PROTECTING HUMAN SUBJECTS

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

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Contents

Selecting Human Research Subjects

Historical Context

In 1932, 400 black men who had syphilis were recruited to participate in the well-known "Tuskegee" study. These subjects participated in research without giving informed consent. The men who enrolled in the study were promised "special free treatment," when in fact the purpose of this public health study was to determine the natural course of *untreated* syphilis. They were denied penicillin as the study continued into the 1940s, when that drug was proven a safe and effective treatment for the disease. Not until the early 1970s, when the popular media disclosed this research, was the study terminated. This media exposure eventually led to the promulgation of the National Research Act of 1974. The Act mandated that institutional review boards (IRBs) approve all federally funded proposed research involving human subjects. *

The Tuskegee study presented many ethical problems. The men were already disadvantaged in terms of socioeconomic status and medical condition. As research subjects, they faced additional risks. They were uninformed about the purpose of the study and misled about the benefits they were to receive. Those who survived were denied treatment long after it became available. The research design was also questionable. The researchers targeted a population to study a problem that was not confined to that group.

The Tuskegee legacy has led to better protections for vulnerable populations. For example, today, rather than recruiting subjects from disadvantaged or vulnerable groups, researchers are likely to select white males for their studies. Nevertheless, selection of human subjects continues to present challenges. In fact, reliance on white males in studies of heart disease or cancer or drug efficacy has raised questions about whether research findings can be generalized to the population as a whole.

Guiding Principles

IRBs have particular responsibility to ensure **equitable selection** of human subjects. The National Commission for the Protection of Human Subjects of Biomedical Research (National Commission), which was established in 1975, recommended that IRBs evaluate the selection of research subjects to determine whether some groups are systematically chosen for research simply because of their easy availability, compromised position, or ability to be manipulated, rather than selected for reasons directly related to the question being studied. An equitable selection process is designed to ensure a fair distribution of the burdens as well as the benefits of research.

In a recent interview, Dr. Joan P. Porter, Senior Policy Analyst at the National Institutes of Health, Office for Protection from Research Risks, discussed key concepts related to the human subjects selection process. The following information is based on this interview as well as the sources cited at the end of this article.

As a rule, IRBs must balance the risks of an individual's participation in research against the benefits to that human subject and and to society. For purposes of evaluation, risks or burdens take several forms, as described by Dr. Porter. **Physical risks** include discomfort or pain related to the research or to the side effects from an intervention. Even drawing blood, for example, may cause bruising or soreness or, occasionally, infection. **Social risks** include loss of confidentiality, stigma as individuals or as a class, or other discomforts such as embarrassment. **Economic risks** include potential loss of insurance, potential loss of employment, and other costs, for example.

The Belmont Report, published by the National Commission in 1979, is the philosophical basis for the current Federal regulation (10 CFR Part 745) that now protects human subjects from research risks. ** *The Belmont Report* discusses two kinds of **justice: individual** and **social.** Both levels must be satisfied to make the research selection process equitable. "Individual" justice is promoted through the researchers' attention to fairness in the selection process. Investigator bias must not influence whether an individual is either included in or excluded from research.

"Social" justice requires researchers to distinguish between groups who should participate in a given type of research and those who should not. The principle of social justice requires the selection of human subjects based on the following order of preference: adults before children, competent individuals before incompetent individuals, and noninstitutionalized persons before institutionalized persons. This order of selection helps IRBs consider the extent to which proposed subjects may already be burdened and decide whether they are suitable populations.

Dr. Porter defined **"burdened" populations** as members of society in situations that put them at a disadvantage and make their lives difficult. These people may have disabilities. Burdens can also emanate from social, cultural, or environmental circumstances. They are often borne by persons who are economically and/or educationally disadvantaged. Institutionalized populations may also be part of the burdened population. Among this group are prisoners, persons with mental disabilities, children in orphanages, and persons in nursing homes. Institutionalized populations, said Dr. Porter, may be sought out as research subjects primarily because they are easy to manipulate or easily accessible to researchers. "These are situations about which an IRB needs to be vigilant," she emphasized.

