PROTECTING HUMAN SUBJECTS

U.S. DEPARTMENT OF ENERGY, OFFICE OF BIOLOGICAL AND ENVIRONMENTAL RESEARCH

No. 11 • Fall 2004

The HSPP and communication issues

This issue of *Protecting Human Subjects* considers several of the various ways that can either assist or impede communication related to Institutional Review Boards (IRBs) and Human Subjects Protection Programs (HSPPs).

More than perhaps anything else, communication between and among people creates either the conditions for success or the ingredient for failure. When the protection of human beings is at stake, clear and effective communication is essential. It may seem that this is a truism, which neither merits nor affords much discussion: Everyone knows it is important; what more is there to say about it?

And yet there is much that needs saying. Perhaps because it seems so obvious, we spend too little time considering better ways to communicate. The unfortunate result of too little consideration is misunderstanding, disagreement, and wasted time.

So in this issue we take a look at a variety of ideas designed to improve the way we relay information, ideas, expectations, and assurances. The form of communication that is most familiar is speaking directly to another person, and so we discuss that in several ways. But communication is increasingly conducted by means of computers, and so we also report about developments in the human subjects database, as well as about an updated Web site designed for the use of IRB community members.

Some of what you read here will be about things you already know, and probably have known for a very long time. But we think they bear repeating because, while they are familiar, we often forget them in the day-to-day involvement of meetings, phone calls, and so forth. When Shirley Fry, who until recently chaired the Beryllium IRB, says that all communication begins with trust, it is not the first time you will have heard that. However, given the widespread presence of distrust, we think it probably needs repeating.

The best communication: people talking to people

Requirements for collaborative research studies

Collaborative research involving investigators at one or more institutions presents unique challenges of communication for the researchers and the Institutional Review Boards (IRBs) that review their protocols, says IRB Program Manager, Sherry Davis of Pacific Northwest National Laboratory (PNNL).

Davis said collaborative relationships with other researchers and institutions are on the increase as investigators expand their knowledge and scope of research by taking advantage of the unique technologies, expertise and equipment that exist elsewhere in the world today.

Advancing research

These collaborations, which have the potential to more quickly advance human subject research, require open and clear communication among the researchers as well as the IRBs that represent their institutions.

Sherry Davis

For example, a researcher might find it advantageous to solicit subjects and gather samples at an established clinical research center but then have the samples analyzed at an institution that has state-of-the-art equipment and expertise. The U.S. Department of Energy's (DOE's) Environmental Research Science

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Laboratory (EMSL) at PNNL is frequently used in this way.

In addition to other research conducted at EMSL, human samples or materials derived from human samples that have been gathered at or supplied by other institutions or by tissue banks are analyzed at the molecular and proteomic levels by visiting scientists and PNNL researchers.

Among the most educational communication tools is to spend time getting familiar with other institutions' processes of approving human subjects research.

The use of these samples must be properly reviewed and approved by the PNNL IRB and, in many instances, by the visiting scientist's IRB, as well.

This ensures that every aspect of the research—from the initial gathering of samples, to the protection of identified or coded samples, and the final distribution of study results—is conducted ethically and in full compliance with federal, state and in some cases, international regulations. Researchers are also responsible for complying with the policies and procedures unique to their institution.

Multiple institutions

These situations are becoming increasingly complex, particularly where multiple institutions or international studies are involved.

With effective communication, everyone associated with these studies should be assured that the research is conducted ethically and that the subjects' rights and welfare are fully considered throughout the life of the project.

In collaborative studies, a variety of communication processes can be employed to ensure that collaborative research protocols are reviewed thoroughly and expeditiously. These may include the following scenarios:

- Each IRB may conduct an individual review and exchange the approvals with the other institutions.

In some instances, Davis said, the PNNL IRB requires the Principal Investigator (PI) to obtain copies of their co-investigator's IRB approval and supporting information.

For instance, when identified or coded samples or data are involved, the IRB requires copies of the current IRB review from the institution(s) that gathered the samples or data. In some instances multiple IRB reviews might be required, particularly when international research is involved.

- In another scenario, the IRBs might be involved in initial discussions, but choose to conduct individual reviews.

Under this scenario, the IRBs might simply discuss the protocol in preparation for their individual reviews.

"Communicating with other IRBs accomplishes two things," Davis said. "First, it establishes a working relationship and opens a line of communication that will prove useful in the future, both to the IRBs and sometimes to the PIs who rely on their collaborative research relationships."

Second, it saves time and effort for everyone by allowing the PIs to address the concerns of all of the IRBs at the same time.

Different institutions, similar problems

"We have found that where one IRB has problems with certain aspects of a study, it usually follows that a collaborating IRB will have similar or, in some cases, different questions and concerns. So addressing all issues up front is very beneficial for everyone. It's double insurance, if you will, for the subjects as well as the researchers.

- IRBs may agree to establish a formal IRB Authorization Agreement (IAA).

To reduce redundancy, in particular where multiple IRB reviews are required, the IRBs may choose to establish a formal IRB Authorization Agreement (IAA).

