IRB Training Modules

The following training and education modules are designed for personnel proposing to conduct, or those reviewing research involving human subjects. Research using human subjects is heavily regulated by the federal government and requires targeted training and documentation of that training.

The following is an excerpt of a message about education and training from Jeffery Cohen, Office for the Protection from Research Risks (OPRR), the federal office responsible for oversight and compliance with human subjects research regulations and guidelines (May 1999)

"There are two basic features of an education program that OPRR looks for - that it is ongoing and that it reaches everyone involved in human subjects research at an institution. The necessity to train IRB members is obvious, as without proper training the IRB cannot make informed decisions. Equally important is the necessity to train the individuals who actually conduct the human subjects research. Unless the IRB can be sure that these individuals understand the issues involved in human subjects research (informed consent, risk/benefit, confidentiality, etc.) it cannot be sure that the subjects in the research are being adequately protected."

Consequently, it is the responsibility of the institution and the IRB to adequately train and educate researchers and IRB members in topics pertinent to the programs ongoing at that institution. The following training and education modules provide that material. Each module targets a different aspect of human subjects research. There is some redundancy between modules, but the information that is found to be in common among the modules is important to the overall understanding of the critical issues involved.

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Module 1: History of Research Abuse of Human Subjects
Institutional Review Board (IRB) Training for Research Involving Human Subjects

Learning Objective: This lesson covers several well-known instances of unethical research involving human subjects, and provides a historical context for why ethical and regulatory requirements for the conduct of research have been developed over the last 50 years in the United States. Upon completion of this lesson, you should be able to recognize some of the historical ethical violations in research that influenced the development of ethical principles and legal requirements currently governing human subjects research.

History

Until the middle of this century, concerns about the ethics of the practice of medicine centered around therapeutic medicine, not research medicine. National and international efforts to protect the rights and welfare of human subjects of research have occurred often in response to ethical violations -- situations in which researchers were found to have ignored the fundamental rights of human subjects. The Nazi Party in Germany committed egregious acts in the name of science that shocked the world community

Infamous Cases - Nazi War Crimes

In order to ensure the supremacy of the Aryan Race, the Nazi party in Germany desired to find a secret way of sterilizing large populations. Three experiments involving sterilization were in progress when WWII ended in 1945.

1. Dried plant juice was put into flour that was fed to the general population. This was supposed to sterilize women predominately.
2. Intrauterine injections of a silver nitrate solution were given to women, without their consent during routine physical examinations.
3. Men stood at a counter to complete forms while being exposed without their knowledge to sterilizing doses of X-radiation.

In addition to sterilization experiments, Nazi physicians and researchers were under great pressure to develop an effective vaccine for typhus fever to administer to German troops. At Buchenwald concentration camp, experiments were conducted in which prisoners were administered vaccine (or placebo) and then injected with blood from patients infected with typhus fever. Between 1942 and 1943 about 729 people were subjected to such experiments, and 154 died. In addition, other prisoners served as a "passage group." In order to keep the virus virulent and alive, the researchers would inject the virus into prisoners, when these people developed the acute illness, their blood was removed and injected into other prisoners.

The horrors of the preceding and many other "experiments," were exposed during and after WWII. The people who conducted these experiments were tried separately from other Nazi war criminals because of their professional status as physicians and researchers, and because of the atrocious nature of their crimes.

During the trial at Nuremberg, fundamental ethical principles for the conduct of research involving humans were codified into the Nuremberg Code, which sets forth ten conditions that must be met before research involving humans is ethically permissible (e.g., the need for voluntary consent of subjects, a scientifically valid design that could produce fruitful results for the good of society). The Nuremberg Code became the first international standard for the conduct of research. You can access it through the NIH web site at http://helix.nih.gov:8001/ohsr/

To date, little has been made of the data generated from the Nazi experiments. There is ongoing discussion in scientific and ethical communities concerning whether it is ethically permissible to use or publish the data.

Infamous Cases - The Willowbrook Study

From 1963 through 1966, studies were carried out at the Willowbrook State School for "mentally defective persons." These studies were designed to gain an understanding of the natural history of infectious hepatitis and subsequently to test the effects of gamma globulin in preventing or ameliorating the disease. The subjects, all children, were deliberately infected with hepatitis virus; early subjects were fed extracts of stools from infected individuals and later subjects received injections of more purified virus injections. Investigators defended the deliberate injection of these children by pointing out that the vast majority of them acquired the infection anyway while at Willowbrook, and perhaps it would be better for them to be infected under carefully controlled research conditions.

During the course of these studies, Willowbrook closed its doors to new inmates, claiming overcrowded conditions. However, the hepatitis program, because it occupied its own space at the institution, was able to continue to admit new patients. Thus, in some cases, parents found that they were unable to admit their child to Willowbrook unless they agreed to his or her participation in the studies. This case caused a public outcry because of the perception that the parents and their children were given little choice about whether or not to participate in research.

Infamous Cases - The Jewish Chronic Disease Hospital Study

In 1963, studies were undertaken at New York City's Jewish Chronic Disease Hospital to develop information on the human transplant rejection process. These studies involved the injection of live cancer cells into patients who were hospitalized with various chronic debilitating diseases. Previous studies had indicated that healthy persons reject cancer cell implants promptly. Patients with widespread cancer also reject homografts, however, rejection is delayed substantially when compared with healthy subjects.

Researchers said that consent had been given orally, but was not documented. They felt that documentation was unnecessary since it was customary to undertake much more dangerous medical procedures without the use of consent forms.

Further, patients were not told that they would receive cancer cells because, in the view of the investigators, this would frighten the patients unnecessarily. Investigators defended this view on the basis that they had good cause to predict that the cancer cells were going to be rejected.

