

PACIFIC LUTHERAN UNIVERSITY

**HUMAN PARTICIPANTS REVIEW BOARD
POLICY & PROCEDURE MANUAL**

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CHAPTER 1: INTRODUCTION

I. Ethical Principles in Research; Role of HPRB

Pacific Lutheran University, through the operation of its Human Participants Review Board (HPRB), protects all human participants in research conducted in connection with the university from unnecessary and morally objectionable exposure to risk. Toward that end the board provides the following policies and procedures. These policies and procedures apply to all university research involving human participants. In particular, they conform to the Federal Policy for the Protection of Human Subjects, endorsed by the Department of Health and Human Service (DHHS) [1] and several other federal agencies that sponsor research. Conformation to the Federal Policy, referred to as the Code of Federal Regulations or “common rule,” is required for funding or other support from agencies endorsing the policy. Should there be any aspect in which the requirements of this policy and any then applicable federal regulation conflict, the federal regulation shall control. There are some situations in which this policy provides greater protection than federal regulations. In such situations, this policy shall control.

The basic ethical principles governing human participant research at PLU are those set forth in the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. [2]. The three main principles are: 1) respect for persons (e.g., applied by obtaining informed consent, giving consideration to privacy and confidentiality, and adding protections for vulnerable populations; 2) beneficence (e.g. applied by weighing risks and benefits); and 3) justice (e.g., applied by ensuring equitable selection of study subjects).

The HPRB has responsibility to ensure adherence to the above ethical principles and the “common rule,” as well as any other required federal or state regulations for the protection of human subjects. [3]. The HPRB is registered with the DHHS Office of Research Protections [OHRP] [registration # 4308] and is obligated to report non-compliance with federal regulations to the OHRP. It also provides ongoing education to the PLU community on human participant compliance issues. In performing its function, the HPRB aims to keep bureaucratic annoyances to a minimum. It seeks to promote research, but of course only that research in which the rights of human participants are protected. It views its role as counselor to investigators, not a mere tribunal that approves and disapproves projects. If the board identifies a potential problem while reviewing a research proposal or monitoring research in progress, it will actively work with the investigator(s) to produce a solution. Furthermore, the board respects the academic freedom of investigators in choices of subject matter and methodology, so long as these choices are consistent with basic human subjects protection guidelines.

[1] The DHHS Code of Federal Regulations cited this document is “Title 45 CFR 46.” The full Code is shown in Appendix A and is posted on the HPRB website: <http://www.plu.edu/~hprb>.

[2] U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report: Ethical Principles and Guidelines for the Protection

of Human Subjects of Research. DHEW Publication No. (05) 78-0012. Washington, D.C.: US Government Printing Office, 1978. [The Belmont Report is posted on the HPRB website: <http://www.plu.edu/~hprb>]

[3] Studies that involve investigations of drugs or other medical devices may also be subject to the Federal Drug Administration (FDA) guidelines [21 CFR 50].

II. Applicability of Policies & Procedures

The policies and procedures in this document apply to all research involving human participants that:

is conducted by or under the direction of any employee or agent of the university in connection with his or her institutional responsibilities (regardless of location of the project), or

is sponsored by the university, or

is conducted using any property, facility, or funds of the university, or

involves the use of the university's nonpublic information to identify or contact human research participants or prospective ones.

CHAPTER 2: DEFINITION OF RESEARCH

The term “research” means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition may be funded or unfunded, or may be conducted as a component of another program not usually considered research. For example, demonstration and service programs may include evaluation components that are research activities.

Precedent and practice has established the principle that certain kinds of activities might be called “human subjects research” but do not require review for protection of human subjects. Examples of such activities include: (a) accepted and established service relationships between professionals and clients where the activity is designed solely to meet the needs of the client; (b) research using only historical documents, and (c) research using only archaeological materials or other historical or pre-historical artifacts.

Pilot studies, pre-tests, and other “preliminary” investigations are research activities and must be reviewed by the HPRB unless they fall into one of the excluded categories listed above.

Classroom activities may include instructing students in research methodologies and techniques.

If the sole purpose of the activity is to teach research techniques or methodology and not to develop or contribute to generalizable knowledge, it is not considered research. However, if the faculty member or students practice the research methodologies on human beings, they are conducting research.

Quality improvement and quality assurance activities conducted solely for the purpose of maintaining or improving quality of services provided by an institution are not considered research activities. However, if the data collected are generalizable and intended to be shared outside of the institution through discussion, presentation, or publication, the activity qualifies as research. Sometimes, data from a quality improvement or quality assurance activity become of interest to the external community after they have been analyzed. In these cases, the research use of the data collected for another purpose must be reviewed by the HPRB.

The same distinction may apply to routine surveillance activities. For example, what began as a disease outbreak investigation by a public health agency may evolve into a research project. The researchers are obligated to seek human participant review as soon as the intent of the data collection or analysis changes. Often, the research activity for review consists of secondary analysis of the data collected originally for the purpose of protecting the public health.

CHAPTER 3: RESEARCH RISKS & LEVELS OF HPRB REVIEW

I. Determining the Level of HPRB Review

The term “risks for human participants in research” refers to possible physical harm as well as to psychological, social, legal, economic, and/or moral adverse effects. The HPRB reviews proposed research for the presence of these risks. The DHHS Code of Federal Regulations [45 CFR 46.101] defines three major categories of research for purposes of HPRB review and approval – 1) exempt, 2) expedited, and 3) full board review. A description of research activities that fall within each of the three categories, and the required HPRB review procedures are described in Sections II, III, and IV below.

