Module—“What Every New IRB Member Needs to Know” (CITI module for subscribers)

William Nebo, community member, Lawrence Livermore National Laboratory

“To prepare someone to fully participate as a community member of an IRB, the following should be done.

- “Describe in formal and practical terms just how the institution deals with human subjects work and how the IRB fits into that task.
- “Then direct the new member to the CITI training site to work through the appropriate parts, which is most of it.
- “Provide written copies of appropriate government policies and institutional policies and then discuss questions and answers about those policies and expectations of community members. This should include discussion about what it means to protect human subjects, including specific examples of cases handled by the IRB.
- “Describe precisely how the institution is involved with human subjects research, being very honest about the pressures of the work. Explain possible institutional prejudices and conflicts of interest that the IRB must address in its deliberations.
- “It would also be helpful to include the history of the institution’s relationship to the community from which the member was selected.

- “Depending upon the community member’s background, it also would be helpful to provide some scientific tutoring on the technology usually covered by the IRB’s protocols.

“All of this could be very requiring of a new community member, which is why I counsel that all other integration into the IRB should be done as part of the board’s usual work as well as its continuing education for members.”

Ann-Marie Bucaria Dake, senior IRB administrator, Lawrence Livermore National Laboratory

“Both the Lawrence Livermore National Laboratory IRB Chair and Program Manager value the importance of our two community members, one of whom has been on the IRB for over 20 years. It is important to have an open line of communication with our entire board, all of whom bring their own level of expertise.

“One of our community members is also a member of both the DOE Human Subjects Working Group and the Central DOE IRB.

“We frequently ask our community members for their opinions. They both volunteer for IRB subcommittee membership and expedited review requests. They are truly engaged and value their roles as community members on the IRB. Their perspectives and contributions are invaluable to the committee.”Δ

Medical screening program has now provided approximately 70,000 medical evaluations

The Former Worker Medical Screening Program's (FWP's) background, purpose, and current efforts were presented at the Spring 2010 Central DOE Institutional Review Board meeting.

Mary Fields, FWP Program Manager, and Isaf Al-Nabulsi, FWP Program Analyst, said the program was established in 1993 with the first former worker projects initiated in 1996 and now serves all former workers (Federal, contractor, and subcontractor) from all DOE sites in locations close to their residences.

Its purpose was to "... establish and carry out a program for the identification and ongoing medical evaluation of ... former DOE employees who are subject to significant health risks as a result of the exposure of such employees to hazardous or radioactive substances during such employment ..."

Its mission is to identify and notify former workers at risk, offer medical screening, and provide information and assistance about medical follow-up and compensation.

The estimated population of former workers who are entitled to receive these medical evaluation services is upwards of 600,000 people.

To date, the FWP has provided approximately 60,000 initial screening exams and 8600 re-screening exams.

Improve protection for current/future workers
One of the program's goals is to use the findings to strengthen safety and health protection for current and future workers, Fields and Al-Nabulsi said.

To ensure objective evaluations of the health of former workers, DOE offers exams by third-party providers.

The program includes several teams, each focused on a distinct group of workers. Their job is to find



Mary Fields



Isaf Al-Nabulsi

former employees, advertise the program, provide medical screening exams, and refer participants with suspicious findings for follow-up medical testing and to the Department of Labor for potential compensation under the Energy Employees Occupational Illness Compensation Program Act, if the findings may be related to occupational exposures at a DOE site.

Two nationwide programs were established to reach as many people as possible. One is the National Supplemental Screening Program, which

is conducted by Oak Ridge Associated Universities, and the other is the Building Trades National Medical Screening Program, which is conducted by The Center for Construction Research and Training.

Also a part of the screening program are six regional projects administered by

Boston University School of Public Health, Johns Hopkins University Bloomberg School of Public Health, Drexel University School of Public Health, Queens College City University of New York, United Steelworkers, and the University of Iowa College of Public Health.

The medical screening itself may include a physical exam, chest X-ray, spirometry, blood chemistry, urinalysis, audiometry, and other tests based on specific exposures, such as to beryllium.

Program accomplishments

The program has been successful in that it has identified conditions at early stages, which allowed for successful treatment. It has also identified nonoccupational health conditions such as high blood pressure, diabetes, and highly elevated cholesterol levels.

In addition, 25 peer-reviewed scientific studies were published between 2003 and 2009 as a result of the data collected and the methods employed by the

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—Mary Fields and Isaf Al-Nabulsi

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Medical screening program -

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program or by employing FWP cohorts as a source of research participants to recruit for scientific studies funded by other sources.