Infamous Cases - Radiation Tests on Mentally Impaired Boys

From 1946 to 1965, 19 boys who thought that they were participating in a science club were fed radioactive milk by researchers who wanted to learn about the digestive system. The experiments were performed at the Fernald State School in Massachusetts. Researchers from Harvard University and the Massachusetts Institute of Technology fed radioactive form of iron and calcium to the boys, sometimes in their breakfast milk, to study the body's ability to digest minerals.

Infamous Cases - The Tuskegee Syphilis Study

This study was conducted in the U.S. and was designed to determine the natural history of untreated latent syphilis. Over 400 black men with syphilis and about 200 men without syphilis, who served as the controls, were the subjects. During the study, the men were told they were being treated for "Bad Blood."

The men were recruited without informed consent. In fact, they were misinformed and told that some of the procedures done in the interests of research (e.g., spinal taps) were actually "free special treatment." By 1936, it became apparent that many more infected men than controls had developed complications. Ten years later a report of the study indicated that the death rate among those with syphilis was about twice as high as it was among the controls. In the 1940's, when penicillin, known to be effective in the treatment of syphilis became available, the men were neither informed of this, nor treated with the antibiotic.

The study continued until the first accounts of it appeared in the national press in 1972, at which time an ad hoc advisory panel was formed by the government to give advice on how to assure that such experiments would never be conducted again. The government continues to pay millions of dollars yearly to surviving subjects and the families of the deceased subjects. “Our challenge in the public health service is to create that system that people can trust, and to continue to strengthen that system,” said CDC Director Dr. David Satcher. In May of 1997, President Clinton issued a formal apology to the last eight survivors of the study.

Summary of Important Points in this Lesson

The three ethical principles of The Belmont Report are: Respect for Persons, Beneficence, Justice (The Belmont Report is the in-depth subject of another training module). In general, the cases that have evoked the greatest public outcry (such as those reviewed here) have violated or seemed to violate the requirements of all three of the fundamental ethical principles in the Belmont Report.

The research activities reviewed in this lesson imperiled the life or health of vulnerable or disadvantaged persons without their informed consent. It was infamous cases such as these and others that focused national attention on the need to protect human research subjects.

Module 2: Introduction to Human Subjects Research

Institutional Training for Research Involving Human Subjects

KWU is committed to assuring that all of its research activities involving human subjects are conducted in a way that promotes their rights and welfare. In accordance with sound ethical principles and federal legal requirements, KWU has policies and procedures to help you fulfill your responsibilities when you conduct or collaborate in research involving human subjects at KWU or elsewhere. KWU designed its policies based on well-established ethical principles for conducting research with humans, as well as in compliance with the Federal Regulations for the Protection of Human Subjects, Title 45 Part 46 of the Code of Federal regulations (45 CFR 46).

Sometimes it isn't easy to see how the policies apply to particular cases, for instance when research deals only with surveys, students or with volunteers. This course is designed to help you identify those research activities that involve human subjects, and to help you understand how to protect the rights and welfare of all human subjects involved in your research activities.

Hypothetical Research Collaboration Project

Let's begin with a hypothetical collaborative research project involving receipt and analysis of human blood samples in your laboratory. Dr. Bronson is an oncologist in an economically-poor, third world country, and has been conducting a trial to develop a vaccine against stomach cancer, a condition highly prevalent in his country. Before he began his study, Dr. Bronson called you and asked if you would collaborate with him by performing some research analysis of blood samples to be drawn from subjects in the proposed vaccine trial, and to help with the subsequent data evaluation. He also suggested that you be identified as a co-author on any relevant publications. You have had professional association with Dr. Bronson, have co-authored several papers with him, and have confidence in his abilities. You judged that your role in the project was peripheral since you would personally have no contact with human subjects. You agreed to help, and have been receiving and analyzing blood samples monthly for over a year. During a recent interview, Dr. Bronson said that without the valuable collaboration of his colleague at KWU, the vaccine trial would not have been possible.

You are surprised to learn during the interview that a clinical trial with the same vaccine had been planned in the U.S., but was not conducted because of unresolvable concern over scientific validity and ethical permissibility. A month later, a journalist's interest is aroused when she learns that 4 of 10 persons in Dr. Bronson's vaccine trial died, allegedly from adverse reactions to the vaccine. When Dr. Bronson notifies you that 4 subjects died, you become concerned, and begin to question whether you have followed KWU's procedures and policies related to collaborations. You become more concerned when the journalist calls you to request information on the vaccine trial related deaths, and inquires about your role in the study. The journalist asks you for a copy of the research protocol and for the Institutional Review Board (IRB) minutes for the meeting that approved the research proposal.

You feel that very distinct tightening in the pit of your stomach. You know that the KWU IRB is responsible for reviewing and approving research with human subjects, but you did not think that KWU IRB approval of the this study was necessary because you were only analyzing blood samples, and would have no direct contact with the human subjects involved in the research. The collaborative research that you performed on this hypothetical case -- samples drawn specifically for research, and analysis of research data -- are considered research with human subjects.

Therefore, before starting this research collaboration, you should have adhered to the relevant policies and procedures of the Human Subjects Committee, which requires review and approval by the KWU IRB.

A true example of a problem with human subjects research that happened here in Kansas

A faculty member and his graduate student decided to perform a survey of middle school aged children in areas of western Kansas. Part of the survey involved questions about specific sexual practices, preferences, and attitudes of the children surveyed. Several parents of children surveyed took exception to the survey that their children were asked to fill out at school, and were angry enough to call the Governor's Office to complain. Predictably, the Governor called the President of the University and pointedly asked, "What's going on down there?" The administration discovered that the graduate student had not submitted his project for IRB approval, and the University was acutely embarrassed.