The HPRB tracks all research conducted at PLU, regardless of the review classification. In all cases the investigator is required to prepare a research proposal before the research is begun. The proposal shall contain a complete description of the planned research, and it shall include provisions for the adequate protection of the rights and welfare of prospective research subjects and insure that any pertinent laws and regulations are observed. Samples of any informed consent forms that are necessary and appropriate should be included. Forms for preparing a HPRB application (with the required research proposal) are posted on the HPRB website [<http://www.plu.edu/~hprb>].

II. Exempt Research

A. Research Eligible for Exempt Status

The Code of Federal Regulations [45 CFR 46.101] identifies six specific types of research activities as “exempt” from the federal regulations due to their low risk potential for research participants. Research proposals that **ONLY** include these “exempt” activities do not need full HPRB review and approval. However, both the HPRB academic unit designate and the HPRB chairperson must approve the exemption.

Exempt activities include:

- (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods;
- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (a) the information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (b) any disclosure of the human subjects' responses outside 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, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior

that is not exempt under paragraph II.A.2 of this section, if: (a) the human subjects are elected or appointed public officials or candidates for public office; or (b) 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. [Note: To qualify for this exemption, the data, documents, records or specimens must be in existence before the project begins.]

(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: (a) public benefit or service programs; (b) procedures for obtaining benefits or services under those programs; (c) possible changes in or alternatives to those programs or procedures; or (d) 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 (a) wholesome foods without additives are consumed, or (b) a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or 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.

B. PLU Policy Regarding Exemptions

If an investigator's research is limited to the above activities, he/she may request that the study be granted "exempt" status when the proposal is submitted for academic unit review. The investigator's application must include a detailed explanation of how the research meets the requirements for exempt status. For example, in the case of a classroom survey in which students are research participants, the investigator would need to give evidence that student's responses are anonymous OR that there are procedures in place to ensure that students' responses will have no influence on grades or other aspects of the course. This would meet the requirement specified as exempt research in Section II.A.2 above.

The term, "anonymous" implies that no person, including the investigator(s), can link the identify of the research participants with the data collected in the research study.

Also note:

An investigator cannot exempt his/her own research proposal from HPRB review. He/she may request an exemption when submitting the proposal for review.

A faculty member supervising a student research project cannot exempt the same students' research proposal from HPRB review. If the supervising faculty member is the current HPRB academic unit designate, he/she must notify the HPRB chairperson of the potential conflict of interest. Another unit member will be assigned on a pro-tempore basis to review the proposal and forward his/her recommendation to the HPRB chairperson.

A research proposal cannot be given exempt status after the research is underway. Exempt status for research is only given for the specific activities outlined in the submitted research proposal. Any modifications in study aims or procedures need additional approval before they may be implemented.

Once a research proposal is granted "exempt" status, the study is not subject to ongoing HPRB monitoring so long as the aims and study procedures do not deviate from those described in the original proposal. Any modifications must be reported to the HPRB and may be subject to additional approval (see #4 above).

The following five categories of research are not exempt and always require HPRB review at the University level:

- studies involving prisoners;
- studies of pregnant women where the focus of the research is on the pregnancy or fetus;
- studies of fetuses in utero;
- studies of "minor" children (e.g., Washington State = under age 18) except for educational research (above) where there is no direct interaction with the child;
- studies using non-public records.

The five research categories above have additional federal requirements, specified in the DHHS Code of Federal Regulations, 45 CFR 46, subparts B, C, and D, that are not detailed in this HPRB Policy & Procedure Manual. Investigators planning research that falls into one or more of these categories are advised to consult the regulatory code. Copies of the regulatory code can be accessed on the HPRB website: [<http://www.plu.edu/~hprb>]

III. Expedited Review [45 CFR §110]

A. Definition of "Expedited Review" and "Minimal Risk"

The expedited review procedure consists of a review of the submitted research proposal by: 1) the HPRB unit designate, and 2) the HPRB chairperson or one or more experienced reviewers designated by the chairperson from among members of the HPRB in accordance with federal requirements. Expedited review is intended for research protocols that only involve "minimal risk." The federal code [45 CFR 46.102 (i)] defines "minimal risk" as situations in which: "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those

ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.”

B. Research Eligible for Expedited Review

The DHHS has established and published in the Federal Register a list of categories that may be reviewed through an expedited review process. FDA [21 CFR 46.111] has its own similar regulation. In general, there are nine categories of research that may qualify for expedited review. The current regulation and publication should be checked before requesting an expedited review. These research activities are not to be considered as “minimal risk” just because they are on the list; they also must meet the “minimal risk” criteria. The nine categories of research are as follows:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
 - a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.
 - b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
 - b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means;
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.
5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment

or diagnosis). Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. Note: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects 45 CFR 46.101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.

8. Continuing review of research previously approved by the convened HPRB, as follows:

- a) where: (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
- b) no subjects have been enrolled and no additional risks have been identified; or
- c) the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption, where categories two (2) through eight (8) above do not apply but the HPRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

C. PLU Policy on Expedited Review

If a proposed research protocol falls within one of the above nine categories, involves only minimal risk to its human participants, uses no more than minor deceptive practices, and the identity of the participants will not be known beyond the investigative personnel, the study qualifies for the PLU HPRB expedited review procedure. Expedited review is typically more rapid than full review. However, if a proposal is submitted for expedited review but is found to require full review, the process may actually be slower. Therefore, investigators should submit a proposal for expedited review only after carefully considering whether the proposed study only includes one or more of the nine activities qualifying for expedited review and meets the criteria for minimal risk.

IV. Research Requiring Full HPRB Review

All research that does not meet the requirements for “exempt” or “expedited review” status described above is subject to full review and approval by the HPRB. The board must review all research that involves more than minimal risks to participants, that incorporates more than minor deceptive practices, that allows the identity of participants to be known beyond investigative

personnel, or that includes the recruitment and/or data collection from children or other vulnerable groups such as, but not limited to, elders, prisoners, and patients in clinical settings.

