

**INVESTIGATOR'S MANUAL
ON RESEARCH WITH HUMAN SUBJECTS**

PLEASE NOTE: THIS MANUAL IS CURRENTLY UNDERGOING MAJOR REVISIONS AND CONTAINS OUTDATED INFORMATION. THE MOST CURRENT INFORMATION IS CONTAINED IN THE FAQs ON THE OPHS WEBSITE. PLEASE CONTACT YOUR PROGRAM ANALYST IF YOU HAVE ANY QUESTIONS

**UNIVERSITY OF OREGON
COMMITTEE FOR THE PROTECTION
OF HUMAN SUBJECTS/
INSTITUTIONAL REVIEW BOARD
(CPHS/IRB)**

TABLE OF CONTENTS

I. INTRODUCTION	3
II. ABBREVIATIONS/DEFINITIONS	4
III. OVERVIEW OF PROCESS	7
DETERMINING WHETHER THE PROJECT NEEDS TO BE REVIEWED	7
COMPLETING THE PROTOCOL.	8
REVIEW AND SIGNATURE OF FACULTY SUPERVISOR (student research only)	8
CHANGES IN APPROVED PROCEDURES (modifications).....	9
CONTINUING PROJECTS AND TERMINATION OF PROJECTS.....	10
REPORTING UNANTICIPATED PROBLEMS AND ADVERSE EVENTS.....	10
IV. CRITERIA FOR APPROVAL	11
EDUCATION REQUIREMENT	11
CPHS/IRB REVIEW AND APPROVAL	11
APPEAL PROCESS	12
V. REVIEW CATEGORIES	13
EXEMPTION CATEGORIES	13
EXPEDITED REVIEW CATEGORIES	14
FULL REVIEW	16
social/behavioral and biomedical IRBs.....	16
VI. RISKS TO SUBJECTS	18
EXAMPLES OF RISKS.....	18
Physical risks	18
Psychological risks.....	18
Social/Economic risks.....	19
Loss of Confidentiality.....	19
Legal risks.....	19
MINIMAL RISK	19
VII. INFORMED CONSENT	21
OBTAINING INFORMED CONSENT.....	21
ADDITIONAL ELEMENTS IF APPROPRIATE	22
Explanation of compensation or medical treatment if injury occurs	
DOCUMENTATION OF INFORMED CONSENT.....	23
WAIVER OF DOCUMENTATION OF INFORMED CONSENT.....	23
PASSIVE PARENTAL CONSENT IN ELEMENTARY & SECONDARY EDUCATION SETTINGS.....	23
VERBAL CONSENT	24
WAIVER OR ALTERATION OF INFORMED CONSENT	24
RETENTION OF SIGNED CONSENT DOCUMENTS	25
CONFIDENTIALITY/ANONYMITY	25
SAMPLE CONSENT FORM: Written Consent, Adults.....	26
CONSENT AGREEMENT FOR VIDEO RECORDING.....	27
SAMPLE ASSENT FORM (young children)	28
SAMPLE CONSENT FORM: NON-SENSITIVE QUESTIONNAIRES	29
PSYCHOLOGICAL RISK LANGUAGE	29
VIII. SPECIAL SUBJECT POPULATIONS	30
DEFINITIONS	30
CHILDREN.....	30
Categories of exempt research when the subjects are children	30
Special considerations in research when subjects are children	30

Informed Consent.....	31
Assent of the children	31
Permission from parent(s) or guardian	31
Information that must be provided in requests for assent and permission; documentation of informed consent	32
MENTALLY DISABLED INDIVIDUALS	32
Categories of exempt research when the subjects are mentally disabled	32
Special considerations in research when subjects are mentally disabled	32
Informed consent	33
Assent of the subjects	33
Permission from competent adults acting on behalf of the subjects	33
Information that must be provided in requests for assent and permission and documentation of informed consent	34
PREGNANT WOMEN AND FETUSES.....	34
Activities Directed Toward Pregnant Women	34
Additional Consent Requirements	34
Research Directly Involving Fetuses.....	34
PRISONERS	34
CPHS/IRB Membership Regarding Research with Prisoners.....	35
Types of Research Permitted	35
Funded Research.....	35
Additional Considerations.....	36
IX. SPECIAL TOPICS.....	36
RECRUITMENT	36
Guidelines for Research Using Classroom Subjects	37
Recruiting Clients of Social Service and Other Institutions.....	37
Advertising for Subjects.....	37
PROTOCOLS USING MAGNETIC RESONANCE IMAGING (MRI).....	37
INFORMED CONSENT AND ABUSE REPORTING REQUIREMENTS	38
Child Abuse	38
Abuse of Elderly Persons	38
Adults who are Mentally Ill or Developmentally Disabled	39
INTERNATIONAL RESEARCH	40
TRANSPORTATION OF RESEARCH SUBJECTS.....	40
COMPENSATION FOR PARTICIPATION IN RESEARCH	40
INVESTIGATIONAL DRUGS/DEVICES REVIEW	40
CLASSROOM INITIATED RESEARCH OR TRAINING PROJECTS INVOLVING HUMAN SUBJECTS	40
REGULATIONS FOR RESEARCH WITH HUMAN SUBJECTS UNDER HIPAA (HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT)	41
GENETIC RESEARCH AND COMPLIANCE WITH STATE LAW	46
RADIOLOGY DEVICES.....	46
DATA SAFETY MONITORING PLANS/BOARDS (DSMP/DSMB).....	47
OTHER COMPLIANCE ISSUES	49
X. REFERENCES	50
XI. APPENDIX A.	51
XII. INDEX	59

I. INTRODUCTION

In accordance with the Federal Policy on the Protection of Human Subjects (DHHS Policy 45 CFR Part 46; Department of Education Policy 34 CFR Part 97; FDA Policy 21 CFR Parts 50 and 56;) and applicable State and local laws and regulations, the University of Oregon assumes the responsibility for the protection of the rights and welfare of human subjects who participate in research and other activity projects conducted by, or under the supervision of, faculty, staff, or students. To carryout this responsibility effectively, the University maintains the Office for the Protection of Human Subjects (OPHS) to support investigators and staff and the Committee for the Protection of Human Subjects (CPHS).

The Committee is comprised of two separate and independent Institutional Review Boards (IRB): Panel #1 (IRB#1) Social/Behavioral and Panel #2 ((IRB #2) Biomedical. The panels review research, training, and other activity protocols, funded and unfunded, involving human subjects and to evaluate both risk and protection against risk for those subjects. It is the function of the OPHS and the CPHS to 1) determine and certify that all projects reviewed by the CPHS/IRB conform to the regulations and policies set forth by DHHS regarding the health, welfare, safety, rights, and privileges of human subjects; and 2) assist the investigator in complying with DHHS and FDA regulations in a way that permits accomplishment of the research activity.

Under the University of Oregon Federalwide Assurance (FWA), the institution commits to Department of Heath and Human Services (DHHS) that it will comply with the requirements set forth in the regulations for the protection of human subjects at 45 CFR part 46. In addition, the University of Oregon assures that all of its activities related to human subjects research, regardless of funding source, will be guided by the ethical principles in the Belmont Report (1979): respect for persons, beneficence and justice. The application of the general principles lead to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects in research (Appendix A).

The OPHS and CPHS aim to provide a service to the University and the public by facilitating ethical treatment of research subjects while at the same time supporting the investigator's endeavor to advance knowledge. This manual is intended to assist investigators in their efforts to perform research and to protect the rights and welfare of human participants.

Notice of Availability of Manual in Accessible Formats

In accordance with the American with Disabilities Act (ADA), the *Investigator's Manual on Research With Human Subjects (Manual)* will be made available in accessible formats (e.g., large print) upon request. Contact the Office for Protection of Human Subjects at (541-346-3106).

II. ABBREVIATIONS/DEFINITIONS

ABBREVIATIONS

CPHS/IRB The University of Oregon's Committee for the Protection of Human Subjects/Institutional Review Board, established for the purpose of review and approval of human subjects in research, in accordance with federal regulations governing the protection of human subjects in research.

OPHS The Office for Protection of Human Subjects, administrative unit on campus (1600 Riverfront Research Park, Suite 105, 541-346-2510) which supports the CPHS/IRB and initiates certification of CPHS/IRB approval to funding agencies.

DHHS U.S. Department of Health and Human Services, the federal agency which enters into agreement with institutions through a signed assurance of compliance for the protection of human subjects in biomedical or behavioral research. The University of Oregon's Federalwide Assurance (FWA) of Protection for Human Subjects number is FWA00005914. The University has two Institutional Review Boards (IRBs) designated under the assurance: IRB #1 - Social/Behavioral IRB; registration number: IRB00000190. IRB #2 -Biomedical IRB; registration number IRB000005841. The FWA number may be required on proposals submitted to funding agencies.

