Human Subjects Research at the Environmental Protection Agency:
Ethical Standards and Regulatory Requirements

Enter Course

This course was developed by the Program in Human Research Ethics at the U. S. Environmental Protection Agency (EPA). It provides training for investigators and others involved in human research supported by EPA and is free of charge.

The course is divided into an introduction and a series of modules, each of which can be taken separately. Module 1 covers the basic federal policy for the protection of human research subjects, also known as the Common Rule. This module was adapted from the course "Protecting Human Research Participants" developed by the Office of Extramural Research at the National Institutes of Health, and permission to use their materials is gratefully acknowledged.

Modules 2 and 3 were developed by the EPA Program in Human Research Ethics specifically for this course. Module 2 covers prohibitions and special protections for vulnerable subjects that are specific to EPA's regulations, and Module 3 covers community engagement.

A fourth module on distinguishing public health practice from public health research in an environmental context is currently under development.

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Human Subjects Research at the Environmental Protection Agency: Ethical Standards and Regulatory Requirements

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Introduction

Human Subjects Research at EPA

Research with human subjects entails an intrinsic conflict for investigators. The goal of research is to make contributions to generalized knowledge, for example improving the understanding of a disease process or determining the efficacy of an intervention. The pursuit of this goal may involve activities with the potential to compromise the interests of individual participants in the research.

Ethical analysis is required to resolve this conflict when it occurs. The regulations, policies, and guidance governing human research are derived from such analyses.

Introduction (continued)

Who?

This course is intended primarily for use by investigators involved in the design or conduct of U.S. Environmental Protection Agency (EPA)-supported human subjects research. It may also be of interest to individuals involved in the oversight of EPA-supported human research, including project officers, IRB members or staff, and others.

What?

This course is designed to facilitate understanding of the ethical obligations and regulatory requirements necessary to protect the rights and welfare of subjects in research. The course material presents basic concepts, principles, and issues related to the protection of research participants.

Why?

As part of EPA's commitment to the protection of human subjects, the Program in Human Research Ethics has designed this course to teach the fundamentals of EPA's ethical and regulatory requirements.

Introduction (continued)

This course assumes that the investigators' research will be funded by EPA and is therefore subject to all EPA regulatory and policy requirements.

The information presented is neither prescriptive nor exhaustive and does not replace or supersede local, state, or Federal regulations applicable to human research or any institutional policies regarding the protection of human subjects.

Introduction (continued)

Course Objectives

Upon completion of this course, you should be able to:

- Describe the history and importance of human subjects protections
- Identify research activities that involve human subjects
- Understand the risks posed by a research project and how to minimize them
- Describe appropriate procedures for recruiting research participants and obtaining informed consent
- Describe additional protections needed for vulnerable populations
- Understand the importance of study design in the protection of research participants
- Understand the importance of community engagement in research projects

Introduction (continued)

Course Organization

This course consists of three modules:

- The Common Rule and its Protections for Human Research Subjects
- Subparts B, C, and D: Protecting Vulnerable Populations
- Community Engagement

Each module can be understood individually, however the course is designed so that each module builds on the previous ones.

Module 1: Section 1: History

Objectives

Before discussing the current system for the protection of human subjects in research, it is important to review two significant historical events that have influenced current ethical guidelines and EPA regulations.

These events are:

- Nazi medical atrocities committed during World War II
- The Syphilis study at Tuskegee

The objectives of this section are:

- To understand the goals and principles of human subjects protection
- To understand how various historical events led to the creation of today's regulations

Module 1: Section 1: History

Goals and Principles of Human Subjects Protection

Human subjects are essential to the conduct of research intended to improve human health. The relationship between investigators and human subjects is critical and should be based on honesty, trust, and respect.

Module 1: Section 1: History

Nazi Medical War Atrocities (1939–1945)

Although not the first example of harmful research on unwilling human subjects, the experiments conducted by Nazi physicians during World War II were unprecedented in their scope and the degree of harm and suffering to which human beings were subjected.

"Medical experiments" were performed on thousands of concentration camp prisoners and included deadly studies and tortures such as injecting people with gasoline and live viruses, immersing people in ice water, and forcing people to ingest poisons.

In December 1946, the War Crimes Tribunal at Nuremberg indicted 20 physicians and 3 administrators for their willing participation in the systematic torture, mutilation, and killing of prisoners in experiments. The Nuremberg Military Tribunals found that the defendants had:

- Corrupted the ethics of the medical and scientific professions
- Repeatedly and deliberately violated the rights of the subjects

The actions of these defendants were condemned as crimes against humanity. Sixteen of the twenty three physicians/administrators were found guilty and imprisoned, and seven were sentenced to death.

Module 1: Section 1: History

The Nuremburg Code

In the August 1947 verdict, the judges included a section called "Permissible Medical Experiments." This section became known as the Nuremberg Code and was the first international code of research ethics.

This set of directives established the basic principles that must be observed in order to satisfy moral, ethical, and legal concepts in the conduct of human subjects research. The Code has been the model for many professional and governmental codes since the 1950s and has, in effect, served as the first international standard for the conduct of research.

The Code provides ten Directives for Human Experimentation:

1. Voluntary consent of the human subject is absolutely essential.

2. The experiment must yield generalizable knowledge that could not be obtained in any other way and is not random and unnecessary in nature.

3. Animal experimentation should precede human experimentation.

4. All unnecessary physical and mental suffering and injury should be avoided.

5. No experiment should be conducted if there is reason to believe that death or disabling injury will occur.

6. The degree of risk to subjects should never exceed the humanitarian importance of the problem.

Module 1: Section 1: History

7. Risks to the subjects should be minimized through proper preparations.

8. Experiments should only be conducted by scientifically qualified investigators.

9. Subjects should always be at liberty to withdraw from experiments.

10. Investigators must be ready to end the experiment at any stage if there is reason to believe that continuing the experiment is likely to result in injury, disability, or death to the subject.

Module 1: Section 1: History

The Syphilis Study at Tuskegee

Arguably the most notorious example in the United States of the violation of the rights and welfare of human subjects was the long-term study of black males conducted by the United States Public Health Service in Tuskegee, Alabama. This study of the natural history of untreated syphilis was initiated in the 1930s and continued until 1972.

The Syphilis Study at Tuskegee involved approximately 600 African-American men: about 400 with syphilis (cases) and about 200 without syphilis (controls). These men were recruited without informed consent and, in fact, were led to believe that some of the procedures done in the interest of research (e.g., spinal taps) were actually "special free treatment."

By 1936, it was apparent that many more infected men than controls had developed complications, and by the mid-1940s, the data showed that the death rate among those with syphilis was about twice as high as it was among the controls. By 1944 penicillin was in widespread use as an effective treatment for syphilis, but the participants were neither offered the treatment nor informed of its effectiveness.