CHAPTER 4 CRITERIA FOR HPRB APPROVAL OF PROTOCOLS

I. General Guidelines; Federal & State Regulations

The criteria for decisions on Human Participant Research Applications are specified in the federal regulations [DHHS 45 CFR 46.111], supplemented by PLU policies in this Policy and Procedure Manual and by applicable laws of the United States and the State of Washington. This section outlines the criteria that are used by the HPRB to make decisions regarding the approval of research protocols.

A. Basic Approval Requirements:

All funded and non-funded research (including research classified as exempt from board review) must meet the following federal requirements for HPRB approval.

1. Risks to subjects are minimized: a) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and b) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to study participants, and the importance of the knowledge that may reasonably be expected to result. *Note:* In evaluating risks and benefits, the HPRB is to consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HPRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
3. Selection of the research participants is equitable. In making this assessment the HPRB must take into account the purposes of the research and the setting in which the research will be conducted and is to be particularly cognizant of the special problems of research involving vulnerable populations such as children, prisoners, pregnant women, mentally disabled, persons or economically or educationally disadvantaged person.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by 45 CFR 46.116. *Note:* Conceptually, some sort of consent of participants is always necessary for research. See Section II below for a listing of the types of allowable consent procedures.
5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117.
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. *Note:* This refers to the safety and monitoring plan required for NIH clinical trials. Chapter 6, Section II.B of this Policy and Procedure Manual details the investigator's responsibility for data monitoring in these types of studies.

7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. *Note:* Research conducted at PLU must always provide adequate privacy and confidentiality.

8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

B. Other Approvals

Research approved by the HPRB may be subject to further appropriate review and approval or disapproval by PLU officials. However, those officials may not approve the research if it has not been approved by the HPRB [45 CFR 46.112].

II. Types of Informed Consent:

The following types of consents can be used for research studies.

A. Written Informed Consent.

Written informed consent is required for all research studies not given waivers for consent or permission for verbal consent by the HPRB. [45. CFR 46.117a]. In the consent form, information about the study is to be conveyed in a manner that is clearly understandable to the potential study participant. After the potential participant (or in the case of minors or incompetent subjects, a parent, guardian, or other interested agent of the subject) clearly understands all aspects of the information and has had any questions answered to the mutual satisfaction of all concerned, the participant or his or her legally authorized representative must sign the consent form before the research may proceed. Each signatory shall receive a signed copy. Investigators must also retain signed copies.

Written consent may be obtained by using: 1) a full consent form approved by the HPRB that includes all required elements for informed consent (see Section III below); or 2) a short version of the consent form, after a summary statement of the full consent information has been presented to the potential participant.

If a short version of the consent form is used, the HPRB must approve both the consent form and the summary statement, and there must be a witness to the oral presentation. The informed participant (or authorized representative) and the witness sign the short consent form. The summary statement is signed by: a) the person doing the presentation of the summary statement, and b) the witness. Copies of the signed consent form and the summary statement are given to the participant and/or his/her representative. [45 CFR 16.117 b(2)].

B. Spoken Informed Consent (verbal consent)

Verbal consent is acceptable for research when: a) the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context; or b) the only record linking

the participant and the research is the consent form, and the principal risk in the study is the potential harm resulting from a breach of confidentiality. [45 CFR 46.117c]
In cases of verbal consent, the investigator must provide potential participants with a written statement, (e.g., invitational letter), describing the research. In this statement, all of the applicable informational elements listed in Section III below must be transmitted clearly to the subject. The date that the information was given, and the potential research participants' verbal refusal or consent, must be documented by the investigator.

C. Child Assent with Parental/Guardian Consent

Assent is typically required of minors who are recruited for research studies [45 CFR 46.408]. The assent procedure should be appropriate to the age of the child. For example, children over the age of 12 typically could be asked to read, discuss, and sign an adult consent form. If the form is to be used by both adolescent and adult participants, it can be titled "assent/consent form. Children aged 7-12 can be given verbal information about a study and asked to sign a simplified version of a consent form. Younger children should be given a verbal explanation of the study aims and procedures and asked if they are willing to participate; if verbally agreeing, a parent/guardian can give written consent.

In general, a parent or guardian is required to sign a consent form for a minor to participate in research. An exception may be made for individuals, *e.g., adolescents*, who have been declared "emancipated" minors and for children in the state of Washington aged 14 years old and older who are seeking diagnosis or treatment for sexually transmitted diseases.

The HPRB can waive the child assent procedure in certain circumstances, as authorized in [45 CFR 46.117(c)] and [45 CFR 46.408 a,b]. Investigators submitting HPRB applications for studies involving children are advised to carefully review the DHHS Federal Code, Subpart D: Additional Protections for Children Involved as Subject in Research [45 CFR 46.401-46.409].

D. Waiver of Informed Consent.

The federal regulations allow the HPRB to modify or waive the requirement for informed consent in the following two situations:

1) a research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate or otherwise examine: a) public benefit or service program, b) procedures for obtaining benefits or services under these programs, c) possible changes in or alternative to those programs or procedures, or d) possible changes in methods or levels of payment for benefits or services under those programs, and the research could not practicably be carried out without the waiver or alteration;

2). a research study that: a) involves no more than minimal risk, b) cannot practicably be carried out without a waiver, c) where the waiver will not adversely affect the rights and welfare of participants, and (d) whenever appropriate, the subjects will be provided with additional pertinent information after participation. [45 CFR 46.116d]

A waiver of informed consent does not absolve investigators of their responsibility to inform the study participants of the nature and benefits of the project, when this is possible. For example, in the case of a mailed survey questionnaire, information that would normally be included in a consent form is included in a cover letter. In other cases, it may be possible to give the study participants additional pertinent information about the study after participation.

III. Required Elements for Informed Consent.

In seeking informed consent the following information shall be provided to each participant. [45 CFR 46.116]

The fact that the study involves research.