DOD Addendum In 2006, the Department of Defense enhanced its human subjects protection requirements. Responsibility for upholding requirements is shared between the researchers and their teams and University administration. In signing an assurance, the University of Oregon will apply Department of Defense regulations when conducting, reviewing, approving, overseeing, and supporting Department of Defense supported research with human subjects. The University has signed an assurance with the Navy. The FWA Addendum number for the Navy: DoD N-A0111.

45 CFR 46 Code of Federal Regulations (Common Rule, Federal Policy for the Protection of Human Subjects, rev. August 19, 1991) implementing Public Law 93-348 (July 12, 1974) establishing institutional review boards and an ethics guidance program.

HIPAA The Health Insurance Portability and Accountability Act of 1996 (HIPAA) is a federal law that has several provisions affecting research that involves health information from human research participants. The Act includes a Privacy Rule that restricts disclosure of protected health information (PHI) for individuals. (Effective April 14, 2003)

DEFINITIONS

Research "Research" means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. 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. For example, some "demonstration" and "service" programs may include research activities.

Human subject "Human subject" 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) in order for obtaining the information to constitute research involving human subjects.

Minimal risk The risk to the subject is said to be minimal when the probability and magnitude of harm or discomfort anticipated in the research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Minimal risk is to be determined with regard to the state of vulnerability of the particular subject or subjects, especially if special populations are used as subjects. Refer to pp. 16-17 for additional guidance in determining minimal risk.

Subject at risk Any individual who is exposed to the probability of injury, physical or psychological, as a consequence of participation as a subject in a research procedure. A subject is beyond minimal risk when participating in a research endeavor in which the risks of harm are greater, considering either probability or magnitude, than those risks encountered in daily life. Refer to pp. 16 for additional information on risk.

Physical risk Any strenuous or unusual physical activity or procedure required of a subject, use of compounds which might alter the subject's biochemical milieu, exposure to strong stimulation, placement in a situation which could lead to violence. The investigator is responsible for anticipating circumstances which might endanger the subject's physical well-being and for bringing these circumstances to the attention of the CPHS/IRB.

Psychological risk Any experimental condition that induces personality change or intense changes in a subject's feelings or motivations, or that may induce such changes which extend beyond the experimental or debriefing period; subjection to deceit, to demeaning or dehumanizing procedures, to humiliation and embarrassment. The investigator has the responsibility to eliminate or minimize the effects of psychological risks to subjects and to bring these matters to the attention of the CPHS/IRB.

Confidentiality Right of privacy and of non-release of disclosed personal information. The investigator should protect subjects against invasion of privacy and loss of confidentiality. Lack of secure handling of completed personality tests, questionnaires, interview protocols or data, and recorded materials, augments risk and must be avoided.

Informed consent Informed consent means "knowing consent," the exercise of a free power of choice without undue inducement, force, fraud, deceit, duress, or other form of constraint or coercion. If the subjects are minors or are not capable of giving consent, parental, guardian or other legal representative consent is required (refer to pp. 27-31). Use of a written consent form that includes all the basic elements of informed consent must be documented by a signature of the subject or legally authorized representative.

Anonymity exists when there are no identifiers whatsoever on project materials which could link the data with individual subjects. Even the research investigator cannot know the identity of participants.

Protocol A protocol is the researcher's plan of a scientific experiment or treatment. A full review or expedited protocol consists of a cover sheet, Investigator's Agreement, Faculty Advisor's Review and Agreement, Human Subjects Protocol Form, informed consent form(s), sample survey instrument(s) or questionnaire(s), and grant proposal, thesis or dissertation, or prospectus, so as to provide complete information regarding activities involving human subjects. Claim of Exemption from CPHS/IRB forms are also available.

Social science and behavioral research The study of human society and of individual relationships in, and to, society. Social and behavioral research is usually conducted in such academic disciplines as sociology, psychology, anthropology, economics, political science, and history. (Amdur, R, and Bankert, E. Institutional Review Board: Management and Function, 2002, Jones and Bartlett Publishers, page 105.) Social and behavioral research is also conducted in areas such as education, public health, marketing, oral history, ethnography, criminal justice, religion, and social services.

Biomedical research The study of biomedical science, which focuses on human physiology, the study of human movement and physical activity or understanding the treatment and prevention of disease.

Other definitions may be found throughout the manual in appropriate sections.

III. OVERVIEW OF PROCESS

STEP 1 -- Design Research

Although scientific concerns are primary in the design of research involving human subjects, the rights of human subjects should be considered from the outset. The principles, policies, and procedures explained in this manual should be kept in mind throughout the design of any research project.

STEP 2 -- Determine Whether the Project Needs to Be Reviewed

All research projects in which human subjects participate, whether funded or unfunded, are subject to the federal regulations governing such research, and to the policies and procedures outlined in the University's Federalwide Assurance of Protection for Human Subjects and this manual. Except for cooperative research projects which may also be subject to review by another institution's IRB, all projects directed or co-directed by UO faculty, students or staff must be reviewed and approved by the UO CPHS/IRB. Such projects include individual or collaborative research projects, as well as any programmatic projects, class surveys or projects, and student government activities with a research component.

Some projects assigned to students in a class may have a research component or constitute training in research methodology. If such projects may contribute to generalizable knowledge (e.g., through publication or dissemination of the findings), they are subject to the regulations and must undergo review. The Committee is unable to give *post facto* approval. Classroom projects that are exclusively for instructional purposes need not undergo review by the CPHS/IRB; however, instructors and students are encouraged to follow federal and University regulations when designing and conducting class projects with human participants. (See page 37.)

Cooperative research between the University of Oregon and other universities or research institutions will usually be reviewed by each institution's authorized Institutional Review Board. The lead institution is responsible for ensuring that all institutions and investigators engaged in the research operate under an appropriate federally-approved Assurance for the protection of human subjects. The lead institution is normally the primary grantee or contractor for funded projects and/or home institution of the principal investigator. The University of Oregon will need documentation of review and approval by another institution's IRB when appropriate. For example, students receiving their degree from another institution who are conducting research at the University of Oregon are required to document approval of the research project by the Institutional Review Board at their home institution. The investigator will need to complete the appropriate application for the University of Oregon for any research that has been approved by another Institutional Review Board other than the UO's CPHS/IRB. A copy of the approved protocol and/or IRB approval letter must be submitted with the UO application.

Certification of IRB approval is required when the research is supported by a federal department or agency. Certification should be submitted with the application or proposal or by the deadline prescribed by the department or agency to which the application or proposal is submitted. These deadlines vary depending on the funding agency and some agencies require certification as part of continuation of the grant. As part of the certification process, the National Institutes of Health (NIH) requires training on the protection of human subjects for all investigators/key personnel submitting NIH applications for research involving human subjects. The UO curriculum in the Collaborative IRB Training Initiative meets this require and is available on the internet at "Human Subjects Training and Certification" (<http://humansubjects.uoregon.edu/>).

Grant proposals lacking definite plans for involvement of human subjects (such as institutional bloc grants, training grants, or those projects in which the human subjects' involvement will depend upon completion of instruments, prior animal studies, etc.), or research undertaken without the intention of involving human subjects, shall be reviewed and certified, but the investigator will be required to submit a protocol to the CPHS/IRB once activities involving human subjects are formulated. In the case of multiple projects, the investigator must agree to take the responsibility for seeing that each individual project involving human subjects will be submitted to the CPHS/IRB for review.

If there are any questions or need of clarifications, the investigator is encouraged to consult with OPHS (346-2510).

STEP 3 -- Complete the Protocol

The protocol provides the CPHS/IRB with the information that it needs to approve the proposed research. Copies of the protocol packet, with instructions for completing the forms are available on the web (<http://humansubjects.uoregon.edu>). As indicated in the instructions, a sample informed consent form must be attached to the protocol. For funded projects and theses and dissertations, a copy of the proposal or thesis must be attached as well, although the material presented in the protocol should be complete in and of itself (i.e., do not refer to sections of the proposal to provide information to the CPHS/IRB).

The principal investigator signs the Investigator Agreement form, indicating that s/he will comply with the federal and University regulations outlined in the Investigator's Manual on Research with Human Subjects.

STEP 4 -- Review and Signature of Faculty Supervisor (Student Research Only)

All student initiated research involving human subjects, whether dissertation, thesis, or other research projects, must be supervised by a faculty member to assure that human subjects are protected.