The term "burdened" is highly contextual in nature, Dr. Porter asserted. That is, certain people are burdened even though they do not fit the various categories described above. For example, not all psychology students are economically or socially burdened, but they are readily available for their professors' research. If these students

feel that their position at school may be compromised (e.g., through lower grades), the decision about whether or not to participate in research may make them feel coerced. Similarly, employees of drug companies are convenient subjects for pharmaceutical research. Their promotions or even job security may depend on those who are recruiting them for research. This circumstance makes the employees susceptible to manipulation. Research participation must be truly voluntary.

Exceptions and Challenges

In designing research, said Dr. Porter, investigators generally call first upon less burdened groups to accept the risks in research. Exceptions occur when the research offers a therapy component or when the subjects of research are affected by the condition or circumstance under study. For example, studies designed to evaluate prison conditions require involvement of prisoners. Research designed to look at cofactors of HIV infection may require people who inject illegal drugs. When a life-threatening virus or environmental problem breaks out in a poor community, inevitably those residents will be the subjects of research. A good example of this point was the research that followed the recent outbreak of a fatal virus in New Mexico's Indian populations.

One of the IRB's recurring challenges is to draw the line between protecting burdened populations and being unduly paternalistic by excluding them. Investigators must avoid repeated targeting of vulnerable groups simply because they are convenient. Yet, investigators must not prohibit free, competent, and eligible subjects from volunteering to participate as often as they wish. ***

In summary, research subjects must—

1. be fully informed before they are asked to decide whether or not to participate in research,
2. make their own decisions about their participation—without coercion, undue influence, or duress—and
3. feel free to participate or withdraw at any time without causing adverse effects on their relationships with researchers.

Sources:

* Arthur L. Caplan. "When Evil Intrudes." *Hastings Center Report 22*, No. 6 (1992): 29-32.

** The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont Report.* Ethical Principles and Guidelines for the Protection of Human Subjects of Research. April 18, 1979.

*** Protecting Human Subjects at the Department of Energy. "Selection of Human Subjects." *Human Subjects Handbook.* June 1992.

Practical Considerations

Several interviews highlighted practical considerations associated with applying the principles Dr. Porter discussed to the selection of human subjects. Persons interviewed were Dr. Bart Gledhill, Chairman of the Human Subjects Committee at Lawrence Livermore National Laboratory (LLNL); Ms. Robin Rawlings, RN,

Clinical Coordinator of the Cholesterol Research Center at Lawrence Berkeley Laboratory (LBL); and Ms. Chris Byrne, Executive Advisor to LBL's Human Use Committee.

Q: What is the typical recruitment process?

A: Dr. Gledhill: The process for recruiting human subjects varies from laboratory to laboratory and from project to project. It depends on the type of research conducted, the purpose of the research, the research setting, the needs of the subject population, and the laboratory's collaborative arrangements with other institutions. At LLNL, a significant percentage of research subjects is recruited from laboratory employees. Most of the research conducted within the laboratory utilizes blood and urine samples collected at the time of occupational medicine examinations. Workers are contacted randomly before their medical exams, except that an effort is made to recruit people who have not already been research subjects. In addition, samples are collected from clinics, hospitals, and other institutions outside the laboratory. The IRB at LLNL carefully scrutinizes the process by which the cooperating institution selects human subjects to ensure compliance with the Federal regulations.

The recruitment selection process is discussed in detail when the project is introduced at the IRB meeting. The principal investigator always attends this meeting. The IRB and investigator "walk through" the recruitment process to determine its fairness. It is not enough to ensure that the research design complies with Federal regulations. Prospective human subjects must also feel they can communicate freely with the principal investigator. In every case, the investigator must provide answers to the following questions: What is the purpose of the research? How does the study relate to research conducted in the past? What does it aim to accomplish? How does the subjects' participation benefit the individual subject or society? What is expected of the research subjects? What risks, however remote, may the subjects encounter?

Q: How do you evaluate whether research subjects have physiological, psychological, or social characteristics that will pose special risks?

