

RAPID POLICY ASSESSMENT & RESPONSE



Module V:

Training Materials

Research Ethics

Purpose and Process

Purpose

- To describe need for ethical oversight of research studies involving humans
- To explain ethical principles that guide research
- To describe important documents relevant to policy research
- To present basic requirements for ethical review
- To facilitate identification and discussion of ethical issues arising in this research
- To train all staff and research team in human subject and information protection procedures for this project and each site.

Process

Discussion of

- potential local ethical issues
- human subject protection procedures as described in project protocol
- informed consent forms and process

Why is Ethical Oversight of Research Studies Involving Humans Important?

Research can be defined as a “systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”¹ A human subject is “a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.”² Research involving human subjects includes a wide variety of scientific endeavors including: basic (non-clinical) science using biological samples, randomized clinical trials of new drugs or devices, epidemiological research of population health and behavior, and policy behavioral research involving surveys, observation, and interviews.

Human subject research has produced important new basic scientific knowledge, established the effectiveness of life saving treatments and vaccines, and advanced our understanding of behavioral and structural factors’ role in health. Not all research, of course, leads to important discoveries. Sometimes research exposes subjects to real or potential risks. Regulation of human subjects’ research aims to reduce these risks and prevent exploitation of research subjects while promoting ethical and well-designed research studies.

Historically, some research has exposed human subjects to real or potential harm, often without their full consent and sometimes without their knowledge. Examples include the Nazi doctors’ experiments that involved exposing concentration camp prisoners to wounds, unnecessary surgery, infectious agents, and extremes of heat, cold, altitude, or other dangerous situations to document the impact on the human body even to the point of causing death. Other examples include the Tuskegee syphilis study in which African-American men with syphilis were deceived about their diagnosis, denied effective treatment when it became available, and observed for up to 30 years untreated. Additionally, throughout the 1940s, 50s, and early 60s, many well-respected researchers conducted studies involving patients without their fully informed consent and some exposed patients to much greater risks from experimental interventions than they would have faced with standard treatment.³

Instances of abuse and harm led to calls for oversight. Regulation, as it has developed in the U.S., has included oversight from courts and regulatory bodies within the government, and from the development of ethical codes and voluntary standards. Ultimately, federal regulation combined with international standards, currently define the requirements for U.S.-based researchers working in other countries. This section introduces the basic principles, documents, and requirements for ethical review of human

¹ 45 (US) Code of Federal Regulations (CFR) 46.102(d).

² 45 (US) Code of Federal Regulations (CFR) 46.102(f).

³ H. K. Beecher, "Ethics and Clinical Research," *New England Journal of Medicine*, 274 (1966): 1354-1360.

subject research and identifies some of the potential ethical issues of policy research in particular.

The Basic Ethical Principles that Guide Research

In the past thirty years a consensus has emerged on basic ethical principles that should guide biomedical research, these are *respect for persons, beneficence and justice*. They appear explicitly stated in the Belmont Report, the Council for International Organizations of Medical Sciences (CIOMS) Guidelines, and are reflected less explicitly in each of the important documents described in the next section. What follows is an excerpt from the most recent CIOMS guidelines describing the basic principles.

“Respect for persons incorporates at least two fundamental ethical considerations, namely:

- a) respect for autonomy, which requires that those who are capable of deliberation about their personal choices should be treated with respect for their capacity for self-determination; and
- b) protection of persons with impaired or diminished autonomy, which requires that those who are dependent or vulnerable be afforded security against harm or abuse.

Beneficence refers to the ethical obligation to maximize benefits and to minimize harms. This principle gives rise to norms requiring that the risks of research be reasonable in the light of the expected benefits, that the research design be sound, and that the investigators be competent both to conduct the research and to safeguard the welfare of the research subjects. Beneficence further proscribes the deliberate infliction of harm on persons; this aspect of beneficence is sometimes expressed as a separate principle, *nonmaleficence* (do no harm).

Justice refers to the ethical obligation to treat each person in accordance with what is morally right and proper, to give each person what is due to him or her. In the ethics of research involving human subjects the principle refers primarily to *distributive justice*, which requires the equitable distribution of both the burdens and the benefits of participation in research. Differences in distribution of burdens and benefits are justifiable only if they are based on morally relevant distinctions between persons; one such distinction is vulnerability. "Vulnerability" refers to a substantial incapacity to protect one's own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities, or being a junior or subordinate member of a hierarchical group. Accordingly, special provision must be made for the protection of the rights and welfare of vulnerable persons.