For thesis or dissertation research, the signature of the faculty advisor is required. If the faculty advisor is unable to sign, another member of the student's committee may sign. **NOTE: For thesis/projects or dissertation projects which will be submitted to the Graduate School, the "Required Clearance for Master's Thesis/Project or Doctoral Dissertation" form must be completed, signed and on file in the Graduate School before subjects may be recruited or collection of data initiated. Forms are available at the Graduate School.**

For student research other than thesis or dissertation projects, a faculty supervisor's signature is required and the student must be enrolled for at least one credit hour of research during that period of the project when human subjects are involved. Graduate students must meet the university requirements of continuous enrollment. The student must register for three graduate credits each term, excluding summer sessions, to be continuously enrolled.

The faculty signature on student research attests that the research procedures comply with federal and University policies with regard to the protection of human subjects. The faculty supervisor also is expected to monitor the research to assure that the approved protocol with human subjects is followed. When approved, the faculty member signs the appropriate section of the Investigator and Faculty Advisor Agreement (included in the protocol packet).

STEP 5 -- Submit the Protocol to OPHS

After the proposed project has been received by OPHS, a preliminary review of the protocol is done to determine whether (a) the project is exempt under the regulations or is to be reviewed under the expedited or full review process (see pp. 12-14 for a description of review categories); (b) the protocol meets the general requirements for review under the regulations; and (c) the informed consent form contains the required elements and is in satisfactory form for CPHS/IRB review. The OPHS will consult with the investigator (and/or faculty supervisor, if student research) when the proposal does not meet the general requirements, the informed consent form is missing required elements, or additional information or clarification is needed to determine the review category.

STEP 6 -- Review and Approval by CPHS/IRB

If OPHS determines that the protocol is exempt under the federal regulations (refer to pp. 12-13 for a list of exempt categories) and everything is satisfactory, OPHS will approve the protocol, indicating that the research may commence.

If the protocol requires expedited review (refer to p. 13 for a list of expedited review categories), the protocol and supporting documents will be reviewed by at least one member of the CPHS/IRB, who will have full authority of the CPHS/IRB (except to disapprove a project) and one Protocol Coordinator (administrative staff member). If the CPHS/IRB reviewer requests, the protocol will be referred to a second CPHS/IRB member for additional review or to the full CPHS/IRB for consideration at their next meeting. If both reviewers approve the project, the chair of the CPHS will sign the cover sheet/investigator agreement page, indicating that the research may commence.

If the protocol is determined to require full review, the protocol and supporting documents will be reviewed by two members of the CPHS/IRB, who will make recommendations to the full CPHS/IRB.

The CPHS/IRB will consider all protocols requiring full review as well as protocols in the expedited category for which at least one of the reviewers determines that the procedures are unacceptable. The CPHS/IRB can approve the research, conditionally approve the research, or disapprove the research.

If the research is approved, the chair of the CPHS/IRB signs the approval page and the research may commence.

If there are correctable problems with the protocol, OPHS will consult with the investigators to seek revisions in the protocol. Conditional approval indicates that problems with the protocol must be corrected before the research may commence; typically, determination of whether the changes made by the investigator satisfy the conditions set forth by the CPHS/IRB can be made by OPHS or the chair, obviating further discussion of the protocol by CPHS/IRB. When the conditions have been satisfied, the chair of the CPHS/IRB will sign the cover sheet and research may commence.

If the protocol is disapproved, the researcher may not conduct the research and the CPHS/IRB will provide, in writing, the reason for its decision. Furthermore, the researcher will have the right to appeal the decision (refer to p. 11 for additional information on the appeal process).

OPHS will report concerns and outcomes of the CPHS/IRB to the investigator and to the faculty member supervising the research when the investigator is a student.

STEP 7 -- Research Commences or Decision is Appealed

Once the protocol is approved, research with human subjects may commence. It is the responsibility of the investigator (and faculty supervisor if investigator is a student) to monitor the research to insure that the approved procedures are being followed. Any harm to subjects should be reported to the CPHS/IRB immediately.

The CPHS/IRB will conduct continuing review of approved projects at intervals appropriate to the degree of risk, but not less than once per year (see Step 10). The CPHS/IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the CPHS/IRB requirements or that has been associated with unexpected serious harm to subjects. Any such termination will include a statement of the reason for action and shall be reported promptly to the investigator, to the faculty advisor if the investigator is a student, to the appropriate University officials, and to the appropriate federal officials. Furthermore, the CPHS/IRB has the authority to observe or have a third party observe the consent process and the research.

If for some reason an investigator is not satisfied with the decision of the CPHS/IRB or with the process by which a decision is rendered, the right to an appeal is maintained (refer to p. 12).

STEP 8 -- Changes in Approved Procedures (Amendments/Modifications)

Any changes in previously approved research must be approved by the CPHS/IRB. Minor changes may be submitted to OPHS on the Amendment/Modification Form with a memorandum describing those changes and the effects of the requested modifications on risks, benefits and consent procedures. The form is available on the Internet (<http://humansubjects.uoregon.edu>). If the changes are determined to be substantial, the investigator will be informed that a new protocol must be submitted. All modifications must be reviewed and approved by the faculty advisor if the researcher is a student.

STEP 9 -- Continuing Projects and Closure of Projects

At regular intervals (and at least once a year, 365 days), the CPHS/IRB will conduct continuing reviews of projects in progress. When the current approval period is nearing an end, the CPHS/IRB will send the investigator a Continuing Review/Final Report Form. If there are no problems, adverse reactions, or changes in activities by the investigator, continuing review will be handled administratively. If any of these conditions are present, review of the project will be conducted by the CPHS/IRB and a revised protocol must be submitted.

An investigator may be granted up to four one-year renewals on each individual human subjects protocol. If the investigator wishes to continue conducting the research in question after the expiration of the fourth renewal, s/he will submit a new protocol application for Committee review.

The National Institutes of Health (NIH) implemented a new training policy for researchers with human subjects (Effective October 1, 2000). Applications submitted for non-competing continuation applications or annual reports on contracts must include a description of the training completed or to be completed prior to award for all key personnel who are listed on the proposal (see NIH Frequently Asked Questions for the Requirement for Education on the Protection of Human Subjects - http://grants.nih.gov/grants/policy/hs_educ_faq.htm). The educational program for the University of Oregon requirement is available on the internet at the Office for Protection of Human Subjects, Collaborative IRB Training Initiative (CITI) link (<http://humansubjects.uoregon.edu/>).

If the project is terminated (i.e., procedures involving human subjects are completed), the investigator should complete the Continuing Review/Final Report Form and send it to the CPHS/IRB. The Continuing Review/Final Report Form is sent to the investigator at a minimum of one month prior to the expiration date of the protocol. The CPHS/IRB shall conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. All consent forms must be kept by the investigator for three years after the research is completed or if funded, 5 years after the final financial report is submitted and the account is closed, unless specified otherwise by the terms of the contract.

STEP 10 – Reporting Unanticipated Problems and Adverse Events

All investigators conducting research with human subjects are required to report unanticipated problems and adverse events to the Office for Protection of Human Subjects within 24 hours. A non-medical research adverse event can consist of an undesirable and unintended consequence of, or reaction to procedures or breach of confidentiality. In medical research, a headache following an activity which lowers the blood pressure or the development of blood clots associated with therapy. In either case, if new information becomes available, as a result of an unanticipated problem, the investigator is required to submit the new information for Committee review for possible inclusion in the consent form or additional consideration by the CPHS/IRB.

The CPHS/IRB relies on the expertise of the investigator to make an assessment and to determine the relationship of the unanticipated problem and adverse events to the research activity (procedure/ intervention) and whether the

event warrants a change to the protocol to minimize risks and/or the informed consent form to better inform subjects of the potential risks and procedures to minimize such risks. Therefore, the reporting of adverse events is based upon the investigator's assessment.

If the event is an unanticipated problem in the opinion of the investigator, the protocol and/or informed consent form requires modification. Examples: identification of a "new trend" (adverse event occurring with greater frequency than anticipated) or a change in the risk/benefit ratio. If the unanticipated problem results in a change in procedures or the consent form, the Amendment/Modification form (<http://humansubjects.uoregon.edu/>) needs to be completed in addition to the Unanticipated Problems and Adverse Event Report Form.

IV. CRITERIA FOR APPROVAL

EDUCATION REQUIREMENT

Beginning February 15, 2007, all UO researchers (faculty, staff and students) conducting human subjects research and faculty advisors of students conducting human subjects research must complete the Collaborative IRB Training Initiative (CITI) program in order for applications to be approved by the Office for Protection of Human Subjects (OPHS). Any UO researcher who has already completed the NIH training module before February 15, 2007, will have a one-year grace period from the date of their NIH training certificate to complete the CITI modules. No NIH training certificates will be honored after February 15, 2008.