In this scenario, one of the IRBs—generally the lead or funded IRB or the one most directly involved with human subject activities—assumes responsibility for conducting the review. The "secondary" IRB receives full documentation and always has the right to comment, require additional information, or disapprove the portion of the protocol submitted by their institution.

Davis recommended that in instances of collaborative projects where serious concerns exist, IRBs might consider conducting a joint review, possibly by telephone or video conference.

—Continued on page 5

Central Beryllium IRB

Involving more IRBs and covering more territory creates special communication hazards

Presenting one of the thorniest problems of communication in the IRB world, the Central Beryllium Institutional Review Board (CBeIRB) has members from throughout the country and reviews beryllium projects from one corner of the nation to the other.

Established in early 2001, the CBeIRB reviews all beryllium-related projects involving human subjects for all DOE sites. It also oversees beryllium projects conducted at other institutions with funding support from DOE or other agencies in which DOE or contractor employees are involved as subjects.

Shirley Fry

"If it weren't for the patience and willingness of everyone involved, it could become a bureaucratic nightmare."

Given the complexity of communications in the endeavor, CBeIRB chair Shirley Fry has neither time nor interest in a communications process that doesn't produce clarity.

"The goal of our IRB," she said, "is to establish effective lines of communication among our principal investigators (PIs), our site IRBs, and members of the CBeIRB."

Creating consensus

'The purpose, she added, "is to create a consensus among those elements, but it is a consensus that is specific for the procedures on each project. There is no blanket process that can be employed for all projects."

Fry, who previously chaired The Oak Ridge Associated Universities/Oak Ridge National Laboratory (ORAU/ORNL) IRB for five years and was a member for 20 year, said that much of the challenge for a central IRB is that it imposes another layer of bureaucracy.

"It is superimposed on the site IRBs and if the PI is at a university, for example, it is superimposed on the university IRB, both of which have to interact with us at the CBeIRB.

"If it weren't for the patience and willingness of everyone involved, it could become a bureaucratic nightmare," she said.

The potential nightmare is avoided because of two things.

Avoid adversarial conditions

"First, we've tried to make sure this process doesn't become an adversarial situation. Second, I think all the IRBs want to help researchers and other IRBs do their jobs. They're interested in scientific progress, but they want to do it right. Third, the investigators almost always want to do it right as well."

Those elements combined ensure that the process gets off on the right track, Fry said. But she said there is one additional element without which the process would fail, no matter how well-intentioned people are.

"The central element is trust," she said. "Like everything else in life, the effort works when we have experience with each other that leads to a sense of trust."

She said this means it is crucial to the endeavor that those involved get to know each other. "We need to

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Given the complexity of communications in the endeavor, CBeIRB chair Shirley Fry has neither time nor interest in a communications process that doesn't produce clarity.

know the people we're working with. We need to understand what their problems are.

"So the first element in developing effective communication is taking the time to learn more about everyone involved. Once that's done, communications generally will improve if there exists a sense of mutual trust and a shared interest in the job."

Recognize the difficulty

The 16 members of the CBeIRB represent a range of disciplines, from occupational and clinical medicine to industry, ethics, law, science, and industrial hygiene. Fry said one reason such a diverse group has been able to succeed at such a complex task of oversight is that they recognize that communication can be difficult.

"If you don't first appreciate that it can be a problem, then it is likely to be more of a problem. Poor communication is more likely to result if one assumes that it will take care of itself," Fry said.

"This is one element of the oversight process that won't take care of itself. You have to ask, 'Where are the potential communication problems and how can they be resolved?' And you must do that before they become problems. The key is to get to know one another, establish trust, and don't rely solely on written communication. Talk to each other. All trust flows from that."Δ

(Shirley Fry was instrumental in the establishment of the CBeIRB for DOE and served as chair for 3 years. She is stepping down as chair but will remain as an ex officio, non-voting member.)

Special web site for IRB community members

Redesigned in 2004, communications hub includes online discussion group

Denise Viator, left, and Amparo Henderson

The Web site "The Community IRB Member: Neighbor and Partner," has been redesigned to expand its scope and offer more services, including additional educational tools.

By Amparo Henderson & Denise Viator, Oak Ridge Institute for Science and Education

Oak Ridge Institute for Science and Education (ORISE), managed by Oak Ridge Associated Universities (ORAU), designed and maintains the site (**http://www.orau.gov/communityirb/**) and an online discussion group that focuses on community IRB members. Both are hosted on ORAU's servers and maintained by ORISE staff.

Established just over two years ago, the site has been redesigned to better address communication issues and provide space for organizations to share educational tools. Organizations use it to disseminate guidelines and checklists that can be downloaded and adapted for use by others.

Several advocacy groups that are interested in community member participation in IRBs and that can offer IRB consultants have provided contact information on the web site.

News, events, and resource links address the need for current information on protection of human research subjects. The web site provides the pathway to a collection of related web sites, where the community member can find news related to IRBs.