Sponsors of research or investigators cannot, in general, be held accountable for unjust conditions where the research is conducted, but they must refrain from practices that are likely to worsen unjust conditions or contribute to new inequities. Neither should they take advantage of the relative inability of low-resource countries or vulnerable

populations to protect their own interests, by conducting research inexpensively and avoiding complex regulatory systems of industrialized countries in order to develop products for the lucrative markets of those countries.

In general, the research project should leave low-resource countries or communities better off than previously or, at least, no worse off. It should be responsive to their health needs and priorities in that any product developed is made reasonably available to them, and as far as possible leave the population in a better position to obtain effective health care and protect its own health.

Justice requires also that the research be responsive to the health conditions or needs of vulnerable subjects. The subjects selected should be the least vulnerable necessary to accomplish the purposes of the research. Risk to vulnerable subjects is most easily justified when it arises from interventions or procedures that hold out for them the prospect of direct health-related benefit. Risk that does not hold out such prospect must be justified by the anticipated benefit to the population of which the individual research subject is representative.”⁴

Important Documents

The current CIOMS guidelines describe many of the key international documents related to human subjects’ research.

“The first international instrument on the ethics of medical research, the Nuremberg Code, was promulgated in 1947 as a consequence of the trial of physicians (the Doctors’ Trial) who had conducted atrocious experiments on unconsenting prisoners and detainees during the second world war. The Code, designed to protect the integrity of the research subject, set out conditions for the ethical conduct of research involving human subjects, emphasizing their voluntary consent to research.

The Universal Declaration of Human Rights was adopted by the General Assembly of the United Nations in 1948. To give the Declaration legal as well as moral force, the General Assembly adopted in 1966 the International Covenant on Civil and Political Rights. Article 7 of the Covenant states "*No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his free consent to medical or scientific experimentation*". It is through this statement that society expresses the fundamental human value that is held to govern all research involving human subjects – the protection of the rights and welfare of all human subjects of scientific experimentation.

The Declaration of Helsinki, issued by the World Medical Association in 1964, is the fundamental document in the field of ethics in biomedical research and has influenced the formulation of international, regional and national legislation and codes of conduct.

⁴ Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects. CIOMS, World Health Organization, 2002, available at: http://www.cioms.ch/frame_guidelines_nov_2002.htm.

The Declaration, amended several times, most recently in 2000 (Appendix 2), is a comprehensive international statement of the ethics of research involving human subjects. It sets out ethical guidelines for physicians engaged in both clinical and nonclinical biomedical research.

Since the publication of the CIOMS 1993 Guidelines, several international organizations have issued ethical guidance on clinical trials. This has included, from the World Health Organization, in 1995, *Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products*; and from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), in 1996, *Guideline on Good Clinical Practice*, designed to ensure that data generated from clinical trials are mutually acceptable to regulatory authorities in the European Union, Japan and the United States of America. The Joint United Nations Programme on HIV/AIDS published in 2000 the UNAIDS Guidance Document *Ethical Considerations in HIV Preventive Vaccine Research*.

In 2001 the Council of Ministers of the European Union adopted a Directive on clinical trials, which will be binding in law in the countries of the Union from 2004. The Council of Europe, with more than 40 member States, is developing a Protocol on Biomedical Research, which will be an additional protocol to the Council's 1997 Convention on Human Rights and Biomedicine.

Not specifically concerned with biomedical research involving human subjects but clearly pertinent, as noted above, are international human rights instruments. These are mainly the Universal Declaration of Human Rights, which, particularly in its science provisions, was highly influenced by the Nuremberg Code; the International Covenant on Civil and Political Rights; and the International Covenant on Economic, Social and Cultural Rights. Since the Nuremberg experience, human rights law has expanded to include the protection of women (Convention on the Elimination of All Forms of Discrimination Against Women) and children (Convention on the Rights of the Child). These and other such international instruments endorse in terms of human rights the general ethical principles that underlie the CIOMS International Ethical Guidelines.”⁵

In addition to these international instruments, the United States has produced key documents of international import. The first, The Belmont Report, was published April 18, 1979, by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, reporting to the Secretary of Health, Education and Welfare. The Belmont Report is a statement of “basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects.”⁶ Although not itself binding, and originally only a statement of departmental policy, the Belmont Report also provided the guiding principles for the

⁵ Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects. CIOMS, World Health Organization, 2002, available at: http://www.cioms.ch/frame_guidelines_nov_2002.htm.

