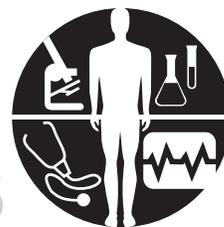


PROTECTING HUMAN SUBJECTS



Office of Biological and Environmental Research • U.S. Department of Energy • Spring 1999

This issue of the newsletter Protecting Human Subjects is devoted entirely to discussion of the important educational role that site reviews play in the effort to protect the dignity and well-being of people who participate in research projects.

Education. That is the single word Dr. Susan Rose uses to describe the purpose of the site reviews her office conducts of the human subjects protection programs across the Department of Energy (DOE).

As manager of DOE's Human Subjects Program, Dr. Rose believes that reviews help to assure that researchers, managers, and administrators understand their responsibilities for protecting the welfare and the rights of people who are subjects of research funded by DOE or conducted by or in a DOE facility.

"A system that only looks for flaws and doesn't educate or reward will never be effective or lasting," she said.

DOE reviews each of its laboratories about once every three years. The

Site reviews: *Protecting the rights and welfare of human subjects*

*By Lisa Carroll,
Oak Ridge Institute
for Science and Education*

review encompasses the policies, practices, and performance of the Institutional Review Boards (IRBs) as well as the oversight of the IRBs by the local DOE office.

The scope of a review varies with the kinds of research conducted at a given site, whether nuclear medicine, genetics, imaging studies, or worker health.

DOE policy requires review by a local IRB familiar with the local community even when an outside investigator performs the research.

In 1998 DOE reviewed four of its largest laboratories, smaller research facilities near them, and the operations

offices. The review teams visited Richland, Washington, home of the Pacific Northwest National Laboratory (PNNL); Albuquerque, New Mexico, where Sandia National Laboratories, and the smaller

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Site reviews

— Continued from page 1

Lovelace Respiratory Research Institute (LRRRI) are located; Los Alamos National Laboratory (LANL) in Los Alamos, New Mexico; and Oak Ridge National Laboratory (ORNL) and Oak Ridge Institute for Science and Education (ORISE) in Oak Ridge, Tennessee.

Recent trends

Two recent trends strongly flavored the 1998 reviews: One is the expanded use of powerful new tools in genetic and molecular biology; and the other is health research on current and former DOE workers.

Although DOE's local IRBs have a long history of reviewing human studies, the rapidly changing technologies in genetics and the increase in the number and scope of health studies have intensified concerns about nonphysical risks to research subjects, such as loss of privacy or entitlements.

These potential risks create a greater need to educate IRB members, researchers, managers, and prospective subjects on understanding and evaluating the studies. The complexity of these studies, which may

involve multiple sponsors, research institutions, DOE sites, and even other nations, increases the need for vigilance in protecting the rights and welfare of participants.

Team members' expertise

For the site reviews, Dr. Rose convenes a team of 5–7 members chosen for their experience with the ethical issues the site may be facing and for their expertise with the kinds of research in progress at the labs reviewed.

The teams may include members and staff from DOE or other IRBs, as well as researchers, ethicists, worker subjects, and staff from other federal agencies, universities, and research hospitals.

Reviewers are also chosen for special expertise relevant to a particular review. For example, Dr. Michael Kelly, chair of the Georgia Tech IRB and a psychologist who conducts ergonomic research, joined the team that reviewed the programs in Albuquerque, where Sandia National Laboratories conducts several projects with ergonomic components.

Participants at the LANL site review included, from left, Jerry Williams, head of occupational medicine and chair of the IRB, LANL; Paula Knudson, University of Texas Science Health Center; Sherry Davis-Cross, PNNL; Mike Kelly, Georgia Tech; Irene Jones, Lawrence Livermore National Laboratory.



Reviewer John Campbell brought his experiences as a former tunnel work supervisor on the Nevada Test Site to review worker health studies. He is also interviewing other retired workers for an oral history of the Test Site and is enrolled as a subject in a current health study.



John Campbell, right, a former tunnel work supervisor on the Nevada Test Site, is now a site reviewer. With him is **Glenn Bell**, a former machinist at the Y-12 plant, Oak Ridge, TN. Bell is a subject in studies of beryllium.

Dr. Marjorie Speers, who chairs the Center for Disease Control and Prevention (CDC) IRB, participated in all three 1998 reviews and provided valuable insights and recommendations based on CDC's extensive experience and her own expertise.

Review agenda

Dr. Rose carefully plans the format and agenda of each review. The team hears presentations by the operations office, laboratory senior managers, and IRB chairs. It interviews IRB members and staff and project investigators. Time is set aside for members to read project files, the lab's human subjects protection policies, and other relevant documentation.

The site visit ends with a close-out meeting on the review team findings. Afterwards, Dr. Rose compiles the reviewers' reports into a brief summary of the program's strengths and weaknesses and recommendations for change. This summary is formally transmitted to the site for response and further action.

Each review offers the IRB staff and researchers opportunities for informal exchanges with review team members, many of whom wrestle with similar issues at their home institutions.

Public education colloquia

- Most importantly, each review includes a public education collo-

quium on a human subjects protection topic chosen by the site. At Richland, team member Susan Katz, a lawyer who served on the Yale University IRB, led a discussion of privacy issues, focusing on the extent of protections offered by the Privacy Act.

- In Albuquerque and Los Alamos, University of New Mexico philosophy professor Joan McIver-Gibson conducted interactive sessions on "Research/Medical Monitoring/and Workers' Rights."

Colloquium participants explored such questions as the overlap between scientific research and occupational health surveillance, the ethics of using data previously collected for other purposes, and the protection of the privacy of personnel records.

Colloquium participants noted that difficulties may arise when researchers as "routine users" obtain legitimate access to personnel records, at times without the prior knowledge or explicit consent of the worker. Although the worker/subject may be supportive of the goals of a health study, he or she may want to know, in the words of one Los Alamos IRB member, "Who's going to have access to my records?"