Completion of the CITI program is required by all UO researchers and research staff, regardless of whether the research is funded or not. "Research staff" includes investigators, researchers, key personnel, graduate or undergraduate students involved in faculty research projects, and faculty advisors on student research projects. Anyone on a research team responsible for the design and conduct of the study (e.g., the informed consent process and/or collecting data through intervention or interaction with an individual, or identifiable private information) need to complete the training. Outside investigators (those unaffiliated with the UO) conducting research at the University of Oregon or for any UO research team may submit documentation from their own institution, provided the training was completed within the last two years, or they may complete the University's CITI modules.

CITI is accessible via the OPHS research website at <http://humansubjects.uoregon.edu/citiprogram.htm>. The program was specifically chosen to provide faculty, staff and students with the greatest ease of access and flexibility to complete the training over multiple sessions according to your schedule. All CITI certificates expire two years from the completion date. At that time, researchers must take the refresher CITI course.

CPHS/IRB REVIEW AND APPROVAL

The CPHS/IRB may approve research when the following conditions are satisfied:

- Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and, whenever appropriate, by using procedures already being performed on subjects for diagnostic or treatment purposes;

●Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result (the CPHS/IRB will consider only those risks and benefits that may result from the research);

●Selection of subjects is equitable (the CPHS/IRB will consider the purposes of the research, the setting in which the research will be conducted, and the population from which subjects will be recruited);

●Informed consent will be sought from each prospective subject or the subject's legally authorized representative and will be appropriately documented, unless informed consent or documentation is specifically waived by the CPHS/IRB (refer to pp. 18-20);

●The research plan makes adequate provision for monitoring the data collected to insure the safety of subjects where appropriate;

●There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data where appropriate;

●Where some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as persons with severe physical or mental disabilities or illness, appropriate safeguards have been included in the study to protect the rights and welfare of these subjects.

●The CPHS/IRB may establish subcommittees as deemed practical to utilize a specific member's expertise, and may consult with individuals outside the CPHS/IRB having competence in special areas to assist in the evaluation of complex issues.

●As specified in the federal regulations, only the CPHS/IRB or a quorum (majority) of its officially appointed membership may give final review and approval to a project involving human subjects. Certification of approval will be issued by OPHS stating that the requirements of the Institution's assurance and federal regulations have been met.

●The CPHS/IRB meets approximately once each month to review protocols, according to the calendar posted on the Office for Protection of Human Subjects website. The CPHS/IRB may 1) approve protocols without question; 2) approve the protocol on condition (such conditional approval will be recorded in the minutes of the CPHS/IRB); or 3) disapprove the protocol and explain the appeal procedure.

●Institutional approval must be granted prior to the commencement of the project. Projects that are not yet approved by the CPHS/IRB prior to receipt of funds by the University will not be allowed use of the funds until such approval is granted. OPHS has the authority to notify the Business Office to withhold all funds until such time as the project is approved by the CPHS/IRB. **NOTE: No Contact with Human Subjects (i.e., recruitment, obtaining consent, etc.,) may occur before CPHS/IRB approval.**

●Compliance with, or exemption from, the regulations will not in itself constitute approval by the institution for conduct of the research. OPHS shall, therefore, review all research involving human subjects to determine whether this institution shall support or sponsor such research.

APPEAL PROCESS

In the event that a protocol is disapproved by the CPHS/IRB, the investigator may appeal the decision as follows:

1. The investigator submits the grievance in writing to OPHS for forwarding to the chair of the CPHS/IRB;
2. The chair discusses the grievance with members of the CPHS/IRB in an attempt to provide resolution;
3. If the grievance cannot be resolved at step 2, the investigator may request a meeting with the CPHS/IRB, and may be accompanied by counsel or other persons with expertise or knowledge of research related to the procedures in questions;
4. The CPHS/IRB may invite a faculty member who is not a member of the CPHS/IRB to act as an observer to the proceedings;
5. Based on the findings of the CPHS/IRB, a final decision regarding the grievance will be made by a majority vote of the CPHS/IRB.

V. REVIEW CATEGORIES

EXEMPTION CATEGORIES (Effective August 19, 1991)

None of these exemptions apply to research involving prisoners, fetuses, pregnant women, or human in vitro fertilization. It is the prerogative of the university to prohibit exemptions that are allowable under federal policy.

Exempt status applies to research activities in which the only involvement of human subjects will be in one or more of the following categories:

- (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.

The above exemption is applicable to mentally handicapped individuals only if research involves no changes in content, location, or procedures of instruction from those a subject would normally experience.

- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless;
 - (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
 - (ii) 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.

This exemption applies to research with children or mentally handicapped individuals as follows:

- *research involving the use of educational tests is exempt;*
 - *research involving survey or interview procedures is **not** exempt;*
 - *research involving observations of public behavior is exempt only when the investigator(s) do not participate in the activities being observed.*
- (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 category (2), if:
- (i) the human subjects are elected or appointed public officials or candidates for public office; or
 - (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- (4) Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- (5) Research and demonstration projects which are conducted by or subject to the approval of [federal] department or agency heads, and which are designed to study, evaluate, or otherwise examine:
- (i) public benefit or service programs;
 - (ii) procedures for obtaining benefits or services under those programs;
 - (iii) possible changes in or alternatives to those programs or procedures; or
 - (iv) 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,
- (i) if wholesome foods without additives are consumed, or
 - (ii) if 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 FDA or approved by the EPA or the Food Safety and Inspection Service of the USDA.

EXPEDITED REVIEW CATEGORIES (Effective November 9, 1998)

Applicability

(A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

(B) The categories in this list apply regardless of the age of subjects, except as noted.

(C) The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing,

employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

(D) The expedited review procedure may not be used for classified research involving human subjects.

(E) IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

(F) Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories:

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, non-pregnant 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 children¹, 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. Examples: (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
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.)

¹ Children are defined in the HHS regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.” [45 CFR 46.402\(a\)](#).

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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 behaviors (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 HHS 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 IRB 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 or subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where 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) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

FULL REVIEW

According to 45 CFR 46.110 (b), full review is necessary for all research proposals which are not Exempt or otherwise subject to Expedited Review (see pp. 6-9 for more information on review procedures).

Projects that potentially pose more than minimal risk to subjects or involve certain populations (e.g., research on prisoners, sensitive interventions with children) may require full review, in which the protocol is reviewed at a convened Institutional Review Board (IRB) meeting. See examples of risk - Section IV.

If the protocol will require full review, please be aware of the IRB meeting dates and protocol submission deadlines (See website for current dates <http://humansubjects.uoregon.edu>). Full Review protocols must be received by the submission deadline to be reviewed at the following meeting. Projects that are determined to be Exempt or Expedited do NOT need to be submitted by the submission deadlines. Contact OPHS (346-2510) for review category determination.

The University of Oregon maintains two Institutional Review Boards. IRB #1 is primarily concerned with projects involving social and behavioral research (e.g., Psychology, Sociology, Education, Political Science, Anthropology, etc. and IRB #2 is reserved for projects that involve medical procedures and/or the biomedical sciences (e.g., Human Physiology).

The submission deadlines and meeting dates for these two committees differ slightly, so please examine the schedules carefully if you are submitting a protocol for full review.

The following table details the types of procedures reviewed by each of the two IRB committees. Use of these procedures does not necessarily require full review.

<u>IRB #1 (Social/Behavioral)</u>	<u>IRB #2 (Biomedical)</u>
Non-Medical <ul style="list-style-type: none"> · Survey/Interviews · Cognitive/Motivational tests · Moderate exercise · Muscular strength testing 	Medical <ol style="list-style-type: none"> 1. Blood Draws 2. X-ray, DEXA Scan 3. IV Work 4. Needle Sticks 5. Nerve Blocks
MRI or EEG for Socio-Behavioral purposes	MRI for Medical purposes
Post-medical procedures, cleared by an M.D.	Pre-medical or treatment procedures
Non-Invasive DNA sampling (cheek swab, hair, etc.)	Invasive DNA sampling (venipuncture, etc.)