This was a serious problem caused by a relatively simple project. The episode could have been prevented if the graduate student and his advisor had reviewed and understood their IRB policies, and complied with the applicable requirements for conducting research involving human subjects.

A Review

In order to better understand the reasons for your responsibilities when performing research using human subjects, let's review a brief history of the ethical guidelines and the Federal regulations In 1946, 23 Nazi physicians went on trial because of research atrocities performed on prisoners of war. Subsequently, the Nazi War Crimes Tribunal issued the Nuremberg Code, which was the first internationally recognized code of research ethics.

The formal codification of the ethical guidelines for the conduct of research involving humans began in the late 1940's. While the Nuremberg Code and subsequent ethical guidelines represented the most enlightened thinking of the time, many well-intentioned researchers did not know about them or did not apply this guidance to their research activities. A series of abuses of research subjects came to public attention in the U.S. between 1953 and 1972, including the infamous Tuskegee Study on the natural history of syphilis conducted by Public Health Service Employees. These studies have led some to conclude that researchers could not be trusted to perform research on humans without oversight. In the 50's and 60's, when Federal funding for biomedical research increased dramatically, ethical safeguards and legal requirements were imposed on research activities involving human subjects.

The U.S. government, in dialogue with the research community, gradually designed one of the most comprehensive systems in the world for the protection of human research subjects. Laws, regulations, and public opinion challenged the research community to make the system accountable and operable. By congressional mandate, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was established in 1974 to make recommendations for the conduct of research involving humans. Oversight of the system was assigned to the Secretary of the Department of Health and Human Services, (DHHS). DHHS set as a goal: "High quality research accompanied by high standards of research ethics." The primary task of the Commission was to identify the ethical principles that would guide all research involving humans. The Belmont Report -- Ethical Guidelines for the Protection of Human Subjects was published in 1979.The principles of the Belmont Report govern all research supported by the U.S. government.

There are three guiding principles that are the cornerstones of the Belmont Report: Respect for Persons, Beneficence, and Justice. The Respect for Persons principle acknowledges the dignity and freedom of every person. It requires obtaining informed consent of all potential research subjects (or their legally authorized representative). The principle of Beneficence requires that researchers maximize benefits and minimize harm associated with research. Research-related risks must be reasonable in light of expected benefits. The principle of Justice requires equitable selection and recruitment, and fair treatment of research subjects.

In the early 1980's, revised regulations for the conduct of research involving humans were published, entitled Title 45 Code of Federal Regulations Part 46, Protection of Human Subjects (45

CFR 46). The Ethical principles of the Belmont Report are embodied in these regulations. Taken together, The Belmont Report and 45 CFR 46 articulate the minimal ethical and legal obligations of those who perform or support research involving human subjects.

Among other things, these regulations require that each institution conducting federally funded research adheres to the principles of the Belmont Report, and sets forth in writing ethical policies, procedures, and guidelines for protecting the rights and welfare of human subjects research. At KWU, this written assurance is done on a project-by-project basis, known as a Single Project Assurance (SPA). A sample SPA can be found online at

http://ohrp.osophs.dhhs.gov/humansubjects/assurance/spa.htm

The SPA places responsibility for protecting the rights of human subjects directly on you, the research investigator, and on KWU as an institution.

KWU feels it is important to comply with the federal guidelines regardless of whether your research is federally funded or not, as a protection for you and for the University. The KWU policies have been designed to help you do that. If you don't understand the requirements of the KWU policy, ask the Dean or the Chair of the IRB for assistance. Not knowing or not understanding the proper procedures is not an acceptable reason for non-compliance with applicable requirements. Failure to comply with the policies may constitute unethical behavior and a violation of the law, and it can lead to loss of research privileges for an individual, a laboratory, or for an entire research program.

Federal regulations and the KWU Human Subjects Committee policies apply to all research involving human subjects. By federal definition, research means a systematic investigation designed to produce generalizable knowledge. Research may involve direct interactions or interventions with subjects, such as obtaining data by taking medical histories, obtaining blood samples, diagnostic procedures, or performing surveys, at least in part for the purpose of gaining generalizable information. Research may also involve indirect activities, such as the analysis of specimens or data from people. Participation in these indirect activities, especially if you plan to publish (or co-author) the results, constitutes human subjects research. Federal policies define a human subject as a living individual about whom an investigator obtains either: data through interaction or intervention with the individual, or identifiable private information.

Research investigators have the fundamental responsibility to safeguard the rights and welfare of those participating in their research activities. In addition, our society has decided by law that that an objective review of human subjects research by a group of diverse individuals is most likely to protect human subjects and promote sound and ethical research. Therefore, when conducting research involving humans, Federal regulations and the KWU policies require prospective and continuing review and approval of the research by a committee called the Institutional Review Board (IRB). The Committee on Research Involving Human Subjects (IRB) is fundamental to the conduct of human subjects research at KWU, and at other research institutions both inside and outside the U.S. One reason IRBs are necessary is because research investigators have an inherent conflict of interest. They should be dedicated to promoting the welfare of individuals, but as researchers, they seek to generalize knowledge applicable to persons or groups other than the individuals in their studies. The second goal may be in conflict with the first.