A: Ms. Rawlings: In a study of lipoprotein levels, for example, participants were recruited who agreed to follow a prescribed, rigid diet in order to evaluate their lipoprotein profiles. Initially, it's important to determine that potential participants do not have medical problems that would pose risks. Questionnaires are very helpful tools to determine an individual's medical eligibility for a given research project. Telephone or personal interviews are also conducted. After these interviews, individuals who meet the protocol requirements must attend an orientation meeting. At this meeting, they are fully informed about the research study and the specific requirements of their participation.

Q: What recommendations do you have for conducting fair evaluations of potential research candidates?

A: Ms. Byrne: To ensure fair evaluation of each research project, it's important to make sure the IRB includes people with special competence in the type of research being proposed (e.g., survey design) or the type of human subject the study targets. The strongest tool for evaluating whether someone should be selected as a human subject is a detailed, thorough, and well-documented research protocol. The research protocol sets the rules for conducting an evaluation. The researcher proposes a complete list of inclusion and exclusion criteria for the IRB's approval.

Q: How do you reduce the pressure to participate for people who are likely to succumb to coercion?

A: Ms. Byrne: The researcher and the IRB must work very closely together. Often, the researcher wants to target the subject group fairly narrowly. He or she may feel the need for a high recruitment rate and thus want to offer inducements to participate. The IRB's role is to determine when an inducement becomes coercion and to assure that coercion does not occur. Here is a fairly common scenario: a researcher needs 10-20 ml of human blood two or three times a week for laboratory experiments. If the researcher walks down the hall to ask a friend or colleague to donate blood, the inducement may be friendship or desire to help a colleague. From the IRB's standpoint, this inducement may represent coercion. The subject could feel pressured even if this reaction is unintended. The IRB cautions against using colleagues as subjects and does not allow researchers to use their subordinates as research subjects. To recruit subjects, the IRB recommends posting advertisements in common areas or using sources outside the laboratory.

Q: What about payment incentives (monetary and also other rewards in lieu of or in addition to money) to participate as a research subject?

A: Dr. Gledhill: This laboratory feels it's appropriate to provide payment incentives when research subjects are inconvenienced. Donating a few milliliters of blood, for example, often requires human subjects to undergo fasting and arrive at work early. The IRB must draw some important distinctions: When do incentives represent undue enticement to participate? What is the appropriate amount of remuneration? Would participants have chosen to participate if they had not been offered a payment incentive? These concerns may exclude a study or a protocol from approval.

Ms. Byrne: The advantage of monetary incentives is that they tend to open up much larger subject pools. It is also true that they may offer an incentive so great that potential subjects feel they cannot refuse the offer. The IRB and investigators must agree on an appropriate scale of payment. At least one nearby medical school reimburses subjects according to the amount of blood drawn. In some cases, however, this too may pose a problem for IRB approval.

One IRB evaluated a study that included a delayed payment structure with a large payment for completing the study. The IRB was concerned that this payment structure might force subjects to continue even though they wanted to drop out in the middle of the study. Another concern was that the proposed population of human subjects included students, who might view the final payment as a very large sum of money. In the worst-case scenario, a person might continue to participate despite feeling ill, in an effort to obtain this payment. Because of these concerns, the IRB asked the investigator to restructure the payment schedule so that the final bonus represented no more than 10-15 percent of the total payment. This decision was consistent with a longstanding policy to allow additional remuneration for completing an experiment as long as it does not represent undue inducement.

Ms. Rawlings: For several studies on the role of diet and cholesterol, subjects are partially reimbursed because they are required to adhere to a strictly prescribed diet. They are getting paid for the inconvenience of eating only the brand names and quantities of foods on the approved list for this research project. When the laboratory advertises for human subjects, the reimbursement procedure is not mentioned. Reimbursement is also not discussed when researchers first talk to a potential subject unless the subject brings it up. This approach eliminates undue inducement.