One of the program's screening tools is the use of high resolution, low-dose computed tomography (CT) scans to screen a select population of workers who have a history of significant occupational exposure for early lung cancer detection (ELCD).

In August 1999, after finding plutonium at the Paducah Gaseous Diffusion Plant (GDP), a protocol was approved to screen former and current GDP workers using low-dose CT scans as a primary screening test for ELCD. The goal was to detect lung cancers early, when they are more easily cured.

Participation was voluntary and informed consent was obtained. The screening was conducted consistent with DOE's ethical guidelines.

Low-dose CT scans

The use of low-dose CT scans for workers with histories of significant occupational exposure began in 2000 at the three GDPs (Oak Ridge K-25, Paducah, and Portsmouth) and continued through 2006.

Congress in 2006 directed a similar program at the Y-12 National Security Complex and ORNL. In 2008, CT screenings were also mandated for workers at Mound and Fernald. In addition, the ELCD program was restarted at the three GDPs.

High risk of lung cancer

As the ELCD program approached its 10th year, the principal investigators of DOE's FWP submitted a proposal to DOE calling for expansion of the ELCD program to include all current and former DOE workers who are at high risk of lung cancer and meet the eligibility criteria. DOE assembled an expert panel to consider the proposal and to provide recommendations to DOE.

While there is concern about possible health effects from radiation exposure during a CT scan, benefits include the ability to detect small lesions that might otherwise not be noticed. Participants are provided full disclosure of potential radiation risks.

Participants are also told that a positive result of scanning does not alone confirm the presence of disease and that there have been no scientific studies to show that CT screening improves medical care or significantly alters outcome. In addition, screening for early detection of lung cancer using CT scans is not currently recommended by any public health agencies, professional societies, or major medical organizations, they said.

DOE has extended the FWP for another five years, from 2010 to 2015.Δ

News notes

■ HS research videos on YouTube

The Office for Human Research Protections (OHRP) has posted videos on YouTube related to IRBs and human subjects research. See <http://www.youtube.com/user/USGOVHHS>

■ African journal articles online

A full-text archive of journal articles published in Africa is now available at www.ajarchive.org. The African Journal Archive is available free of charge.

Funded by Carnegie Corporation of New York and managed by South Africa-based Sabinet Online, the collection currently includes 150,000 pages of journal archives of academic, scholarly, institutional, museums, and professional research organizations in Africa.

Over the next three years, Sabinet's goal is to digitize, index, and provide access to more than 200 journals consisting of 90,000 indexed articles in the sciences, social sciences, and humanities.

Central DOE IRB is up and running -

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“As a result, beryllium research projects—and more recently the former worker medical screening projects—now have informational materials and consent forms that are clear, accurate, and consistent.”

In January 2010, the Central IRB’s mission was expanded to also serve as the DOE IRB of record for the entire Former Worker Medical Screening Program (FWP), not just the beryllium component, as well as multisite studies of current worker health and productivity.

Includes diverse membership

Its membership, White said, includes people with medical and scientific backgrounds as well as an attorney, a psychologist, community members, current and former workers from DOE sites, coordinators from several projects, and administrators or chairs from three DOE site IRBs.

Alternate members also are included but may vote only if the primary member is unavailable. When the voting member rotates off the board, the alternate has the option of taking that place.

Targeted medical screening

All research using personally identifiable information must comply with DOE requirements for the protection of this information.

White said that the board might also be employed for future research studies on emerging issues and technologies.

The central IRB’s current projects include a study of the health impacts of beryllium exposure and a study of genetic and exposure factors in beryllium sensitization and disease.

Another is the development of a beryllium biorepository that will make deidentified information available to the research community for the purpose of increasing our understanding of the diagnosis, progression, and treatment of disease. This includes blood and tissue samples from: a) exposed individuals who are not beryllium sensitized, b) sensitized individuals, and c) individuals who have chronic beryllium disease.

Still another is the FWP, which is the largest DOE-funded effort looking at health impacts of previous work at DOE sites and has since 1996 provided targeted medical screening to DOE’s 600,000 former workers. In addition, the Central IRB is responsible for reviewing several new multisite studies which

will look at the health and productivity of the current employees at DOE sites.Δ

News notes

■ **Non-English consent forms**

Readability issues in non-English consent forms are addressed in the July–August 2010 issue of *IRB: Ethics & Human Research*.

The authors say that when consent forms are created in English and then translated into another language, they are often not sufficiently comprehensible to readers. For more information, see <http://www.thehastingscenter.org/Publications/IRB/Default.aspx>.