Educational opportunities open to the community IRB member are advertised on the site, such as details about conferences and workshops being held across the country.

The online discussion group, developed in 2002, currently has 356 active subscribers. It is a growing

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avenue, in addition to the web site, available to the community IRB member to foster communication.

http://www.orau.gov/communityirb/

Interactive listserv
Subscribers to the listserv enjoy a more interactive experience because they have the ability to generate discussions and offer feedback to postings related to human subjects issues.

Subscribers have posted about 300 messages since its inception, beginning with 29 postings during the latter part of 2002, increasing to 159 in 2003, and continuing to increase in 2004.

Recent postings include a query for suggestions on how to find the ideal community representative for an IRB, opinions about clinical research practices in the news, and information about available positions in the field of human research at a specific location.

Ensuring integrity
The list is moderated by ORISE staff to ensure the integrity of postings; however, all posts receive careful consideration. Information about subscribing to the discussion group is available on the web site.

Subscribers can also forward information to be posted on the web site by contacting the ORISE site administrator at hendersa@orau.gov.Δ

People talking to people

(Continued from page 2)

If feasible, the lead IRB could host a meeting to which one or more IRB member from the other institution(s) would be invited to participate in the deliberations and perhaps in the vote.

Classified research
Reviewing classified research presents additional unusual and difficult problems in addition to those caused by IRBs not having a quorum of members with the necessary clearances.

When a classified review is required, but a full IRB cannot be convened at the institution where the research is to be conducted, it is possible, Davis suggested, that an IAA could be established with a standing classified IRB.

If possible, an IRB member or members of the requesting IRB should participate in the deliberations as a representative of their institution. This would require establishing careful lines of communication between the IRBs and the PI and perhaps establishment of a standing IAA between the IRBs.

In working with researchers, Davis said, person-to-person communication is the process by which she can best explain both the need for protecting subjects and the most reasonable and effective way to go about it.

"Our researchers truly want to do the right thing. When I explain why it is so important to protect the rights and welfare of the people that make their research possible and provide the guidance and tools for doing so, I find that they are more than willing to do what it takes—as long as those expectations and requirements make sense.

Some have become human subject field advocates who assist other investigators, which is probably the most effective kind of communication.

"Good communication," Davis said, "is a matter of establishing mutual respect. In the field of human subject research, it requires trust that everyone involved has the same goal: protecting the people who make this important research possible."

Spend time getting familiar with other institutions' processes of approving research.

Among the most educational communication tools is to spend time getting familiar with other institutions' processes of approving human subjects research.

Davis said her experience interacting with other IRBs has taught her that "each institution has its own special way of looking at protocols, at what constitutes research, and at how reviews should be conducted. Their applications and consent forms differ; sometimes greatly."

These differences often lead to development of alternative, sometimes much more efficient ways of doing things. "Interacting with other IRBs is always a learning experience for me," she said.Δ

IRB decision quadrant

Guide developed for use by PNNL ensures consistent, comprehensive IRB deliberations

Two important elements of IRB deliberation are consistency and comprehensiveness.


Tim Ledbetter

Both are specifically addressed in a now well-proven tool created for use by the Pacific Northwest National Laboratory's (PNNL's) IRB.

Called the "IRB Decision Quadrant," it was developed by PNNL IRB community member Tim Ledbetter, a hospital chaplain and ethicist, and IRB administrator Sherry Davis. *(See pages 12–15 to view the complete IRB Decision Quadrant.)*

Systematic, thorough

The Decision Quadrant is a nearly four-page guide designed to walk an IRB through most possible issues and questions that can arise during the process of IRB considerations. One of its strengths is that it makes the communication of information more systematic, more thorough.

Nothing is taken for granted, nothing assumed, and a wide range of difficulties are avoided.

It is a checklist intended to ensure that nothing is taken for granted, nothing assumed, and a wide range of difficulties are avoided—which, of course, is perhaps the most important goal of communication.

"One of the advantages I see in using this," Ledbetter said, "is that it demands a methodical approach. It reins in those who might be tempted to rush through the process because they have prejudged the project being considered. There can be no rubber stamping."

Another advantage is that it focuses the deliberations. "At times," he said, "it's easy to wander off on tangents that might be interesting but are not related to the task. Using the checklist tends to keep us on track, going through each point, one at a time."


Sherry Davis

Because the checklist requires carefully attending to each item, the deliberation can also have the effect of expanding the thinking of those who may tend to focus on only one area.

It is the combination of all these advantages, Ledbetter said, that prevents the danger of being erratic and inconsistent.

Davis said the focus and consistency required by the Decision Quadrant have worked well for PNNL's IRB. "We don't find ourselves after a meeting wondering why we didn't think of this or talk about that. Everything gets considered and nobody is left thinking we missed something," she said.

The Decision Quadrant follows the fundamental ethical elements of the Belmont Report.

Ledbetter originally developed the guide for use by the hospital ethics committee he chairs. Davis, who sits on the same committee, suggested he adapt it for use by the laboratory IRB. Both worked on the project to make it fit the specific requirements of a research laboratory. It can be adapted, however, to be used by any IRB.