Human Subjects Database

On April 4, the Office of Health and Environmental Research (OHER), U.S. Department of Energy (DOE), delivered to Senator John Glenn's Senate Governmental Affairs Committee summary statistics and individual reports on all projects using human subjects—a total of 175—that are conducted at DOE facilities or funded by DOE at other institutions. (See database statistics.) The same day, DOE provided Internet access to the database used to generate this information. These actions fulfilled a commitment made by Secretary Hazel O'Leary in January.

We would like to express sincere appreciation to everyone who made this achievement possible. It was the result of cooperation and hard work by people throughout the DOE system. We ask for your continued support in helping us refine the database and ensure that it continues to be updated with complete and reliable information.

Thank you.

Susan Rose
Human Research Subjects
Program Manager

Spotlight on Pacific Northwest Laboratories: *An IRB Strives for Excellence*

In July 1993, Pacific Northwest Laboratories (PNL) was granted a multiple project assurance by the Department of Energy (DOE). Mr. Harold Harty, who chairs the IRB, stated that in part PNL's expanded responsibility was warranted because of the strong working relationship with the Richland Operations Office and DOE Headquarters.

These relationships began, Mr. Harty stressed, with good communications between PNL's IRB and the Operations Office. He reported that PNL keeps the Richland Operations Office fully informed, at least annually, about all human subjects activities so that the Operations Office can communicate authoritatively with Headquarters. Communication does not stop there. Two-way communication with DOE Headquarters also drew favorable comments from Mr. Alan Rither, Senior PNL Attorney and IRB member. Both Mr. Harty and Mr. Rither expressed gratitude for the support received from Headquarters' personnel.

In particular, they recalled that Dr. Susan Rose, DOE Human Subjects Program Manager, observed a PNL IRB meeting in action and asked several investigators challenging questions about research design. Mr. Harty said that Dr. Rose's questions helped the IRB members "confirm that their own approach to questioning investigators was appropriate." In a recent interview, Dr. Rose said she was impressed with the IRB's responsiveness and dedication to quality. She attributed much of the IRB's success to its excellent leadership.

Reasons for Seeking a Multiple Project Assurance

Nearly 2 years ago, PNL began to pursue a multiple project assurance for many reasons. "Perhaps the most compelling reason for any laboratory to obtain a multiple project assurance," Mr. Rither said, "is to establish credibility with other Government and private organizations that conduct human subjects research, such as the Department of Health and Human Services (DHHS) and university hospitals and health agencies."

Mr. Harty emphasized other advantages to having a multiple project assurance. It allows new projects to begin, following IRB approval, without waiting for DOE Headquarters' concurrence. This provision reduces administrative work for the laboratory and review responsibilities for Headquarters. He commented particularly on the fact that IRBs at institutions with multiple project assurances may conduct expedited reviews without Headquarters' approval for those projects that qualify.

This process benefits all IRB members, said Mr. Harty. The IRB members who are selected by the chairperson to conduct expedited reviews examine proposed research in depth and report their findings to the full IRB. This thoroughness helps win trust and establish a standard for all IRB reviews.

IRB Composition

The IRB's makeup also influenced Headquarters' decision to award PNL a multiple project assurance. The IRB composition at PNL more than satisfies the Federal requirements. For example 10 CFR Part 745 requires IRBs to have a minimum of five members. PNL's board has seven members, and Mr. Harold Harty noted that five of the seven IRB members have been on the board for 15 years or more. The Common Rule (10 CFR 745) requires diversity in race, gender, and culture. PNL's board is multi-racial, and two of the seven members are women. While the Common Rule requires at least one member who is not affiliated with the institution, PNL's IRB has three community members, who provide contact with a variety of cultures.

For research involving vulnerable subjects, the Common Rule requires IRBs to include one or more individuals knowledgeable about and experienced in working with these groups. To review a project involving people with AIDS, Mr. Harty said, PNL's board used another IRB whose members had expertise in this area. He also added that "when PNL research involves a minority not represented on the IRB, the laboratory invites researchers with knowledge of that group to work with the IRB to promote cultural sensitivity."