■ **Sex and research subjects**

Ethical dilemmas related to sexual relationships and research are discussed in an article by Timothy Murphy, University of Illinois College of Medicine at Chicago.

Published in the June 23, 2010, issue of *The American Journal of Bioethics* (Vol. 10, No. 7, pp 30–38), the article says that professional standards rule out sex with research subjects who are also patients but do not necessarily apply to nonclinical relationships.

Murphy says that sex in nonclinical research relationships might be treated as it is elsewhere among adults, as a matter of individual choice and responsibility. Alternately, one could ask oversight bodies to draw lines between research that can safely accommodate sexual relationships and research that cannot. The deficiencies of various options suggest the need for a professional code of conduct for nonclinical researchers.

At the end of the day, the real protection in research using biorepositories is going to be in oversight, not in informed consent. And absent oversight, there will be no protection for participants.

IRBs and data sharing

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Increased pressure to share data will affect our way of thinking about informed consent, oversight, return of results, and identifiability, she said, “especially because we have much more data available to many more investigators over a much longer period of time.”

On the one hand, the increased access resulting from more sharing will lead to more results and more knowledge, which leads to improved human health. “On the other hand, we’re not sure how

We’re not sure how much choice research subjects will have regarding future uses of samples.

much choice research subjects will have regarding future uses of samples.

“At the end of the day, the

real protection in research using biorepositories is going to be in oversight, not in informed consent,” Clayton said. “And absent oversight, there will be no protection for participants.”

The issue of returning results of research on biorepository samples is “enormously controversial,” she said, with opinions ranging from nothing should be returned to everything should be returned.

If results have to be returned to the people who originally provided the material, how far in time and distance does that obligation extend? The material can be used by many people down the road, not just the investigator who first gathered it. Does everyone who uses it, no matter how long from now, have an obligation to return results? “The problem,” Clayton said, “raises both legal and practical issues.”

If results are going to be returned, there must be an ethically acceptable way to do it so that people understand the implications. “So, who will return

them? How will it be done? Who ensures that the research participant and the clinician understand the results?

“And what about people who don’t want the results? People will say they want results of genetic tests, but a substantial proportion choose not to get them when they become available, especially for cancer predispositions and Alzheimer’s. It would be a little peculiar to call someone and say I know something about you; do you want to know it?”

Who is going to decide what results are important enough to return? “The challenges for IRBs will be enormous in deciding these questions,” she said.

Removing identifiers also carries uncertainty for researchers and IRBs, Clayton said. “But removing identifiers is more difficult to achieve given the prevalence of online data bases. Samples can be triangulated and identified. Going into the future, with our robust computing tools and the Internet, it’s going to be harder to say someone is deidentified,” she said.

Making the issue even more difficult—“if we have to return results to donors, we have to retain identifiers for them. But this isn’t possible if removing identifiers is required to deposit samples in repositories and to protect from risk of identification,” she said.

Finally, “about the issue of oversight and accountability, where does the buck stop? I’ve been thinking about biorepositories for almost 20 years and have come to think that almost all the action is in oversight, and yet we have defused oversight accountability.

“This means the only real accountability will be with IRBs deciding how things go into repositories and how downstream investigators access the repository. It will be interesting to see how this will work,” she said.Δ

Dan Ariely: While it may seem that if people are given enough of just the right information, they will be able to make a truly informed decision about participating in human research. This might be true if people were different. They aren't.

Don't count on people to make rational choices -

Behavioral economist Dan Ariely says there is a difference between how people actually act and how they would perform if they were completely rational. Those who design research protocols and consent forms should take note.



Dan Ariely

He cited several examples of people thinking they are making the right decision and employing the correct information, whereas they are actually doing something very different. This is especially true if people are given too much information, as they might be on a consent form. It is also true if they are given information designed to make them choose in a specific way.

Organ donation

For example, the various European countries seem to have very different views on willingness to donate organs and body tissue after death. In some countries the willingness is very high. In Sweden, 86% of people choose to donate, whereas in Denmark it is only 4%, even though culturally there does not seem to be that much difference.

"What caused the difference," Ariely asked.

The forms used by the two countries to seek approval for donation was different in only one way, but a significant way.

In Denmark, the form asks that a box be checked "if you want to participate in the organ donor program." The result was that people don't check the box," he said, "because the path of least resistance is the default, which is to do nothing."

In Sweden, however, the form asks that a box be checked "if you don't want to participate." Again, the default is to do nothing, which is what people do. They don't check the box and so they have implicitly agreed to donate their organs. The difference between these two methods is called opt in and opt out."