VI. RISKS TO SUBJECTS

The University of Oregon accepts as a basic principle that it has an ethical and moral obligation to safeguard the rights and welfare of all subjects involved in research, training, educational development and other activities where subjects are exposed to a risk that could be detrimental to their health or well-being. In those cases where risk may exist, even with informed consent, approval of a research project will be made only if the risk to the individual is outweighed by a clear explanation of the potential benefit to the person (as in the case where an activity involves therapy, diagnosis, management, etc.). In evaluating risks and benefits, the CPHS/IRB shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies the subjects would receive even if not participating in the research), and shall not consider long-range effects of applying knowledge gained in the research as among those risks that fall within the CPHS/IRB's purview of responsibility.

The university shall be responsible for physical or psychological injury to human subjects attributable to university-sponsored research, development, and related activities, to the extent that the university may be found liable under federal and state laws. Therefore, the obligation of researchers to conduct activities in a manner and at such locations as will assure the proximity of adequate medical attention if warranted, and to provide appropriate referrals to subjects for adequate facilities and professional attention should subjects suffer physical, psychological or other injury, is of paramount importance when designing research involving human subjects. (Refer to p. 19 for further information on university liability.)

The seriousness of a risk to subjects is a function of the magnitude of the harm and the probability of the harm. A risk may be serious or significant because it has a probability (even a low probability) of great harm (e.g., a low probability of death), or because it has a high probability of slight harm (e.g., a near certainty of physical discomfort or psychological distress).

The risks of participation in research may be part of the research design or may be a consequence of the research procedures, or both (e.g., the risks of an adverse reaction to an investigational drug are part of the research design, while the risk of hematoma from blood drawn in the research is not part of the design but a consequence of the research procedures). Risks may be a consequence of the methods of recording, maintaining, or reporting data, and they may be a consequence of methods of obtaining informed consent.

EXAMPLES OF RISKS

Physical risks include physical discomfort, pain, injury, illness or disease brought about by the methods and procedures of the research. A physical risk may result from the involvement of physical stimuli such as noise, electric shock, heat, cold, electric magnetic or gravitational fields, etc. Engaging a subject in a social situation which could involve violence may also create a physical risk.

Psychological risks include the production of negative affective states such as anxiety, depression, guilt, shock and loss of self-esteem and altered behavior. Sensory deprivation, sleep deprivation, use of hypnosis, deception or mental stresses are examples of psychological risks. (See page 26 for sample informed consent language for research with psychological risks.)

Occasionally, some degree of deception is involved in a research study. Minor deception, such as failing to tell the subject what the specific points of interest are in an attempt to prevent biasing the results, can be acceptable provided the subject is fully debriefed after participating. Risks stemming from major deceptions, such as leading a subject to believe that s/he has committed a crime or has a disease, must be clearly counterbalanced by the benefits of the research. **Withholding information cannot be used as a means to secure the participation of subjects in research.**

The use of deception imposes special responsibilities on the investigator. One of these responsibilities is to provide appropriate debriefing to the subjects. In each case, the CPHS/IRB will require information sufficient to understand why deception is needed, how the potential benefits justify its use, and how debriefing will be done.

If information was temporarily withheld from the subject during the study, or if deception was employed, a separate debriefing statement should be presented at the end of the procedure. This statement should clearly indicate why information was withheld during the study, and/or the purpose of the deception.

Social/Economic risks include alterations in relationships with others that are to the disadvantage of the subject, including embarrassment, loss of respect of others, labeling a subject in a way that will have negative consequences, or in some way diminishing those opportunities and powers a person has by virtue of relationships with others. Economic risks include payment by subjects for procedures not otherwise required, loss of wages or other income and any other financial costs, such as damage to a subject's employability, as a consequence of participation in the research.

Loss of Confidentiality: In all research involving human subjects, confidentiality of identifiable information is presumed and must be maintained unless the investigator obtains the express permission of the subject to do otherwise. Subjects have the rights to be protected against injury or illegal invasions of their privacy and to preservation of their personal dignity. The more sensitive the research material, the greater the care that must be exercised in obtaining, handling, and storing data.

Investigators should be cognizant of the following guidelines to ensure confidentiality:

- acquiring of personal information should be limited to that which is absolutely essential to the activity;
- data should be securely stored and accessible only to the investigator and authorized staff;
- data should be coded as early in the activity as possible, and plans for the ultimate disposition of the data should be made;
- identities of individuals should not be released without express permission of the individual;
- use of stored data which was originally obtained for different purposes and which involves identifiable subjects, requires examination of the risk involved, a determination of whether the new use is within the scope of the original consent or whether obtaining additional consent is necessary and feasible, and provision made for the preservation of anonymity of the subjects.

Identifiers linked to the subject can include name, code or reference that could be used to identify an individual outside of the context of the research setting. Names, student numbers, and social security numbers on the data are obvious examples. An identifier that links a subject to a list of names or identifiers kept elsewhere can also lead to loss of confidentiality. If records are linked to a second set of records (e.g., test scores linked to school grades) and the second set of records is identified, then the first set would also be identified. A subject's privacy may be invaded simply by being identified as a qualified participant for a study (such as membership in Alcoholics Anonymous). The investigator should determine whether the information or data could be traced back to an individual subject, and make appropriate safeguards to ensure that confidentiality will be maintained (refer to pp. 21-22 for additional information on confidentiality/anonymity). Please refer to p. 33 for information on accessing subjects' records.

Legal risks exist when the research methods are such that the subject or others will be liable for a violation of the law, either by revealing that the subject or others have or will engage in conduct for which the subject or others may be criminally or civilly liable, or by requiring activities for which the subject or others may be criminally or civilly liable.

MINIMAL RISK

Defining "minimal risk" in research involving human subjects is useful for both the investigator and the CPHS/IRB, in that research involving more than minimal risk requires additional elements in the informed consent documents, including the official liability clause (refer to p. 19), and full review by the CPHS/IRB. Projects with minimal risk may be reviewed through the expedited process, or in some cases may be exempt from review altogether if the research so qualifies under the regulations.

The federal regulations governing research with human subjects define "minimal risk" as follows: "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."

In broad terms, a project may be determined as involving minimal risk if:

- the participant experiences no pain or physical danger;

- the participant experiences no emotional arousal or psychological stress beyond the levels normally to be expected in everyday life;
- the project neither induces nor attempts to induce long-term significant change in the participant's behaviors (including attitudes toward self and others);
- the data would not embarrass or socially disadvantage the participant, were confidentiality to be violated; and
- any concealment on the part of or misinformation provided by the investigator with regard to the specific purpose of the project is such that there is no basis for believing the participant would choose not to participate in the research had the true state of affairs been made known to him or her.

Additional considerations for making this determination might include whether the project provides a novel environment for the subject, or whether the subject will be exposed to situations which would not be considered a risk for the general public but might be risky for a special population such as disabled, young or elderly subjects.

It is difficult to develop a rule that can be applied across all disciplines and in all situations, to determine whether a project involves minimal risk or more than minimal risk. It is assumed that the researcher will apply the customs and practices associated with his/her discipline, such as outlined in a published code of ethics, in making this initial determination. The CPHS/IRB will make the final determination as to the project's level of risk and the safeguards required to minimize risks for subjects.

VII. INFORMED CONSENT

Informed consent is the knowing consent of an individual or her/his legally authorized representative which is obtained without undue inducement or element of force, fraud, deceit, duress, or other forms of constraint or coercion. A consent form documents informed consent and is designed to protect the investigator and the institution against legal liability.

One of the most common reasons for delay of approval of a protocol is an inadequate consent form. The consent form should be a statement addressed to the subject and should read as such. Ordinarily, it is best worded in the second person. It must be in language the subject can understand (avoid or define technical terminology, adjust for educational background and ages, provide translations in other languages when subjects do not understand English). Separate forms may be required for different subject groups (parents, children, UO students, etc.), as well as for release of particular kinds of information (photographs, video recordings). (See page 24.)

Templates for several types of informed consent forms can be found at the end of this section. Researchers need not copy this language verbatim, so long as all required elements are included in the informed consent form. Sample protocols with examples of well-written informed consent forms are on file at OPHS and may be reviewed in that office.

OBTAINING INFORMED CONSENT

Research investigators are responsible for obtaining informed consent and for insuring that no human subjects will be involved in the research prior to obtaining their consent. In obtaining informed consent, investigators must avoid the possibility of coercion or undue influence. Unless otherwise authorized by the CPHS/IRB, investigators are responsible for insuring that legally effective informed consent shall:

- be obtained from the subject or the subject's legally authorized representative;
- be in language understandable to the subject or the representative;
- be obtained under circumstances that offer the subject or the representative sufficient opportunity to consider whether the subject should or should not participate; and
- not include exculpatory language through which the subject or representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the research investigator, the sponsor, the institution or its agents from liability for negligence.