The purpose of the research, the expected duration of participation, and the procedures to be followed and identification of any procedures which are experimental.

Any reasonably foreseeable risks or discomforts to the participant.

Any reasonably expected benefits to the participant or others from the research.

Any appropriate alternate procedures or courses of treatment, if any, which might be advantageous to the subject.

The extent to which confidentiality of records that identify the participant will be maintained.

Any additional costs that the participant might incur from the research.

For research involving more than minimal risk, an explanation as to whether any compensation or follow-up medical treatment will be provided if injury occurs, and if so, what that consists of and where further information about it may be obtained.

Whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in event of a research-related injury to the subject.

A statement that participation is voluntary, and that refusal to participate or to continue to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled.

Where appropriate, a statement that the particular treatment or procedure may involve risks to the participant that are currently unforeseeable.

A statement that any significant new finding developed during the course of the research which may relate to the participant's willingness to continue participation will be provided.

Where appropriate, the following information will also be provided to participant:

Anticipated circumstances under which participation may be terminated without the participant's consent.

The consequence of a decision to withdraw and procedures for the orderly termination of participation.

The approximate number of participants in the study.

Furthermore, this information shall:

be in language understandable to the participant or the participant's legally authorized representative.

be conveyed under circumstances that all the participant or the participant's legally authorized representative sufficient opportunity to consider whether to agree to participate.

not include exculpatory language through which the participant or the participant's legally authorized representative is led to waive any of the participant's legal rights or release the investigator or university from liability for negligence.

IV. Deception in Research

In cases where the HPRB finds and documents that full disclosure of information to potential research participants is not possible without compromising the aims/goals of the research, the HPRB may approve a procedure that departs from the above requirements of informed consent. HPRB must find and document that the research will: a) involve no more than minimal risk to the participants or it can be persuasively claimed that they would have consented had they been fully informed in these additional respects, b) not adversely affect the rights and welfare of participants, and c) not practically be carried out without the waiver or alteration of consent procedures, and (d) whenever possible, the subjects will be provided with additional pertinent information after participation. If the data obtained in any way preserve their individual identity, they must consent to its further use. The necessary consent must be obtained in the manner described in Sections II and III above.

CHAPTER 5: HPRB APPLICATION & REVIEW PROCEDURES

I. Advance Submission

HPRB applications (research proposals) are to be submitted to the HPRB unit designate for review at least 30 days before the planned start-up date for the research. No definitive action such as recruiting participants, expending funds, or submitting a grant proposal to an outside agency may proceed before written approval for the research is obtained.

II. Content of Research Proposal.

Proposals submitted for review shall include the following :

a rationale explaining the nature, purpose, and potential benefits of the research;

a description of the research methods, with particular emphasis on procedures that pose a risk to participants, involve deception, or do not maintain the participant's anonymity to all parties beyond investigative personnel.

description of the potential participant pool and the means of recruitment; and

copies of any written recruitment materials and consent forms, or of information given retroactively to participants.

III. Review and Approval of Proposals

All research proposals are first submitted to the investigator's HPRB unit designate. The unit designate reviews the proposals for completeness, clarity, and eligibility for exempt or non-exempt status. He/she then forwards the proposals to the chairperson of the HPRB with either conditional approval as exempt or a recommendation for either expedited or full board review.

A. Requests for Exempt Status

Investigators seeking "exempt" status for research should prepare a research proposal, using the standard application form on the HPRB website. The proposal should clearly explain why the research is believed to be low risk and should qualify for exempt status.

The HPRB unit designate, (in consultation with the supervising faculty in the case of student research) will review the proposal. If the unit designate determines that the research proposal meets the requirements for exempt status, he/she will conditionally approve the study and forward two copies of the proposal (with the conditional approval) to the HPRB chairperson. The HPRB chairperson will review the submitted proposal and either approve the exempt status for the research, or designate the proposal for expedited review or full board review. He/she will forward one copy of the proposal (with his/her decision regarding the review status) to the Provost office and will retain the other copy of the proposal for his/her files.

When the research proposal is received in the Provost office, the HPRB administrative staff will notify the investigator and unit designate of the outcome of the review. If the study has been approved with exempt status, a "Certification for Exemption" will be sent

to the investigator. The research may proceed when the investigator receives the exempt certification. If the HPRB chairperson does not approve the exempt status for the research, the investigator will be advised of procedures to obtain the required review. Research studies approved for exempt status are not routinely monitored by the HPRB while the study is in progress. However, the investigator (or supervising faculty member in the case of student research) is responsible for informing the Provost office of the completion date of the approved research study.

B. Expedited Review:

From the viewpoint of the investigator, the procedures for expedited review are the same as those for full board review. An HPRB application form is completed and submitted with the research proposal and supporting documents. The proposal shall contain a complete description of the proposed research or study, including provisions for the adequate protection of the rights and welfare of prospective human research participants and assurance that the pertinent laws and regulations are observed. Samples of study materials, communications with prospective participants and any informed consent forms shall be included.

For studies meeting the eligibility criteria for expedited review, a recommendation for expedited status is made by the unit designate, and two copies of the research proposal are submitted to the HPRB chairperson. The proposal is read by at least one board member who takes one of two actions: (i) referral of the proposal to the full board for review, or (ii) approval of the proposal with or without adding stipulations and/or recommendations. Note: Reviewers doing expedited reviews cannot disapprove research proposals.

In the case of stipulations, the approval is conditional, and the investigator must respond to the stipulations in a communication with the HPRB member. Upon receipt of a satisfactory response to the stipulation(s), the HPRB member may then grant final approval. In the case of recommendations, the investigator may proceed without further communication from the HPRB. If the board member judges the proposal to require full board review, the proposal shall be relayed to the full board and the investigator notified in writing to that effect.