- In Oak Ridge, a panel (pictured on page 4) addressed "Issues Involving Workers as Research Subjects." Panelists were Reed Durham, a

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Each review offers the IRB and researchers opportunities for informal exchanges with review team members, many of whom wrestle with similar issues at their home institutions.



A panel meeting during the ORNL site review addressed issues including the protection of privacy. From left are moderator Dr. Tom Lincoln and panelists Dr. Howard Friedman, Amy Rothrock, Reed Durham, and Dr. Donna Cragle. All are from Oak Ridge.



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The sites reviewed indicated a high level of confidence that all projects with human subjects were being brought to the IRB.

chemist at the Y-12 Plant analytical lab, who is beryllium sensitized as a result of his occupational exposure; Dr. Howard Friedman, a psychologist who facilitates a Y-12 Plant support group for beryllium workers; Dr. Donna Cragle, an ORISE epidemiologist conducting a long-term study of beryllium health effects among DOE workers; and Ms. Amy Rothrock, the DOE Oak Ridge Freedom of Information Act officer, who explained the controls on access to medical and exposure records.

Finding the projects

In 1998, reviewers looked closely at how well the IRBs were doing in such essential areas as identifying projects, making and documenting review decisions, educating researchers and managers about the needs and the procedures, and adequacy of funds to maintain the program infrastructure.

Reviewers also looked at the interest, support, and oversight of the site program by the operations office. In each of these areas, the site reviews identified strengths and weaknesses at the sites.

The sites reviewed indicated a high level of confidence that all projects with human subjects were being

brought to the IRB. This is due to the IRB chairs and administrators making educational outreach to research staff a central mission.

Administrative checks in both DOE labs and operations offices help identify human subjects in proposals and research plans. At Albuquerque, for example, staff who oversee work for other federal agencies and partnerships with private industry participated in the review both to learn about the issues and to communicate their efforts to identify projects that need IRB review.

Human Subjects Research?

The sophisticated technologies developed by DOE labs attract research clients and partners from many organizations. In some cases, a federal agency or an industry may identify a human use for a lab invention or invite the lab to conduct follow-on work. When this happens, or when the researchers are engineers, they may not easily recognize that the research is a human subject project and thus requires that human subjects be used to evaluate the actual operation of the invention.

For example, several years ago, the National Institute of Justice proposed a crowd control foam and contracted with a DOE lab to test



the ability of this substance to immobilize humans. The engineers had no previous experience in research with human subjects.

The project was delayed until the lab's IRB reviewed and approved the project. Past problems heightened DOE attention in the labs to nontraditional projects that involve human subjects and the importance of IRB review. The solution to solving this problem is in education/communication involving lab engineers and other non-bio-medical researchers. The researchers must be made aware of human subjects definitions and issues and should contact the IRBs concerning potential research. The determination of when it is research rests with the IRBs and not with the researcher.

But is it research?

Another debate surrounding the DOE worker health studies has been conflicting interpretation as to whether a given project is occupational health *research* or occupational medical *surveillance*.

Occupational medical departments, researchers, and sponsors as well as workers themselves may view a health study as primarily for the benefit of the participant, and surveillance or medical monitoring, by itself, does not fall within the regulatory requirements for human subjects protection.

However, many current projects have a strong research component with expectations that findings will lead to "generalizable knowledge" to be used in setting more protective workplace standards, identifying genetic predictors of disease, or refining future research hypotheses.

At one site where a health study principal investigator had asserted that a project did not meet the criteria for research, the reviewers found in the study materials clear references to generalizable knowledge and future research applications of the data to be gathered.

During all three 1998 reviews, Dr. Speers explained the basic CDC criterion for handling such "mixed" projects: participants must be protected as research subjects whenever a project is conducted both to obtain information for use in diagnosis and possibly treatment of the individual and to obtain generalizable knowledge.

Informed consent!

Assuring the quality of the consent process

and forms is an ongoing concern for IRBs everywhere. The review teams in the 1998 site visits looked hardest at how well the informed consent documents and protocols communicate the purpose of the research, explain the risks (and benefits) to subjects, and describe what subjects will experience, as one reviewer commented "from the subject's viewpoint." Not surprisingly, they found that DOE investigators, like their counterparts elsewhere, have difficulty translating specialized scientific terms into lay language the prospective subject can understand.

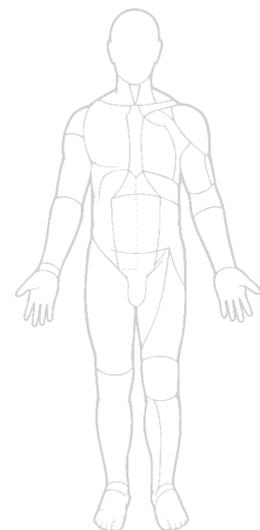
The participation of scientific and technical staff as volunteers in some of the projects in the IRB files complicated the choice of appropriate language for the informed consents.

The reviewers repeatedly stressed the need to keep the language simple, to describe measures in

*"Mixed"
projects create
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problems*

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Not surprisingly, they found that DOE investigators, like their counterparts elsewhere, have difficulty translating specialized scientific terms into lay language the prospective subject can understand.



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Better informed consent

New policy at Brookhaven Lab requires random reviews

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The IRB Administrator and one or two IRB members will act as observers when a research subject is given the consent form and discusses it with the member of your group designated to obtain informed consent.

A new policy went into effect recently at Brookhaven National Laboratory (BNL) requiring random reviews of the informed consent process.

In a memo from M.C. Bogosian, chairman of BNL's Institutional Review Board (IRB), all human research subjects principal investigators were told that the informed consent process for one of their protocols would be reviewed.

Bogosian's memo explains that once a month a protocol will be randomly selected and the principal investigator contacted. The IRB administrator and an IRB member will arrange to be present during the informed consent process. The text of the memo follows:

“According to Federal regulations, the Institutional Review Board (IRB) has the authority and is encouraged to review and observe the informed consent process.

“Once a month, a protocol will be chosen at random to review, and you will be contacted when one of your protocols has been chosen. The IRB Administrator and one or two IRB members will act as observers when a research subject is given the consent form and discusses it with the member of your group designated to obtain informed consent. They are there simply as observers, and should be introduced to the subject as such.