REQUIRED ELEMENTS FOR ALL INFORMED CONSENT FORMS

A written consent form must include the following items. In addition, special provisions are required when subjects are from special populations (refer to pp. 27-33).

- A statement that the study involves research;
- An explanation of the purposes of the research;
- A description of the procedures to be followed;
- The expected duration of the subjects' participation;
- A description of any reasonably foreseeable risks or discomforts to the subject;
- A description of any benefits to the subject or to others which may reasonably be expected from the research;
- A statement describing how confidentiality of records identifying the subject will be maintained;
- An explanation of whom to contact
 - a. for answers to pertinent questions about the research (researcher's name and phone/address, and that of faculty advisor if investigator is a student);
 - b. regarding research subjects' rights (OPHS); and
 - c. in the event of a research-related injury to the subject (OPHS);
- A statement that
 - a. participation is voluntary;

- b. refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and
 - c. the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;
- An indication that the subject may keep a copy of the consent form.

ADDITIONAL ELEMENTS IF APPROPRIATE

- For research involving more than minimal risk, an explanation as to whether any compensation or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained, and who is responsible for payment of medical expenses; The following language is suggested:

If you are physically injured because of the project, you and your insurance company will have to pay your doctor bills. If you are a UO student or employee and are covered by a UO medical plan, that plan might have terms that apply to your injury. (revised 4/02)

- For research involving more than minimal risk, the following statement must be included (updated 7/09):

If you experience harm because of the project, you can ask the State of Oregon to pay you. If you have been harmed, there are two University representatives you need to contact. Here are their addresses and phone numbers:

*General Counsel
Office of the President
1226 University of Oregon
Eugene, OR 97403-1226
(541) 346-3082*

*Office for Protection of Human Subjects
5237 University of Oregon
Eugene, OR 97403-5237
(541) 346-2510*

A law called the Oregon Tort Claims Act limits the amount of money you can receive from the State of Oregon if you are harmed. The most you could receive would be \$100,000, no matter how badly you are harmed. If other people are also harmed by the project, all of you together could only receive \$3,000,000.

- For research projects that involve video recording, a video recording release form must be attached to the written consent form (a sample is on p. 24). If the investigator anticipates use of the recordings beyond the scope of the initial research project, the written consent form must indicate (a) who will view the recordings; (b) for what purpose; (c) when the recordings will be destroyed.
- If subjects will be paid, all information concerning payment, including amount and schedule of payment;
- A statement that the particular treatment or procedure may involve risks to the subject which are currently unforeseeable;
- Identification of any procedures which are experimental;
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- Any additional costs to the subject that may result from participation in the research;
- The consequences of the subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
- The approximate number of subjects involved in the study.

TYPES OF CONSENT DOCUMENTS

The consent form may be 1) a written document that contains the required elements of informed consent, to be read by the subject or the subject's representative or by the investigator to the subject; or 2) a short written form stating that the basic elements of informed consent have been presented orally to the subject or representative.

DOCUMENTATION OF INFORMED CONSENT

Investigators shall be responsible for insuring that informed consent is documented by the use of a written consent form approved by the CPHS/IRB and signed by the subject or the subject's legally authorized representative, unless this requirement is specifically waived by the CPHS/IRB. Each person signing the written consent form must be given a copy of that form.

WAIVER OF DOCUMENTATION OF INFORMED CONSENT

Under certain conditions, the CPHS/IRB can waive the requirement that the subject sign the consent form. However, waiver of documentation of informed consent does not constitute waiver of informed consent. The CPHS/IRB may waive the requirement to obtain a signed consent form for some or all of the subjects if one of the following conditions exists:

1. The consent document is the only record linking the subject and the research and the principle risk would be potential harm resulting from a breach of confidentiality. Subjects will be asked whether or not they want documentation linking them to the research, and their wishes will prevail.
2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
3. For projects of minimal risk involving the use of questionnaires, the required elements of informed consent may be included in an introductory letter attached to the instrument, which includes a statement that completion and return of the questionnaire will constitute consent to participate. (A sample letter may be found at the end of this section, on page 26.)

In cases where documentation is waived, the CPHS/IRB may require the investigator to provide subjects with a written statement regarding the research.

POLICY ON PASSIVE PARENTAL CONSENT FOR RESEARCH IN ELEMENTARY AND SECONDARY EDUCATION SETTINGS

1. Under current policy, as set forth in the Investigator's Manual on Research With Human Subjects, the CPHS/IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent, if:
 - a. The research involves no more than minimal risk to the subjects and involves no procedures for which written consent is normally required outside of the research context;
 - b. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
 - c. The research could not practicably be carried out without the waiver or alteration.
 - d. Subject selection is based on classroom membership and not exclusionary .
2. The investigator must provide the parent(s) with a written document containing all the required elements of informed consent, as outlined in the Investigator's Manual, pp. 18-20. Note: The *Method of Obtaining Informed Consent* section of the application must indicate assurance that the parent will receive the written document (e.g., the letter will be mailed by the school).
3. Investigators who propose the use of passive consent in a study to be conducted in an elementary or secondary school must (a) obtain permission from the relevant research review mechanism for that school (e.g., school district) and (b) provide the CPHS/IRB with documentation of such approval prior to initiation or recruitment, and (c) if the research involves a change of curricula by the school or school district, provide written documentation on official letterhead from the participating school or school district indicating that the school

district's procedures for adopting the curricula have been followed. The letter documenting curricula adoption must be submitted with the protocol to allow review with passive parental consent.

4. The Office for Protection of Human Subjects may bring protocols which do not clearly meet the requirements of waiving or altering consent before the CPHS/IRB for further review.

If the proposed study meets the conditions needed to obtain a waiver of informed consent, use of a passive consent mechanism may be granted.

VERBAL CONSENT

Only in special and/or unusual circumstances can the consent of the subjects be obtained orally. Waiver of prior written informed consent must be approved by the CPHS/IRB. A waiver of prior written informed consent might be granted in the case where: a) the risk to the subject is minimal; b) use of primary procedures for obtaining consent would invalidate important research objectives; or c) alternative means would be less advantageous to the subjects.

Oral presentation of the elements of informed consent should be used only when it is the most appropriate means of conveying relevant information to the subject, thus adapting the presentation to the subject's capacities. The presentation may be made in either of two ways: 1) A written consent document that sets forth the required basic components of informed consent may be read to the subject or the subject's representative and the investigator will allow the subject or representative ample time to read and consider the document before it is signed; or 2) the CPHS/IRB may approve a short written form describing the particulars of required informed consent that are to be presented orally to the subject or representative.

Where oral consent is allowable, investigators shall insure that:

- a witness is present at the oral presentation;
- the short form is signed by the subject or the representative;
- the witness signs both the short form and a copy of the written summary of the oral presentation;
- the person obtaining consent signs a copy of the summary;
- a copy of both the short form and summary is given to the subject or the representative;
- the written summary of what is to be said to the subject or the representative receives the prior approval of the CPHS/IRB.

WAIVER OR ALTERATION OF INFORMED CONSENT

The CPHS/IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent, provided one of the following sets of conditions exists and is documented:

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine a) programs under the Social Security Act, or other public benefit or service programs; b) procedures for obtaining benefits or services under those 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. The research involves no more than minimal risk to the subjects; the waiver or alteration will not adversely affect the rights and welfare of the subjects; the research could not practicably be carried out without the waiver or alteration, and, whenever appropriate, the subjects will be provided with additional pertinent information after participation.

RETENTION OF SIGNED CONSENT DOCUMENTS

Investigators are responsible for placing the consent documents signed by research subjects in a repository approved by the Office for Protection of Human Subjects and for retaining signed consent forms for three years after termination of the project.

CONFIDENTIALITY/ANONYMITY

By current federal and University policies, subjects in research, evaluation, and training projects give their informed consent to participate. In the informed consent procedure, subjects are often given assurances of protection against loss of confidentiality or for total anonymity. Despite the assurances and subsequent efforts, subjects may yet be identifiable. Two legal conditions are at stake.

1. Loss of confidentiality can occur when a court requires that research files be submitted as evidence in a legal matter. The court decides who has access to the files and whose identity will be revealed.
2. Loss of confidentiality can occur under the so-called "Freedom of Information Act." Under this Act, citizens can gain access to files of federal agencies, except as provided by law.

The University is obligated to protect subjects' identities when the promise of protection is made in obtaining their consent to participate. This obligation can be fulfilled in the following ways:

- If the research files are arranged so that the investigators cannot know the identity of participants, then loss of confidentiality cannot occur by court order. This can be accomplished by routinely destroying master code lists. Confidentiality may not be preserved by locating the master code lists outside the jurisdiction of the court, i.e., in another country. Anonymity may be assured when there are no identifiers whatsoever on project materials which could link the data with individual subjects.