⁶ The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report. April 18, 1979. Available at: <http://ohsr.od.nih.gov/guidelines/belmont.html>.

development of the federal regulations that govern research in the US, referred to as the Common Rule.”⁷

The Common Rule and institutional policies designed to comply with US federal regulations have direct impact only on U.S. researchers and institutions. However, they also have an enormous impact on research conducted around the world by U.S. researchers or funded by U.S. institutions since they require such research to adhere to U.S. standards for review and approval, *in addition to*, local and international requirements.

See documents and web sources at the end of these training materials.

The Basic Requirements of Ethical Review

General Requirements

As a general rule all research involving human subjects should conform to the international standards for research described in CIOMS and Helsinki, as well as respecting human rights, and complying with relevant local (national) law regarding the rights of research subjects and the responsibilities of investigators.

The primary responsibility for ensuring research is ethical and conforms to local, national and international standards rests with the investigators. It is the responsibility of the investigator to ensure that all persons involved in the project have a sufficient understanding of ethical issues in research to protect the rights of subjects during the project. First, investigators and staff must familiarizing themselves with the basic documents governing research and understand the steps necessary to protect subjects in their particular protocol. Additionally, a local board or committee whose mandate is to provide ethical review of new and ongoing protocols involving human subjects can assist investigators to identify ethical issues and solutions through the process of local review of their research plan. Local review may result in dialog between investigators and the committee to identify potential ethical issues, reduce research risks, protect subjects’ confidentiality and physical well-being, and provide adequate procedures to meet requirements. In the U.S., such committees are usually called an Institutional Review Board(s) (IRB).

Research involving U.S. institutions

For research funded by the United States government or involving U.S. institutions the specific requirements that must be met through ethical review include:

- obtaining prior ethical review and approval by an IRB within the US;
- minimizing research risks in relation to possible benefits;

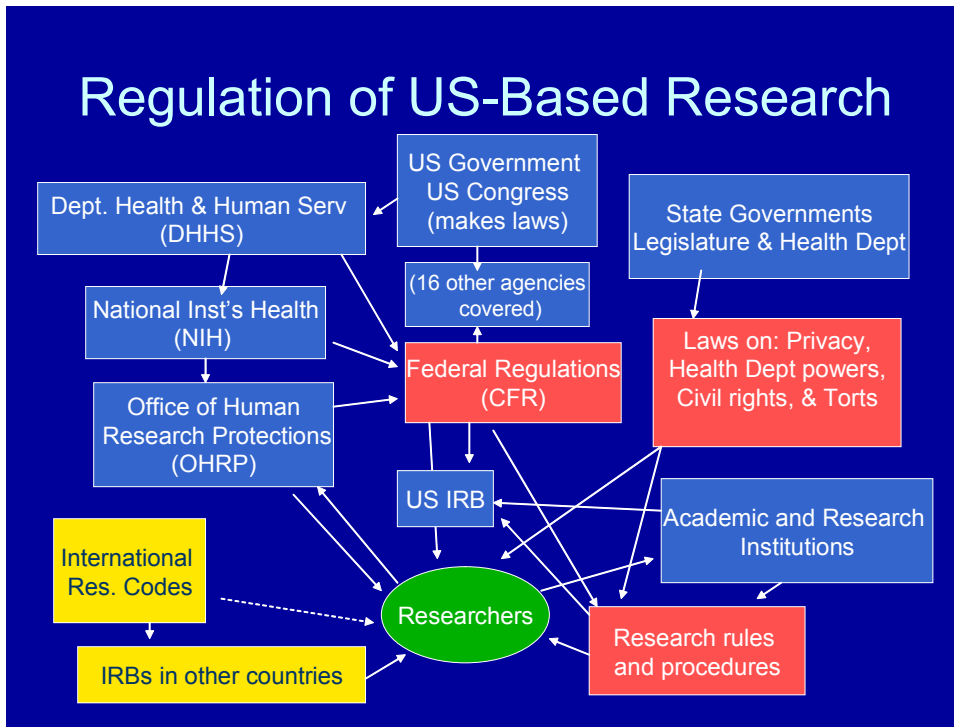
⁷ 45 CFR 46, and 21 CFR (governing the Food and Drug Administration’s activities).

- ensuring that the informed consent process and documentation is sufficient for fully informed and voluntary consent by research subjects or their legally authorized representatives;
- informing subjects of their rights as research subjects to withdraw from the study at any time;
- selecting subjects fairly;
- protecting confidential or identifying information about subjects;
- establishing safety monitoring, where appropriate;
- protecting vulnerable populations;
- re-reviewing the study at least once a year to monitor compliance with ethical rules and identify unanticipated risks.