The power of defaults only gets larger, Ariely said, when the situation is more complex and the amount

It often seems that if people are given enough of just the right information, they will be able to make a truly informed decision about participating in human research.

Dan Ariely, a behavioral economist at Duke University, says that might be true if people could be counted on to make rational choices.

But they can't.

Author of the books, *Predictably Irrational: The Hidden Forces that Shape Our Decisions* and *The Upside of Irrationality: The Unexpected Benefits of Defying Logic at Work and at Home*, Ariely was a keynote speaker at the Advancing Ethical Research Conference in Nashville.

Ariely studies how people actually act in the marketplace, as opposed to how they should or would perform if they were completely rational.

Informed consent

He suggests that if researchers designed informed consent procedures with a better understanding of people's real motivations—which are much messier than the rational decision-making that theoretically should motivate them—the process might work better.

Too much information isn't necessarily going to get the desired result.

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Ariely said his research tries to get more understanding about how we can so often think we know what we're doing, and have intuitions about right and wrong, but we get it wrong.

Rational choices

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of information is larger. For example, in a study of physicians who are giving advice to a 67-year-old farmer with hip pain, the physicians are divided into two groups. Both refer the farmer for hip replacement surgery.

One group, however, is told that “the next day you realize you forgot to suggest that the farmer first try ibuprofen before getting surgery.” The question is, do you call the farmer and say, wait, try ibuprofen first. Basically, all the physicians agree that this is what they will do.

The second group is told that “the next day you realize you forgot to suggest that the farmer tries two medications as options rather than proceeding with surgery.” The question for them is, do you call the farmer and offer one or both of the medications instead of surgery.

The second group had a more complex set of options, two medications or one medication, and in this case most of the physicians let the farmer proceed with surgery rather than calling to recommend medication. Why? Because as the information becomes more complex, all of us (even if we are highly paid professionals) are more likely to choose the default.

Buying jam

Similarly, he said, an experiment was tried that placed six sample jars of jam that could be sampled in a supermarket. Customers were given coupons that could be used to buy any jams in the store. On the next day, 24 jars of jam were placed in the display and customers were given coupons again.

The result was that 30% of the customers who had only six jars to sample actually bought jam using the coupon. Only 3% of those who had 24 jars to sample actually bought jam.

“The people who had to choose from 24 jars found the question too complicated. They were given too much information, and they didn’t know what they wanted to do.

“So, if it’s too much for people to know what to do about buying jam, think about other decisions they have to make—financial decisions, health care decisions.”

More choices makes it harder

What do we do, he asked, when we doubt how able people are to make wise choices for themselves.

“It’s easy to say people know what’s best for them and we’ll give them all the options and choices to make up their own minds. But the reality is that when we give more choices we’re making it harder for them.

“That puts more responsibility on the people designing the choices and deciding what the default and information presentation will be. Often, in research, the default is not to participate. Is this the right thing?” he asked.

If it's too much for people to know what to do about buying jam, think about other decisions they have to make—financial decisions, health care decisions.

Ariely, who has had considerable experience as a patient when he was being treated for third degree burns over 70% of his body, said he remembers trying to express his opinion to nurses about better and worse ways to help him.

They didn’t want to hear it. “They want patients to be passive; they said ‘we know what we’re doing.’” Later, conducting experiments as a researcher, he said he learned that indeed there are better and worse ways to treat people in especially painful conditions.

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People don't know their own preferences and the implications of that. This makes it more difficult to protect people in situations like research studies when they don't know what they want.

Rational choices -

(Continued from page 9)

"In standard economic theory it is believed that people can make the right decisions on average. Some people get it wrong in this way, some in others, but on average, it will work out.

"But here we have nurses who were getting it wrong all the time, nurses with good intentions who were wrong consistently."

Ariely said his research tries to get more understanding about how we can so often think we know what we're doing, and have intuitions about right and wrong, but we get it wrong.

He said vision is one of the skills humans are best at doing, "with a huge part of our brain dedicated to the task." Even so, he said, when shown optical illusions, including the standard ones of straight lines, bent lines, and so forth, we get it wrong consistently.

"If we make so many mistakes, predictable mistakes, at something we're so good at, what do you think is going on with more important things?"

The attractive version

In another experiment, Ariely was able to manipulate people's choices when they were asked to choose from three photographs the person they were most attracted to. By starting with two very different people—Tom and Jerry—and then adding a third who was an unattractive version of Tom, people almost invariably chose the more attractive version of Tom, rather than Jerry. The people who designed the experiment skewed people's choices by ensuring that they saw the attractiveness of Tom by having the contrast.