IRBs, on the other hand, have one paramount responsibility: To protect the rights and welfare of human subjects. IRBs take into account national, and when appropriate, international ethical standards of research on a protocol-by-protocol basis. Protecting human research subjects is their primary responsibility. Protection of the rights and welfare of research subjects is a high priority worldwide. It is reflected in the Nuremberg Code, the United Nations Charter of Human Rights, the Declarations of Helsinki, the guidelines of the World Health Organization, and the ethical codes of many professional societies. The KWU IRB infrequently disapproves proposed research activities. Instead, they strive to work interactively with research investigators to assure that research design is excellent, that risks are minimized and expected benefits are maximized, and that consequent procedures are adequate. IRB members bring diverse skills, insights, and perspectives to the responsibility of reviewing research activities involving humans. Although the IRB system is not perfect, conscientious IRBs reassure the American public that the rights and welfare of human subjects are seriously considered by people who do not have a vested interest in the outcome of research. By exercising their responsibility, IRBs promote the protection of human subjects. IRB approval provides a significant affirmation of the scientific and ethical quality of the research, and therefore offers important validation to the research investigator and the institution. Keep in mind that the application of ethical principles, the Federal regulations (45 CFR 46), and KWU's policies are intended to balance society's interest in advancing scientific knowledge with its mandate to protect the rights and welfare of human subjects. IRB review of proposed research helps achieve this balance. Experience has shown that sound ethics and good science are compatible. The system, though not perfect, has worked well in the U.S. for over 30 years.

Please remember that the members of the KWU Institutional Review Board (IRB) are available to assist you. If you need advice or guidance, please contact a member of the committee.

Module 3: The IRB Review Process

Institutional Training for Human Subjects Research

Learning Objectives

Upon completion of this lesson, you should be able to identify:

1. Whether policies for the protection of human subjects apply to your research
2. When IRB review and approval are or are not required
3. What you are expected to do if your research involves human subjects, but you believe it is exempt from IRB review and approval.
4. Steps you must take before you collaborate in research involving human subjects at other institutions

Before beginning a research activity, you need to answer three critical questions about it:
1. Is the activity in which you will be engaged defined as RESEARCH?
2. Will the activity involve HUMAN SUBJECTS?
3. Does the activity require IRB REVIEW and APPROVAL

The following decision tree will help you answer these questions.

***The Institutional Review Board (IRB) will ultimately determine if the proposed project is exempt from review and approval, not the investigator*

Question 1. Is the proposed activity RESEARCH?

The definition of research in the KWU IRB policies is: a systematic investigation designed to develop or contribute to generalizable knowledge. Compare your proposed activity with the definition of research. And ask yourself the following questions:

Is the activity designed to produce generalizable knowledge? In other words, will the information derived from the activity be applicable to other cases?

Will the information be gathered systematically? In other words, will it be arranged so that conclusions can be drawn, and so that others can review those conclusions (i.e. activities which may later be published or publicly presented)?

If your answers to the previous questions are NO, then your proposed activity does not meet the definition of Research, and the KWU IRB does not apply to the activity.

However, if your answers to the previous questions are YES, then the activity IS research and you should proceed with Question #2 of the decision tree.

Important clue: The intent to publish the results of an activity, almost always means that it is research.

Question 2. Does the proposed activity involve HUMAN SUBJECTS?

If the activity is defined as research, then you need to ask, does the research involve any Human Subjects? A human subject is involved if:

The person is alive and

Data pertaining to the person will be obtained through:

Intervention (e.g., taking a blood sample)

Interaction (e.g., taking a medical or personal history).

A private/confidential source (e.g., from medical or personnel records).

Types of activities that are NOT covered by the definition of Human Subjects and are NOT subject to the IRB include research use of:

Samples from dead or cadaverous individuals

Samples or data available from commercial or public repositories or registries

Established cell lines available to qualified scientific investigators

Self-sustaining free-cell derivative preparations including viral isolates, cloned DNA or RNA

Note: Some of these activities may be subject to other laws or regulations. In most cases, the determination as to whether a particular research activity involves human subjects or not is not difficult.

Sometimes, the issue is not so clear. When in doubt, contact the Chair of the IRB for help or clarification.

If your proposed activity is RESEARCH, AND involves HUMAN SUBJECTS, you must submit a proposal to the KWU IRB. The KWU IRB will decide if your proposed activity is EXEMPT from review.

Question 3. Is your proposed activity exempt from IRB review and approval?
*** Remember that the KWU IRB makes the final determination if a project is exempt or not.*

There are six categories of Research involving Human Subjects that are EXEMPT from the provisions of IRB review and approval. The general rationale behind the six exempt categories is that, although the research involves human subjects, it exposes them only to very small physical, social, or psychological risks that are similar to the risks they take in everyday life - such as applying for a job, answering telephone surveys, tasting food, etc. Adults who engage in these and similar activities can be expected to understand and accept the small risks they are taking. Therefore, for this reason, they need no special protection offered by IRB review and approval.

Some of the most frequently conducted research activities that are EXEMPT from IRB review involve the study or collection of existing records or samples (e.g., pathological specimens, data) if these sources are publicly available or if the information is recorded by the investigator so that subjects cannot be identified directly or through identifiers linked to subjects. The Six Exemptions from 45 CFR 46 are:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as research on regular and special educational instructional strategies; or effectiveness of, or the comparison among instructional techniques, curricula, or classroom management methods.
2. Research involving the use of educational tests (cognitive diagnostic attitude achievement), survey procedures, interview procedures or observation of public behavior, unless information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers, linked to the subjects, and any disclosure of the human subjects responses outside of the research could reasonably place the subjects at risk of criminal or civil liability, or be damaging to the subjects financial standing, employability, or reputation.
3. Research involving the use of educational tests (cognitive diagnostic attitude achievement), survey procedures, interview procedures or observation of public behavior that is not exempt under #2 if the human subjects are elected or appointed public officials or candidates for public office or federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens if these sources are publicly available, or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
5. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine public benefit service programs, procedures for obtaining benefits or services under these programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.
6. Taste and food quality evaluation and consumer acceptance studies if wholesome foods without additives are consumed, or a food is consumed that contains a food ingredient at or below the level

and for a use found to be safe, an agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

An example of an exempt project: research analysis of stored human blood samples from which all identifiers have been completely removed. In this hypothetical example of exempt research, the samples stored are “existing,” (e.g., they are stored in a freezer), and there are NO IDENTIFIERS, therefore, subjects cannot be identified. Note that the identifiers can include names, initials, social security numbers, patient numbers or codes, or student ID numbers. Investigators should be cautious when using such identifiers in their research and should not assume that the use of codes renders research data exempt from IRB review.