Belmont Report

The Decision Quadrant follows the fundamental ethical elements of the Belmont Report (See *Protecting Human Subjects*, Summer 2004, No. 10, for a full discussion of the Belmont Report).

It also incorporates the ideas of moral philosopher A. R. Jonsen, who suggested the idea of considering medical issues within a framework of four quadrants: medical indications, quality of life, patient preferences, and contextual features. ➢

The Decision Quadrant Ledbetter and Davis created for PNNL is structured around four elements: research design, subject selection (applying principles of justice), risk/benefit (applying principles of beneficence and/or nonmalfeasance), and subject protection (applying principles of respect/autonomy).

It considers the full range of problems associated with data collection, protection of privacy, consent, subject recruitment, risk, biological samples, and so forth.

The guide begins by listing several areas of consideration within each of these four elements. For example, under "subject selection" is a list of issues to be examined. They include appropriate inclusion/exclusion criteria, equitable selection of subjects, benefit to the community, freedom from coercion, and special protections for vulnerable subjects.

Issues
The guide provides a detailed listing of all the issues that might arise related to any of the basic elements. It considers the full range of problems associated with data collection, protection of privacy, consent, subject recruitment, risk, biological samples, and so forth.

The last section of the guide suggests "other considerations." It includes such concerns as whether the research might generate public concern, whether there are potential conflicts of interest, whether other IRB reviews are involved, and whether it is Food and Drug Administration-regulated research.

Expedited review
PNNL's IRB does not always employ the full guide in its deliberations because some protocols are below minimal risk. In those cases, the review is expedited.

For all other projects, however, the IRB has concluded that the Decision Quadrant provides a sense of comfort that they have asked the important questions and carefully looked at the proposed project.

"Some might think it is cumbersome," Ledbetter said, "but the more proficient we get, the quicker we can cover the checklist. In the long run, it seems to avoid headaches by ensuring good communication among IRB members and between the investigators and the IRB."

(The PNNL IRB Decision Quadrant is printed at the end of the newsletter. For information about the guide, contact Tim Ledbetter at **ledbet@kadlecmed.org**).Δ

News notes

Articles for next newsletter?

The next issue of the *Protecting Human Subjects* newsletter will focus on the PRIM&R and ARENA meetings in San Diego October 28–31. Coverage will include reports about the annual IRB meeting and presentations related to protecting human subjects.

In addition to the meeting coverage, we will include a variety of other human subjects news and articles. If you have something that might be of interest to the protecting human subjects community, please contact Gloria Caton at **catongm@ornl.gov**.

Bioethics resource

The American Society for Bioethics and Humanities (ASBH) has published archives of its ASBH Exchange for 1998–2004 at **http://www.asbh.org/resources/exchange/index.htm**

It includes articles on clinical, research and public policy issues. The archives also include the ASBH Bibliographic Tour, which lists references to recent articles on bioethics and medical humanities. Also in the archives is a partial listing of dissertations published each year addressing bioethics and medical humanities issues.

Communication between sites

You need to have a lot of ready answers, or know where you can quickly find the answers

By Terry Reser, IRB Administrator, Sandia National Laboratories

Who ya gonna call? When you have questions, and you're the only one at your site who does what you do, you'd better have someone outside to turn to. That's good sense whether your business is widgets or weapons, but it's crucial if your job is protecting human subjects.

IRB administrators are human subjects experts, the ones other folks turn to for answers about human subject research. And at most DOE sites, you can't defer questions to anyone else because you're it.

Terry Reser

The Working Group

So, you need to have a lot of ready answers or know where you can get some pretty quickly. That's why DOE's Human Subjects Working Group (HSWG) has become such an important resource.

These are experienced professionals who share your passion for doing things just right.

The HSWG consists of representatives from each DOE site that conducts human subject research. These are experienced professionals who do similar work, face similar problems, are equally adept at getting the most from their hard-fought budgets, and share your passion for doing things right — just the sort of people you want to talk to when you need straight answers to thorny problems!

New challenge

I regularly call or email colleagues on the HSWG whenever I'm up against a new challenge or curious whether someone else's procedure might run a little more smoothly than one that's currently giving me fits.

Sometimes I get just the information I was hoping for right away. Other times it takes a few days, but it's generally worth the wait. And when I see an incoming email from someone on HSWG saying "HELP!!," I try to respond as quickly as I hope they would. Here are a few examples of how effective this communication system can be:

Examples

A couple of years ago, I developed a policy and procedures manual for our site and had the Sandia IRB members review it. Most of them liked it well enough, but I wasn't satisfied that it was as good as it ought to be.

Bree Klotter, who was then the IRB Administrator at Lawrence Livermore National Laboratory, had just revised her own policy and procedures manual and called to see if I would consider critiquing it for her. I agreed, and we soon negotiated the terms—I would provide a comprehensive review if she would allow me to "borrow" liberally from her more complete tome.