Module 1: Section 1: History

Outcomes of the Syphilis Study at Tuskegee

The first accounts of this study appeared in the national press in 1972. The resulting public outrage led to the appointment of an ad hoc advisory panel by the Department of Health, Education and Welfare (which later was split into the Department of Education and the Department of Health and Human Services [HHS]) to review the study and develop recommendations to ensure that such experiments would never be conducted again.

Outcomes included:

1. National Research Act of 1974

2. HEW Policy for Protection of Human Subjects

3. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Module 1: Section 2: Codes and Regulations

Objectives

The Objectives For This Section Are:

- To identify the three principles of ethical human subjects research identified in the Belmont Report
- To understand the current EPA regulations, including:
  - Risks associated with participation in research and appropriate protections against risks
  - Vulnerable populations that need specific protections
  - Situations in which research involving humans is exempt from regulatory requirements

Module 1: Section 2: Codes and Regulations

The Belmont Report

Following the public outrage over the Syphilis Study at Tuskegee, Congress established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1974. The National Commission was charged with:

1. Identifying the ethical principles to guide all research involving human subjects

2. Developing guidelines for the conduct of ethical research involving human subjects

In 1979, the National Commission published The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research. The report was a product of many meetings held over four years, with a very productive one occurring at the Smithsonian Institution's Belmont Conference Center in 1976.

The Belmont Report identified three principles essential to the ethical conduct of research with humans:

1. Respect for persons
2. Beneficence
3. Justice

These three principles serve as the foundation of the current basic federal regulations and guidelines for the ethical conduct of human subjects research. EPA adopted the basic regulations in 1991, along with over a dozen other federal agencies. In 2006, EPA added additional regulations that incorporate special protections for vulnerable populations. These special protections will be discussed in greater detail in the "Subparts B,C, and D: Protecting Vulnerable Populations" module.

Module 1: Section 2: Codes and Regulations

Respect for Persons

"To respect autonomy is to give weight to the autonomous person's considered opinions and choices while refraining from obstructing his or her actions..." – The Belmont Report

The principle of respect for persons incorporates two basic ideas:

1. Individuals should be treated as autonomous agents

An autonomous person is able to:

- Consider the potential harms and benefits of a situation
- Analyze how those risks and potential benefits relate to his or her personal goals and values
- Take action based on that analysis

Prospective research participants must be given the information they need to determine whether or not they want to participate in research. There should be no pressure to participate and ample time to decide. Respect for persons demands that participants enter into the research voluntarily and with adequate information. This is called informed consent, and will be covered in detail in other sections of this training.

2. Persons with diminished autonomy are entitled to additional protections

According to the Belmont Report, "special provisions may need to be made when an individual's comprehension is severely limited or when a class of research participants is

Module 1: Section 2: Codes and Regulations

considered incapable of informed decision making (e.g., children, people with severe developmental disorders, or individuals suffering from dementias). Even for these groups, however, respect for persons requires giving them the opportunity to choose, to the extent they are able, whether or not they wish to participate in research activities. In some cases, respect for persons may require seeking the permission of other parties, such as a parent or legal guardian."

The challenges in applying the Belmont principle of respect for persons include:

- Making sure that potential participants comprehend the risks and potential benefits of participating in research
- Avoiding influence of potential participants' decisions either through explicit or implied threats (coercion) or through excessive compensation (undue influence)

Module 1: Section 2: Codes and Regulations

Beneficence

"Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term beneficence is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation." – The Belmont Report

Two general rules have been articulated as complementary expressions of beneficent actions:

1. Do no harm
2. Maximize possible benefits and minimize possible harms

The challenge inherent in applying the Belmont principle of beneficence is how to determine when potential benefits outweigh considerations of risks and vice versa.

Module 1: Section 2: Codes and Regulations

EPA Regulations – Protection of Human Subjects

The ethical principles for research involving human subjects described in the Belmont Report are codified by EPA in the Code of Federal Regulations at 40 CFR 26. These regulations include The Common Rule at Subpart A. The Common Rule has been adopted by over a dozen government agencies including HHS and EPA. Both EPA and HHS have incorporated protections for vulnerable subjects beyond those in the Common Rule into Subparts B-D of their rules, although the specific protections in those subparts differ between the two agencies.

Subpart A – basic federal policy for protection of human research subjects, also referred to as The Common Rule

Subpart B – prohibition of intentional exposure research on pregnant women, their fetuses, nursing women, and children

Subpart C – special protections for pregnant women and fetuses involved in observational research

Subpart D – special protections for children involved in observational research

More detail on the EPA regulations governing the vulnerable populations in Subparts B-D can be found in the "Subparts B, C, and D: Protecting Vulnerable Populations" module.

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Subpart A – Basic Federal Policy for Protection of Human Research Subjects

Subpart A, also called The Common Rule, describes the required protections for all human subjects.

Subpart A defines a human subject as "a living individual about whom an investigator... conducting research obtains:

1. Data through intervention or interaction with the individual, or
2. Identifiable private information"

Subpart A defines research as "a systematic investigation...designed to develop or contribute to generalizable knowledge."

This definition includes:

- Research development
- Testing
- Evaluation

Module 1: Section 2: Codes and Regulations

Exemptions

The federal regulations describe categories of human subjects research that may be exempt from requirements described in the regulations including Institutional Review Board (IRB) oversight. Studies proposing only research that falls under one or more of the exempt categories of research do not require IRB review and approval. The HHS Office for Human Research Protections (OHRP) has issued guidance that institutions should have a clear policy in place on who shall determine what research is exempt under 26.101(b). This authority generally rests with the institution's IRB or Human Research Protection Program (HRPP) Office. Investigators themselves should never determine whether or not their own human research is exempt.

The exemptions can be found at 40 CFR 26.101(b) (PDF) (35pp, 480K).

Module 1: Section 2: Codes and Regulations

Requirements for Federal Support of Human Subjects Research

The federal regulations require that federal departments and agencies that conduct or support human subjects research must evaluate all applications for research using the following criteria:

- Risks to the subjects
- Adequacy of protection against these risks
- Potential benefits of the research to the subjects and others
- Importance of the knowledge to be gained

Module 1: Section 2: Codes and Regulations

Summary

This module examined:

- The three basic ethical principles described in the Belmont Report
- The subsequent codification of these principles in 40 CFR 26 of the Code of Federal Regulations

The Belmont Report summarizes the three basic ethical principles of clinical research as:

1. Respect for persons
   - Individuals should be treated as autonomous agents
   - Persons with diminished autonomy are entitled to additional protections
2. Beneficence
   - Do no harm
   - Maximize possible benefits and minimize possible harms
3. Justice
   - Requires that individuals and groups be treated fairly and equitably in terms of bearing the burdens and receiving the benefits of research

Module 1: Section 3: Respect for Persons

Objectives

What This Section Covers:

- The informed consent process
- Requirements for documentation of informed consent
- Waivers of informed consent
- Diminished autonomy and legally authorized representatives
- Assent from children and permission from parents
- Community consent

The Objectives For This Section Are:

- To outline the requirements for informed consent
- To state when waivers of informed consent and legally authorized representatives are appropriate

Module 1: Section 3: Respect for Persons

Respect for Persons

"To respect autonomy is to give weight to the autonomous person's considered opinions and choices while refraining from obstructing his or her actions..." – The Belmont Report

The principle of respect for persons can be broken down into two basic ideas:

1. Individuals should be treated as autonomous agents
2. Persons with diminished autonomy are entitled to additional protections

Module 1: Section 3: Respect for Persons

Informed Consent

The Belmont principle of respect for persons is primarily applied by requiring that all human subjects research participants provide valid voluntary informed consent to participate in research.