Even if you believe your proposal is Exempt from IRB review and approval, you must complete the IRB Application for Review for a project involving Human Subjects.

Research Protocol Format

The format for a research protocol submitted by the principal investigator (PI) to the Committee on Research Involving Human Subjetcs (IRB) includes:

- A description of, and scientific rationale for the proposed research activity
- A discussion of the human subjects protection issues which addresses at a minimum:
  - The risks to subjects.
  - All experimental procedures that may be a risk.
  - The anticipated benefits to subjects, if any.

The usual format for a research protocol submitted by the principal investigator (PI) to the IRB includes:

- Subject selection, recruitment procedures, and the anticipated number of subjects.
- The proposed consent document and process to be used.
- Appropriate additional safeguards if potentially vulnerable subjects are to be enrolled. Potentially vulnerable subjects include the elderly, prisoners, children, cognitively impaired people, or people who are economically or educationally disadvantaged.

IRBs review research from the vantage point of protecting the rights and welfare of human research subjects and are required to evaluate proposed research activities using the following criteria:

1. The design of the study is consistent with sound scientific principles, ethical guidelines, and legal requirements.
2. Risks to subjects are minimized by using procedures that are consistent with sound research design and do not unnecessarily expose subjects to risk.
3. Risks to subjects are reasonable relative to anticipated benefits, if any, to subjects and the importance of the knowledge that may reasonably be expected to result.
4. The necessary elements of informed consent have been met and documented, and additional elements added when appropriate.
5. Additional appropriate safeguards have been provided if potentially vulnerable subjects are to be studied (e.g., children, prisoners, financially or educationally disadvantaged people).
6. Subject selection is equitable, with attention to the inclusion of minorities and both genders in study populations so that research findings can be applied to all persons at risk for the disease or condition under study.

In exercising their authority, IRBs may approve, disapprove, or table research protocols. However, IRBs are obligated not to approve any protocol that does not meet the criteria previously presented. Most often, the IRB approves a research protocol with required changes, referred to as stipulations.

Research may not begin until the stipulations have been met in writing by the P.I. Once the IRB approves your protocol and you reply to any stipulations that are required by the committee, you will receive an approval letter authorizing you to proceed with your project as described in your protocol. As part of its statutory responsibility to monitor ongoing human subjects research activities on campus, you will be required to update the committee at least annually on the status of your project.

Collaborative Research

Special provisions must be made if you intend to collaborate in non-exempt research involving humans at sites other than KWU. These provisions are required because when you collaborate, you accept some measure of responsibility for protecting the rights and welfare of the human subjects involved.

What constitutes "collaboration" by an investigator? Collaboration exists if the investigator expects "something in return" as a result of having participated in a research activity. "Something in return" could include data, authorship on a publication, samples, or even patent rights. KWU views authorship as prima facie evidence of collaboration. Collaborative activities may include but are not limited to:

Collection of specimens

Visits to institutions to perform research activities or clinical research

Exchange of information containing personal identifiers

Preliminary data collection activities involving human subjects

Substantive intellectual contributions to research techniques, protocol design, or interpretation of data.

More remote participation -- such as supplying important reagents, performing laboratory analyses, or analyzing data, may also constitute collaboration.

The degree of review required for collaborative research projects depends on the nature and the extent of the collaboration. In order to collaborate in research where subjects are enrolled other than at KWU, you should ask your collaborator if his/her institution has an IRB. Most organizations with which you are likely to collaborate will have a Multiple Project Assurance (MPA). A list of MPA-holding institutions is at a National Institures of Health (NIH) web site at http://helix.nih.gov:8001/ohsr. When you are collaborating with an investigator in an institution with an MPA in non-exempt research with human subjects, research may begin only when both you and your collaborator have formal documentation of IRB approval. When you want to collaborate in research at any non-MPA domestic site or in foreign countries, you need assurance that the rights and welfare of human subjects involved are appropriately protected. This is done by negotiating a Single Project Assurance (SPA). An SPA is a formal agreement between an institution and the NIH's Office for the Protection from Research Risks (OPRR) that the institution will abide by the ethical principles of The Belmont Report and 45 CFR 46 in its conduct of a specific collaborative research project.

Summary of Important Points in this Lesson

1. The requirements of the KWU IRB apply to all research involving human subjects, including collaborative activities that enroll subjects at sites other than KWU.
2. If you apply the decision tree shown in this lesson, you will be able to analyze whether or not a particular research activity involves human subjects.
3. When your research involves human subjects, you should not begin until it has received IRB review and approval OR is determined by the IRB to be exempt from IRB review.
4. The mandate of the IRB is to review research in order to protect the rights and safeguard the welfare of human subjects at KWU.

Module 4: The Belmont Report

Institutional Training for Research Involving Human Subjects

As a result of the revelations of serious abuses of human research subjects during the Nuremberg War Crimes Trials, The Nuremberg Code was formulated. It set standards for physicians and scientists using human subjects and was the Prototype code for human subjects research. Immediately after World War II, many questions were raised about the ethical propriety of use of human subjects in biomedical research. In July 1974, Congress passed The National Research Extension Act (PL 93-348), that created the Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. "In 1979, the Commission produced The Belmont Report, a statement of ethical principles and guidelines that assists in resolving the ethical problems that surround the conduct of research with human subjects"

The Report defined boundaries between PRACTICE and RESEARCH. Practice was defined as "interventions designed solely to enhance the well-being of an individual that has a reasonable expectation of success." Research was defined as an activity designed to test a hypothesis, draw conclusions, or develop or contribute to generalized knowledge, which uses a protocol format with objective procedures.