Value gained

My review took a couple of weeks by working it in among other priorities. But the time spent was a pittance compared with the value I gained. In the end, we were both pleased, and each of our sites ended up with a much better manual.

Another example occurred last November, when I was preparing for a presentation to our board of directors.

I wanted to orient them to Sandia's place in the larger DOE complex. A quick search on the web didn't locate the kind of information I needed, so I drafted a table to indicate human subjects activity at several DOE sites.

The table just had labels on the rows and columns and a lot of blanks cells waiting for data. I was seeking a lot of information that no one was likely to have handy, yet I was confident in my colleagues.

Well-placed confidence

My confidence was well placed. In short order, I had current information for each blank space—all obtained by querying my colleagues in the HSWG. Once the table was filled, I distributed it back to the

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group and we all now have useful information to share with upper management at our respective sites.

A third example occurred in August of this year. I used the same strategy to poll other DOE sites on the volume of classified research projects involving human subjects and to gauge interest in this as a discussion topic for the upcoming HSWG October meeting in San Diego.

Each IRB administrator in the HSWG has a distinct skill set and expertise

My quick poll showed that both volume and interest in this area were very scant, sparing HSWG folks a planned lengthy discussion on the topic, and allowing redirection to a topic more likely to be well received.

Other sources

Other sources of wisdom regarding human subjects research are also available, but one size doesn't fit all. The "IRB Forum" is a good example. This is an excellent online discussion group and I've learned a lot from this resource over the years, but it requires a lot of time and effort.

The majority of those who participate engage in research that is very different from research done at Sandia. While it's interesting, it means I have to wade through a lot of non-pertinent information, and in the end, I may or may not find anything useful for my site. It's not unlike an upper-crust estate sale—lots of great stuff, but nothing that seems to fit very well. The HSWG, on the other hand, is more like a favorite sweater— it usually fits just right and it's always comfortable.

Email groups

Although the HSWG as a group have a lot in common, each IRB administrator is unique and has a distinct skill set and expertise. For example, if I have a question about some vagary in the regulations, I call Chris Byrne at Lawrence Berkeley National Laboratory. If I need to know about clinical research, Darcy Mallon at Brookhaven National Laboratory is on my speed dial. If understanding cell lines is my quest, Sherry Davis at Pacific Northwest National Laboratory is where I start. When I don't know who to contact, I just send e-mails to everyone.

So the next time some problem is nagging you, call someone on the HSWG. And if by some strange quirk they don't have a ready solution, at least you'll have a kindred soul on the line to commiserate with! A good adjunct to this might be to establish regional email groups that could provide a continuing venue for questions, discussions, and problems.Δ

News notes

Brookhaven National Lab

Brookhaven National Laboratory's new Standards Based Management System (SBMS) for its human subjects protection program is complete and available at this address: **https://sbms.bnl.gov/standard/2v/2v00t011.htm**.

The new version includes a section detailing revisions since the previous version. This listing may be helpful to other sites that are still updating their SBMS.

Community-based research

The U.S. Agency for Healthcare Research and Quality has released the report *Community-based Participatory Research: Assessing the Evidence* in PDF form on its Web site at **http://www.ahrq.gov/clinic/evrptpdfs.htm#cbpr.**

The review consolidates literature on health-related community-based participatory research. More information can be obtained from Community-Campus Partnerships for Health at **http://www.ccph.info**.

Database update details DOE funding

The annual update reports $45 million in funding from DOE for human subjects-related projects

By Don Watkins and Kathy Olsen, Oak Ridge Institute for Science and Education

The fiscal year (FY) 2003 annual update of the U.S. Department of Energy (DOE) Human Subjects Research Database (HSRD) is now on the World Wide Web at **http://hsrd.orau.gov**.

The database contains information on research projects that involve human subjects and that are funded by the DOE, conducted at DOE facilities, or performed by DOE or contractor personnel.

Previous yearly updates were performed by the DOE Environmental Measurements Laboratory (EML). In 2003, EML became part of the Department of Homeland Security, and the Oak Ridge Institute for Science and Education (ORISE) assumed responsibility for maintenance and update of the database.

New database includes 255 active projects, 77% at DOE facilities, 23% at non-DOE facilities.

Projects
The FY 2003 database includes 255 active projects with 77% being performed at DOE facilities and 23% at non-DOE facilities.

Forty-three research facilities provided data for the current database. Thirteen of these facilities are DOE laboratories and 30 are non-DOE laboratories.

Sixty percent of the active projects are performed at five DOE facilities—Brookhaven, Los Alamos, Lawrence Berkeley, and Lawrence Livermore national laboratories and ORISE. Lawrence Livermore National Laboratory has the largest number with 48 active projects.

Funding
Funding from DOE for projects that were active in FY 2003 amounted to approximately $45 million. Other federal and private sources provided about $10 million, to bring total funding for the human subjects research projects described in the database to approximately $55 million.

Funding for individual projects ranged from $200 to $11.3 million, with the median project receiving $112,500.