“Thank you for your anticipated cooperation.”Δ

Workers as research subjects

Meeting June 24–25 in Bethesda

“Workers as Research Subjects” will be the topic of a meeting June 24–25, 1999, at the National Library of Medicine in Bethesda, MD.

DOE Human Subjects Program Manager Susan Rose organized the meeting and will chair it.

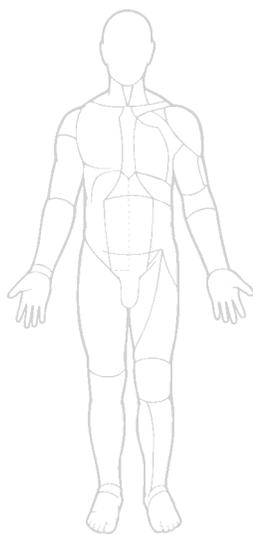
The meeting will focus on unique issues that arise when the work force (federal, military or industry) becomes the subject of research.

Speakers include representatives from industry, the National Institute for Occupational Safety and Health, the Centers for Disease Control, the Equal Employment Opportunity Commission, academia, the Depart-

ment of Energy (DOE) work force, congressional staff, and unions.

This meeting is the latest in a series of DOE interagency educational meetings. The original goal of these meetings was to educate and increase awareness among DOE staff, but the success of the meetings and the need for this knowledge in the larger community led to the decision to invite everyone interested in the topic.Δ

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email: dawnm@orau.gov



Human subjects data

DOE-funded projects on the web

Information on research projects that involve human subjects and that were funded by the Department of Energy (DOE), conducted at DOE facilities or performed by DOE personnel is available on the World Wide Web.

The database, begun in 1994, now contains Fiscal Year 1998 project information. The new entries profile 258 research projects at 35 research facilities and includes a variety of activities ranging from actual experimentation to simple questionnaires.

The DOE's Human Subjects Research Database can be accessed through:

<http://www.eml.doe.gov/hsrd/>

Some of the projects described are therapeutic in nature; some include efforts to develop new instrumentation or techniques; some involve the use of trace quantities of radioactive material in imaging studies; others involve the analysis of blood or urine samples from volunteers; and still others involve follow-up studies on workers previously employed at sites that stored or used radioactive materials.

Funding

Eighty-three percent of the projects were conducted at DOE facilities and 17% at non-DOE facilities. The funding from DOE that was directly associated with tasks or portions of projects involving the use of human subjects was about \$27 million.

A total of 166,200 human subjects were reported; however, about 95% of this total is based on records from registries, questionnaires, surveys, and epidemiological studies.

More will be added to the database, including overdue CDC/NIOSH projects funded by the Office of Epidemiologic Studies (EH-62), and some additional Former Worker Projects funded by the Office of Occupational Medicine and Medical Surveillance (EH-61).

For more information, contact Richard Larsen by e-mail at: larsenr@eml.doe.gov.Δ

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Web sites

DOE Protecting Human Subjects Program home page:
<http://www.er.doe.gov/production/ober/humsubj/>

DOE Human Subjects Research Projects Database:
<http://www.eml.doe.gov/hsrd/>

DOE News and Hot Topics, including DOE Directives and Orders:
<http://www.explorer.doe.gov:1776/htmls/directives.html>

Former workers program is for former employees at DOE sites.
<http://tis.eh.doe.gov/workers/>

DOE Chronic Beryllium Disease Prevention Program.
<http://tis.eh.doe.gov/be/>

DOE Occupational Medicine and Medical Surveillance Program.
<http://tis.eh.doe.gov/med/>

DOE Epidemiologic Studies
<http://tis.eh.doe.gov/epi/>

A genomics lexicon, a searchable database of terms and definitions, from the Pharmaceutical Research and Manufacturers of America and the Foundation for Genetic Medicine, Inc.
<http://www.phrma.org/genomics/lexicon/index.html>

A primer on Molecular Genetics, Human Genome Management Information System, Oak Ridge National Laboratory, U.S. Department of Energy:
<http://www.ornl.gov/hgmis/publicat/primer/intro.html>

A glossary from the primer:
<http://www.ornl.gov/hgmis/publicat/primer/prim6.html>



Obstacle to be survived? or opportunity?

Varying Perspectives on Site Reviews

When hospital chaplain Tim Ledbetter prepared for meeting Dr. Susan Rose and the other site reviewers who came to evaluate the IRB at Pacific Northwest Laboratories, the nervousness set in early.

“We’re not looking specifically at the details of whether all the ‘t’s are crossed and the ‘i’s dotted,” she said. “We’re more interested in the larger picture, in the institution’s general attitude.”

Now a consultant working with IRBs, Elliott was until recently director of the Health Sciences IRB at the University of Wisconsin. She was previously the compliance officer at the Office for Protection from Research Risks.

On Both Sides

Elliott has been on both sides of the review process, most recently as a reviewer, but also as one of those who experience the fear and trembling of anticipating what is often feared as the arrival of an attack team.

“I understand the concern,” she said. “The review is often viewed as an obstacle, as something to be survived.”

Survival is exactly what Tim Ledbetter had on his mind. A community representative on the IRB, he said, “There was

terrific nervousness in the days before the review.”

Forget the fears and the nervousness, Elliott counsels. “Forget staying up all night every night for

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We’re not specifically looking at the details of whether all the t’s are crossed and the i’s are dotted . . . We’re more interested in the larger picture, in the institution’s general attitude.



Marianne Elliott

Until recently director of the Health Sciences IRB at the University of Wisconsin, Marianne Elliott said that as a reviewer, she is more interested in the institution’s general attitude than in finding out whether every ‘i’ is dotted and ‘t’ crossed. She was previously the compliance officer at the Office for Protection from Research Risks. She is now a consultant working with IRBs.

But Marianne Elliott, one of the reviewers who would be on the panel looking at the IRB, says he should have relaxed.



the week before reviewers arrive. If you haven't already got things together, your last minute scurrying isn't going to change that."