C. Full Board Review:

If the unit designate recommends full board review of a submitted proposal, five copies of the proposal are to be forwarded to the HPRB chairperson with the recommendation of the unit designate. When the application is received, it will first be screened for completeness. If information is missing from the application, the investigator will be contacted and requested to supply the missing information. Applications are assigned to one of the monthly Board meetings for review on a “first come, first served” basis. A week or more before the scheduled meeting, applications are posted on the confidential HPRB website for review by board members.

Upon review, the Board shall make one of three determinations:

1. Approval.

Approval only if specified modifications are made. The Board will explain in writing why the proposal, as submitted, is considered unacceptable. The investigator may not take any definitive action such as recruiting participants, expending funds, or submitting a grant proposal to any outside agency that requires institutional review board certification until a proposal, with modifications be approved by the Board.

2. Disapproval.

If neither of the two previous options received at least three votes, the proposal will be considered “disapproved” by the Board. If a proposal is not approved, the Board will in explain, in writing, the rationale for the disapproval and notice of the appeal options under this policy. Without approval the investigator shall not use any university facilities or funds for the research, nor in any way claim university sponsorship. The university will not incur any obligation to protect an investigator who proceeds with the research nevertheless.

IV. Approval Timeframes:

Research activities are approved for no longer than a period of one year and may be approved for a shorter period of time commensurate with the level of risk posed by the research and the projected project duration. [45 CFR 46.109]. The approval letter sent to the investigator will specify the time period that research activities may be conducted. No research data may be collected outside of the designated time period. Research projects that cannot be completed in the approved time period will need a continuation approval (see Section V below).

When reviewing the initial proposal, the following criteria will be used by the HPRB to determine the frequency of study review: 1) the probability or magnitude of anticipated risks to participants, 2) any medical conditions of the proposed participants and their susceptibility to problems as a result of enrollment in the protocol, 3) qualifications of the investigator and other members of the research team, 4) past history of the investigator(s) and research team in adherence to HPRB guidelines, 5) specific experience of the investigator(s) in similar research protocols, 6) the nature and frequency of adverse events in similar research, 7) the general vulnerability of the population being studied, and 8) other factors deemed relevant to the HPRB.

V. Applications for Continuation of Previously Approved Studies

The HPRB shall be informed at least annually of the status of all research. As a courtesy to investigators, administrative staff assigned to HPRB support functions will send a notice and Status Report Form to the investigator two months before the end of a given approval period. An investigator who does not receive such a reminder should contact the Provost Office as soon as possible to request a copy of the Status Report. If the research is proceeding in relation to participants as outlined in the research protocol, the investigator is to note this on the Status Report Form. If there are any significantly increased risks to participants, deceptive practices in the research, or if any other changes have occurred (or are expected to occur) that could affect the rights and choices of participants, the investigator shall not wait until the annual status report but shall promptly submit updated information to that effect to the board for its review.

VI. Study Modifications.

It is recognized that changes to a research study and informed consent documents may be required as the research proceeds. However, proposed modifications must be approved by the HPRB before they are implemented. The only exception to this requirement is a procedural change that may be necessary to eliminate an apparent immediate hazard to a research participant. If this occurs, the investigator must submit an amendment to the original proposal to make it consistent with the changes.

If a research study is completed prior to the end of the approval period, the investigator should submit a Status Report Form to the HPRB, noting the date of study closure.

VII. Appeal Process

If an investigator believes that the HPRB review process was not fairly executed and that it resulted in an unduly restrictive decision regarding the proposed research, he/she may appeal the decision. He/she should first discuss the matter with the HPRB chairperson, taking care to explain the reasons for believing that the research procedures are in compliance with University policy and federal and state regulations. If the issue cannot be resolved satisfactorily by negotiation, the investigator may appeal the decision of the reviewer(s), in writing, to the Provost.

Upon receipt of an appeal the Provost shall convene an ad hoc committee, constituted so as to fulfill federal requirements, and with the majority of members being past but not current members of the HPRB. The ad hoc committee will consider the appeal, and within 60 days, communicate its decision in writing to the Provost, giving its reasoning for the decision. A copy of the decision will be given to the investigator and the current HPRB chairperson, and documented in the minutes of the next convened HPRB meeting.

Any person who proceeds with collecting or analyzing research data, intentionally disregarding the need for official approval of the HPRB for the research, will be in violation of HPRB policy and will be subject to administrative sanctions, including the termination of research privileges at the University.

CHAPTER 6: MONITORING THE CONDUCT OF RESEARCH

I. Oversight Responsibilities

Protection of human participants in research is a shared responsibility of many persons in the academic community, including those directly engaged in the conduct of the research (e.g., investigators and study personnel), those with specific review and oversight responsibilities (HPRB and its academic unit designates), University administrative officers, and the wider academic community.

All persons engaged in the conduct of research are expected to be aware of PLU policies regarding human participants research and are obligated to report observed violations to the HPRB. The HPRB provides ongoing education on human participant[s] research for the University community through new faculty orientation sessions, online education/training modules, and individual consultations as requested. Members of the HPRB, the academic unit designates, and all investigators are required to complete human participants research training approved by the HPRB. Persons engaged in research support roles are encouraged to complete the HPRB approved training modules or the online Human Subject Assurance Training, available at the OHRP website.

A. Investigator Responsibilities and Reporting Requirements

The primary responsibility for the day-to-day protection and welfare of research subjects lies with the investigator who submitted the HPRB application. This person is expected to implement the study in a safe and timely manner, according to the approved proposal, and to keep the HPRB informed of any unanticipated problems or adverse events. During the course of the study, and up to three years after completion of a study, he/she must keep detailed records of all research-related activities, (e.g., lists of enrollments, copies of consent and assent forms, minutes of meetings, lists of meetings and attendees), and make the records available for HPRB review upon request.