Human subjects
In FY 2003, a total of 1,503,947 human subjects were involved in DOE-funded, DOE-site, or DOE-related projects, with 29% affiliated with DOE facilities and 71% with non-DOE facilities.

Funding ranged from $200 to $11.3 million, with the median project receiving $112,500.

Of the number of projects, 99% were records-related from registries, questionnaires, surveys, and epidemiologic studies. As an example, one epidemiological records-based study this year by the National Institute for Occupational Safety and Health included 600,000 subjects, 40% of the total number of subjects reported.Δ

Web sites

International Calendar of Bioethics Events
http://www2.umdnj.edu/ethicweb/upcome.htm

Medbioworld: Bioethics Journals
http://www.medbioworld.com/med/journals/ethics.html

World Health Organization Ethics & Health page
http://www.who.int/ethics/en/

Analyzing your HRPP structure

A systematic approach to an effective program

Priscilla Craig and Paula Waterman, of the Human Subjects Working Group (HSWG), have developed a model designed to systematize analysis of Human Research Protection Programs (HRPPs).

The complete 11-page version of the model can be found on the *Protecting Human Subjects* Web site—**http://www.science.doe.gov/ober/humsubj/hrppanalysis.pdf**.

Priscilla Craig

Their proposed approach may be useful to other organizations seeking to delineate the mechanics of their own programs.

The structure serves as a detailed guide to the processes and documentation required for the successful operation of an IRB within the larger HRPP.

Craig said the entire structure is based on the principle that communication is the single most crucial element in the system.

Everything about the model points to clearly articulating standards, expectations, processes, and goals. In this formulation, good communication includes maintaining documentation and clarifying the roles of the various elements involved in an HRPP

Not in isolation

Most important, the model emphasizes that the IRB does not function in isolation but, rather, is central to and is a crucial element in an institutional/organizational system whose job it is to protect research participants.

Craig and Waterman's structure thus extends beyond the IRB to encompass the total effort. This includes the investigators and their staff who actually conduct the research, the department/office/individuals who have responsibility for meeting the obligations imposed by the assurance, and the sites where the research is being done.

An overarching system

Depending on the type of research being done, other groups, committees, and departments could also be considered part of the HRPP. Craig said institutions and organizations should think in terms of such an overarching system.

"At the same time," she said, "it is important to emphasize that the IRB is central to this system, and plays a pivotal role in its functioning, as opposed to simply being one committee operating within it. If the IRB is not functioning properly, it can be said the HRPP is not functioning properly."

In such a system, she explained, "communication plays an important role in the successful operation of any HRPP. Such communication may be written, or oral; however, it is extremely important that the communication does occur."

Describe lines of communication

For this reason, she added, "it is a good idea to develop standardized operating procedures that describe lines of communication and how the communication will be accomplished within the HRPP."

> *The entire structure of the model is based on the principle that communication is the single most crucial element in the system.*

Craig and Waterman's model begins with a systematic analysis of the elements of an HRPP, the roles and responsibilities of each, lines of authority and responsibility, and the way each of the elements relates to the others.

It also covers written procedures, as well as the specifics of how documentation is maintained, the way research projects are examined, and the process by which the IRB maintains oversight. Additional sections cover adverse event reporting, protocol files, patient records, self assessment, and many other topics.Δ

PNNL's IRB Decision Quadrant

Reprinted here is the IRB Decision Quadrant used by Pacific Northwest National Laboratory's IRB. The guide for IRB decisionmaking is discussed in the article on page 6 of this newsletter. For information, contact Tim Ledbetter at **ledbet@kadlecmed.org**..

Date: _____
IRB No.: _____

PNNL IRB Decision Quadrant

(Basic Ethical Principles of the Belmont Report)

Research Design		Risk/Benefit (Beneficence)	
___ Is scientifically sound with clear objectives ___ Supports proving hypothesis ___ Human subjects necessary ___ Peer review documented		___Benefits to subject and/or society outweigh risks to the subject ___Benefits maximized and risks fully considered and minimized ___Appropriate safeguards in place ___Emergency response plan in place	
Acceptable		Acceptable	
Comments:			
Subject Selection (Justice)		**Subject Protection (Respect/Autonomy)**	
___Inclusion and exclusion criteria are appropriate ___Equitable selection of subjects. Results benefit community being studied ___Free of coercion and undue influence ___Special protections in place for vulnerable subjects		___Consent process is free of coercion and undue influence ___Informed consent appropriate and clearly written ___Clear explanation of risks ___Identity of subjects protected ___Data and privacy are secure Assurance that no conflict of interest exists	
Acceptable		Acceptable	
Comments:			

Risk/Benefit Analysis

___ The risk to subjects is reasonable in relation to the anticipated benefits and/or to the significance of the knowledge that may reasonably be expected to result from the research.
___ This research involves the prospect of direct benefit to individual subjects.
___ This research involves no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition.
___ This research involves the prospect of indirect benefit to the individual subject because of direct benefit to the society in which the individual participates.