The three fundamental aspects of a valid informed consent are:

Disclosure

EPA regulations (40 CFR 26.116(a) (PDF) (35pp, 480K)) require that researchers disclose:

1. The purpose of the study
2. Any reasonably foreseeable risks to the individual
3. Potential benefits to the individual or others
4. Alternatives to the research protocol
5. The extent of confidentiality protections for the individual
6. For research more than minimal risk, compensation in case of injury due to the research
7. Contact information for questions regarding the study, participants' rights, and in case of injury
8. The conditions of participation, including right to refuse or withdraw without penalty

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This disclosure must be made in such a way that it provides a reasonable person the information she or he would need in order to make an informed decision.

Comprehension

Individuals must have the mental or decisional capacity to understand the information presented to them in order to make an informed decision about participation in research.

Voluntariness

Individuals' decisions about participation in research should not be influenced by anyone involved in conducting the research: "...consent must be freely given or truly voluntary."[1]

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Informed Consent

Subpart A regulations (40 CFR 26.116 (PDF) (35pp, 480K)) require that investigators obtain legally effective informed consent from prospective participants in a way that allows them to consider whether or not to participate and that minimizes the possibility for coercion or undue influence.

Potential participants must understand that enrolling in the research is voluntary and that they may withdraw from the study at any time without penalty or loss of benefits (40 CFR 26.116(a) (PDF) (35pp, 480K)).

In order for participation in research to be voluntary, the potential for coercion and undue influence must be minimized.

Module 1: Section 3: Respect for Persons

Informed Consent

Informed consent should be understood as an on-going process rather than a level of legal protection for an institution. It is not intended to be a one-time act of having a participant sign a form.

Informed consent is designed to inform research subjects about the purpose, risks, potential benefits, and alternatives to the research, thus allowing people to make a decision about whether or not to participate based on their own goals and values. This exchange of such information should occur at enrollment and throughout the study.

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Informed Consent

Investigators are responsible for providing information during the informed consent process in a manner that is understandable to the potential participants. Investigators should not enroll anyone in a study unless the investigator is confident that the individual comprehends all information disclosed and agrees freely to procedures described during the informed consent process.

Investigators can use methods in addition to a consent form to enhance individuals' comprehension. Some examples include:

- Oral presentations that provide potential participants with the opportunity to discuss the information and ask questions
- Additional educational materials, such as brochures, about research in general and/or the specific procedures that will be used in the study
- Video presentations that familiarize potential participants with the procedures that will be used in the study

The informed consent process must be delivered in "...language that is understandable to the subject..." (40 CFR 26.116 (PDF) (35pp, 480K)). This may mean adjusting the reading levels of documents provided or translating documents and presentations into the language with which participants are most comfortable.

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Waivers of Informed Consent

Regulations (40 CFR 26.116(d) (PDF) (35pp, 480K)) allow IRBs to waive or alter some or all of the required elements of informed consent if all of the following conditions are met:

1. The research involves no more than minimal risk to the subjects
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects
3. The research could not practicably be carried out without the waiver or alteration
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation

Module 1: Section 3: Respect for Persons

Waivers of Informed Consent

Regulations (40 CFR 26.116(c) (PDF) (35pp, 480K)) also allow IRBs to waive or alter some or all of the required elements of informed consent if all of the following conditions are met:

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; (iv) possible changes in methods or levels of payments for benefits or services under those programs, and

2. The research could not practicably be carried out without the waiver or alteration.

Module 1: Section 3: Respect for Persons

Practicability and Waivers of Informed Consent

Decisions about waivers of informed consent often concern the issue of practicability. Although practicability is not defined in the federal regulations, it is not sufficient for an investigator to argue simply that seeking consent would be time-consuming or incur additional cost.

In some situations, a waiver of informed consent may be appropriate for a medical record review or for using existing data or specimens that can be linked to identifiable individuals. Specific decisions regarding practicability are made by the IRB.

Module 1: Section 3: Respect for Persons

Case Study: New Analyses of Existing Data

An investigator has collected identifiable data from participants in a research study. She has completed the analyses that were originally proposed and described in the EPA grant application, the protocol approved by the IRB, and the informed consent document approved by the IRB. The informed consent document made no mention of using the data in additional research but gives permission for the investigator to re-contact the participants.

Now, based on new hypotheses, the investigator has obtained another EPA grant to conduct new analyses to fulfill purposes different from those described in the original informed consent document. She knows that she needs to obtain approval for the new research from her IRB and the EPA Human Subjects Research Review Official (HSRRO).

Does the investigator need to obtain new informed consent from the participants?

The investigator needs to obtain informed consent unless:

- The criteria for a waiver are met, and
- The IRB has approved a waiver of informed consent.

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Requirements for Documentation of Informed Consent

In addition to obtaining informed consent, the federal regulations require that informed consent be documented. This may be done by either a written form that contains all of the required elements (40 CFR 26.116(a) (PDF) (35pp, 480K)) or a short form that states that all of the required elements have been presented orally. This form must be signed by either the participant or the participant's legally authorized representative (40 CFR 26.117 (PDF) (35pp, 480K)).

The federal regulations (40 CFR 26.117(c) (PDF) (35pp, 480K)) allow IRBs to waive the requirement for documenting informed consent but not for obtaining the informed consent itself, if they find that either:

1. The only record linking the participant to the research would be the informed consent document and the principal risk to the participants would be the potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern, or

2. The research presents no more than minimal risk to the participants and involves no procedures for which written consent is normally required outside of the research context.

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Diminished Autonomy

An individual's autonomy can be affected by several factors including age, cognitive impairment, illness, and treatments. An individual's capacity to consent to a particular study should be assessed based on:

1. The individual's level of capacity, and

2. The complexity and risks of the study, i.e., the capacity needed for an individual to be able to understand the study well enough to consent to participate

Module 1: Section 3: Respect for Persons

Decisional Capacity and Legally Authorized Representatives

The Belmont principle of respect for persons states that investigators need to make special provisions when including individuals in research who have diminished capacity for making decisions in their own best interests.

The regulations, therefore, require that legally authorized representatives provide voluntary informed consent for individuals participating in research who have diminished capacity (40 CFR 26.116 (PDF) (35pp, 480K)).