In the case of student research, the student and supervising faculty member share responsibility for monitoring the safety of human participants, and are held accountable for these activities.

B. Unexpected Events and Adverse Reactions

During the course of a research study, unexpected events and adverse reactions may occur to a study participant, other individuals associated with the participant, or to key personnel associated with the research study. An unexpected event is an unanticipated problem associated with any aspect of the research study that may involve risks to the enrolled study participants and/or to other individuals who may or may not be directly associated with the research study. This type of event can happen in both clinical and non-clinical (behavioral or social science) studies. An adverse reaction is an undesirable and unintended, though not necessarily unexpected, result of therapy, study interventions or activities. These generally occur in clinical research and only apply to participants enrolled in the study. Investigators are responsible for ongoing monitoring of their studies for unexpected events and adverse reactions, and reporting these situations to the HPRB if they arise.

For further clarification of the investigator role for human participant protection, see the document, “Investigator Role in the Responsible Conduct of Research,” posted on the HPRB website.

II. HPRB Monitoring of Approved Studies

The HPRB tracks all research studies. It also has procedures for systematic monitoring of all non-exempt studies while they are being conducted. If it finds any human subject concerns or violations (or if these are reported to the HPRB), it will make every attempt to work collaboratively with the principal investigator to ensure that corrective actions are taken.

A. Routine Monitoring

The following HPRB procedures are used for routine monitoring of approved studies:

Review of investigators’ credentials and HPRB training certifications

Primary Investigators must show evidence of having completed the HPRB-approved human participant research training before start-up of a research project.

A copy of the training certificate can be attached to the HPRB application or sent to the Provost office.

Computerized tracking of research studies, with documentation of HPRB application approval dates, annual reviews, and notations of any protocol changes or reported human subject concerns;

Annual (and other required) Status Reports;

Administrative staff assigned to support HPRB functions routinely monitor non-exempt research studies in the tracking system for timely submission of Status

Reports and any other required documentations from investigators. Quarterly reports are generated and submitted to the HPRB. An alert will be sent to any investigator having a delinquent Status Report, reminding him/her that the approved study period has lapsed and the study may not proceed. If there is no acknowledgement within 10 days, direct contact will be made with the investigator to determine whether the research study has been completed. In the event that the study is still in progress (without the required Status Report), it is in violation of HPRB policy, and the investigator will be instructed to desist from all project activities. The violation will also be recorded in the HPRB minutes.

Student research projects are often associated with coursework and have HPRB approval (if needed) for one or two semesters. The supervising faculty member is responsible for ensuring that the HPRB is kept informed of the status of the student project. If the approved project period has lapsed without notification of

project completion, the faculty member will be contacted and asked to submit the required status report.

1. Random audits

Random samples of non-exempt studies in progress may be selected for periodic audits. When this occurs, a designated person from the HPRB meets with the investigators of the audited studies to discuss the progress of the studies and review the study records. A report is generated for the HPRB and feedback is given to the investigators.

2. Unexpected Events/Adverse Reactions

If a report of an unexpected event or adverse reaction is filed with the HPRB, an investigation is held to determine the seriousness of the situation and its potential effect on the safety of study participants and other persons (risk/benefit analysis). If the safety concerns can be adequately addressed by modifications of study procedures, the investigator will be asked to make the modifications and submit an amendment to the original proposal, verifying his/her intent. If risks to the research participants or other persons cannot be adequately addressed by procedural modifications, the research study will be suspended or terminated.

3. Follow-up on reported human subject concerns and/or violations

Any telephone calls or other verbal or written communications that come to the attention of the Provost office concerning human participant matters in individual studies will be forwarded to the HPRB chairperson for follow-up. An investigation of the concern or allegation will be initiated within 10 working days.

B. Additional Monitoring and Verification of Safety and Compliance

There may be situations in which the HPRB determines that it needs to do additional monitoring, and/or collect information from sources other than the investigator to verify that no material changes have occurred in the study since previous HPRB review or that no other human subject violations have occurred. Situations that may require additional monitoring and/or verification include: a) studies that involve unusual levels or types of risks or that include vulnerable groups as research participants, b) a study conducted by an investigator who has previously failed to comply with HPRB or federal regulations, or c) concerns raised about changes occurring in a study, based on information in submitted Status Reports, or d) human participant concerns reported to HPRB members or the Provost office. .

Various sources may alert the HPRB of the need for an independent review of an ongoing study. Inquiries may be submitted from: committees or administrative units within the University; community agencies collaborating on a project; enrolled research participants or family members; the news media; a funding agency; the Office of Research Protections (OHRP) or other federal or state agencies.

In these cases, the HPRB will determine whether: 1) an audit of the research study needs to be conducted by the Provost's office, 2) the research should be suspended, and/or 3) if

additional administrative actions need to be taken. If an investigation is required, a designated person from the HPRB will meet with the investigator to discuss the reported concerns/violations (without revealing the identity of the person(s) initiating the report). He/she is authorized to review any study documentations, interview study staff and/or study participants, or directly observe the research proceedings to obtain information needed for an impartial assessment of the situation. Needed corrective actions will be discussed with the investigator, and a written report will be given to the HPRB and Provost. Additional follow-up visits or contacts may be initiated by the HPRB to verify that corrective actions have been taken. Oversight of assigned senior researchers and/or HPRB members can be used to ensure that no more violations occur.