"One of the things we learned from this is that people don't know their own preferences that well, and the implication of that is that people can be made to do what the people who design their decisions environment (supermarkets, advertising, researchers) want them to do. This also makes it more difficult to protect people in situations like

research studies when they don't know what they want," he said.

Paternalism

This makes the issue of paternalism even more important and troublesome because when consent forms are designed, how do you know what to include and what to exclude if you cannot trust people's decisions about what is in their best interest?

Conflict of interest for researchers is similarly troublesome, he said, because his studies suggest that when a physician, for example, tells patients that a conflict exists, the physician may well be more likely to wrongly try to benefit from that conflict.

He said conflicts can not be managed; they must be eliminated entirely—or at least as much as possible. This means, for example, that researchers should do whatever is necessary to divest themselves of any financial interests in the studies they conduct.

"The standard economic view is of human nature as noble, true, and beautiful, that if we let people alone to make decisions they will do what's best."

The evidence suggests otherwise, he said.Δ

Web sites

International Bioethics Exchange Program
<http://bioethics.georgetown.edu/ibep/itr.htm>

Is the IRB Model Relevant in Africa?
<http://www.bioethicsforum.org/ethics-review-of-medical-research-in-Africa.asp>

Research Ethics Committees in Africa
<http://www.hopkinsmedicine.org/bioethics/news/africa.html>

Aboriginal Community Values (from the Journal of Empirical Research on Human Research Ethics)
http://www.csueastbay.edu/JERHRE/notes/AboriginalComm_Values.pdf

Using local IRB review began in the 1970s when the world was a different place, when it was a single site and a single investigator looking at a handful of subjects.

The case for centralized IRB review

Law professor says disclosing researchers' conflicts of interest has little effect on people's willingness to participate in studies



Dan Nelson

Centralized IRB review is the only logical approach to providing effective and efficient oversight of multisite research, according to Dan Nelson, director, Office of Human Research Ethics, University of North Carolina, Chapel Hill.

Using local IRB review began in the 1970s when the world was a different place than it is today, when it was a single site and a single investigator looking at a handful of subjects, Nelson said during a talk at the Advancing Ethical Research Conference in Nashville.

"Now it's phase III studies with thousands of subjects at hundreds of sites across the country or the world. The oversight system has failed to evolve to keep pace with the volume, complexity, and nature of the research it oversees."

Multi-site studies

Depending on the trial, before a local IRB ever reviews a multisite study, a committee designs the study, a steering committee reviews it, external DSMB and protocol committees review it, the FDA and/or the NIH reviews it, the investigators and institutions are selected and vetted, study-specific consent templates are created and reviewed, and a central IRB may review it.

This means, Nelson said, that the reality is that multi-center research is a take it or leave it proposition for individual sites because the identical protocol is used across all sites. Local IRBs don't get to tinker with it.

"Even if major issues are found by the local IRB, the likely result will be exclusion of that site because there is little that can be done to modify the underlying protocol."

Local IRBs are left to tinker only with the one thing they can control, which is to write a consent form,

the result of which in a multisite study is 100 versions of the form.

Alternative models have been suggested, he said, including various forms of IRB cooperation and reciprocity. The barriers to these are various combinations of history, inertia, isolationism, lack of awareness of alternatives, and especially fear. Nelson said fear comes from concerns about liability, sharing

Today, it's phase II studies with thousands of subjects at hundreds of sites across the country or the world. The oversight system has failed to evolve to keep pace with the volume, complexity, and nature of the research it oversees.

authority and responsibility, ensuring quality of review, costs, and loss of revenue.

Most of these concerns can be addressed, he said, by establishing a good relationship between the institution and the external IRB "with trust, transparency, and good communication."

Nelson said SACHRP supports collaborative and alternative IRB models and has requested the U.S. Department of Health and Human Services to encourage the National Institutes of Health director to "explore more widespread use of collaborative IRB models, including the expanded use of centralized IRBs for NIH-sponsored research."△

(Note: See article on DOE's Central IRB, page 1.)

Local IRBs are in a better position to keep an eye on noncompliance, to quickly see what is occurring so that problems are resolved before they become worse.

The competing case for local IRB review -

The history of research scandals from the 1960s resulted in the current system of local control. Local IRBs have knowledge of the community, they know the investigators and staff, and are better able to keep an eye on developing problems



David Forster

“Local IRBs are better able to follow up on subject complaints and problems because they are local and can resolve issues more effectively, face-to-face,” he said.