Instead, she said the way to approach a review is to be honest, be flexible, and be candid about what is being done well and what needs improvement: "If you've got problems, say that's not your best area, say you need some help with that."

Not a one-way street

The site review is a good way to get information, to get help, Elliott said.

"Try to get as much out of the experience as you can. Too often, people think this is a one-way street, that we're coming to inspect. But it needs to be a cooperative arrangement," she said. "We'll always find something wrong, but that's not the purpose of the review. We aren't expecting to see a perfect system. The purpose is to help you improve your program, to find ways to do better, all in the context of protecting human subjects."

The real concern of reviewers is to get an idea of whether the institution's general attitude is in giving protection to subjects or not. They look at whether there is enough staff for the IRB to adequately do its work. They look at the facility and want to know if it has the right tools.

"All of those things are indicators of the institution's culture and whether it gives primacy to human subjects," Elliott said.

Enough resources?

More than anything else, Elliott wants to know how the IRB fits into the larger institution. Are they considered a critical part by those who are designing the research, by

those doing the research, and by those administering the work? Is the institution providing necessary resources, especially education for the IRB and its staff?

"I always want to approach this from an educational view. Let us look at what you're already doing, and then we can make suggestions about what you might do better."



Tim Ledbetter

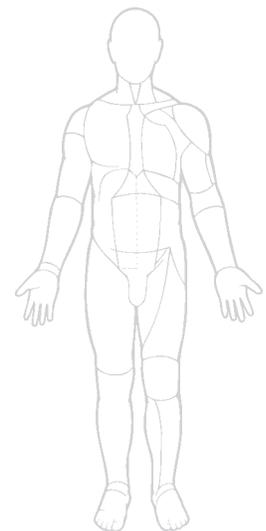
A chaplain and medical ethicist, Tim Ledbetter said the review process was most valuable in providing a connection between the local IRB and the national system. He is one of five community members on the IRB at Pacific Northwest National Laboratory in Washington.

It's just as important to tell people what they're doing right, she said.

"A lot of what we do is give people the opportunity to get to know us, to see us face to face. Often the IRB administrators feel as if they are out there all alone, very unsupported, without enough resources, and working in isolation. I want them to know that they are part of a larger network, and I want to show them how they can tap into a lot more resources than they ever imagined were available."

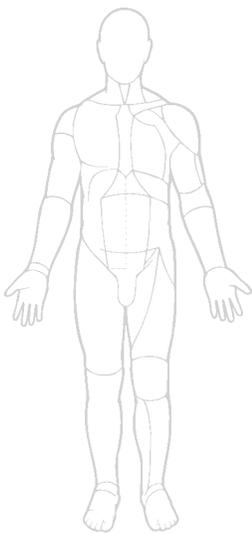
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Among the changes is that people years ago generally did not want to be involved as research subjects and now people desperately want to be research subjects to get access to medical care.



It was that sense of connection that most impressed Ledbetter about the review at PNL.

“They really did seem to be there to provide information as much as to evaluate the IRB’s operation,” he said. The experience also gave Ledbetter and the others on the IRB a chance to meet people who usually exist only as names on official documents.

“I was interviewed separately, which really was a little nerve-racking until I got in there and discovered it wasn’t so bad after all. Still, I’m relatively new on the board, and I spend most of my time keeping quiet and trying to learn my way around.”

Ledbetter said one of the most helpful parts of the process was that Elliott and the other reviewers provided a connection between the local IRB and the national system.

“I don’t think I’d ever felt that connection before meeting Dr. Rose and the others,” he said.

Which is exactly as the review should go, Elliott said.

Commonalities

“One of the things we can do is provide information about commonalities of concern. In some ways the concerns of IRBs today are not much different from those two decades ago, but in other ways the concerns are very different indeed,” Elliott explained.

“Among the changes is that people years ago generally did not want to

be involved as research subjects and now people desperately want to be research subjects to get access to medical care. The changes have partly been a result of the activism associated with HIV/AIDS and partly a result of rapidly developing technology in medications and devices. People see promise, opportunity, and hope in biomedical research.”

The difficulty for IRBs, she said, is that institutions have become overwhelmed with the changes in both technologies and concerns about protecting human subjects.

“Things are getting harder and more complex. There is more re-

search. And the average institution doesn’t support its IRB as well as it does other departments because IRBs are not money-makers.

Human beings

“Our job,” she said, “is to find ways to help the institutions see that IRBs are an integral part of the research process. There will always be people who think there is no need for the IRB because they don’t see its value to their research. The goal is to get everyone to understand the need to protect human subjects in research.”

The experience of being reviewed has generally tended to accomplish this. That was clearly the result of the recent evaluation at PNL, where Laboratory Director William Madia said in a letter to Dr. Rose that the review had been both educational and pleasant. The complete text of the letter is on the next page.Δ

Finding commonalities of concerns and solutions



November 20, 1998

Dr. Susan L. Rose
Human Subjects Program Manager
U. S. Department of Energy
Germantown, MD 20874-1290

**Human Subjects Performance Review - April 29-30, 1998,
Pacific Northwest National Laboratory**

Dear Dr. Rose:

Pacific Northwest National Laboratory (Pacific Northwest) was pleased to host you and your review committee during the recent Performance Review of our Human Subjects Program. The depth and breadth of knowledge, experience, and expertise of the committee contributed greatly to the review. We appreciate the committee's efforts and take their interesting and thought-provoking recommendations seriously as we continue our commitment to fully protect the rights and welfare of humans who are subjects of research at Pacific Northwest and the Hanford Site.

We were very appreciative of the positive comments regarding the quality of our board, the administration, and educational activities, and are very proud to hear that our Institutional Review Board is recognized as a role model for other institutions. I was especially pleased to know that your Federal Regulations experts found our program in full compliance with the Common Rule.