C. Federally-Funded Clinical Trials.

Federally-funded research studies that include activities classified as Phase I or Phase II clinical trial research by the National Institutes of Health (NIH) or other federal funding agencies are required to have a “Data and Safety Monitoring Plan” in place to document safeguards for research participants. The HPRB follows and endorses federal policy with regards to the need for additional monitoring for such intervention studies. If an investigator intends to submit a protocol that entails clinical trials research, a preliminary Data and Safety Monitoring Plan should be submitted with the HPRB application. The HPRB will consult with the investigator on development of the Data Safety and Monitoring Plan or provide advise on external resources. Investigators planning to participate in multi-center collaborative research are encouraged to seek guidance from established clinical trials networks and the DHHS Office of Research Protections (OHRP). This should be done in addition to completing the required HPRB-approved human participant research training.

D. Suspension or Termination of Research

The HPRB has the authority to suspend or terminate at any time its approval of research that is not being conducted with the HPRB’s requirements or that has been associated with unexpected serious harm to subjects [45 CFR 46.113]. Any suspension or termination shall be conveyed promptly to the principal investigator, with reasons for the board action conveyed in writing.

E. HPRB Reporting Requirements

The DHHS regulations [45 CFR 46.103(a) and (b) (5) require that institutions have written procedures to ensure that the following incidents related to nonexempt research conducted under an OHRP-approved assurance are promptly reported to the OHRP:

any unanticipated problems involving risks to subjects or others;

any serious or continuing noncompliance with federal policy or requirements or determinations of the HPRB;

any suspension or termination of HPRB approval.

Any of the above problems will be promptly reported to appropriate institutional officials, and to the DHHS Office of Research Protections (OHRP) when applicable.

Incident reports submitted to the OHRB will include the following information: a) name of the University (PLU); b) full title of the research study; c) name of the primary investigator (person currently responsible for conduct of the research); d) number of the study assigned by the HPRB (and any number of any applicable federal award, e) a detailed description of the problem, and f) actions the University is taking or plans to take to address the problem.

The Provost or his/her appointed representatives are responsible for communications with the OHRP and/or other governmental or regulatory agencies for compliance purposes. The HPRB will cooperate with any compliance investigations initiated by the University or the OHRP.

CHAPTER 7: HPRB DOCUMENTATIONS

I. Maintenance of Research Records

A. The university shall maintain adequate documentation of HPRB activities, including the following:

Copies of all research proposals submitted for notification or review.

Copies of all progress reports, changes in research as related to the rights of participants, and reports of injuries to participants.

Minutes of HPRB meetings, in sufficient detail to show attendance, board actions, the vote on these actions in terms of the number of members voting for, against, or abstaining, the basis for requiring changes in a proposal or disapproving it, and a brief summary of the discussion of controverted issues and their resolution.

Records of continuing notification and review activities and copies of all correspondence between the board, its unit designates, and investigators.

The written policies and procedures of the board.

B. For each non-exempt study approved by the HPRB, the retained records shall include: the research proposal and supporting documents;

copies of all correspondence between the HPRB and investigators; including copies of all progress reports, changes in research as related to the rights of participants, and reports of injuries to participants.

adverse event reports of injuries to participants or unapproved changes in study procedures;

records of initial and continuing review and any amendments to the proposal and/or consent forms;

progress reports submitted by investigators and statements of significant new findings provided to study participants.

C. Studies granted exempt status by the HPRB are not subject to ongoing HPRB monitoring and record retention so long as there is not a change in the proposed aims or procedures. However, the dates of the project start-up and completion of exempt studies are recorded in the HPRB tracking system.

II. Timeframes for Record Retention

All HPRB records required by this policy shall be retained for at least three years. Records related to research that is conducted shall be retained for at least three years after completion of

research, and will be accessible for inspection and copying by authorized representatives of the OHRP and other federal agencies.

Investigators conducting exempt studies are advised to retain study forms and documentation of research activities for three years or as required by the academic administrative unit, and they are responsible for notifying the HPRB of the date of completion of the study.

CHAPTER 8: HPRB MEMBERSHIP & MANAGEMENT

I. Board Member Appointments & Responsibilities.

- A. The HPRB consists of five members appointed by the university president.
1. At least three members of the HPRB shall be faculty.
 2. One member shall not be otherwise affiliated with the university and shall not be a part of the immediate family of someone who is affiliated with the university.
 3. Members shall include at least one whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.
 4. The HPRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the HPRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas.
- B. Members of the HPRB are appointed by the president for three-year overlapping terms. The Provost, deans, and other faculty information sources may be consulted in order to identify appropriately qualified members to serve on the board.
- C. Members shall not vote on proposals in which they have a conflict of interest. The board may invite individuals with special competencies to assist with proposal review. These individuals will not vote.

II. Unit Designates

- A. Administrative units of the university in which research is conducted with human participants shall have HPRB unit designates.

The unit designates shall be chosen within units that conduct research with human participants.

The key responsibilities of the unit designates are to: a). receive all proposals from investigators in their units; b) conditionally approve proposals that are judged by the designate to have exempt status; and c). forward all proposals to the chairperson of the HPRB with either a designation of exempt or a recommendation for either expedited or full board review.

The unit designates also facilitate communications between the HPRB and staff and faculty in their respective units.

III. Liability

The university will defend and indemnify the HPRB members and unit designates for claims that arise from their good faith performance of duties as HPRB members or unit designates.

IV. Physical Resources and Administrative Support

The HPRB operates out of the Provost office, where physical space is available for storage of confidential materials and convening of board meetings. The HPRB also has access to other conference rooms on campus that are adequate for proposal presentations and discussions.

The Provost office provides administrative staff support for HPRB functions. Typical support tasks include activities such as facilitating communications between the HPRB and investigators regarding the submission and disposition of research proposals, maintaining confidential research files, managing the computerized tracking system (including entry of new studies, status report notifications, reports for HPRB review), and managing HPRB correspondence. Additional support for compliance oversight is provided via internal faculty/staff assignments or by external consultation contracts as the need arises.