They are also in a better position to keep an eye on noncompliance, to quickly and easily see what is occurring and talk to those involved so that problems are resolved before they become worse.

Protecting image of local IRB

In addition, Forster said, local oversight is better able to protect the image of the IRB in the eyes of the investigators and the community. Because they are local and are tied to the institution and the institution’s standing in the community, they can guard the interests of everyone involved. Similarly, they can “manage risks for the institution by such things as having a local legal office that can oversee the IRB’s compliance and intervene on the institution’s behalf as necessary.”

By using a local IRB, the institution can provide and control the resources necessary to support the IRB and the research infrastructure. “If you’re using a central

IRB, the institution has no control over funding,” he said. And, having its own IRB provides a cost-effective means of providing IRB review for unfunded research such as that done by students or initiated by the institution’s own investigators.

Conflicts of interest

Also, because local IRB members are not paid, there is likely to be less of a problem with conflicts of interest, Forster said.

He cited the 1978 National Commission’s Report and Recommendations: Institutional Review Boards, which said “the rights of subjects should be

Those who argue against the effectiveness of local IRBs ignore the history of research scandals from the 1960s that resulted in the current system of local control, according to David G. Forster, of Western IRB, a commercial review board.

“There was a good reason to establish local IRBs and there remains good reasons,” he said.

Local IRBs have knowledge of the community, including racial, cultural, ethnic, and religious characteristics that cannot be detected by looking at census demographics, he said.

Knowledge of investigators

Local IRBs also know the investigators and their staff. “They know who skirts the requirements, who almost lost hospital privileges the year before, and who causes legal risk to the hospital. They also know who always plays by the book, and they can use that knowledge in reviewing the research.”

They are also better able to judge the acceptability of research given the resources available, including whether there is appropriate nursing staff to support a study, and such resources as the availability of expertise in the hospital for adverse events.

Because local IRB members are not paid, conflicts of interest are less likely.

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The case for local IRBs

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protected by local review committees operating pursuant to federal regulations and located in institutions where research involving human subjects is conducted."

That report also said that "Compared to the possible alternatives of a regional or national review process, local committees have the advantage of greater familiarity with the actual conditions surrounding the conduct of the research. . . . Such committees can work closely with investigators to assure that the rights and welfare of human subjects are protected and, at the same time, that the application of policies is fair to the investigators."

Finally, Forster said that when local IRBs review protocols for multisite trials, it means more people will be examining the ethics, which means there are more oversight and more of a chance they will find problems that might exist.Δ

Web sites

High School Bioethics Curriculum Project
(Georgetown University)
<http://highschoolbioethics.georgetown.edu/>

FDA Information Sheets for IRBs
<http://www.fda.gov/oc/ohrt/irbs/appendixc.html>

The National Academies Institutional Review Board
<http://www7.nationalacademies.org/irb/>

Human Subjects Research Training, sponsored by The Collaborative IRB Training Initiative (CITI) and The University of Miami
<http://www6.miami.edu/citireg/>

Office for Human Research Protections (OHRP), Department of Health and Human Services
<http://www.hhs.gov/ohrp/>

Office for Human Subject Protections (OHRP)—IRB Guidebook
http://www.hhs.gov/ohrp/irb/irb_guidebook.htm

New resources

■ Ethical issues in consent

The Ethics of Consent, ed. by Franklin Miller and Alan Wertheimer. 432 pp. Oxford University Press, 2009. \$49.95.

This book includes contributions from several distinguished scholars discussing the ethics of consent in theory and practice. Part one addresses theoretical perspectives on the nature and moral force of consent, and its relationship to key ethical concepts, such as autonomy and paternalism.

Part two examines a broad range of contexts, including sexual relations, contracts, selling organs, political legitimacy, medicine, and research.

A reviewer says the book is "a contemporary, general and multidisciplinary treatment of the topic of consent, which has not been previously addressed in this way in a book-length format . . . because the book is written by experts working in a variety of disciplines, the book will be relevant for a wide cross-section of academics, in bioethics, but also in law, political theory, and gender and sexuality studies."

■ New research journal

The American Journal of Bioethics has begun a new journal, *AJOB Primary Research*. The first issue was published in February 2010.

This journal will publish empirical research in bioethics and the social sciences on a wide range of topics from end-of-life care to medical professionalism to stem cell research.