Preparation for IRB Responsibilities

Mr. Harty devotes time and energy to orienting IRB members and preparing them for meetings. He sends each committee member information on PNL's corporate and human subjects research policies. Well in advance of each IRB meeting, committee members receive the agenda, research protocols, and other relevant materials. PNL also offers its IRB members opportunities to stay abreast of human subjects concerns by attending national meetings. For example, Mr. Rither participated in the most recent DOE-sponsored human subjects workshop and other members have attended DHHS-sponsored meetings relevant to PNL's research activities. One of the newer IRB members attended a national workshop that focused on women and minorities in research. On her return, she reported that she had gained a deeper understanding of the role of informed consent, the need for clear statements about risks and benefits, and the need for appropriate remuneration of subjects who participate in research. She added that the meeting increased her awareness of the ways in which various ethnic groups shared certain cultural sensitivities while they differed in other respects.

IRB Interactions

Both Mr. Harty and Mr. Rither emphasized that all IRB members must contribute constructively to the interplay of personalities, perspectives, and interests. Mr. Rither said that members must appreciate differences of opinion and express their viewpoints in a nonconfrontational manner. The chairperson, Mr. Harty said, must help members feel comfortable exchanging information and ideas and contributing to the consensus-building process. This support is often particularly important for lay persons or community representatives, who may be reluctant to participate fully in an IRB because they feel intimidated by the specialized knowledge of the professionals. Above all, said Mr. Rither, the IRB members must dedicate themselves to resolving conflicts in a way that keeps the group focused on the bottom line: assuring an appropriate balance of benefits to risks for the human subjects.

A Case in Point

The PNL IRB recently reviewed a research project involving vulnerable populations—youth aged 12 to 15 who were at risk of developing sexually transmitted diseases. The research protocol required them to identify their sources of information regarding a variety of sensitive health practices. If the sources were individuals, they in turn were to be interviewed without being told the name of the person who identified them as a source. The interview process was to continue until the network and quality of information available in the community could be determined.

Mr. Harty and Mr. Rither described the IRB review of this project as very challenging: the research subjects were vulnerable because of race, ethnicity, and age, and the research topic and methods were highly sensitive. At first, the IRB rejected the project. It decided, they explained, that the potential negative consequences (such as gang retribution or parental interrogation and abuse) were too great, although the IRB recognized the eventual benefits might be significant.

Subsequently, the IRB's concerns were addressed by principal investigators, researchers from cooperating institutions, additional community representatives, and reviewers from the sponsoring organization. After more protections were added and privacy concerns addressed, the project was approved.

Mr. Rither reviewed the steps taken to reach the decision. He noted that the informed consent form (which required the signature of the subject and a parent) was reworked several times to ensure the language was understandable and culturally appropriate to each ethnic group involved. "We went over each part of the informed consent form with a fine-tooth comb to make sure it met the requirements of the Common Rule (10 CFR Part 745)," said Mr. Rither. Then, the consent forms and questionnaires were tested on the youth and their parents or guardians. The goal was to check their understanding of the consent forms and to determine their reaction to the questionnaires. Mr. Rither and Mr. Harty noted that the results to date have been very gratifying. "Using community 'gatekeepers' in addition to interviewers has led to a high degree of acceptance of, and participation in, the research," they reported.

This project is one among several research studies reviewed by PNL's IRB but conducted outside the laboratory. In addition, PNL's considerable experience in reviewing human subjects research funded and approved by several Federal agencies, said Dr. Rose, is yet another strong qualification for becoming a multiple project assurance institution.

PNL Characteristics

Main Topics of Human Subjects Research:

Statistical Health Studies of Worker Populations

Collaborating Institutions:

Projects often undertaken in partnership with Hanford Environmental Health Foundation, a DOE facility that maintains databases on past and present Hanford plant employees.

Single Project Assurance Institutions and Multiple Project Assurance Institutions

Key Similarities and Differences

Institutions that use DOE funding, facilities, or personnel to conduct research involving human subjects must provide DOE with assurance that they are complying with 10 CFR Part 745. Many DOE laboratories hold a "single project assurance" (SPA). Some have qualified for a "multiple project assurance" (MPA). The key difference between the two is whether DOE Headquarters must approve new human subjects projects before work begins.