Additionally, for research occurring outside the U.S., the study must also be reviewed by a local ethics committee or board (IRB) or the U.S. IRB must be advised by someone who is aware of ethical issues in the site where the research will occur.

The complex structure of institutions and documents that govern human subject research involving U.S. and foreign institutions is displayed in the following diagram. For the purposes of the RPAR it is important to know that:

- U.S. regulations cover even policy research relying mainly on interview data;
- The project must be reviewed both in the U.S. and by a committee or board that has knowledge of the local research environment (usually an in-country research ethics committee registered with the NIH);
- That the research must comply with both the international documents discussed above and the U.S. federal regulations; and
- For policy research, meeting these requirements should be easily achievable.



Informed Consent

Researchers and staff should be aware of the basic requirements of informed consent wherever they are responsible for recruiting subjects and / or obtaining informed consent from subjects, documenting informed consent, designing research protocols, or storing research data and informed consent documentation.

Informed consent is a process, not a form. Although, federal regulations and most projects require that research subjects sign and complete very specific informed consent forms and that investigators maintain records of such forms, subjects actually give fully informed and voluntary consent, only as part of a process. The *informed consent process* includes 1) disclosure of information about the project by someone involved in the project, or by documents prepared for this purpose; 2) discussion of the purpose, procedures, and other aspects of the project by the potential subject and the project representative including enough time for the subject to ask any questions she has; and 3) deliberation of the risks and benefits of the project by the potential subject. If, after weighing all these, the subject chooses to enroll, then she or he signs the consent form, a copy is given to the subject and another stored in the research records.

In order for informed consent to be possible, the subject must meet at least two pre-conditions – that the subject have the capacity to make an informed decision and that the decision be made free of coercion. Additionally, the researcher must provide sufficient information to the subject to make an informed choice. First, in order to have the capacity to make a decision, the potential subject must be capable of *understanding* the risks and benefits of the study, *deliberating* the balance of risks and benefits in the context of his or her own life, and *communicating* a choice clearly to the investigator or

staff. Thus, adults are assumed to be able to give consent unless there is evidence that they are unable to understand, deliberate or communicate. Children, however, are assumed not capable of consent, and permission to enter research is usually necessary from their parent or legal guardian. Adults with mental disabilities, dementia, mental illness, or those unconscious or heavily medicated, may or may not be able to give consent and must be evaluated on a case-by-case basis. The second precondition is that the subject must make the decision whether or not to participate freely, voluntarily and without coercion.

If both these pre-conditions are present, then the subject must be fully informed. This means that they have been presented the following information and have had an opportunity to ask questions and receive answers to those questions. Informed consent should include:

- the purpose of the study;
- reasonably foreseeable risk and discomforts to the subject;
- potential benefits to subjects;
- how risks will be minimized including protection of confidential information;
- possible alternative (non-research) procedures or treatments;
- participation is voluntary;
- subject may withdraw at any time;
- if the study poses greater than minimal risk, the subject should receive any information about potential compensation for harm or medical treatment;
- who to contact with questions about the research and their rights as subjects.

Documentation of informed consent is usually required, by a form that lists all the above information at a level of language understandable to the potential subjects, and is signed by the subject. Some institutions require a witness's signature or the signature of the person obtaining the consent.

See the informed consent forms in the Tools section of this Module (V) for examples of forms that meet these requirements.

Protecting subject's confidentiality

In many research projects, including those involving mainly interviews or surveys, the only risk to subjects is that confidential or sensitive information about them will be improperly disclosed. In all studies researchers have an obligation to protect subject identities and information. Common measures to protect information include:

- conducting interviews in private or in settings where the information disclosed cannot be overheard by other persons;
- keeping the identities of all research subjects confidential, even the fact that an individual *is* a research subject should be protected;

- identifying research data by code rather than name;
- not using names or other identifiable information in any published or circulated summary of the data or discussion of the results;
- storing research data, including informed consent forms in locked rooms or file cabinets, or on pass-word protected computers, to limit outsider's access to information;
- educating staff not to share interesting anecdotes from the research outside of the research setting.

Confidentiality in research:

Interviewers may know their research subjects from other settings such as street outreach, health clinics, on-going therapy groups, or other settings. They may have even recruited subjects in those settings. However, in all cases interviewers should not acknowledge the identity of a subject as a participant in a study in any setting, unless the subject identifies himself as such. Interviewers may even encounter research subjects socially at a later time. Once again, interviewers should not acknowledge their previous contact with the subject unless the subject does so.