Issue 2 includes articles about pharmacist conscientious objection, religion and genetics and genomics, understanding informed consent, and the impact of written policies on euthanasia in the Netherlands. For information, see <http://www.tandf.co.uk/journals/uabr>

Individual autonomy and informed consent is the basis of moral research, but the Western emphasis on individual autonomy does not predominate in all cultures.

Belmont Report -

(Continued from page 1)

Jonsen said the Advisory Board was briefly set up but soon disappeared. The result has been that the evolving nature of biomedical research has posed new problems that Belmont does not appear to address.

“For example, we are much concerned about cultural distinctiveness of research populations that make some principles, such as Respect for Persons, difficult to realize,” he said. “Although in recent years, the Office of Protection of Research Subjects has instituted an advisory body, this work of continued re-evaluation of Belmont has not taken place.”

It would be useful to expand on those principles . . . to apply them in settings where the people and cultures are very different.

Jonsen, Emeritus Professor of Ethics in Medicine at the School of Medicine, University of Washington, also pointed out that the three principles of

Belmont were crafted precisely as ethical principles relevant to the research enterprise.

“Although the words in which they are stated reflect general notions of moral philosophy, the Commissioners did not espouse any particular theory of moral philosophy. They hoped that their formulation would address the very special moral issues raised by research.

“For example, the principle of Respect for Persons, despite its roots in the moral philosophy of Kant, Mill and others, must be seen as a challenge to the utilitarian views that often spur research.

“The drive to better health care or add to scientific knowledge cannot,” said Jonsen, “override the fundamental moral principle that no one should be forced to take risks for the good of others without their free and voluntary consent.

“Thus, each of the principles needs to be tailored to the research enterprise. Belmont, he said, should be seen as a sort of Constitution for the Republic of Research, in which all researchers and all subjects participate voluntarily to promote a public good,” he said.

Research in resource-poor settings

Panelist Lynnette Neufeld, Chief Technical Advisor at the Micronutrient Initiative in Canada and former director of the Division of Nutritional Epidemiology at the National Institute of Public Health, Cuernavaca, Mexico, said that research conducted in resource-poor settings illuminates a limitation of Belmont, especially when people have limited availability or accessibility to health services.

It is not necessary to modify the principles of Belmont, she said; instead, it would be useful to expand on those principles to get more understanding about how to apply them in settings where the people and cultures are very different than the cultures where the Belmont originated.

It's unreasonable to think that a population will obtain access to drugs or procedures in a health care system that's not functioning.

For example, the report's requirement to respect persons emphasizes individual autonomy that is implemented by informed consent.

“This is the basis of moral research. But the Western emphasis on individual autonomy does not predominate in all cultures,” she said.

Instead, she said she has observed in some groups in Mexico and elsewhere that decision-making is some-

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Rather than modifying the principles of Belmont, Neufeld said, “we need clear guidance on how to apply the principles in resource-poor settings.”

Belmont Report

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times “a collective process occurring in the community or extended family.”

Not recognizing this, Neufeld said, “does not provide adequate respect for communities or adequate protection for the individuals who are a part of them.”

Another concern when conducting research in resource-poor countries is that the people who live in marginalized communities with a history of cultural discrimination may be illiterate, have minimal or no education, and may not understand the languages that might be used.

“There are 28 languages spoken in various parts of Mexico, and access to health care might require a 10 or 15 kilometer walk and boat rides.

“How can we ensure that information comprehension and voluntary participation are occurring in a disempowered population?”

Another of the Belmont principles is justice, the emphasis for which “is on ensuring that risks are not disproportionately borne by the disadvantaged and benefits by the privileged,” Neufeld said. It also requires that research not be “conducted in populations that will not eventually benefit in some way from the research.”

“Even when both conditions can be met, it’s unreasonable to think that a population will obtain access to drugs or procedures in a health care system that’s not functioning.”

The third Belmont principle is beneficence, which implies doing no harm. For this to be the case, we would need a full understanding of the potential risks and benefits for the population being studied, including the physiological, social, economic, and emotional implications of the research.

“It may be impossible to assess the risks and benefits without an in-depth understanding of social, cultural, and political settings, especially when research is being conducted in multiple sites,” Neufeld said.

Further, “how can we adequately assess potential risks and benefits if we do not have complete knowl-

edge of the functioning and failings of the health system?”

“It seems clear that it’s not ethical to conduct research in these settings, but the truth is that it happens all the time all over the world.”

Rather than modifying the principles of Belmont, Neufeld said, “we need clear guidance on how to apply the principles in resource-poor settings.