While the regulations allow for legally authorized representatives to make substituted decisions for individuals who need assistance, investigators should obtain consent from the participants to the extent possible. Because some individuals may be only temporarily or intermittently incapacitated (e.g., due to injury or medications), investigators should attempt to approach these individuals at a time when they do have the capacity to consent to research. If a participant regains the capacity to consent to research after the research has begun, investigators should obtain the participant's informed consent before continuing his or her participation in the study.

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Children's Participation in Research

Children are unable to provide "legally effective informed consent" as required by the federal regulations at 40 CFR 26.116 (PDF) (35pp, 480K).

Because children cannot provide informed consent, children provide assent to participate in research, to the extent that they are able, and parents/guardians give permission for a child to participate in research.

The additional regulatory requirements of assent and permission for research involving children (40 CFR 26.408 (PDF) (35pp, 480K)) are intended to make sure that investigators respect the decisions of both children and their parents. Parental permission must be obtained for research involving children "in accordance with and to the extent that consent is required by 40 CFR 26.116 (PDF) (35pp, 480K)."

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Community Consultation

In some cultures it is not appropriate to obtain informed consent solely from the individual participants, because the individual's interests may be considered to be intimately entwined with their community's interests, or, conversely, diverge from them. The appropriate way to attain community consent may vary widely, but is often achieved through meetings with large groups of community representatives or community leaders.

It is also appropriate to consult a community before conducting research when the research involves risk to discrete, identifiable populations. For example, members of a community may feel stigmatized if members of that community participate in research that may reveal unpopular or dangerous traits.

More information on community consultation can be found in the "Community Engagement" module.

Module 1: Section 3: Respect for Persons

Summary

During the informed consent process, the principle of respect for persons is applied by requiring that all human subjects provide voluntary informed consent to participate in the research.

Practical application of this principle means that potential study participants must:

- Be provided complete information about the study in order to make an informed decision
- Have the decisional capacity to understand the information presented to them
- Give their consent freely and voluntarily

This module has examined:

- Information that should be included during the informed consent process
- The types of situations that can be considered for waiver of informed consent
- The appropriate involvement of legally authorized representatives for consent
- Vulnerable subjects
- The need to undertake community consultation when appropriate

Module 1: Section 4: Beneficence

Objectives

What This Section Covers:

- Risks and benefits
- Privacy and confidentiality
- Institutional Review Boards
- Data and safety monitoring

The Objectives For This Module Are:

- To understand what aspects of research may constitute a benefit to research participants
- To identify possible risks to be considered in evaluating research
- To discuss methods to protect privacy of individuals and confidentiality of data
- To define the role of an IRB to ensure the rights and welfare of human subjects

Module 1: Section 4: Beneficence

Beneficence

"Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term beneficence is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation." – The Belmont Report

Two general rules have been articulated as complementary expressions of beneficent actions:

1. Maximize possible benefits and minimize possible harms
2. Do not harm intentionally

Investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation.

Module 1: Section 4: Beneficence

Risk

Risk is the likelihood that a harm of a specified magnitude will occur.

All research involves some level of risk. We often think of risks in terms of direct harms that may occur as a result of participation in research protocols, but harms may also result from aspects of participation other than from research procedures. For example, harms may result from simply agreeing to be a participant in research, or they may result from disclosure of findings from a research study.

Most risks encountered by participants in research fall into the following categories:[2]

A. **Physical** – Physical risks may include pain, injury, and impairment of a sense such as touch or sight. These risks may be brief or extended, temporary or permanent, occur during participation in the research or arise after.

B. **Psychological** – Psychological risks can include anxiety, sadness, regret and emotional distress, among others. Psychological risks exist in many different types of research in addition to behavioral studies.

C. **Social** – Social risks exist whenever there is the possibility that participating in research or the revelation of data collected by investigators in the course of the research, if disclosed to individuals or entities outside of the research, could negatively impact others' perceptions of the participant. Social risks can range from jeopardizing the individual's reputation and social standing, to placing the individual at-risk of political or social reprisals.

D. **Legal** – Legal risks include the exposure of activities of a research subject "that could reasonably place the subjects at risk of criminal or civil liability."[3]

E. **Economic** – Economic risks may exist if knowledge of one's participation in

Module 1: Section 4: Beneficence

research, for example, could make it difficult for a research participant to retain a job or to find a job, or if insurance premiums increase or loss of insurance is a result of the disclosure of research data.

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Minimizing Risks

Since research involves risks, investigators, IRBs, and other members of the research team must take responsibility for protecting participants against the risks of participating in research. Protections vary according to the kind of risk:

A. **Physical** – In many situations, physical risks in research can be minimized by carefully and skillfully following protocols, by having trained individuals conduct research procedures, through careful monitoring of research participants' health status, by recruiting appropriate populations, and by providing clinical care when needed.

B. **Psychological** – Possible ways to protect against psychological risks include reminding participants of their right to withdraw from research or limit their participation if they become uncomfortable, providing counseling or psychological support for participants who experience distress, or thoroughly debriefing research participants after research sessions are completed.

C. **Social** – Often, minimizing social risks to participants involves protecting confidential data, including not only the data collected, but the fact of participation in the research project itself.

D. **Legal** – Protections against legal risks often involve protecting the confidentiality of research data. For studies conducted in the United States, investigators can apply for Certificates of Confidentiality, which are intended to prevent investigators from being forced to disclose data that can be linked to identifiable research participants in legal proceedings.

E. **Economic** – Protecting confidentiality of data is one method for protecting against economic risks, such as those to employability and insurability. Investigators may elect to keep research data separate from medical records in order to prevent employers and insurance companies from obtaining information that could put the participants at risk.

Module 1: Section 4: Beneficence

Designing Research: Anticipated Benefits Greater than Potential Harms

In general, the goal of research is to benefit society by contributing to generalizable knowledge about diseases, disorders, public health concerns, etc. Participation in research may:

- Benefit individual participants or communities
- Neither benefit nor harm individual participants or communities
- Pose risks to individual participants

The federal regulations apply specifically to individual participants in research and require that:

- Risks are minimized
- Unavoidable risks are justified as necessary for sound scientific design
- Research studies are anticipated to make progress toward important, generalizable knowledge

Module 1: Section 4: Beneficence

Assessing Risks and Potential Benefits

Assessing risks and potential benefits is inexact, but investigators need to be able to explain to the funding agency, the IRB, and the potential research participants how and why the potential benefits of research outweigh the risks of participating in a particular study.

In applying the principle of beneficence, investigators should consider a number of factors including:

- Protecting the privacy of research participants and the confidentiality of research data
- Establishing oversight mechanisms to protect the rights and welfare of research participants and to determine the significance of the data

Module 1: Section 4: Beneficence

Regulatory Requirement for Explaining Benefits and Risks

After minimizing risks to the extent possible, the federal regulation requires that investigators consider:

1. Protections against risks: Where appropriate, investigators must describe procedures for minimizing potential risks, including risks to confidentiality, plans for ensuring any necessary medical or professional intervention, etc.