Requirements Checklist

Requirements	SPA Institutions	MPA Institutions (DOE or DHHS)
Must obtain Field Office and Headquarters (HQ) approval before new project begins.	yes	no
May conduct expedited review.	yes	yes
Must provide HQ with annual reports, including a project summary form for every project.	yes	yes
Must notify HQ immediately if human subjects experience adverse effects in any way.	yes	yes
Must notify HQ immediately if there is any evidence of noncompliance with the Federal regulation.	yes	yes
Must notify HQ if any research is conducted abroad or with foreign collaborators.	yes	yes

Following approval for each new project by the institutional review board (IRB), SPA facilities must seek Headquarters' approval. For each new project, SPA institutions must send complete documentation, both the assurance of compliance with 10 CFR Part 745 and the project information, to the cognizant Field Office for

transmittal to Headquarters. Headquarters must provide approval before each human subjects research project may start.

By contrast, MPA institutions are independently responsible for approving new human subjects research projects. While cognizant DOE Field Offices and Headquarters exercise general oversight, they rarely, if ever, participate in granting initial project approval. Once the IRB approves a project, it may begin. Under the Federal regulation, however, DOE may waive any prior approvals and examine any DOE-supported project.

After the initial approval of new projects, IRBs at both types of institutions must (1) review and approve projects at least once annually, and (2) annually report all approved projects to Headquarters. Any adverse effects must also be reported immediately to the IRB, to DOE Headquarters, and to all funding sources.

Both SPA and MPA institutions may conduct expedited reviews of certain human subjects research. Under Title 10 Part 745 Section 27.110, a single, experienced IRB member selected by the IRB chairperson may conduct reviews when (1) approved research requires only minor changes within the review period or (2) research under review presents only minimal risk. Minimal risks are defined as being no greater in probability or magnitude than risks encountered in daily life or during the performance of routine physical or psychological tests. Note that if the reviewer disapproves the research, the full IRB must convene to decide.

Once expedited review and approval has occurred, however, SPA institutions must obtain Headquarters' approval before the new project can begin.

By Federal regulation, DOE and all other Federal agencies must recognize MPAs granted by the Department of Health and Human Services (DHHS). Thus, laboratories like Lawrence Livermore National Laboratory and Lawrence Berkeley Laboratories, with DHHS-approved MPAs, are eligible to confer initial approval of human subjects research that relies on DOE funding, facilities, or personnel. These laboratories are also able to approve research conducted at or funded by other Federal agencies.

Common Requirements for SPA and MPA Institutions

All institutions must submit Project Summary forms each year for each approved project, whether new or continuing. This requirement applies whether an institution uses an SPA or has obtained MPA status from either DOE or DHHS.

Further, all institutions must immediately report the following events to Field Offices and Headquarters:

- Any injuries to human subjects, unanticipated problems that involve risks to human subjects or others, and serious or continuing noncompliance with the requirements or determinations of the IRB.
- Any suspension or termination of the IRB's approval of research.
- Any change in the IRB membership.

How to Qualify for MPA Status

To qualify for MPAs granted by DOE, institutions must demonstrate competence in protecting human subjects. Key factors are often the qualifications and experience of IRB members, evidence of their sensitivity and good judgment with respect to human subjects issues, and the production of orderly, complete, timely records and reports. (See Title 10 Part 745 Section 27.107 for IRB composition requirements.)

How To Apply For MPA Status

To apply for an MPA granted by DOE, institutions must complete the sample MPA assurance forms located in the Human Subjects Handbook.* The form covers all features of 10 CFR Part 745 requirements. A roster of the current IRB membership must be attached.

* *Protecting Human Subjects Research Subjects at the Department of Energy—Human Subjects Handbook* is currently being updated. Limited copies are available from Headquarters.