“The usual ethical training for researchers does not adequately provide the kind of training to take these things into consideration in the design and implementation of their studies. There is also a lack of guidance to ethics review boards here and abroad about how to adequately take these challenges into account in the review of research studies.”

Neufeld said part of the solution is to bring more people into the process from communities and regions where research is being conducted, including ethicists, researchers, and others who can provide better understanding of the local context.

“We should also encourage a dialogue between U.S. IRBs and research ethics committees in the countries themselves, which would take advantage both of the know-how that exists there and the know-how that comes from the U.S.”^Δ

Research ethics

The National Reference Center for Bioethics Literature: A specialized collection of books, journals, newspaper articles, legal materials, regulations, codes, government publications, and other relevant documents concerned with issues in biomedical and professional ethics.
<http://www.georgetown.edu/research/nrcbl/nrc/bibliographies.htm>

The National Information Resource on Ethics and Human Genetics
<http://www.georgetown.edu/research/nrcbl/nirehg/index.htm>

News notes

■ International compilation

The 2010 edition of the International Compilation of Human Subject Protections has been released and is now available online.

The document can be seen at <http://www.hhs.gov/ohrp/international/HSPCompilation.pdf>.

The 2010 version lists about 1,100 laws, regulations, and guidelines on human subject protections from 96 countries. This year's compilation includes listings from 5 new countries: Dominica, Guatemala, Honduras, Kyrgyzstan, and Qatar.

Many of the listings include the web address, allowing the reader to link directly to the law, regulation, or guideline of interest.

It was prepared by the Office for Human Research Protections of the U.S. Department of Health and Human Services. It is designed for use by IRBs, researchers, sponsors, and others involved in human subjects research around the world.

■ Listing of research ethics activities

The Alden March Bioethics Institute maintains a comprehensive listing of conferences, educational programs, and other activities related to research ethics and related issues. For information, see <http://www.bioethics.net/events.php?page=1>

For a listing of bioethics news generally, see the institute's site at <http://www.bioethics.net/>

■ Online research ethics seminar

North Carolina State University has developed a free, online "Open Seminar in Research Ethics" to provide the research community with an ongoing forum for discussion of continuing issues. Information about the seminar is at <http://openseminar.org/ethics/>

The online forum is part of a research ethics program that includes an initiative funded by the National Science Foundation, "A Model Curriculum for Land Grant Universities in Research Ethics" (LANGURE), which is a national network of eight land grant and historically black universities developing a model curriculum in research ethics.

Resources

IRB resource links

<http://www.peacehealth.org/IRB/links.htm>

U.S. Department of Health & Human Services (HHS) Office of Research Integrity

<http://ori.dhhs.gov/>

Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule

http://privacyruleandresearch.nih.gov/pr_02.asp

Bioethics blogs

Bioethics blog, written by the editors of The American Journal of Bioethics

<http://blog.bioethics.net/>

The Hastings Center bioethics forum

<http://www.bioethicsforum.org/whatis.asp>

Women's bioethics project

<http://womensbioethics.blogspot.com/>

Business ethics (includes discussion of the bioeth industry in the developing world)

<http://www.businessethics.ca/blog/>

Meetings

■ American Society for Bioethics and Humanities 12th Annual Meeting

Oct. 21–24, 2010

San Diego, California

For information, see <http://www.asbh.org/meetings/annual/index.html>

■ 17th Annual Pitts Lectureship

Oct. 29–30, 2010

The Medical University of South Carolina, Charleston, South Carolina

“Ethical issues in clinical and translational research”

For information, contact Chris Rutigliano at rutiglia@musc.edu

■ Research and Children Conference

Nov. 8, 2010

Bethesda, Maryland

This meeting is sponsored by the Drug Information Association.

For information, contact Constance Burnett at Constance.Burnett@diahome.org, or 215/293-5800

■ 2010 Advancing Ethical Research Conference

Dec. 6–8, 2010

San Diego, California

Pre-Conference programs are on Dec. 5

For information, see <http://www.primr.org/Conferences.aspx?id=56>

■ 2011 ELSI Congress: Exploring the ELSI Universe

April 12, 2011

University of North Carolina, Chapel Hill

A research community congress to explore ethical, legal, and social implications (ELSI) of the new genomics, sponsored by the National Institutes of Health and others.

For information, see <http://genomics.unc.edu/genomicsandsociety/html/ELSIcongress>



Protecting Human Subjects

This newsletter is designed to facilitate communication among those involved in emerging bioethical issues and regulatory changes important to both DOE and the human subjects community.

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<http://humansubjects.energy.gov/doe-resources/newsletter/>