Investigators can be held in contempt of court for failing to submit the research files or for destroying the master code lists only because of knowledge of the intent of the court. Investigators will not be held in contempt of court for not revealing the identity of the subjects, when they routinely take steps to keep the identity of subjects unknown to themselves (i.e., subject responses are anonymous).

- If identifying information is not sent to a federal agency, then loss of confidentiality cannot occur under the Freedom of Information Act. Federal files are subject to the Act. University files are not subject to the Act. Participants should be informed if identifying information will be sent to a federal agency.

Refer to p. 19 for additional information on safeguarding subject confidentiality.

SAMPLE CONSENT FORM: Written Consent, Adults

*This sample is a template from which a consent form can be developed. The language does not have to be repeated verbatim. **THE CONSENT FORM SHOULD BE WRITTEN IN TERMS UNDERSTANDABLE TO THE SUBJECT** (avoid or define technical terminology, adjust for educational background and ages, provide translations in other languages when subjects do not understand English). A detailed description of the basic elements of consent is in the Investigator's Manual on Research with Human Subjects. Investigators with projects involving more than minimal risk, and/or those working with special populations (children, mentally disabled, prisoners, pregnant women) **must** consult the Manual for additional informed consent elements.*

You are invited to participate in a research study conducted by [name of investigator], from the University of Oregon [departmental affiliation]. I hope to learn [state what the study is designed to discover or establish. If a student, indicate that results will contribute to thesis or dissertation]. You were selected as a possible participant in this study because [state why subject was selected].

If you decide to participate, [describe procedures, including their purpose, how long they will take, their location and frequency. If activities are to be audio or video recorded, indicate this]. [Describe risks, discomforts, inconveniences, and how these will be managed. Describe any alternative procedures or courses of treatment, if applicable. Indicate costs of participating, if any.] [Describe benefits to subjects and humanity expected from the research]. However, I cannot guarantee that you personally will receive any benefits from this research. [If subject will receive compensation, describe amount and when payment is scheduled.]

[If project is more than minimal risk, the standard language regarding responsibility for medical expenses and liability must be included. See p. 19 "Additional Elements If Appropriate" for this language. Other elements of informed consent may be required for a particular study. Refer to pp. 19 and 34-36 for this information.]

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or as required by law. Subject identities will be kept confidential by [describe coding procedures and plans to safeguard data]. [If information will be released to any other party for any reason, state the person/agency to whom the information will be furnished, the nature of the information, and the purpose of the disclosure.]

Your participation is voluntary. Your decision whether or not to participate will not affect your relationship with [name agency, school, etc. where subject was recruited]. If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without penalty.

If you have any questions, please feel free to contact [provide phone number and department address. If student, also provide advisor name and phone, and identify as your advisor.] If you have questions regarding your rights as a research subject, contact the Office for Protection of Human Subjects, University of Oregon, Eugene, OR 97403, (541) 346-2510. This Office oversees the review of the research to protect your rights and is not involved with this study.

Your signature indicates that you have read and understand the information provided above, that you willingly agree to participate, that you may withdraw your consent at any time and discontinue participation without penalty, that you will receive a copy of this form, and that you are not waiving any legal claims, rights or remedies.

Print Name

Signature

Date

NOTE: Language may be altered to obtain parental consent for participation of their child (e.g., "If you decide to allow your child to participate in this study, the child will be asked to..."). Children may also sign this form if they understand the information provided, or a separate assent form may be given to young children (see following sample). If subjects are mentally disabled, the language should be appropriate to their understanding, and additional signatures are required (refer to pp. 27-31).

●For research projects that involve video recording, a video recording release form must be attached to the written consent form. If the investigator anticipates use of the recordings beyond the scope of the initial research project, the written consent form must indicate (a) who will view the recordings; (b) for what purpose(s); (c) when the recordings will be erased or destroyed.

SAMPLE CONSENT AGREEMENT FOR VIDEO RECORDING

(to be attached to written consent form)

I have received an adequate description of the purpose and procedures for video recording sessions during the course of the proposed research study. I give my consent to allow _____to be video recorded during participation in the study, and for those video recordings to be viewed by persons involved in the study, as well as for other professional purposes [*clarify purposes*] as described to me. I understand that all information will be kept confidential and will be reported in an anonymous fashion, and that the video recordings will be erased after an appropriate period of time after the completion of the study. I further understand that I may withdraw my consent at any time.

Print Name

Signature of parent/guardian Date
(if subject is a child)

Print Name

Signature of participant Date

SAMPLE ASSENT FORM (young children)

Child's name:

I am interested in what attention is, so that one day we can try to help people who find it hard to concentrate on things, and I'd like you to help me. I'd like you to play a kind of game on a computer. All you'll have to do is press a button when some lights come on. It will take about an hour, but you can rest as much as you'd like, and you can stop the game whenever you want.

If you want to rest, or stop completely, just tell me--you won't get into any trouble! In fact, if you don't want to play the game at all, you don't have to. Just say so. Also, if you have any questions about what you'll be doing, or if you can't decide whether to do it or not, just ask me if there is anything you'd like me to explain.

If you do want to try it, please sign your name on the line below. Your parent(s) have already told me that it is alright with them if you want to play the game. Remember, you don't have to, and once you start you can rest or stop whenever you like.

Print Name: _____

Signed: _____ Date _____

SAMPLE CONSENT FORM: NON-SENSITIVE QUESTIONNAIRES

I would appreciate your assistance with this research project on *[state purpose of research. If student, indicate that results will be used in thesis/dissertation]*. This research will help me understand *[state benefits to subjects and humanity expected from the research]*.

All you need to do is complete this short questionnaire, which should take approximately *[state time needed to complete questionnaire]*. If you do not wish to participate, simply discard the questionnaire. Responses will be completely anonymous; your name will not appear anywhere on the survey. Completing and returning the questionnaire constitutes your consent to participate.

Keep this letter for your records. If you have any questions regarding the research, contact *[give name, department, phone number, and department address if applicable. Include advisor name/phone if student, and identify as advisor]*. If you have any questions regarding your rights as a research subject, please contact the Office for Protection of Human Subjects at the University of Oregon at 346-2510. Thank you again for your help.

SAMPLE CONSENT LANGUAGE FOR RESEARCH WITH POTENTIAL PSYCHOLOGICAL RISK

Cover statement/Informed Consent:

If you feel uncomfortable answering any of the questions, you may discontinue at any time or skip to the next question. If you experience any stress, anxiety or psychological discomfort as a result of participation in this research, you may contact my advisor _____, the University Counseling Center at x63227, or the University of Oregon Psychology Clinic, x64954.

Debriefing Statement:

Answering personal questions about one's life can be a disconcerting experience. If answering any of these questions has upset you, or made you think of your own questions, or if you have experienced any stress or discomfort as a result of participation in this research, you may contact the University Counseling Center at x63227, the University of Oregon Psychology Clinic at x64954, or you can call the investigator or his/her advisor for other names and numbers that may be helpful to you.

VIII. SPECIAL SUBJECT POPULATIONS

DEFINITIONS

Child means any person younger than 18 years of old unless s/he has been legally emancipated. (However, college or university students 15-17 years of age may be considered adults for the purpose of participation in a research project with no more than minimal risk.)

Parent means a child's biological or adoptive parent.

Guardian means a person who is authorized by law to consent on behalf of a child or disabled individual to general medical care.

Permission means the agreement of the parent(s) or guardian to the participation of the child, disabled individual, or ward in the research.

Assent means an affirmative agreement to participate in research; mere failure to object does not constitute assent.

CHILDREN

When research subjects are children, additional considerations must be met by the researcher. Two limitations are that 1) some research which would fall in the exempt category if the subjects were all competent adults is not exempt, and 2) some research involving more than minimal risk to the subjects is prohibited. Additional requirements pertain to informed consent.

For the purpose of these rules, a "child" is any person younger than 18 years old unless he or she has been legally emancipated. A young person is legally emancipated if he or she is married or if a court has declared him or her emancipated. People younger than 18 who are living independently of their parents are not for this reason alone legally emancipated. However, college or university students 15-17 years of age may be considered adults for the purpose of participating in a research project with no more than minimal risk.

Categories of exempt research when the subjects are children

Some types of research are considered exempt even when children are subjects (refer to pp. 12-13 for a list of exempt categories). However, some types of research considered exempt when subjects are competent adults are not exempt when children are subjects. Research involving survey or interview procedures is not exempt when children are subjects. Research involving observation of public behavior is exempt only if the researcher does not participate in the activities being observed. All other research with children must be reviewed by the CPHS/IRB.