To request a copy, write—

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Attention: Handbook Request
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Occupational Medicine Programs at the Department of Energy

By John Peeters, Office of Occupational Medicine

The Department of Energy's (DOE's) increased focus on the cleanup of U.S. weapons facilities has contributed to the ongoing efforts within the Department to provide state-of-the-art employee health protection. **Occupational medicine**, the medical specialty that focuses on recognizing, treating, and preventing work-related diseases, is involved in ensuring employee health protection.

DOE's Office of Occupational Medicine (EH-43) is responsible for promulgating and enforcing DOE Order 5480.8A, which outlines the requirements for DOE contractor occupational medicine programs. This Order establishes that all DOE contractors will provide routine medical surveillance examinations and tests for employees, in order to detect and prevent occupational illness or injury. EH-43 assesses contractors' occupational medicine programs and provides technical assistance. Technical assistance includes improvements in medical informatics and quality assurance activities.

In addition to assessing occupational medicine programs at DOE contractor sites, EH-43 also conducts health services research in **preventive medicine**. Preventive medicine initiatives include the DOE Medical Surveillance Program, which started as a pilot program in 1993. Medical surveillance in the workplace refers to the periodic, systematic collection and analysis of data about workers' health and workplace conditions. It attempts to detect "illnesses or health trends that indicate a possible adverse effect of workplace exposures" before serious disease has become evident or the worker would normally seek medical advice. *

The DOE Medical Surveillance Program will provide a means of analyzing medical and exposure records to determine subtle effects of hazardous exposure. This process will allow the occupational medicine physician to detect precursors of disease before the actual onset of illness. In 1993, four pilot sites were selected, the study design for hardware and software was completed, and a common data set for use at all DOE sites was defined. The process of defining a common data set was long and challenging; yet without this common framework, it would be impossible to compare information from different sites.

The need to monitor employee health at DOE gained Congressional support with the passage of the National Defense Authorization Act for FY 1993 (Public Law 102-484). Section 3162 of this Act mandates that DOE establish a comprehensive program to monitor not only its present contractor employees but also *former* contractor and *subcontractor* employees who have been significantly exposed to hazardous and radioactive substances. The current DOE Medical Surveillance Program provides the foundation for this ambitious program, which ultimately may serve an estimated one million past and present DOE workers across the country. Regulations to implement the program will be jointly drafted by DOE and the Department of Health and Human Services.

The DOE Medical Surveillance Program is a clinical program aimed at proactive preventive health care and will ultimately function across all DOE contractor occuational medicine programs. **It is not a research program and thus is not subject to human subjects regulations.** This program must meet the normal physician-patient confidentiality requirements. Only summary information that does not identify individual patients either directly or indirectly will be made available in the future.

Some other activities under the purview of DOE's Occupational Medicine Program, however, are subject to human subjects research regulations. For example, an institutional review board (IRB) recently evaluated a study to compare the ability of different medical tests to detect chronic beryllium disease. Conducted by the Oak Ridge Institute for Science and Education (ORISE), the study is designed to compare blood lymphocyte testing to more traditional screening tests (e.g., chest x-radiography and pulmonary function testing). The subjects are 1,000 workers who were exposed to beryllium at the Oak Ridge Y-12 Plant. Although the study poses minimal physical risks to the subjects, the IRB was concerned about the negative effects (for example, potential loss of future employment opportunities) that could result from labeling someone as either "ill" or "susceptible to beryllium." As a result, informed consent materials were developed to address the physical and social risks of participation in the project. Development of these materials was a cooperative effort by DOE Occupational Medicine personnel, labor representatives, Y-12 plant management, and ORISE's IRB. The ORISE IRB approved the informed consent materials and study protocol.

In summary, EH-43 has major, cross-cutting responsibilities spanning occupational medicine and worker-related research. Both responsibilities involve a commitment from qualified personnel including both workers and onsite medical departments. Cooperation among laboratory officials, medical officers and their departments, and workers at all DOE and contractor facilities is vital. EH-43 activities require surveillance and close attention to privacy issues and regulatory concerns.

Articles planned for future issues of this bulletin will further explore distinctions between occupational medicine and human subjects research. They may also highlight medical surveillance activities at onsite facilities.