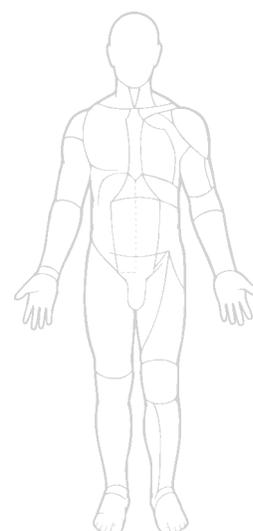
We have carefully reviewed the issues and recommended areas for improvement and, where possible, have taken immediate action. In other areas, we are escalating or implementing plans for improvement. In an effort to fully address each issue and recommendation, I have attached a report that includes the items discussed and a detailed response and intended action for each. Please call Sherry Davis-Cross if you have questions regarding the report.

Thank you again for your helpful review. We found it an enlightening, educational, and thoroughly pleasant exchange.

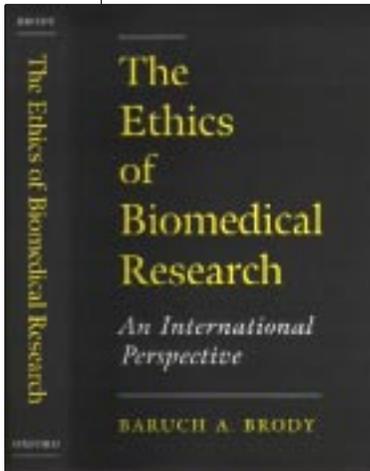
Regards,
William J. Madia
Director

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*The depth and
breadth of
knowledge,
experience, and
expertise of the
committee
contributed
greatly to the
review.*



Books



The Ethics of Biomedical Research, An International Perspective. By Baruch A. Brody. Oxford University Press. 1998. 386pp.

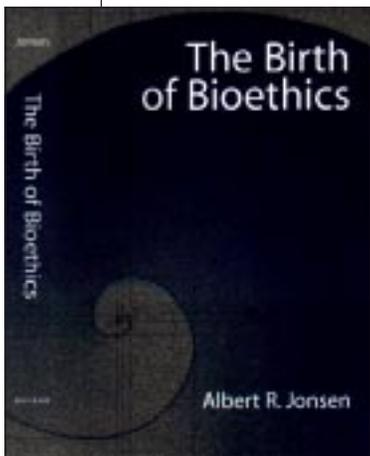
A comprehensive analysis of the ethical issues raised by scientific research on animal and human subjects, Brody's new book emphasizes the emergence of an international dialogue about the topic.

Among the issues covered are animal research, research on human subjects, epidemiological research, genetic research, reproductive research, research on vulnerable subjects, clinical trials, drug approval, and research on women and minorities.

Brody evaluates the content and methods of developing research policies by philosophically examining their rational underpinnings and likely results.

Brody, one of the best-known experts on biomedical ethics, provides a detailed review of official policies from different parts of the world. Considerable selections of official policies from research-intensive countries are reprinted in the appendix, which features close to 150 pages of material collected in one place for the first time.

Brody is the Leon Jaworski Professor of Biomedical Ethics and Director of the Center for Medical Ethics and Health Policy at Baylor College of Medicine.



The Birth of Bioethics. By Albert R. Jonsen. Oxford University Press. 1998. 431pp.

This is the first broad history of the growing field of bioethics. Covering the period 1947–1987, it examines the origin and evolution of the debates over human experimentation, genetic engineering, organ transplantation, termination of life-sustaining treatment, and new reproductive technologies.

Bioethics represents a dramatic revision of the centuries-old professional ethics that governed the behavior of physicians and their relationships with patients. This venerable ethics code was challenged in the years after World War II by the advances in biomedical sciences and medicine that raised questions about the definition of death, the use of life-support systems, organ transplantation, and reproductive interventions.

Jonsen's work assesses the contributions of philosophy, theology, law, and the social sciences to this expanding discourse in bioethics.

The book is based on extensive archival research into sources that are difficult to obtain and on interviews with many of the leading figures in the moral debates in medicine.

Jonsen is chairman of the Department of Medical History and Ethics and Professor of Ethics in Medicine at the School of Medicine, University of Washington.



Community members . . .

Bringing both caution and encouragement to IRB discussions

IRBs rely on their community members as external, objective voices that bring a valuable perspective to the group's discussion. One of their strengths is the diverse background they bring to what can otherwise be a singularly scientific endeavor. The people whose ideas are heard in this article reflect that diversity.

Pastor Bill Nebo says that people in his California community are often more willing to proceed with scientific research in the face of possible ethical conflicts than are the scientists who submit research proposals to Lawrence Livermore National Laboratory's IRB.

Nebo, who is senior pastor at the First Presbyterian Church of Livermore, California, has for six years been one of two community members of the IRB.

"This works both ways, of course," Nebo said. "There are times when the community wants to be more careful than the investigators would like. But very often the community is crying out to move things along. This is especially true when research holds the promise of helping to cure a really nasty disease."

Like many other community representatives serving on IRBs, Nebo believes that providing this kind of information is the most valuable service he brings to the IRB: "They need to know when they're moving too quickly or going too far and

when they need to keep proceeding on."

Getting the whole story

This same sentiment was suggested by Dr. Al Corrado, a physician who serves as a community representative on the Pacific Northwest National Laboratory (PNNL). "Some of what we community members do is just public relations work," Dr. Corrado said. "We help get across the message that things aren't being done with no concern for what the general public thinks. We're the ones who say, 'Here's the other side of the story.'"

Dr. Corrado is one of the longest-serving community members of any IRB, having been first appointed 25 years ago when the board was called the human subjects committee.

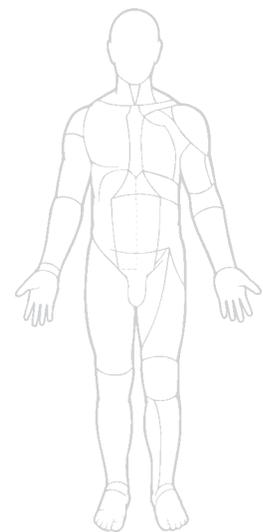
"Back then," he says, "we pretty much did whatever the director wanted. But the thing was, he was far more careful than we were. Many members of the committee were willing to take a fairly liberal view about ethical risks because we saw that the research needed to proceed. But the director generally held us back. He'd say we ought to consider this and reconsider that and be very careful about how we proceeded, especially when it came to dangers to research subjects."