Risk/benefit to children involved in this research is best represented in Federal Regulation 45 CFR 46.40 _____.

Risk Assessment: ____ Minimal Risk _____ Greater Than Minimal, But Acceptable Risk _____Unacceptable Risk

In accordance with 45 CFR 46, Subparts A B, C, and D, I recommend this project be:

_____ Approved as presented.

_____ Given preliminary approval under the following condition(s), subject to final approval by the IRB Administrative Team:

_____Tabled or _____ Disapproved for the following reason(s):

And suggest the following for consideration by the Board:

This protocol meets the qualifications for waiver of consent. Yes _____ No_____
The IRB should conduct a compliance review of the approved protocol. Yes _____ No_____
The IRB Administrative Team should "Expedite" minor changes to the protocol/consent. Yes _____ No_____
Continuing Review should be conducted at intervals of every: ____Mo. ____ 6 Mo. ____ 12 Mo.

IRB Decision Quadrant – Supporting Information

1. Research - Scientific Design and Purpose

- Scientific peer review has been conducted and documented.
- The hypothesis (purpose and overall objective) is clearly stated.
- The study design is scientifically sound and appropriate to prove the hypothesis
- Scientific peer review is documented.
- The research will contribute to generalizable knowledge.
- The anticipated results justify exposure of subjects to (any) risk, discomfort, or inconvenience.
- The proposal provides results from previous animal, human, or other supporting research.
- The participation of human subjects is necessary to meet research objectives.
- Subjects' rights and welfare are considered as integral part of study design.

2. Subjects

Subject Population

- Are the inclusion/exclusion criteria: sex, age, health status, ethnicity, number of subjects clearly stated?
- Is the proposed subject population appropriate for the goals of the study?
- Are subjects likely to benefit individually from participation in the study?
- Is the selection of subjects equitable, given any restrictions imposed by justifiable inclusion/exclusion criteria?
- Will any particular physiological, health, psychological, sociological, or cultural characteristics of the subject population pose special medical, ethical, or legal problems?
- Have appropriate steps been taken to minimize these potential problems?
- Could "secondary subjects," such as family or social groups, be affected by this study (genetics/social exposure)?

Subject Selection and Recruitment

- Is the method used to identify the subject population ethically and legally acceptable?
- Is the process used to recruit potential subjects appropriate and free of coercion?
- Do the advertisements or solicitations used to recruit subjects contain sufficient information?
- Is compensation reasonable in relation to the requirements for subject participation? Is it coercive in any way?

Vulnerable Subjects

- Additional safeguards are required for subjects likely to be vulnerable to coercion or undue influence such as children, prisoners, pregnant women, mentally disabled or economically or educationally disadvantaged persons. The IRB should confirm that the inclusion of any vulnerable subject population is justified and in compliance with guidance found in Federal Regulation 45 CFR 46 Subparts, B, C, and D.

Research Involving Children

- When reviewing research that involves children, the IRB must document the appropriate risk/benefit category.
  - 45 CFR 46.404 - Research that involves no more than minimal risk.
  - 45 CFR 46.405 - Research that involves greater than minimal risk but also presents the prospect of direct benefit to individual subjects.
  - 45 CFR 46.406 - Research that involves greater than minimal risk and no prospect of direct benefit to the individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition.
  - 45 CFR 46.407 - Research not otherwise approvable that represents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

3. Risks/Benefits

Risk

A risk is a potential harm or injury associated with the research that a reasonable person in the subject's position would likely be considered injurious. Risks can be categorized as physical, psychological, sociological, economic, and legal. Risks to subjects must be reasonable in relation to anticipated benefits, if any, to subjects and to the importance of knowledge that may reasonably be expected to result from the research.

"Minimal Risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily activities or during the performance of routine physical or psychological examinations or tests."

- What are the potential risks/discomforts/inconveniences associated with the research?
- Has full consideration been made of the risk to vulnerable subjects and/or other special populations?
- What is the overall risk classification: less than minimal, minimal, greater than minimal or, is it unacceptable?
- What are the estimated probability, severity, average duration, and reversibility of any given harm?
- Have adequate safeguards been adopted to minimize the possibility of an occurrence and the magnitude of the risks?
- What steps will be taken to treat subjects who suffer an injury? Is an Adverse Event Plan required?

Benefits

A research benefit is considered to be something of health-related, psychosocial, or other value obtained by the individual research subject, or something that will contribute to the acquisition of generalizable knowledge. Compensation for participation in research is not considered a benefit, but rather to provide compensation for research-related inconveniences.

- What are the potential benefits to the subject?
- What are the potential benefits to society?

Risk/Benefit Assessment

- Is the potential risk to subjects outweighed or balanced by the potential benefit to them or to the society in which they participate?
- Research involving children, pregnant women and fetuses, prisoners: Is the risk/benefit relationship acceptable according to the requirements of 45 CFR 46 Subparts B, C, or D?
- Is the research designed to maximize benefits and minimize risks to subjects?
- What is the magnitude and importance of the risk and benefit to the subject?
- How does the Principal Investigator assess risk/benefit?