*** Source**

U.S. Congress. Office of Technology Assessment. *Hazards Ahead: Managing Cleanup—Worker Health and Safety at the Nuclear Weapons Complex.* OTA-BP-O-85. Washington, DC: U.S. Government Printing Office, February 1993.

Statistics: Current DOE Research Involving Human Subjects

[*NOTE: The following data was extracted from the FY 1994 DOE Human Subjects Research Projects Database.*]

	No. of Projects	Funding	No. of Subjects
TOTALS	175	$56,864,316	724,303*
Support DOE only	88	$45,317,320	326,743
DOE and other(s)	15	$2,137,048	62,107
Non-DOE only	72	$9,409,948	335,453
Site DOE facilities	139	$26,724,701	702,099
Other facilities	36	$30,139,615	22,204
RADIATION EXPOSURE	41	$34,586,450	5,056
Minimal, tracer levels	31	$8,833,950	3,208
Health studies using diagnostic x-rays	7	$24,457,500	1,288
Therapeutic levels	3	$1,295,000	560

* Total number of human subjects in the United States. The number includes 360,000 people involved in two epidemiologic studies and another 321,000 who participated in a questionnaire study of runners and their health.

General Resources

Associations

The Applied Research Ethics National Association (ARENA) and Public Responsibility in Medicine and Research (PRIM&R) are both located at—

132 Boylston Street
Boston, MA 02116
Tel: (617) 423-4112
Fax: (617) 423-1185

ARENA is a national service organization for researchers, administrators, institutional review board members, and other professionals interested in biomedical ethics. The association promotes educational activities and distributes a quarterly newsletter, free of charge, to all members.

PRIM&R sponsors conferences on bioethical issues in the areas of human subjects and animal research. This organization also publishes comprehensive summaries of its conferences and provides educational packets.

Newsletters/Periodicals

The *Hastings Center Report* and *IRB: A Review of Human Subjects Research* are published bimonthly by—

The Hastings Center
255 Elm Road
Briarcliff Manor, NY 10510
Tel: (914) 762-8500
Fax: (914) 762-2124

The *Hastings Center Report* covers topics in bioethics from the perspectives of several disciplines and professions—philosophy, medicine, law, the natural and social sciences, and theology. *IRB: A Review of Human Subjects Research* addresses substantive concerns in research ethics and keeps readers abreast of the Federal regulations governing human subjects research. It is designed for members of institutional review boards, researchers, administrators, and public policymakers.

Videotapes

To help individuals responsible for safeguarding the rights and welfare of human subjects, NIH has developed a series of three instructional videotapes. *Evolving Concern* provides historical perspective on behavioral and biomedical research. *Balancing Society's Mandates: Criteria for Review* shows an IRB in action. *The Belmont Report: Basic Ethical Principles and Their Application* looks at underlying ethical principles and how they apply to human subjects research. Concepts explored are beneficence, respect for persons, and justice. To obtain a free copy of these videotapes, contact—

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Meetings

Focus on Protecting Human Subjects in the Federal Government
June 13, 1994

Sponsored by the Interagency Human Subjects Research Committee
To be held at the Uniformed Services University, Bethesda, Maryland

Speakers

- Dr. Robert J. Levine, Yale University, *Human Subjects Protections: Past/Present/Future*
- Dr. David J. Rothman, Columbia University, *Current Events in Perspective*

Agenda Topics

- Risk/Benefit Assessment
- International Research
- Assurance/ Compliance Considerations
- Compensation Issues
- Special Populations

Research Using Human Subjects: Past and Present Viewpoints
June 14, 1994

Organized by the Department of Energy
To be held at the Uniformed Services University, Bethesda, Maryland

Agenda Topics

- Status of the Historical Record Collection & a Laboratory's Perspective
- Occupational Medicine vs. Human Subjects Research
- Database Issues: Current Research
- IRB Issues
- Compliance/Auditing

For registration information, consult Susan Dallas by mail at ORISE, P.O. Box 117,Oak Ridge, TN 37831-0117 or by fax (615) 576-0202 or at the address above.

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DOE Human Research Subjects Program

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