2. Potential benefits to individual participants: The proposed research has a favorable ratio of potential benefit to risk. This balancing act is often called a risk-benefit analysis.

3. Importance of the knowledge to be gained: Investigators reasonably anticipate that the research will contribute to generalizable knowledge. This generalizable knowledge is considered a benefit to others, and risks to research participants must be reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

Module 1: Section 4: Beneficence

Minimal Risk

The Common Rule defines situations as minimal risk when "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 life or during the performance of routine physical or psychological examinations or tests." (40 CFR 26.102(i) (PDF) (35pp, 480K))

Minimal risk is a regulatory concept used by IRBs to make decisions about which regulatory requirements apply in certain situations. It is not the same as risk minimization and the two should not be confused. A study that qualifies as "minimal risk" must have those risks minimized nonetheless. Conversely, a study that minimizes all risks still may not be categorized as "minimal risk."

Module 1: Section 4: Beneficence

Compensation for Research Participation

Some types of research involve a significant commitment from research participants in terms of time or effort, and investigators may wish to provide compensation.

Institutions should consider establishing standards for fair and appropriate compensation.

During the informed consent process, investigators should explain to potential research participants:

1. If there will be compensation for their participation in the research
2. Appropriate expectations for receiving full, partial, or no compensation if research participants complete the study or withdraw prior to its completion
3. That compensation is meant to reimburse research participants for their time, research-related inconveniences and/or research-related discomforts

Compensation should not be considered a benefit of the research when doing a risk-benefit analysis.

Module 1: Section 4: Beneficence

Avoiding Undue Inducement

While the use of inducements to participate in research is considered appropriate under many circumstances, sometimes inducements can be unduly influential and inappropriate. These are referred to as "undue inducements." As discussed in the Respect for Persons section, the level and kind of compensation must take into consideration the vulnerabilities of the research population to minimize the possibility of undue inducement.

"Undue inducements are troublesome because:

1. offers that are too attractive may blind prospective subjects to the risks or impair their ability to exercise proper judgment; and
2. they may prompt subjects to lie or conceal information that, if known, would disqualify them from enrolling – or continuing – as participants in a research project."[4]

Careful consideration of compensation is not only critical for beneficence, but may be critical for sound research. Considerations should include, but are not limited to, issues like participants' "medical, employment, and educational status, and their financial, emotional, and community resources."[4]

Module 1: Section 4: Beneficence

Avoiding the Therapeutic Misconception

Some research studies include examinations, diagnostic tests, and/or interactions with healthcare providers in addition to experimental interventions. These aspects of a research protocol may benefit participants by helping them to better understand a disease or condition, and may help in the participants' medical decision-making. While it is often appropriate to include treatment procedures in the conduct of research studies, there is a risk that research participants may misunderstand the benefits of research if they think that potential benefits of participation in research are certain. This is called the therapeutic misconception.

Therapeutic misconception is the tendency for research participants to "...downplay or ignore the risks posed to their own well-being by participation … [due to] the participants' deeply held and nearly unshakeable conviction that every aspect of their participation in research has been designed for their own individual benefit."[5]

Investigators should not harbor the therapeutic misconception themselves and should discuss the risks and benefits of research as part of the informed consent process in order to minimize the possibility of therapeutic misconception in potential subjects.

Module 1: Section 4: Beneficence

Privacy and Confidentiality

Investigators are responsible for

- Protecting privacy of individuals
- Confidentiality of data

Privacy means freedom from unwanted intrusion.

Confidentiality means maintaining the secrecy of an individual's private information unless the individual permits disclosure.

Module 1: Section 4: Beneficence

Case Study: Confidentiality in Research

After the conclusion of a study in a small rural community, an investigator is anxious to publish findings. Understanding the policies encouraging the reporting of demographic differences in intervention effect, and concerned about protecting the confidentiality of research participants, the investigator publishes only general demographic data such as sex, age, state, and county.

Is this an appropriate and acceptable way to protect the confidentiality of research participants?

Publishing demographic information is not acceptable in situations where the population is small or the disease/condition is rare because it is possible for research participants to be identified using only general demographic data. For example, these protections were not sufficient after a hantavirus outbreak on an Indian Reservation in the United States. The information published made the identity of one of the individuals who died obvious to the local tribal leaders. In this case the published report not only compromised the identity of the research participant, it also violated the cultural taboo about not speaking of the recently deceased.

Module 1: Section 4: Beneficence

Confidentiality

The need for maintaining confidentiality of private information exists in virtually all studies in which data are collected from or about living individuals. In most research, maintaining confidentiality is a matter of following some established practices, for example:

- Properly disposing of data sheets and other paper records
- Limiting access to identified data; and/or
- Storing research records in locked cabinets or secured databases

It may also be appropriate for investigators to remove direct identifiers from human specimens and data so that they may be analyzed without risk of accidental disclosure of private information. De-identifying data can be done in several ways, including coding and anonymizing.

Module 1: Section 4: Beneficence

Coded Private Information and Human Subjects Research

Human subjects research with coded private information or specimens is subject to risk of breach of confidentiality when:

- the investigator(s) can readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain, or
- the information can be associated with the identity of the individual(s) to whom the coded private information or specimens pertain.

Module 1: Section 4: Beneficence

Institutional Review Boards

Institutional Review Boards (IRBs) are specialized committees required by EPA regulations that safeguard the rights and welfare of human subjects. IRBs determine "the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice" (40 CFR 26.107 (PDF) (35pp, 480K)).

The major roles of IRBs in the oversight of research are:

1. To review and approve or disapprove of the proposed research activity

2. To ensure that the proposed informed consent process meets all of the requirements of 40 CFR 26.116 (PDF) (35pp, 480K)

3. To provide continuing oversight for progress reports and protocols for ongoing research studies

Module 1: Section 4: Beneficence

IRB Membership

The EPA regulations (40 CFR 26.107 (PDF) (35pp, 480K)) require that IRBs have at least 5 members from a variety of backgrounds. The experience, expertise, and diversity of the IRB members should allow the IRB to provide a complete and adequate review of the research activities conducted at the institution.

Research may involve issues about which IRB members lack specific expertise. In these situations, IRBs should identify and invite individuals with specialized knowledge to assist in the review of applications and protocols where the expertise is required.

Module 1: Section 4: Beneficence

Working with the IRB

In order to approve research, IRBs have a responsibility to ensure that research participant protections are adequate.

EPA regulations provide the following criteria for IRB approval of research at 40 CFR 26.111 (PDF) (35pp, 480K):

- Risks to human subjects are minimized
- Risks to human subjects are reasonable in relation to anticipated benefits, if any, to human subjects and the importance of the knowledge that may reasonably be expected to result from the research
- Selection of human subjects is equitable
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §26.116
- Informed consent will be appropriately documented, in accordance with, and to the extent required by §26.117
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects
- When appropriate there are adequate provisions to protect the privacy of human subjects and to maintain the confidentiality of data

Module 1: Section 4: Beneficence

Expedited IRB Review

Protocols may be reviewed either at a meeting of the full IRB or by "expedited review."