More caution

Dr. Corrado said that when the government mandated formation of IRBs, members took a far more active role in understanding the issues and requiring caution than had the original human subjects committees.

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But very often the community is crying out to move things along. This is especially true when research holds the promise of helping to cure a really nasty disease.



“It can be hard being a community representative on these IRBs,” he said. “It takes time, and most people don’t have it.”



Dr. Al Corrado

The oldest practicing allergist in the country, Dr. Corrado has a common sense understanding and quiet wit that make him an especially valuable resource. He is much admired by other IRB members both for the determination that led him to keep working after losing his sight several years ago and for his compassionate understanding of other human beings.

Genetics

Concerns about research in genetics is becoming especially troublesome for IRBs, Dr. Corrado said.

“I think that as people in the community come to know more about the research and what it can do, we’ll have more and more people demanding that they get really good explanations for where the work is heading.”

Pastor Nebo agrees. “There is a lot of ignorance in the community about most research. This is especially true about work in genetics. People feel there is a danger that someone will tweak around the human genes and create monstrosities. But when you take the time to find out more of what people are thinking, they believe that there are some genetically based diseases they’d like to not have and like their progeny to not have.

“So there is both a desire to have the good that can come of the research and yet there is also trepidation about the possible costs. People get nervous when you talk about germ cell alterations.”

It is in discussions about this tension in the public’s view that community representatives

do the most good on IRBs, Nebo said. Providing this kind of informa-

tion is one of what Nebo says are three major contributions from people like him. “It’s telling the scientists that whether they think a view is irrational or not, here’s how people would perceive what you’re doing, here’s what an outsider sees.”

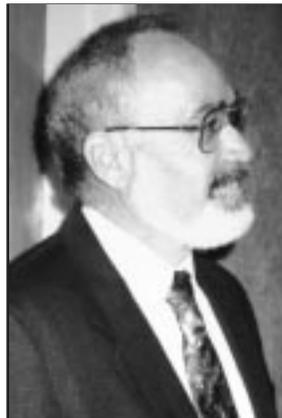
The second contribution is that the community representative is an indication of good faith. It means the institution isn’t trying to keep all the doors and windows locked securely against public prying. “The lab can’t tell me to keep quiet; it has no control over me. That gives people some comfort that the community’s interests are being heard. And a part of this role is for me to ensure that this research is explained to the public in language we can all understand.”

The third contribution Nebo tries to provide is to make the researchers more comfortable that they are not overreaching. “I’m often the one who encourages them. When they have some worries about the ethics of some protocol, I can often be the one who reminds them to keep in mind the ethics of their responsibility to assist the community by providing ways to make all of us more healthy. I tell them that what they’re doing may be of such enormous benefit that some risks are worth it.”

Taking on ethical risks

When the first discussions were being held about research into the health effects suffered by cleanup workers at the Chernobyl nuclear plant, Nebo said, many scientists were concerned that the workers being studied had not been protected by an IRB.

“Many of these people were sick, they had short life spans, they’d been subjected to fierce radiation, and we needed to know more about what had happened to them. We said that it would be letting them die in vain if we couldn’t use lab samples and other data taken from those workers just because no IRB had obtained a fully informed consent.”



Bill Nebo

Senior pastor of the First Presbyterian Church, Bill Nebo has for six years sought to represent on his IRB both his parishioners and the diversity of his community



Nebo said the involvement of community representatives in the debate was important because the researchers were assisted in feeling more comfortable pressing ahead with important analyses even though the data were not obtained with all the protections required by U.S. institutions.

“There are times when we’ve got to accept cultural differences and understand that not all places are going to institute the same protections we’d like them to use. In the case of the Chernobyl research, it was important that what happened to those workers be used to help others,” Nebo said.

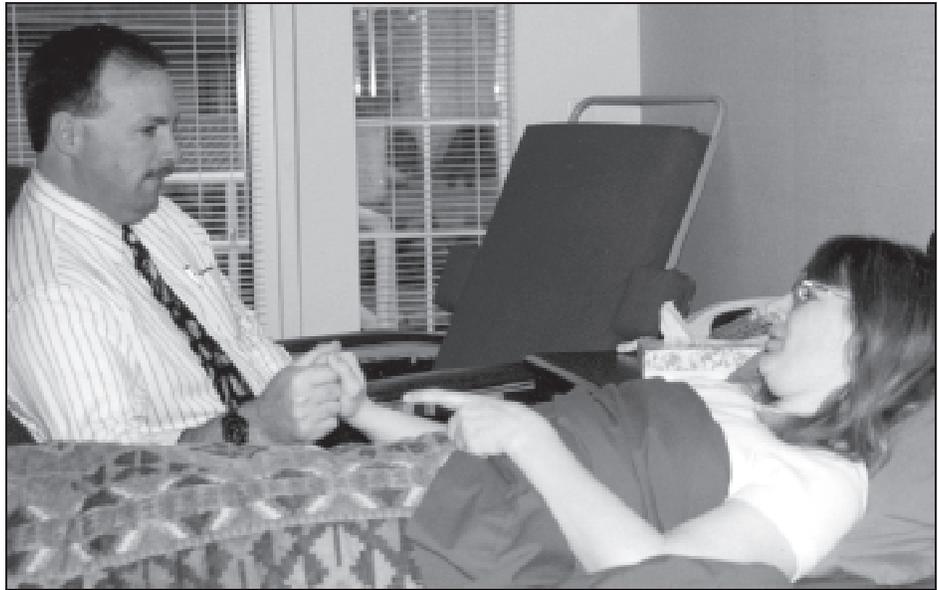
Nebo said one of the lessons he has learned from his work on the IRB is that more often than not it is the scientists who are most cautious about the social and ethical difficulties of their research. “They feel very responsible for the use to which their work will be put,” he said.