The Belmont Report developed three Basic Ethical Principles: Respect For Persons, Beneficence, and Justice.

Respect for Persons

This first principle incorporates at least two Ethical Convictions: that individuals should be treated as autonomous agents, and that persons with diminished autonomy are entitled to autonomy. It also incorporates at least two Moral Requirements: a requirement to acknowledge autonomy, and a requirement to protect those with diminished autonomy. An Autonomous individual is defined as being capable of self-deliberation and acting under direction of such self-deliberation. Not every individual is capable of self-determination. The extent of protection afforded certain individuals is dependent upon the risk of harm and the likelihood of benefit.

Beneficence

This second principle of the Belmont Report translates into two strict actions:

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

THE DILEMMA - deciding when it is justifiable to seek certain benefits despite the risks, and when benefits should be foregone because of the risks.

Justice

The Belmont Report considers the third principle of "Justice." Who should receive the benefits of research - and who should bear its burdens?? The selection of research subjects should be scrutinized in order to determine whether some classes (welfare patients, particular racial and ethnic minorities, or institutionalized persons) are selected because of their easy availability, compromised position, or manipulability rather than for reasons related to the problem.

During the 19th and early 20th century, the burden of serving as research subjects fell largely upon poor ward patients, while the benefits of knowledge and improved medical care flowed primarily to private patients. This violated the basic ethical principle of Justice.

Practical application of the three Basic Ethical Principles of The Belmont Report leads to consideration of the following requirements: Informed Consent, Risk/Benefit Assessment, and Selection of Subjects

Informed Consent

Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall, or shall not happen to them. This opportunity is provided when adequate standards of informed consent are met. The Consent Process contains three elements: Information, Comprehension, and Voluntariness

Information is the first of the three elements of the informed consent process. Specific items for disclosure generally include the research procedure, the purposes of the procedure, the risks and anticipated benefits, alternative procedures where appropriate, the provision to ask questions, and the freedom to withdraw at any time.

Comprehension is the second of the three elements of the informed consent process. It is critical that the subject understand the information conveyed. Since the ability to understand is a function of intelligence, maturity, language, it is necessary to adapt the presentation of information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information.

Voluntariness is the third of the three elements of the informed consent process. Agreement to participate in research must be secured under conditions free of coercion and/or undue influence. Coercion is defined as an overt threat of harm to obtain compliance. Undue Influence is defined as excessive, unwarranted, inappropriate, or improper reward to obtain compliance, especially with vulnerable subjects.

Assessment of Risks and Benefits

This process presents both an opportunity and a responsibility to gather systematic and comprehensive information about the proposed research. For different players, assessment of risk/benefit means different things. For the investigator, it is a means to examine whether research is properly designed. For the IRB, it is a means for determining whether risk to subjects are justified. For the participant, it is a means for assisting the determination of whether or not to participate. The requirement that research be justified on the basis of a favorable Risk/Benefit assessment relates to the ethical principle of Beneficence.

RISK refers to the possibility that harm may occur. Discussions of risk deal in "probabilities." BENEFIT implies something of positive value related to health or welfare. Benefits do not deal in probabilities. Risk/Benefit assessments are concerned with probabilities of possible harm, and with magnitudes of anticipated benefits. Risks and Benefits must be "Balanced" and in a "Favorable Ratio." This requires a systematic nonarbitrary analysis of risks and benefits insofar as possible.

There should be a systematic determination of the validity of the presuppositions of the research; of the nature, probability, and magnitude of risk that the investigator's estimate of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

There are several Important factors in the Assessment of the JUSTIFIABILITY of research. First, brutal or inhumane treatment of human subjects is never justified. Second, risks should be reduced to only those necessary to achieve the research objective. Third, researchers should consider alternatives, including the elimination of human subjects from the research design. Fourth, when significant risk is involved, strong justification is demanded. Fifth, when vulnerable subjects are involved, appropriateness of their inclusion must be demonstrated. Last, any relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the consent process.

Selection of Subjects

The final practical application of the ethical principles of the Belmont Report is Selection of Subjects. The principle of Justice gives rise to the moral requirements that there be fair procedures and outcomes in the selection of research subjects.

The Principle of Justice is relevant to the Selection of Subjects at two levels - Individual and Social Justice. In Individual Justice researchers must exhibit fairness and not offer potentially beneficial research to only some patients who are in their favor, or select only “undesirable” persons for “risky” research. Social Justice requires that distinction be drawn between classes based upon the ability of classes to bear burden of research, not placing further burden on already burdened persons. This means that there may be an order of preference for classes, i.e. adults before children, and that some classes (prisoners, mentally infirm, etc.) may be involved only in certain conditions.

When proposed research involves risks without a therapeutic component, less burdened classes than the infirm and/or institutionalized should be asked to accept the risks of the research - except where the research is directly related to specific conditions of the class involved. Certain groups such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may be continually sought because of their availability in settings where research is conducted. They should be protected against being involved in research for administrative convenience, or their socioeconomic condition.

Summary of Important Points in The Belmont Report module

1. The Belmont Report is a statement of ethical principles and guidelines that assists in resolving the ethical problems that surround the conduct of research with human subjects.
2. The three key ethical principles that are the cornerstone of The Belmont Report are: Respect for Persons, Beneficence, and Justice.
3. The investigator and the IRB must carefully evaluate the Risk/Benefit ratio to ensure that a proposed study has a reasonable chance for benefits in relation to probable risks.
4. Agreement to participate in research must be completely voluntary, and secured under conditions free of coercion and/or undue influence.
5. A key concept of The Belmont Report is the special consideration for and protection of potentially vulnerable subject populations - children, prisoners, certain racial minorities, those with diminished autonomy, etc.
6. The Belmont Report is a key reference document influencing federal regulations and guidelines for research using human subjects.