Ethical Issues in Policy Research and this Project

Avoiding harm to subjects and others

Although policy research focusing on behavior is relatively low risk in comparison to some types of clinical trials or behavioral research, any research related to drug use or other illegal behavior poses some risks to subjects. For those not engaging in illegal activity themselves, the main risk is that sensitive or critical information revealed in an interview or focus group might be disclosed to their colleagues, friends, or associates. Or, there might be some possible stigma associated with working with the researchers identified with an "AIDS project" or a "drug user project."

For subjects engaged in or knowledgeable about illegal behaviors such as drug use, potential risks include both disclosure of stigmatizing information and potential legal risks if law enforcement authorities use information obtained in research for criminal justice purposes. These subjects, who may be reluctant to talk to researchers, deserve protection from possible mis-use of their information. For example, collecting data without personally identifiable information on subjects may be one way to insulate them from harm. Subjects could give their initials or use pseudonyms. Other precautionary measures include not recording precise locations where subjects were interviewed or illegal activity occurred so as to prevent police use of the information to conduct surveillance or make arrests.

Finally, in some cases the potential for harm comes from the implications of the results of the research. In these cases, researchers must balance the probable benefits of

the research against the possible harms that might occur from documentation of the results.

Case Study: do no harm – an ethical dilemma in prison

During planning for an investigation of HIV in a prison researchers were concerned that a backlash would result from prison staff and administration if the researchers revealed that there was injection drug use and sex in the prison. On balance the team decided that research was vital to convince policy makers and politicians to implement penal reform.

Neutrality

Researchers will need to have a non-judgmental stance. This means respecting the life choices that informants have made and any opinions they hold. During a rapid assessment, researchers should never attempt to change the behavior, beliefs or attitudes of an informant. Where conflict exists in a locality, either between individuals or political groups, researchers should avoid being associated with either side.

Case study: neutrality - an ethical dilemma

During street interviews with young heroin injectors, a researcher was often asked whether she thought they should be tested for HIV. Rather than express her own opinion about HIV testing, at the end of the interview she would give the interviewee a card with contact details for a free, confidential HIV testing and counseling service.

Consent

Informants should normally give their consent to being involved in the study. Where researchers record the identity of the respondent, consent is required. However, where researchers are only observing behavior, or where they have been advised not to explain what they are doing by a key informant, *and* the identity of the subject of the information is not recorded, the researcher must assess the most ethical course of action.

Case study: informed consent - an ethical dilemma

During research in a Baltic country, members of the team became involved in a conversation at a party. The young person they spoke to revealed, during the conversation, that she was involved in sex work and used drugs. She spoke quite openly about her experience and provided useful information about sex work and drug use in the city. However, the members of the research team did not reveal to the young person that they were researchers or the nature of their work. Since there was no informed consent, the researchers were faced with the ethical dilemma of whether or not to use the useful information.

Feedback

Those people who were involved in the rapid assessment should be given a chance to comment on the findings. As well as being ethical, this is often a useful final check on the validity of any results and the feasibility of any recommendations.

Consequences

Researchers should always be aware of the consequences of their actions. What seems ethical in strict research terms may have unethical consequences for others.

Example: Alcohol and ethics, Ireland

Research team members were interested in how 'poitin' is made. 'Poitin' is a home-made spirit that a lot of young people drink in our community. The only person who could show them how to make the drink was currently undergoing alcohol treatment. The team was aware that by asking this person prepare the drink, they could be placing the individual in a situation where she might be tempted to drink the solution. This ethical dilemma was solved when the opportunity arose to witness the 'poitin' production by individuals not in alcohol treatment.

Protecting Human Subjects in Policy Research and this Project

Investigators should develop a plan specific to their research project that foresees potential risks to research subjects (and staff), adopts means to reduce risks and establishes procedures to ensure that risks are minimized and subjects are protected throughout the course of the research project.

See Protection of Human Subjects in the tools section of this Module (V).

Documents and Sources:

The Belmont Report. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. April 18, 1979, available at:
<http://ohsr.od.nih.gov/guidelines/belmont.html>

Code of Federal Regulations (US) 45 CFR Part 46, available at:
<http://www.nihtraining.com/ohsr/site/guidelines/45cfr46.html>

Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects. CIOMS, World Health Organization, 2002, available at:
http://www.cioms.ch/frame_guidelines_nov_2002.htm

Nuremberg Code, 1947. available at: <http://ohsr.od.nih.gov/guidelines/nuremberg.html>

Universal Declaration of Human Rights, 1948. available at:
<http://www.un.org/Overview/rights.html>

World Medical Association, Declaration of Helsinki, available at:
<http://www.wma.net/e/policy/pdf/17c.pdf>