Finding community members

Finding people to serve as community members can be difficult. It requires people who have time not only to attend meetings, but also to do the reading and other legwork necessary to understand the issues and make a contribution to the IRB’s discussion.

“Trying to understand discussions about genetics and about the possible effects of research in that area is very difficult,” Nebo said. “And the issues are complex. There is one side that is science, but there is another side that is legal and another that is moral. The discussions can get very rarified.”

One way IRBs might improve their relationship with communities is to



Tim Ledbetter, a hospital chaplain and medical ethicist, brings a perspective that bridges many issues: the spiritual and the ethical.

hold more community forums, Nebo suggested. These are often resisted because the tendency is that only a few people attend them, and everyone in the research community fears that the forums can turn into sessions that are more argumentative than informative.

“But that is just one of the things IRBs will have to go ahead and deal with,” he said. “Even if the forums draw some of the nuttier types, the lab is better off facing that. It would be much worse to give people reason to think you’re hiding something and that’s why you don’t want to hold public forums.”

Tim Ledbetter, a hospital chaplain and medical ethicist serving on the IRB at PNNL with Dr. Corrado, has found that his experience on a hospital ethics committee provided skills and understandings that have been helpful in his IRB work.

“The deliberative process is very similar in both groups,” he said. “The way we address dilemmas from a medical ethics perspective is parallel to that concerning human subjects.

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Site reviews

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The other aspect of IRB procedure closely examined by the site teams was the decision to exempt projects, permit expedited review, or require full board review.

familiar units, and to avoid acronyms. In one project, where most subjects were technical personnel, the IRB had permitted the use of a glossary to explain terms to the nontechnical subjects, a decision reviewers challenged as more involved than writing the forms in language accessible to all subjects.

Multinational studies

The review teams looked carefully at informed consent materials for multinational studies. They noted that investigators must not only obtain accurate language translations of informed consent documents, they must also assure that the process supports crosscultural “translation” of the underlying concepts, perhaps even the basic idea of voluntary participation.

One reviewer cautioned that these issues become especially important when DOE labs conduct research in former Soviet states, “where there is no history of democracy.”

Exempt, expedited, or full board?

The other aspect of IRB procedure closely examined by the site teams was the decision to exempt projects, permit expedited review, or require full board review.

Review team members expected to see justification for exemption or for expedited review clearly explained (with reference to the lab’s Multiple Project Assurance) in outreach materials and in guidance given

researchers. These were not always found.

They also scrutinized project files for documentation giving explicit justification for decisions to exempt or expedite a project. The teams made a number of recommendations to each IRB for strengthening its

documents, providing specific justifications for exemptions, and fully communicating its decisions.

One of the great strengths the teams identified in the IRBs reviewed during 1998 was the attention the IRB staff gave to developing and sharing templates and examples to help researchers

understand and address human subjects protection.

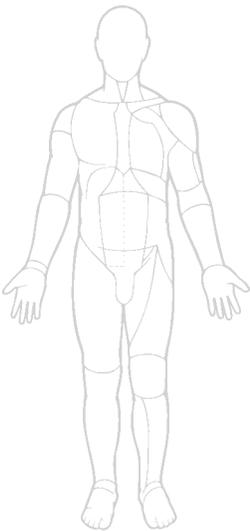
The site reviewers also examined the guidance the IRB staff provided to researchers on development of informed consent to see if it contained all of the “required elements” and offered enough direction to help the research team create a good draft. Reviewers also recommended checklists and worksheets for IRB members to use in evaluating informed consent documents.

Although reviewers suggested specific improvements in some materials, they praised the overall quality of the efforts they reviewed.

IRB Composition & structure

Diversity—of all kinds—was the focus of much concern the site teams raised about IRB membership. For example, reviewers asked:

Keep the Language Simple and Straightforward!



- Does the membership turn over frequently enough to give younger people opportunities to participate?
- Does the membership include workers or workers' representatives?
- Does the membership reflect the ethnic diversity of the region or community?
- Are community members truly independent of the laboratory or are they retired lab employees?

Finding volunteers

Even when the IRBs have policies to encourage diversity and turnover, they may not be able to achieve their targets. At the more isolated DOE sites, IRBs may struggle to find community members who are willing to volunteer their time but have no past association with the lab.

Worker participation is especially important to reviews of DOE health studies, but finding a single worker member for an IRB may be difficult on sites with multiple bargaining units. Team members suggested the formation of ad hoc committees of workers or other stakeholders to consult on reviews of specific projects as a way the IRB could expand input without increasing its permanent membership.

The quality of the IRB chair and the administrator was a strength identified at every site reviewed. Many IRB chairs are medical doctors who have many years of experience in occupational medicine and research in the DOE labs.

The IRB administrators were long-term employees—known, respected by colleagues, and able to fill the role of educator. With several IRB chairs

and administrators nearing retirement, the reviewers identified a need to prepare successors, for example, by establishing and filling a vice chair position on the board.

Management support & resources

Site reviewers found evidence at most sites of good communication with the general counsel, the lab director, the research integrity office, the work for others office, and all levels of management.

IRB chairs could point to management support for their decisions. In Oak Ridge, Albuquerque, and Los Alamos, senior managers attended the review sessions and voiced their endorsement of the work of their IRBs.

Looking at the adequacy of staff time and other resources allotted to the IRB, reviewers found

instances where resource allocation did not meet the current work load.

The review teams preferred to see an IRB supported through overhead funds rather than as a direct charge on project accounts. Direct charging, it was feared, may tempt investigators to avoid IRB oversight to save program dollars. The other risk, in the words of one reviewer, is that “When an IRB has to fight for its funding on a project-by-project basis, this takes time and resources away from the IRB’s objectives.”

Demands increased

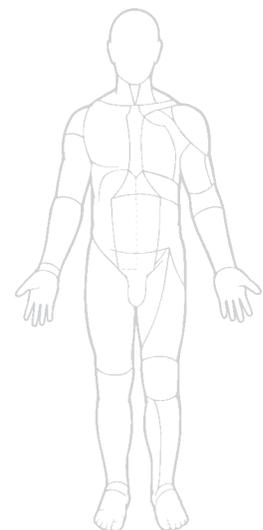
Several of the 1998 reviews noted that demands on some IRBs had increased with the need to address the worker health studies.