Module 5: Identifying, Assessing, and Minimizing Risks of Social and Behavioral Research

Institutional Training for Research Involving Human Subjects

*adapted from a presentation by Jeffrey Cohen, OPRR

The Institutional Review Board (IRB) - called the Committee for Research Involving Human Subjects, is responsible for reviewing and approving activities involving all research with humans at KWU. The performance of non-medical research in the social and/or behavioral arena has the potential for significant risks that go beyond invasive procedures or physical injury. These potential risks must be identified and considered by the IRB during the review and approval process.

Institutional Review Board (IRB) Responsibilities

As with other forms of research involving human subjects, KSU IRB review responsibilities include:

Identify risks to human subjects

Determine that risks are minimized

Determine that "risks to subjects are reasonable in relation to anticipated benefits"

Determine that subjects are adequately informed about any "reasonably foreseeable risks or discomforts"

Identifying Risks

Physical risks are fairly easy to identify. They would include injury, illness, or allergic reactions. However, it is important to remember that social and psychological risks are real risks too. Examples of social and psychological risks include: emotional distress, psychological trauma, an invasion of privacy, embarrassment, loss of social status, and loss of employment.

IRB's should not rely solely on investigators to identify risks. They should use investigator's knowledge coupled with resident or consultative expertise of the IRB to identify risks.

Minimizing Risks

The three best ways to minimize risk in social and behavioral research are to incorporate precautions, to incorporate safeguards, and explore alternative methods to achieve the same goals.

Risk/Benefit Analysis

IRB's must make a Risk/Benefit Analysis. This evaluation of a Risk/Benefit ratio is a subjective judgment. The IRB must decide whether anticipated benefit justifies asking subjects to undertake risks.

IRB should take into account different subject populations and individual differences among subjects. Some people are more sensitive or "at risk" than others, and some people would benefit from participation more than others would.

Informed Consent

Consent process should empower subjects to make their own determination about risk. Therefore, risks should be explained in simple terms that subjects can relate to everyday life experiences. Risks should be stated clearly and directly, not minimized or excused away. It must be clear to the subject that they are participating in research, and they should have enough information about what is expected of them to rationally decide whether or not they choose to participate.

Module 6: Ethics of Research with Human Subjects
American Psychological Association – April 2nd, 1998
Institutional Training for Research Involving Human Subjects

The American Psychological Association (APA) originally published "Ethical Principles in the Conduct of Research with Human Participants" in 1973, revised in 1983. Dramatic shifts have occurred in the context in which research occurs. This has resulted in new ethical challenges:

1. Behavioral research is expanding into biomedical contexts and settings where research priorities are being integrated with non-research institutions, communities, and diverse populations
2. Research involves a broad range of populations that may have special concerns, i.e., children, substance abusers, teen mothers, chronically ill, mentally ill or challenged, minorities, etc.
3. Sensitive issues have been added to research agenda, i.e., domestic violence, incest, sexual practices. These create tension between right to privacy and the need for careful research.
4. Advances in electronic technologies for gathering, analyzing, storing, and sharing data have raised new ethical issues not covered by earlier guidelines

Therefore, new codes published by Office for the Protection from Research Risks (OPRR) and the APA need to be addressed.

Ethics of Research with Human Subjects
Responsibilities of researchers can be sorted into four sets: Responsibilities to
science
society
students, apprentices, or trainees in research, and
participants of the research
The primary focus of this information will be on responsibilities to participants in research

Five basic principles are covered in the APA guidelines
Respect for Persons and their Autonomy
Beneficence and Nonmalfeasance
Justice
Trust
Fidelity and Scientific Integrity

Principle I - Respect for Persons and their Autonomy

Researchers should respect the human participants in their investigations as persons of worth whose participation is a matter of their autonomous choice. If persons have diminished autonomy, whether because of immaturity, incapacitation, or circumstances that severely restrict their liberty, they require special concern.

Principle II - Beneficence and Nonmalfesance

In the planning and conduct of research with human participants, the researcher should maximize the possible benefits and minimize possible harms from the research

Principle III - Justice
Risks and benefits of research should be equally shared by all. Unfortunately, this ideal is rarely fully achieved. Historically, risky new procedures were traditionally tried on ward patients with the benefits enjoyed largely by patients in private care. Threats to justice in psychological research arise from the almost inherent power differential between the experimenter and the research participant. Real or perceived power differentials necessitate safeguards against exploitation. Additionally, to

prevent gender inequities, Justice may require sampling designs that pertain to women as well as to men.

Principle IV - Trust

Researchers must establish and maintain a relationship of trust with participants in their research. Participation is based upon explicit agreement about the

Participant's experience
Consequences of the participation
Researcher's obligations, privacy, confidentiality, etc.

Principle V - Fidelity and Scientific Integrity

The researcher is committed to the discovery and promulgation of truth. The researcher must do good science, and must not falsify, misrepresent data, or falsely claim the work of others.

Scientific integrity -- truthfulness, is not open to compromise.

Informed Consent

Psychologists should have concern for the rights, dignity, and welfare of their research participants. They must carefully inform potential participants about the studies for which they are volunteering. This should include a clear statement of the purpose and procedures, the risks and benefits, and the obligations and commitments of both participants and researchers.