For "certain types of research involving no more than minimal risk and for minor changes to existing research," an IRB may choose to use an expedited review procedure. The expedited review may be conducted by the IRB chair or by designated experienced IRB member(s) (40 CFR 26.110 (PDF) (35pp, 480K)).

Investigators should understand that expedited review is conducted by fewer individuals, but is no less stringent and not necessarily faster than a full IRB review. If any individual reviewer who conducts an expedited review is unable to approve a proposed study, the study must be discussed by the full IRB.

Module 1: Section 4: Beneficence

Data and Safety Monitoring

Data and Safety Monitoring Plans describe protections for research participants and data integrity, and research oversight at a level that is commensurate with the risks of participating in the research. That is, the method and frequency of monitoring is directly related to the possible harms to research participants in the research.

The EPA regulations require that studies involving human subjects should have a monitoring plan when appropriate (40 CFR 26.111 (PDF) (35pp, 480K)).

Module 1: Section 4: Beneficence

Summary

The Belmont principle of beneficence involves maximizing possible benefits and minimizing possible harms to research participants.

Issues covered under beneficence include:

- Protections against risks
- Definition of minimal risk
- Methods of weighing risks against anticipated benefits
- Potential benefits for the research participants
- The use of compensation for participation in research
- Privacy and confidentiality of research participants and research data
- Use of coded private information to protect confidentiality
- Use of an IRB to provide oversight for research involving human subjects
- Situations that allow for an IRB expedited review procedure

Module 1: Section 5: Justice

Objectives

What This Section Covers:

- Fair distribution of the benefits and burdens of research
- The importance of integrating local cultural norms into the research process

The Objective For This Module Is:

- To understand the concept of fair and equitable sharing of the benefits and burdens of research

Module 1: Section 5: Justice

"Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects." – The Belmont Report

The definition of justice has two parts:

- Fair procedures and outcomes are used to select research participants, and
- There is a fair distribution of benefits and burdens to populations who participate in research

Module 1: Section 5: Justice

Individual Justice and Social Justice

The Belmont Report distinguishes social justice and individual justice in the selection of subjects:

Individual justice requires that investigators "should not offer potentially beneficial research only to some patients who are in their favor or select only 'undesirable' persons for risky research."

Social justice "requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons."

Module 1: Section 5: Justice

More on Social Justice

The Belmont Report states that "the choice of participants in research needs to be considered carefully to ensure that groups (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are not selected for inclusion mainly because of easy availability, compromised position, or manipulability."

Selection should depend on reasons directly related to the research questions. When research leads to the development of new treatments, procedures, or devices, justice demands both that:

- These advancements are provided to those who can benefit from them, and
- The research should involve persons from groups who are likely to benefit from subsequent applications of the research

Module 1: Section 5: Justice

Equity vs. Equality in Human Subjects Research

The meanings of "equity" and "equality" are similar, but not the same. The difference between equity and equality has important implications for justice in research.

To treat "equitably" means to treat fairly; to treat "equally" means to treat in exactly the same way.

Research should strive for equitable distribution of the risks and potential benefits of the research. This means that investigators are treating the groups involved in the research fairly and justly. It does not necessarily mean that all groups are equally represented, but that their representation is fair and just based on the risks and potential benefits associated with the research.

Module 1: Section 5: Justice

Equitable Distribution

In order to achieve an equitable distribution of the risks and potential benefits of the research, investigators must determine the distribution of different groups (men and women, racial or ethnic groups, adults and children, age, etc.) in the populations that:

1. May be affected by the disease or condition under study, and

2. That are anticipated to benefit from the knowledge gained through the research

Investigators must ensure that the participants recruited for the research will not be unduly burdened and that recruitment reflects the diversity of the population that may benefit from the knowledge generated from the study.

Module 1: Section 5: Justice

Case Study: Environmental Exposures and the Development of Migraines Study

A researcher seeks to study a link between indoor and outdoor air pollution and the development of migraines. Because women are three times more likely to experience migraines than men, he proposes to enroll three times as many women as men. They will be recruited from racially and ethnically diverse communities.

Does this study design fulfill the principle of justice?

The research includes women and men in proportion to the rates of severe migraines experienced by each sex, and is designed to have racial and ethnic diversity. The study provides both sexes and racial/ethnic communities with the opportunity for benefits, and does not unfairly burden any single group with the risks of research. The design is fair.

Module 1: Section 5: Justice

Sustaining Benefits Locally

Investigators should think about how benefits to individual research participants and the local population may be sustained after the study is complete.

When planning a study, researchers and sponsors may:

- "... make reasonable, good faith efforts before the initiation of a trial to secure, at its conclusion, continued access for all participants to needed experimental interventions that have proven effective for the participants ..."[6]
- Consider how any effective treatment emerging from the research could be provided to the rest of the population

Module 1: Section 5: Justice

Local Cultural Norms and Informed Consent

In unfamiliar settings, investigators should:

- Become familiar with local cultural norms, and
- Seek guidance from community advisors and the IRB

Investigators should incorporate cultural norms into the research process when appropriate. Examples of cultural norms include community consent and informed consent from family representatives.

If community consent is the cultural norm, it may be appropriate to obtain community consent in advance of obtaining informed consent from individuals. Community consent cannot replace the informed consent from individuals.

If cultural norms require permission from a family member before an individual may enroll in research, it may be appropriate to obtain permission from the family member in addition to informed consent from the prospective research participant.

Module 1: Section 5: Justice

Summary

Justice requires:

- Fair procedures and outcomes in the selection of research participants, and
- Distribution of benefits and burdens among the populations participating in research.

Individual justice requires that:

- Benefits of participation in research are offered to a diverse eligible population, and
- Risks of participation in research are shared by a diverse population

Social justice requires that consideration is given to classes of subjects that ought, and ought not, to participate in research. Considerations are based on:

- The ability of members of that class to bear burdens and
- The appropriateness of placing further burdens on already burdened persons.

Module 1: Section 5: Justice

Contact Information

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Module 1: Section 5: Justice

Citations

1. Emanuel, EJ et al., eds. 2003. Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary. Baltimore, MD: The Johns Hopkins University Press, p.189.

2. This list originated from: National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. 1979. The Belmont Report -- Ethical Principles and Guidelines for the Protection of Human Subjects of Research. Washington, D.C.: U.S. Department of Health and Human Services: Part C, section 2, "Assessment of risks and benefits" http://www.nihtraining.com/ohsrsite/guidelines/belmont.html EXIT Disclaimer

3. 40 CFR 26 406.101 (b)(2) (PDF) (35pp, 480K)

4. Penslar, RL and JP Porter, Office for Human Research Protections (OHRP). 2001. IRB Guidebook, 2nd ed.: Ch. III, Section G http://www.hhs.gov/ohrp/irb/irb_chapter3.htm

5. Emanuel, EJ et al., eds. 2003. Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary. Baltimore, MD: The Johns Hopkins University Press, p.194.