Because external research is neither a source of direct funds nor a con-

The Focus of Most Concerns: Diversity

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Because external research is neither a source of direct funds nor a contributor to laboratory overhead, the work load it imposes may exceed the planned resources.



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Site reviews

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tributor to laboratory overhead, the work load it imposes may exceed the planned resources.

Reviewers were concerned that funding for the IRB ought to cover continuing education of IRB staff and members. Although the DOE Human Subjects Program directly supports the attendance of IRB staff at national meetings such as the Public Responsibility in Medicine and Research Conference, site reviewers sought evidence of the local laboratory's commitment to educating its IRB through special meetings and through opportunities for members to participate in regional networks and workshops.

Was It Educational?

Site reviews do not stand alone. The DOE Human Subjects Working Group provides a forum for collaboration on issues of mutual concern. This group consists of DOE IRB members, field office staff, community members, program staff, and research subjects. In addition to the working group, the Human Research Subjects Program maintains numerous print and on-line resources, and offers a wealth of educational materials.

At each site, a constructive dialogue resulted in a strengthened, energized, and more knowledgeable human subjects program.Δ

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Site reviewers sought evidence of the local laboratory's commitment to educating its IRB through special meetings and through opportunities for members to participate in regional networks and workshops.

Community members

—Continued from page 15

The issues are also similar, especially in questions of privacy and informed consent.”

A religious approach

But Ledbetter's training and experience as a clergyman brings an even greater breadth to his work on PNNL's IRB. He says he can help people with a mostly scientific orientation understand how people approach life from a religious orientation. “It is a very different perspective, but sometimes the distance between the two is not as far as it might appear at first.”

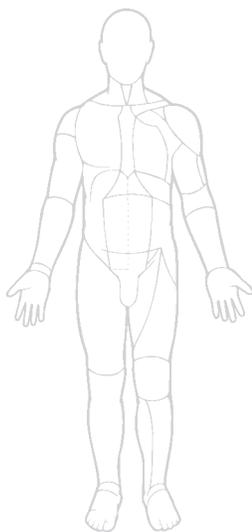
After a year and a half on the IRB, Ledbetter says he still spends a lot of time listening and trying to clarify questions.

“I'm still very new,” he says, “and I don't pretend to understand all the science involved in the discussions. But that can be helpful, because I try to ask the questions that the average

lay person might ask. Once we start talking about the human effect, that is the area in which I have the most understanding.”

The issue that most concerns Ledbetter is privacy. “We're in a very conservative neck of the woods up here. Most people's real concern is that their privacy not be intruded upon, which means that one of the areas I'm most attentive to is record keeping, keeping computer records isolated away from networks. The concern is who might get access to the information.”

Nebo, Ledbetter, Dr. Corrado, and other community representatives say that their concerns are taken very seriously by the scientific people on their IRBs. “They may not always agree,” Ledbetter said, “but they listen, and they are usually willing to consider other viewpoints. That's one of the reasons this IRB works so well.”Δ



Protecting Human Subjects

This bulletin is designed to facilitate communication among those involved in human subjects research and to inform persons interested in human subjects research activities.

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This newsletter is available at no cost to anyone interested or involved in human subjects research at DOE. Please send name and complete address (printed or typed) to the address below. Please indicate whether information is to (1) add new subscriber, (2) change name/address, or (3) remove name from mailing list. Enclose a business card, if possible.

Send suggestions, contributions, and subscription information to —

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Meetings

June 24–25, 1999

Workers as Research Subjects: A Vulnerable Population?

National Library of Medicine • Bethesda, MD

Sponsor: DOE, Human Subjects Program

Details of this meeting can be found on page 8 of this newsletter.

Contact: Susan L. Rose, meeting organizer and Human Subjects Program Manager, Office of Biological and Environmental Research, DOE, 19901 Germantown Rd., Germantown, MD 20874.

Registration: Mikki Dawn; phone: (423) 576-9278; fax: (423) 241-2727; email: dawnm@ornl.gov.

June 18, 1999

OPRR/FDA Town Meeting: Evolving Concern for Protection of Human Subjects

Ohio State University, Novice Fawcett Center • Columbus, Ohio

Participants: Representatives from OPRR, FDA, DOE, and other federal agencies that support human subjects research will participate.

Dr. Susan Rose will represent DOE at the meeting, which is designed to facilitate understanding of federal guidelines. The town meeting will be held from 8:30 a.m.–3:30 p.m.

For information, call (614) 292-3238.

July 19–22, 1999

Occupational Medicine in the 21st Century: Health Technologies, Los Alamos and Sandia National Labs

Sheraton Old Town • Albuquerque, NM

Contact: Linda Sharp, Oak Ridge Associated Universities, MS 50, PO Box 117, Oak Ridge, TN 37831-0117.

For information: <http://tis.eh.doe.gov/med/occmecconf/agenda.html>

October 28–31, 1999

American Society for Bioethics and Humanities—2nd Annual Meeting

Wyndham Franklin Plaza • Philadelphia, PA

Contact: <http://www2.umdj.edu/ethicweb/upcome.htm>

December 5, 1999

Annual ARENA IRB Meeting

Sheraton Boston Hotel & Towers • Boston, MA

Contact: PRIM&R, 132 Boylston St., 4th floor, Boston, MA 02116; phone: (617) 423-4112; fax: (617) 423-1185; email: prmr@aol.com; website: <http://www.aamc.org/research/prmr>

December 6–7, 1999

Annual PRIM&R IRB Meeting

Sheraton Boston Hotel & Towers • Boston, MA

Contact: PRIM&R, 132 Boylston St., 4th floor, Boston, MA 02116; phone: (617) 423-4112; fax: (617) 423-1185; email: prmr@aol.com; website: <http://www.aamc.org/research/prmr>



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