The resulting explicit agreement is generally documented through the use of a written consent form, which should be clear, fair, and not exploitive. Consent by the potential participant should be voluntary, informed, and given by a competent individual. It is the responsibility of the researcher to guarantee that such consent has been obtained prior to allowing a volunteer to participate in a research protocol.

The consent process is more than simply obtaining a signature from the potential participant, it is communicating necessary information to the participant. In order to do this, the researcher must first assess the participant's mental and legal ability to provide informed consent, as well as the participant's ability to comprehend the information being communicated. Individuals with limited autonomy (e.g., children, prisoners, psychiatric patients, etc.) are special populations in which specific safeguards are required.

The following areas are among those to be addressed in ensuring informed consent

1. Invitation to Participate - makes clear that participant is volunteering for research
2. Purpose of the Research - includes over all purpose of the research including research goals at the individual and group level, when appropriate
3. Basis for Participant Selection - is a clear statement as to why the participant is appropriate for the study. Allows prospective participants to exclude themselves if they do not believe they meet criteria for inclusion

The following areas are among those to be addressed in ensuring informed consent

1. Study Procedures - should be clearly described
   where will it take place
   who will be involved,
   what kind of work output will be involved
   any therapeutic interventions
2. Description of Risks and Discomforts - volunteers are unable to make informed decisions about whether to participate if they are not adequately informed.
3. Description of Benefits - In general, benefits can be summarized under the general category of anticipated additions to a systematic body of knowledge

4. Available Alternatives - primarily for therapeutic studies in which nonvalidated interventions are being studied

5. Noncoercive Disclaimer - participation should always be voluntary, and the decision to participate or discontinue participation should result in no penalty or loss of benefits to the participant. It is appropriate for researchers to

use reasonable noncoercive inducements to complete a study

state the consequences of early withdrawal (e.g., loss of monetary bonus for completing study).

6. Data Withdrawal - participants should also be informed they may withdraw their data from the study, stating time constraints for that data withdrawal

7. Incomplete Disclosure - information for participants to make an informed decision is necessary. At times, however, information may be withheld. Although not usually the first choice, it is sometimes necessary to omit information in order to protect the validity of the data collected

8. Offer to Answer Questions - it is important that participants know whom to contact if they have any problems or are injured during the study

Barriers to Informed Consent

Comprehension - the participant must understand the information imparted

Limited Competence - should consider those who lack legal capacity to provide consent, e.g., children, prisoners, mentally disabled, etc. (Federal regulations require that parents "permit" or "deny" permission for a child to participate in a research protocol)

Insufficient Time - participants need time to consider all relevant information

Study Design - There are some studies in which full information disclosure would confound study design, e.g. drug vs. placebo studies

Longitudinal Studies - in the course of long-term studies, conditions can change. It is important to remember that consent is an ongoing process

The consent process is a negotiation between the researcher and each potential participant, and requires clear and appropriate communication by researchers - coupled with respect for the autonomy of the individual considering research participation.

Privacy and Confidentiality

Respect for privacy is at the heart of the conduct of ethical research with human subjects. Privacy and confidentially derive from our respect for the autonomy of persons, our desire to do good (beneficence), and the principle of trust. Privacy refers to a person's interest in controlling other people's access to information about themselves. Confidentiality refers to the right to maintain private information divulged in the course of a professional relationship with a researcher.

Research participants can file a suit for "invasion of privacy under tort law. However, if the researcher has taken reasonable precautions and if the activity is approved by the IRB, they are usually dismissed.

Privacy has two major aspects. The first is the freedom to pick and choose the time and circumstances under which facts about a person, e.g., attitudes, beliefs, opinions, etc., are shared or withheld from others. The second is a person's right not to be given information that he or she does not want, ie., HIV testing results, standardized testing scores , etc.

Concerns about privacy can result from many sources; sociocultural values, characteristics of the physical environment, and characteristics of the cultural environment.

Anonymity provides excellent protection of privacy. Anonymity means that the identity of participants is not attached to the data, and can never be inferred from the data through any means, ie., social security numbers, addresses, etc.

Confidentiality refers to agreements with persons as to what may be done with their data. Researchers should refrain from sharing private information with others, unless authorized by the participant, or some other justification. Authorization is obtained through the informed consent process.

Confidentiality is becoming increasingly hard to maintain. It can be threatened in many ways
- legal actions
- government statutes
- access by third party groups
- data sharing
- technical lapses in security
- breaches during presentation of data

The best safeguard is to be well-informed about the law, understand the limits to confidentiality, have a well formed consent agreement, and understand techniques that protect data and preserve the participant's anonymity and privacy.

Maintaining Trust

The trusting relationship between the researcher and participants, established during the informed consent process, should be maintained as the research unfolds. The research team should continue to foster trust by treating research participants and research assistants as respected partners in the research.

Safety of Participants

Federal regulations require that "When appropriate, the research plan makes adequate provision for monitoring data collected to ensure safety of subjects." Unintended harms can occur during research. Ongoing monitoring may be necessary to evaluate this. Aside from obvious illness or injury, adverse reactions can take the form of shame, anxiety, embarrassment, or an actual pain or distress reaction to a physical stressor

One mitigation response may be to debrief participants at the end of a study, providing them with appropriate reassurances and information about normal reactions

Debriefing

One of the benefits to participants in research is an educational one. Researchers generally inform participants at the end of a study why it was conducted and how the results fit into what is already known. A debriefing session continues the information and education process for both the researcher and the participant. Establishing and maintaining trust and monitoring the safety of research participants is an ongoing process during research.

Researchers should take steps to ensure that:
- privacy of participants is continuously protected
- actual and potential harms are continuously monitored and acted upon as needed
- unique vulnerabilities of participants be given special attention
- there be appropriate and effective debriefing procedures
- when deception is used, steps to remove any residual negative effect be taken