PROTECTING HUMAN SUBJECTS

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

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Contents

Introducing This Bulletin

The Office of Health and Environmental Research (OHER), within the Office of Energy Research at the Department of Energy (DOE), supports research to ensure that the potentially adverse health and environmental impacts of energy technologies are fully understood and to advance the biomedical and environmental sciences. Among its many additional contributions to the Department's mission, OHER is responsible for formulating human subjects research policies and for ensuring Department-wide compliance with the Federal regulations that protect human subjects from research risks. Dr. David Galas, the Associate Director for Health and Environmental Research, oversees the three divisions: the Environmental Sciences division, the Medical Applications and Biophysical Research division, and the Health Effects and Life Sciences Research division. Dr. David Smith is the Director of the Health Effects and Life Sciences Research division. This division has been delegated responsibility for activities directed toward protection of human subjects research at the Department. Dr. Susan Rose of this division manages these activities.

OHER is pleased to present the first issue of *Protecting Human Subjects*. This bulletin is designed to inform and educate the DOE address solutions to the wide range of challenges encountered in human subjects research, a working group of field office, national laboratory, and Headquarters personnel meets regularly to exchange ideas, discuss problems, and plan DOE human subjects meetings. The working group meetings are open, and members of the DOE community are welcome to attend.

For more information on working group activities, contact—

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Federal Policy for the Protection of Human Subjects (10 CFR Part 745)

On July 18, 1991, 10 CFR Part 745–the Federal Policy for the Protection of Human Subjects (known as the Common Rule)–was signed into law. This event represented a milestone for those involved with human subjects research in Federal Government agencies. For the first time, all Federal Government agencies were formally required to comply with the same set of rules for protecting human subjects from research risks. In addition, agencies conducting both intramural and extramural research activities must require identical protections for both types of funding.

Background

Between 1975 and 1978, the National Commission for the Protection of Human Subjects issued a series of reports that later became the basis of the Department of Health and Human Services regulations governing the protection of human subjects. In 1978, that commission became the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. Their mandate was to study and report to the President, Congress, and appropriate Federal departments and agencies on the ethical and legal implications of a variety of issues in medicine and research. The President's Commission reviewed the adequacy and uniformity of the rules, policies, guidelines, and regulations of all Federal departments and agencies regarding human subjects protections. In 1981, the President's Commission recognized the need for a Model Federal Policy to protect human subjects. Subsequent human subjects subcommittees (now under the Federal Coordinating Council for Science, Engineering, and Technology (FCCSET)) began the effort to draft a carefully crafted Model Federal Policy and finally succeeded in 1991 in securing its passage. Dr. Charles McCarthy and Dr. Joan Porter from the National Institutes of Health's (NIH) Office for Protection from Research Risks (OPRR) ably led these efforts.

FCCSET and Its Subcommittees

FCCSET is a large umbrella organization of Federal agencies that addresses problems and developments in science, engineering, technology, and related fields. Through its various committees and subcommittees, FCCSET reviews, recommends, and implements policies and other measures designed to:

- Plan and administer Federal scientific, engineering, and technological programs more effectively.
- Identify research needs, including areas requiring additional emphasis.
- Utilize government scientific, engineering, and technological resources and facilities more effectively.
- Encourage international cooperation in science, engineering, and technology.

Chartered in 1982, the Ad Hoc Committee for the Protection of Human Research Subjects developed the Model Federal Policy that established a uniform governing regulation for all federally conducted or supported research involving human subjects. In 1983, the Interagency Human Subjects Coordinating Committee was chartered to provide continued interagency cooperation concerning human subjects research issues. The current committee is chaired by the director of NIH's OPRR and is composed of representatives of all Federal departments and

agencies that conduct, support, or regulate research involving human subjects. OPRR continues to be the lead agency for promoting the protection of human subjects and establishing policies for the Federal community. Upon promulgation of the Common Rule in 1991, the Interagency Committee was redesignated the Human Subjects Research Subcommittee of FCCSET's Committee on Life Sciences and Health.