6. 2001. Ethical and policy issues in international research: clinical trials in developing countries (2 volumes). Bethesda, MD: National Bioethics Advisory Commission. http://www.bioethics.gov/reports/past_commissions/nbac_international.pdf (PDF) (154pp, 6.4M)

Module 2: Subparts B, C, and D: Protecting Vulnerable Populations

Objectives

The objectives of this section are:

- To understand why special protections are needed
- To identify which groups are defined as "vulnerable" in EPA's regulations
- To understand the difference between observational and intentional exposure research
- To describe the protections specified in subparts B-D

Module 2: Protecting Vulnerable Populations

Overview

In the context of research, vulnerable individuals are defined as those who cannot fully protect their own interests.

Examples of vulnerable populations include:

- Fetuses
- Nursing infants
- Children
- Mentally impaired persons
- Prisoners
- Other individuals who cannot fully protect their own interests

Subparts B, C, and D of EPA's human studies rule provide additional protections for three specific vulnerable groups:

- Children
- Nursing infants
- Fetuses

Module 2: Protecting Vulnerable Populations

Why are special regulations in place?

The Common Rule (Subpart A) contains the general requirement that Institutional Review Boards (IRBs) incorporate additional safeguards to protect the rights and welfare of subjects who may be vulnerable.

The special regulations at Subparts B, C, and D define specific additional protections and prohibitions that must be implemented in EPA-conducted or supported research involving children or nursing or pregnant women.

Module 2: Protecting Vulnerable Populations

Types of Research Covered by the Regulations Protecting Vulnerable Populations

In EPA's regulations, the additional protections that are implemented depend on the type of research being conducted. EPA recognizes two basic study types:

1. Intentional exposure research

2. Observational research

Module 2: Protecting Vulnerable Populations

Distinguishing Intentional Exposure and Observational Research

Research involving intentional exposure of a human subject is defined as a study where the exposure experienced by the subject would not have occurred but for the human subject's participation in the study. This includes any research in which the subject's exposure is artificially manipulated or controlled.

Observational research means any research that does not involve intentional exposure. Studies that involve naturally occurring environmental exposures may meet the regulatory definition of observational. However, so would studies that do not involve an exposure of any kind, even if they are not intuitively "observational."

Module 2: Protecting Vulnerable Populations

Details on Intentional Exposure Research

The key part of the exposure research definition is that the exposure would not have occurred but for participation in the study.

- In intentional exposure research, the researcher controls some aspect of the exposure under study.
- One way to do this is by intentional dosing where the study substance is administered directly.
- Another way is by controlling the subject's behavior to bring him or her into contact with a study substance already in the environment.

Risk level (including zero or minimal risk) is irrelevant to the determination of whether the research involves intentional exposure or is observational.

Module 2: Protecting Vulnerable Populations

Examples of Intentional Exposure Research

A direct dosing study: Asthmatics and non-asthmatics are exposed, in a chamber, to varying levels of air containing particulate matter in order to determine the effects on their breathing.

A controlled exposure study without direct dosing: Participants are asked to walk, according to a scripted protocol, on a deck treated with commercially available wood preservative. Exposure to the chemicals is measured by wipe samples collected from the bottom of their shoes.

Module 2: Protecting Vulnerable Populations

Examples of Observational Research

Floor samples are taken inside homes to determine the levels of pesticides naturally brought in.

Families living in varying proximities to a cement factory have air samples taken inside the home to determine air quality.

Both of these examples involve an exposure that is already in the environment and the study participants do not alter their normal day-to-day activities for participation in the study.

Module 2: Protecting Vulnerable Populations

Case Study: Beach Pollution

Suppose John, an EPA grantee, conducts a study seeing how much pollution people are exposed to by playing on a beach. This study involves collecting samples from 100 individuals after they play for at least one hour on the beach. Tim does not direct when or for how long the participants play; he merely collects his data after they have been on the beach longer than an hour.

Is this intentional exposure or observational research?

This is observational research because the exposure is not controlled or influenced in any way by the researcher.

Module 2: Protecting Vulnerable Populations

Case Study: Beach Pollution

Suppose John decides that merely collecting samples from the participants will not produce quality data. As a result, Tim decides to structure their time on the beach by keeping them on certain parts of the beach for exactly one hour per day, and then collecting the samples. On average, this will reduce the participant's time on the beach and, therefore, decrease their exposure to any harmful pollutants.

Is this intentional exposure or observational research?

This is intentional exposure research because the participant's exposure to pollutants has been determined by the researcher. It is irrelevant that the people likely would have been exposed in the same or greater amounts anyway.

Module 2: Protecting Vulnerable Populations

Subpart B

Subpart B of the regulations prohibits intentional exposure research, under all circumstances, in children and women who are pregnant or nursing.

The ban is categorical and is not based on a risk-benefit ratio, including prospect of direct benefit.

Module 2: Protecting Vulnerable Populations

Subpart C

Establishes rules for studies that involve pregnant women (and thus their fetuses) participating in observational research.

Research of this nature can be conducted when there is direct benefit to the woman or the fetus.

However, in the absence of direct benefit, if the risk is no greater than minimal to the fetus and the research is important for biomedical knowledge which cannot be obtained in any other manner, the research is permissible.

Module 2: Protecting Vulnerable Populations

Subpart D

Establishes rules for studies that involve children participating in observational research.

Research of this nature can be conducted on children as long as it involves no more than minimal risk. Research that involves greater than minimal risk can only be conducted when there is direct benefit to the subject.

There is no provision in the EPA rule for the conduct of research when there is greater than minimal risk and no direct benefit to the child.

Module 2: Protecting Vulnerable Populations

Differences from HHS Regulations

Unlike the regulations adopted by the Department of Health & Human Services, EPA's regulations:

- Define a child as someone less than 18 years of age (whereas HHS regulations defer to state or local law).
- Contain no exceptions to the rule prohibiting intentional exposure research involving children, nursing women, and pregnant women and fetuses
- Do not recognize a category of research on children involving "a minor increase over minimal risk."
- Have no provisions for "research not otherwise approvable" for children, nursing infants, or fetuses.
- Do not further regulate research involving prisoners, beyond those additional protections found in the Common Rule.

Module 2: Protecting Vulnerable Populations

Authorization of Research under Subparts B, C, and D

EPA's regulations use three terms to signify authorization of research:

- Consent: agreement to participate made by a fully competent adult
- Assent: agreement to participate made by an individual without full capacity to consent, such as a child or a person with cognitive impairment, if developmentally appropriate
- Permission: an agreement to participate made by a parent on behalf of a child; does not replace the need for assent from the child

Module 2: Protecting Vulnerable Populations

Authorization of Research in Pregnant Women

A pregnant woman gives consent for herself.