Financial resources are available thru the Provost office to support any required human participants research training for the HPRB, unit designates, and investigators. Additional funding is available for institutional memberships in organizations that support human participant research standards, and for the HPRB chairperson or other designated Board members to purchase needed education materials or attend national and regional conferences on human participant research.

CHAPTER 9: DEFINITIONS

1. “Risks for human participants in research” refers to possible physical harm as well as to psychological, social, legal, economic, and/or moral adverse effects.
2. “Research” means a systematic investigation designed to develop, demonstrate, or contribute to generalizable knowledge. Activities that meet this definition constitute “research” for purposes of these regulations, whether or not they are supported or funded under a program which is considered research for other purposes. For example, some “demonstrations” and “service” programs may include research activities. [46.102d]
3. “Human subject” or “participant” means 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. “Intervention” includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes. “Interaction” includes communication or interpersonal contact between investigator and subject. “Private information” includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) to constitute research involving human subjects. [46.102f]
4. “Investigative personnel” are all persons who conduct the research.
5. “Classroom research” is all research conducted as part of instruction in an approved Pacific Lutheran University course; as long as the study participants are or have been students, instructors or assistants. The participants must be informed of the connection with the course.
6. “Non-classroom research” is all research to which HPRB guidelines are applicable and which is not “classroom research” as defined in subsection d above.
7. Research involving “virtually no risk” is that in which there is no increase in a participant’s risk due to participating in the research, as ascertained to the best of our current knowledge. This designation is not precluded simply by the possible risk that it might be said is present merely because we do not know that it is not.
8. “Minimal risk” means that the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [46.102.i]
9. “Minor deceptive practices” (“minimally deceptive practices”, “minimal deception”) are those practices of withholding or altering the information required by informed consent which: a)

involve a situation of no or minimal risk, and b) do not create the expectation by subjects of more than minimal risk.

10. “More than minor deceptive practices” are those practices of withholding or altering the information required by informed consent.

11. “Conflicts of interest” by a board member involve being an investigator, a subject, a financial supporter, or an administrative supervisor of an investigator in or financial supporter of the research being reviewed. This list exemplifies but does not exhaust potential conflicts of interest.

12. “Certification” means the official notification by the university to the U.S. Department of Health and Human Services in accordance with the requirements that a research project or activity involving human subjects has been reviewed and approved by the HPRB in accordance with the approved assurance on file at DHHS. [46.102,j]

13. “University” means Pacific Lutheran University

14. “Board” means the Human Participants Review Board of Pacific Lutheran University

15. “Stipulations” are modifications in the research protocol that are required by the HPRB before approval can be granted.

APPENDICES

The Belmont Report

Office of the Secretary

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

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

April 18, 1979

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

SUMMARY: On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, there-by creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: **(i)** the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, **(ii)** the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, **(iii)** appropriate guidelines for the selection of human subjects for participation in such research and **(iv)** the nature and definition of informed consent in various research settings.

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It 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. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402. Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a

statement of the Department's policy. The Department requests public comment on this recommendation.

**National Commission for the Protection of Human Subjects
of Biomedical and Behavioral Research
Members of the Commission**

Kenneth John Ryan, M.D., Chairman, Chief of Staff, Boston Hospital for Women.

Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University.

Robert E. Cooke, M.D., President, Medical College of Pennsylvania.

Dorothy I. Height, President, National Council of Negro Women, Inc.

Albert R. Jonsen, Ph.D., Associate Professor of Bioethics, University of California at San Francisco.

Patricia King, J.D., Associate Professor of Law, Georgetown University Law Center.

Karen Lebacqz, Ph.D., Associate Professor of Christian Ethics, Pacific School of Religion.

**** David W. Louisell, J.D., Professor of Law, University of California at Berkeley.*

Donald W. Seldin, M.D., Professor and Chairman, Department of Internal Medicine, University of Texas at Dallas.

**** Eliot Stellar, Ph.D., Provost of the University and Professor of Physiological Psychology, University of Pennsylvania.*

**** Robert H. Turtle, LL.B., Attorney, VomBaur, Coburn, Simmons & Turtle, Washington, D.C.*

**** Deceased.*

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Ethical Principles & Guidelines for Research Involving Human Subjects

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the prototype of many later codes(1) intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects. This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

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Part A: Boundaries Between Practice & Research

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called "experimental" when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.⁽²⁾ By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.⁽³⁾

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

Part B: Basic Ethical Principles

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions.

Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence and justice.

1. Respect for Persons. -- Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

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

complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children -- even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. Justice. -- Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

Part C: Applications

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. 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 for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires

the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension. Special provision may need to be made when comprehension is severely limited -- for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disable patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence -- especially where possible sanctions are involved -- urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits. -- The assessment of risks and benefits requires a careful array of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike, "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harm and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been

protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: **(i)** Brutal or inhumane treatment of human subjects is never morally justified. **(ii)** Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. **(iii)** When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject -- or, in some rare cases, to the manifest voluntariness of the participation). **(iv)** When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. **(v)** Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. Selection of Subjects. -- Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

(1) Since 1945, various codes for the proper and responsible conduct of human experimentation in medical research have been adopted by different organizations. The best known of these codes are the Nuremberg Code of 1947, the Helsinki Declaration of 1964 (revised in 1975), and the 1971 Guidelines (codified into Federal Regulations in 1974) issued by the U.S. Department of Health, Education, and Welfare. Codes for the conduct of social and behavioral research have also been adopted, the best known being that of the American Psychological Association, published in 1973.

(2) Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual, and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not confuse the general distinction between research and practice. Even when a procedure applied in practice may benefit some other person, it remains an intervention designed to enhance the well-being of a particular individual or groups of individuals; thus, it is practice and need not be reviewed as research.

(3) Because the problems related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.

Link to DHHS regulations - <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>

Link to FDA regulations - <http://www.fda.gov/oc/ohrt/irbs/appendixb.html>