Benefits of the Common Rule to DOE

The Common Rule benefits DOE in these ways:

- It clearly defines the concept of human subjects research.
- It simplifies and streamlines the human subjects project approval process. The DOE Headquarters and field office personnel and laboratory researchers follow one set of policies.
- Laboratories and universities that conduct research for a variety of sponsors are no longer required to follow a variety of policies and procedures. Thus, a formerly ambiguous situation for laboratories and universities has been resolved.
- It allows DOE to establish approval authorities and the lines of responsibility, write uniform orders, and establish policies and procedures systemwide.
- It provides for exemptions, procedures for reporting adverse affects, and expedited review.
- It provides a mechanism to establish "equivalency" with other Federal agencies, which simplifies the approval process when multiple funding agencies are involved.

The Informed Consent Process–The Key to Effective Protection

In 1945, the world was shocked to learn about unethical experiments conducted by German physicians on concentration camp prisoners. In that same decade, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease not confined to that population. These subjects were not offered effective treatment long after such treatment became generally available.

Abuses like these generated awareness of the need to protect human subjects and to assure their informed voluntary consent. The Nuremberg trials of accused World War II criminals represented the first prosecution for the crime of forcing people to participate in experiments against their will. For this trial, a set of principles, known as the Nuremberg Code, was developed. These principles embodied moral, legal, and ethical standards for judging human experimentation. The principles have since been refined and incorporated into professional codes and Federal and State laws and regulations. Three tenets of the Nuremberg Code deal specifically with informed consent issues. They are as follows:

- The *voluntary* consent of the human subject is essential.
- During an experiment, the human subject must be free to leave the experiment if he or she feels that, mentally or physically, continuation of the experiment is unacceptable.
- During the experiment, the scientist in charge must be prepared to end the experiment at any stage if he or she has probable cause to believe that continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Informed consent is a process designed to give human subjects all the information they need about a study, to ensure that they understand the information, and—most importantly—to give them an opportunity to decide freely whether to volunteer to participate in the study. This process is codified in 10 CFR Part 745, the Federal Policy for the Protection of Human Subjects.

Too often, informed consent documents fail to cover all required elements, or they fail to cover the elements completely and comprehensively. The following guidelines outline key elements that investigators and reviewers must use in designing informed consent documents, and offer advice on preparing and reviewing forms that are clear, complete, and useful.

Informed Consent Forms: Critical Points To Review

The informed consent document must present information in a way that genuinely enables the individual to decide whether to participate as a research subject. It must educate people in easily understood terms. It must use short sentences and plain, direct words. It must avoid medical, technical, or legal terminology unless all the participants have training in those fields. For example, it could say, "We will draw a blood sample," not "We will perform venipuncture." It must present information to non-English-speaking subjects in a language they understand. It should not use first-person language (e.g., I understand that this research involves testing. . .). This phrasing may be too coercive and place too much responsibility or burden on the subject. Instead, it could say, "You are being asked to participate in a research study that involves testing. . . ."

Elements of Informed Consent

The informed consent document must provide *all* the required elements of informed consent in complete terms. The reviewers of these forms must ensure that the investigator states:

- That the study involves human subjects research.
- The purpose of the research.
- The length of subject participation.
- The experimental procedures to be followed.
- Any procedures that are experimental (e.g., a new drug or extra tests).
- Any foreseeable risks or discomforts and any benefits to the subject or others.
- Alternative procedures or treatments, if any.
- The extent of confidentiality to be maintained.
- Compensation, if any.
- Procedures to be followed if an injury or accident occurs.
- Names of contacts who can answer questions about the research, explain the human subject's rights, and help out in an emergency.
- That participation is voluntary and that refusal to participate will in no way involve penalty or loss of benefits to which the person is otherwise entitled.
- That participation may be discontinued at any time without penalty or loss of benefits.

Each research activity must be customized to meet the specific needs of its participants. If a particular study involves risks currently unforeseeable (for example, risks to an embryo if a subject becomes pregnant), then the informed consent form must say so. If additional risks are identified during the research, the informed consent form must be revised, and human subjects must be so informed.

Sources

The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects Research. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. April 18, 1979. An OPRR Report. National Institutes of Health. Office for the Protection from Research Risks.

Robert A. Greenwald, et al. *Human Subjects Research: A Handbook for Institutional Review Boards.* New York: Plenum Press (1982).

Protecting Human Subjects at the Department of Energy. Fall 1992.