4. Informed Consent

The Consent Process

- Are the mechanisms used to solicit subjects appropriate and without coercion or undue influence?
- Who will conduct informed consent? At what point in the process?
- Will the timing and setting for consent be conducive to rational and thoughtful decision-making? Will subjects be given the opportunity to review the consent and discuss their participation with family members or others beforehand?
- Is there anything in the process that might be perceived (real or otherwise) as undue influence or coercion?
- Should subjects be re-educated and re-consented at critical periods during the study?
- Will the nature of the research or other factors potentially inhibit a subject's desire/ability to withdraw from participation? If so, have appropriate steps been taken to minimize this problem?
- Will the subjects be physically and mentally competent to give informed consent? If no, is the proposed proxy consent procedure acceptable?
- Should a subject advocate or other individual be present during the consent process?
- Is assent required for children?
- If a waiver of some or all of the elements of informed consent is requested, do the nature and/or importance of the research justify such a waiver? Is the waiver in compliance with Federal regulations?

The Consent Form

- The Informed Consent is written clearly at the appropriate level and includes, at a minimum:
  - A clear explanation of the procedures to be followed, including an identification of those that are experimental.
  - A description of the potential benefits (to the subject or to society) and the attendant discomforts and risks.
  - A description of appropriate alternative procedures that would be advantageous to the subject if applicable.
  - An offer to answer any inquiries concerning the study and provides project manager and IRB contacts to do so.
  - A clear explanation of the results to be expected and information that will be provided to the subjects.
  - A clear explanation of methods employed to protect the subject's privacy.
  - Instructions that the subject is free to withdraw his consent and discontinue participation at any time.

5. Data Collection/Protection of Privacy/Confidentiality

- How will research data be collected and recorded?
- How sensitive is the data?
- Are special privacy and confidentiality issues properly addressed, e.g., the use of genetic information?
- Will personal identifiers or codes be associated with the data?
- How will the data be stored and maintained (secured) during the study?
- How will the data be stored or destroyed at conclusion of the study? At other sites?
- Who will have access to the data?

- Is there potential for medical and research data to be mixed?
- How will data be handled if more than one site is involved?
- Would a breach of confidentiality be harmful to the volunteer? What provisions exist to protect subjects' privacy?
- Does this study require a Data Management Plan? Should it be read and signed by all project staff?
- Do HIPAA regulations apply?

6. Biological Samples, Tissues, DNA, Cells or Cell Lines

- How will samples or tissues be collected, recorded, stored and disposed of?
- If embryonic stem cells, do they meet current Federal requirements?
- Are personal identifiers associated with the samples?
- Will private information be protected by code?
- How long will samples, tissues, cell lines, etc., be retained?
- Are there genetic or DNA issues?
- Will samples, tissues, cell lines, etc., be used for any other purpose than this research?
- Are samples obtained from licensed or registered suppliers, not on a warning list?
- Will subjects or their families receive results of the study? Should they?

7. Other Considerations

- Is the research controversial? Could it generate public concern or does it require implementation of special recommendations/protections?
- Does the potential for conflict of interest exist? By researchers, the IRB, or the sponsor?
- Does the research involve the use of ionizing or non-ionizing radiation? Chemical, biological or physical risk?
- Is this collaborative research? Is other IRB review required?
- Will human subject involvement take place at PNNL or another location?
- Is this FDA-regulated research? Investigational New Device (IND) or Investigational Device Exemption (IDE) involved?
- Does this project require more than annual continuing review? If so, how often and at what level?
- Does this research require compliance review?

8. Items for Discussion/Special Consideration

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.

DOE Human Subjects Protection
Interim Program Manager Michael Viola, M.D.

This newsletter is prepared at Oak Ridge National Laboratory, managed by UT–Battelle, LLC, for the U.S. Department of Energy, contract DE-AC05-00OR22725.
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Meetings

CATHOLIC HEALTH CARE ETHICS: FOUNDATIONS & APPLICATIONS
March 3–4, 2005
Loyola University medical Center, Maywood, Illinois
For information, see http://www.bioethics.lumc.edu

CLINICAL ETHICS CONSULTATION: SECOND INTERNATIONAL CONFERENCE
March 17–20, 2005
Basel, Switzerland
Sponsored by the Institute for Applied Ethics and Medical Ethics, University of Basel, the Department of Bioethics at the Cleveland Clinic Foundation, Ohio, and the Swiss Academy for Medical Sciences.
For information, see http://iaeme.ch

WORKSHOP ON ETHICAL ISSUES IN INTERNATIONAL HEALTH RESEARCH
June 13–17, 2005
Boston, Massachusetts
For information, see http://www.hsph.harvard.edu/bioethics/

AMERICAN SOCIETY FOR BIOETHICS AND HUMANITIES—2005 CONFERENCE
October 19–23, 2005
Washington, D.C.
For information, see http://www.asbh.org/