A pregnant woman also gives permission for her fetus.

In some cases, permission is also required from the father of the fetus.

Module 2: Protecting Vulnerable Populations

Authorization of Research in Children

Children (those under 18 years of age) cannot give informed consent for research under EPA's regulations.

Instead of informed consent, the regulations generally require the assent of the child and the permission of the child's parents.

Waivers:

- Assent may be waived, if the child, due to age, maturity, or psychological state is reasonably incapable of being consulted.
- Assent may also be waived if the observational study holds the prospect of direct benefit to the child's health or well-being and that benefit is available only in the context of the research study.
- If an IRB determines the same conditions exist that would permit an IRB to waive the written informed consent requirement for adults, either assent, or permission, or both, may be waived.

Authorization documents should always contain age-appropriate language.

Module 2: Protecting Vulnerable Populations

Check for Understanding

Suppose an EPA researcher wants to test the efficacy of a new pollution reduction system. As part of the proposed experiment, the researcher will, in a controlled environment, expose children to levels of some pollutants that match the levels found in ambient air.

May the researcher conduct this activity?

(A) Yes, because exposing someone to the same pollutants that children would encounter anyway is minimal risk.

(B) No, because the research involves intentional exposure of children.

The correct answer is B.

Module 2: Protecting Vulnerable Populations

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Module 3: Community Engagement

Objectives

The objective of this module is:

To appreciate that respect for subjects and communities who participate in research is fundamental to the ethical conduct of research.

This module is designed to expand the concept of respect when doing research in a community setting.

Topics covered include:

- Definition of a community
- Community participation in informed consent
- Community consultation
- Importance of trust

Module 3: Community Engagement

Communities

Communities are comprised of groups of people who share an attribute.

Defining a particular community can be difficult since

- communities may lack precise borders; and
- individuals may be members of several, overlapping communities.

CDC has examined four factors to aid in identifying, describing, and understanding communities:

- People (the demographics of the community)
- Location (especially geographic boundaries)
- Shared or common ideas and values
- Formal and informal power relationships (including how communication occurs)

For more information, please see CDC's 1997 report, Principles of Community Engagement

Module 3: Community Engagement

Who Represents the Community?

Like the process of defining a community, determining who represents the community can be a difficult task.

- The lines of authority within a community may be well-defined.
  - Native American Indian tribes, for example, tend to have a formal governing structure.
  - Many religions also have clearly identifiable leaders.
- In other communities the lines of authority may be quite informal, unclear, or nonexistent.
- Many "activists" can be vocal on a particular issue and appear to be the community leaders. However, it is important to note that vocal activists may or may not represent the community.

In unfamiliar settings, investigators should:

- Become familiar with local cultural norms; and
- Seek guidance from community advisors and their Institutional Review Board (IRB).

Module 3: Community Engagement

Individuals and their Communities

The relationship between individuals and society at-large can vary from culture to culture. In some cultures, protecting individual liberty from interference by society takes near-absolute precedence.

- Ethical guidelines may reflect this liberty from interference by including very strong prohibitions against violating a subject's privacy.

Other cultures place more emphasis on the involvement of the community, sometimes injecting the community's input into areas that, elsewhere, might be thought of as strictly individual decisions.

Module 3: Community Engagement

Communities versus Stakeholders

It is also important to distinguish stakeholders from the community. A stakeholder has some interest in the activity being conducted but is not necessarily a member of the community.

- For example, suppose EPA conducts an observational study on the use of a particular pesticide in a city's apartment complexes. The community would comprise residents of the apartment complexes. The manufacturer of the pesticide is clearly a stakeholder in the study but will likely not be a member of the community in which the research is conducted.

The interests of stakeholders may or may not be in harmony with those of the community.

In determining who represents a community, it is important not to confuse stakeholders with community representatives.

Module 3: Community Engagement

Application to Research

A community that requires engagement by the researcher may be present in any human study.

Community engagement is especially likely to be needed in the following settings:

- Public health-related research
- Research involving cultures or populations known to have different or unusual norms
- Research involving populations where the norms are unknown to researchers

The need for community engagement should always be considered in research conducted or supported by EPA.

Module 3: Community Engagement

Informed Consent in a Community Setting

In some cultures it is not appropriate to obtain informed consent solely from individual participants since the individual's interests may be considered to be intimately entwined with their community's interests. The appropriate way to attain community consent may vary widely.

- It is often achieved through meetings with large groups of community representatives or community leaders. It is usually appropriate to obtain community consent before obtaining individual consent.
- In some cultures, one may need to get permission from a family representative before conducting research on a member of that family.

Researchers will also find that community consultation, when appropriate, aids them in carrying out their research. Members of certain communities may be hesitant to volunteer for research, not because they do not want to participate, but because they are unsure about how their community leaders feel about the research.

Incorporating members of the community or members of a family into the decision-making process is always ***in addition to*** – **never in substitute of** – other individual protections required by EPA regulations. EPA regulations do not permit disregarding individual protections contained in the regulations based on local norms.

Community or family permission never overrides the need to obtain informed consent from a competent adult.

Module 3: Community Engagement

Other Areas of Community Participation: Consultants

There are several ways for researchers to include a community in the research process, including using community members as consultants.

- Consultants can contribute significant knowledge about the community to the research staff.
- Due to their knowledge about their community, community consultants can contribute to recruiting research subjects and retaining the subjects once recruited.
- Consultants may be paid or unpaid, but researchers must be mindful of the potential for conflict of interest when using paid consultants.

Module 3: Community Engagement

Other Areas of Community Participation: Community Consultation

Researchers can rely on the broader community as a good resource to help them design, recruit participation in, and monitor public health research.

When relying on the broader community, it is imperative that researchers and the community maintain an open dialogue.

- Researchers should ensure that information shared with the broader community is both accurate and understandable to a non-scientific audience.
- Researchers should be receptive to listening to concerns of the community and, when appropriate, modifying studies to address those concerns.

Module 3: Community Engagement

Trust in Research

Trust between a researcher and participants is important to all human subjects research.

Participants have the right to expect that research will be conducted responsibly.

This is important for:

- Research logistics
- Scientific quality of data
- Ethics (respect for participants)

Module 3: Community Engagement

Trust in Community Research

Maintaining a strong dialogue with the broader community is a key feature in establishing trust between researchers and the community at large.

Community trust is especially important considering the types of research EPA is often engaged in.

- In studies related to the environment and public health, community cooperation is invaluable in producing reliable data.
- Some of EPA's research can be complex and difficult to understand. Proper community involvement in the research is imperative in order to prevent confusion about the nature of the research taking place.

More detailed information about this kind of research at EPA can be found in a 2008 reference document developed by the National Exposure Research Laboratory, entitled Scientific and Ethical Aspects for Observational Exposure Studies (PDF) (133 pp, 1.2M).

Module 3: Community Engagement

Prev

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