DOE-Wide Training Workshop on Protecting Human Subjects To Take Place in Winter 1993

A workshop on the issues and challenges associated with implementing a program for the protection of human subjects in research is scheduled for February 1993 in Washington, DC. This third DOE-wide human subjects workshop is designed for DOE personnel from Headquarters, field offices, and laboratories. Because this is the first workshop since the Common Rule has been published, 10 CFR Part 745, the Federal Policy for the Protection of Human Subjects, will be the focus of discussion. The workshop will highlight and explain the principles underlying protection of human subjects and offer a historical perspective on how the regulation evolved.

Specific agenda items include:

- A keynote speaker well versed in current bioethics issues.
- Procedures required by DOE for implementing human subjects research.
- Special types of research (research involving children, research with security implications, and research involving foreign countries).
- A mock institutional review board review session involving attendees and facilitators.
- Discussion by attendees of unique concerns or issues requiring further attention.
- Challenges for the future.

More details on this 1 1/2-day workshop will be available soon. To receive more information or to offer suggestions, contact

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Update: Ethical, Legal, and Social Issues Regarding the Human Genome Program

At the Human Subjects Research Subcommittee meeting held in early April at the National Institutes of Health (NIH), Dr. Dan Drell of the Office of Health and Environmental Research (OHER) presented information about ethical, legal, and social issues (ELSI) related to the Human Genome Program at DOE. Dr. Drell is the DOE liaison to the DOE/NIH Joint ELSI Working Group that meets to discuss ethical, legal, and social issues related to the mapping and sequencing of the human genome. Findings of the Human Genome Program raise interesting and complex ethical, legal, and social questions that complicate research involving human subjects. The Human Genome Program is providing biomedical researchers with new, powerful tools to identify defective genes that cause diseases and to develop better treatments for the health problems they cause. Results of this research make previously unavailable human data accessible to researchers and others, thus raising issues of confidentiality and privacy, employment, and related fields.

In his talk, Dr. Drell noted that the Human Genome Program funded applications in a variety of ELSI activities for the program's first 2 years, but it is now focusing more on human genome research data and implications for individual privacy and confidentiality. Knowledge of genetic information can affect an individual's relations with family members, employers, insurers, and others. Unlike some forms of medical information, genetic information can have predictive power long before cures or effective therapies become available. Genetic tests raise questions because they can predict future disease in apparently healthy individuals. The controversy surrounding genetic testing increases as computers gain more ability to assemble, store, and organize data (including genetic data) into large databases—capabilities that make issues of security and access control more acute.

In his presentation, Dr. Drell discussed several studies in the area of genetic testing. One study explores legal issues associated with protecting the confidentiality of genetic data. Another investigates genetic discrimination by comparing local genetic testing, screening, and counseling programs and their impact on two different ethnic and socioeconomic communities. Yet another project looks at the implications of genetic knowledge in relation to the right of privacy and the uses of genetic information in public health planning.

To help direct ELSI activities toward privacy and confidentiality of genetic data, the DOE/NIH Joint ELSI Working Group has recently established a Task Force on Privacy.

Dr. Dan Drell contributed information for this article.

For more information on ELSI, contact

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Human Subjects Resource Handbook Set for Publication

To facilitate Department-wide education on the Common Rule and the related human subjects research policies and implementation issues, OHER has developed a comprehensive resource handbook titled *Protecting Human Subjects at the Department of Energy*. It will be available soon at DOE program to protect human subjects. It will be distributed to Headquarters and field office personnel, laboratory officials, principal investigators, and contracting officers. Material to help readers interpret and comply with the DOE project approval process is included, and roles and responsibilities are defined. Directions for preparing annual institutional review board approvals are included, as is guidance on classified research and international research, answers to frequently asked questions, tips on informed consent, checklists for performing IRB review board self-evaluations, and a glossary of terms. Arranged in a three-ring binder format, the handbook is designed to be revised and updated as policies change and new problems or issues arise.

Protecting Human Subjects at the Department of Energy will be available from

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Newsletter Information

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

DOE Human Research Subjects Program

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This bulletin is available at no cost to individuals interested or involved in human subjects research at DOE. Please send name and complete address (printed or typed) to the address below. Please indicate whether information is to—

1. add new subscriber,
2. change name/address, or
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