In all cases, the assent of the children, and consent of parent(s) or guardian, must be obtained prior to conducting the research.

Special considerations in research when subjects are children

- Research that poses only minimal risk to the subjects:
Adequate provisions must be made for obtaining assent of the children and permission from their parent(s) or guardians, as described below. (Minimal risk is defined on pp. 16-17.)
- Research that poses more than minimal risk but which promises to benefit the individual child directly or involves a monitoring procedure likely to contribute to the child's well-being will be permitted if:
 1. the risk is justified by the expected benefit to the child;
 2. the relationship between the risk and benefit is at least as favorable to the child as that presented by other available approaches; and

3. adequate provisions are made for obtaining assent of the children and permission from their parents or guardians, as described below.

● Research that poses more than minimal risk and does not promise to benefit the individual child directly is permitted only if:

1. the risk is only slightly greater than minimal;
2. the research will subject the child to experiences that are reasonably commensurate with those inherent in the child's actual or expected medical, dental, psychological, social or educational situation;
3. the research is likely to yield generalizable knowledge about the child's disorder or condition which is of vital importance to understanding or ameliorating the child's disorder or condition; and
4. adequate provisions are made for obtaining assent of the children and permission from their parents or guardians, as described below.

In addition, if the child is a ward of the state or any other agency, institution, or entity, he or she may be a research subject only if the research is 1) related to his or her status as a ward or 2) conducted in a school, camp, hospital, institution or similar setting in which the majority of the children involved as subjects are not wards. An advocate must be appointed for each child who is a ward. This advocate must be a person who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except as advocate or member of the CPHS/IRB) with the research, the investigator or the guardian organization. The requirement for an advocate is in addition to the requirement that permission be obtained from any other person acting on behalf of the child as guardian or *in loco parentis*.

● Research with children which exposes the subjects to more than minimal risk and which does not satisfy the conditions set out above cannot be approved by the CPHS/IRB. However, the federal regulations governing research with human subjects provide a special procedure for seeking approval for such research that involves getting approval of the Secretary of DHHS. OPHS has information about this process.

Informed Consent

Assent of the children: Assent must be obtained from the child if the child is 7 years old or older. However, the CPHS/IRB may waive the assent requirement if some or all of the children lack the capacity to give meaningful assent, or the research holds out the prospect of direct benefit that is important to the health or well-being of the children that is available only in the context of the research.

The federal regulations do not set a minimum age at which a child's assent must be solicited but instead say that assent is required whenever in the judgment of the CPHS/IRB the children are capable of providing assent, taking into account their ages, maturity, and psychological state. The CPHS/IRB has set this age at 7 years based on consultations with a child development expert on the University of Oregon faculty. Therefore, when research subjects are younger than 7, their assent does not have to be solicited, but the CPHS/IRB encourages researchers to explain to younger children what they will be asked to do in the course of the research and to secure their agreement to participation if possible.

Permission from parent(s) or guardian: If the research involves only minimal risk, or it poses more than minimal risk but promises to benefit the child directly, permission must be obtained from at least one of the child's parents, or the child's guardian. If the research poses more than minimal risk and no direct benefit to the child, both parents or the child's guardian must give permission for the child to participate in the research. However, the permission of a parent who is deceased, unknown, or incompetent, or not reasonably available, or who does not have legal responsibility for the care and custody of the child is not required.

If a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the children (for example, neglected or abused children), the CPHS/IRB may waive the requirement that parental permission be sought, provided that there is an appropriate

alternative mechanism for protecting the children which is not inconsistent with the law. The choice of an appropriate alternative mechanism depends on the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the children, and their age, maturity, status and condition. In such cases the researcher should propose an alternative mechanism, explaining why it will protect the children. The CPHS/IRB will then review the adequacy of this proposal.

Information that must be provided in requests for assent and permission; documentation of informed consent: When parents or guardians are asked for permission and children are asked for assent, they must be given the same information that is generally required when informed consent for participation in research is sought, and their permission and assent must be documented in writing. The general requirements are discussed on pp. 18-22.

The assent form for children should, of course, be written in language appropriate to their age and understanding (a sample form for use with younger children can be found on p. 25). If the parents are not also research subjects themselves, it may be appropriate to have them sign the same form their children sign. If the parents are also research subjects, ordinarily a separate form should be drafted for them, addressing their own participation as well as that of their children.

In circumstances in which the CPHS/IRB may alter or waive the usual requirements for securing and documenting informed consent when the subjects are competent adults (refer to pp. 20-21), the CPHS/IRB may waive or alter the requirements for seeking permission and assent when children are subjects.

MENTALLY DISABLED INDIVIDUALS

The CPHS/IRB has adopted special rules that apply when research subjects are mentally disabled. Most of the general requirements for approving research with human subjects apply, but with some exceptions and additions. The major exceptions are that 1) some research which would fall in the exempt category if the subjects were all competent adults is not exempt, and 2) some research involving more than minimal risk to the subjects is prohibited. Additional requirements pertain to informed consent.

For the purpose of these requirements, a "mentally disabled" person is a person who, because of mental illness, mental retardation, emotional disturbance, or senility, is incapable of giving informed consent.

Of course, some persons who have these conditions are also able to give informed consent, but the CPHS/IRB cannot determine the capacity of persons with these conditions on the basis of labels alone. Therefore, whenever proposed research involves subjects who have been diagnosed with one of these conditions or who may have such a condition, the researcher should explicitly tell the CPHS/IRB whether the subjects are able to give informed consent because of the condition. If the subjects are able to give informed consent, the special rules in this section do not apply, and only the general requirements for research with human subjects must be satisfied.

Categories of exempt research when the subjects are mentally disabled

Some types of research are considered exempt even when subjects are mentally disabled (refer to pp. 12-13 for a list of exempt categories). However, some types of research considered exempt when subjects are competent adults are not exempt when subjects are mentally disabled. Research in category 1 (conducted in established or commonly accepted educational settings involving normal educational practices) is exempt only if the research involves no changes in the content of instruction, location of instruction, or procedures used during instruction from those a subject would normally experience. Research involving survey or interview procedures is not exempt. Research involving observation of public behavior is exempt only if the researcher does not participate in the activities being observed. All other research with mentally disabled subjects is subject to review by the CPHS/IRB.

Special considerations in research when subjects are mentally disabled

- Research that poses only minimal risk to the subjects: No special limits are placed on this type of research, except that adequate provisions must be made for obtaining assent of the mentally disabled subjects and permission from their representatives, as described below. (Minimal risk is defined on pp. 16-17.)

- Research that poses more than minimal risk but which promises to benefit the individual subject directly

will be permitted if:

1. the risk is justified by the expected benefit to the subject;
2. the relationship between the risk and benefit is at least as favorable to the subject as that presented by other available approaches; and
3. adequate provisions are made for obtaining assent of the mentally disabled subjects and permission from their representatives, as described below.

In addition, if the mentally disabled subjects are wards of the state or any other agency, institution, or entity, they may be the subjects of research that poses more than minimal risk only if the research is 1) related to their status as wards or 2) conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of the subjects involved are not wards. Furthermore, if the research poses more than minimal risk, an advocate must be appointed for each mentally disabled person who is a ward. The advocate must be a person who has the background and experience to act in, and agrees to act in, the best interests of the mentally disabled person for the duration of the person's participation in the research. The advocate cannot be associated in any way with the research, the investigator(s) or the guardian organization. A person can be the advocate for more than one person. The requirement for an advocate is in addition to any other person acting on behalf of the mentally disabled person as guardian.

● Research that poses more than minimal risk and does not promise to benefit the individual subject directly will be permitted if:

1. the risk is only slightly greater than minimal;
2. the research will expose the subject to experiences that are reasonably commensurate with those inherent in the subject's actual or expected medical, dental, psychological, social or educational situation;
3. the research is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance to understanding or ameliorating the subject's disorder or condition; and
4. adequate provisions are made for obtaining assent of the mentally disabled subjects and permission from their representatives, as described below.

In addition, if the mentally disabled subjects are wards the requirements described previously apply.

Informed consent

Assent of the subjects: Ordinarily, a mentally disabled person may not be the subject of research unless the person gives assent. The CPHS/IRB may waive the assent requirement if 1) the capability of some or all of the subjects is so limited that they cannot reasonably be consulted or 2) the intervention involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the subjects that is available only in the context of the research.

Permission from competent adults acting on behalf of the subjects: Ordinarily, a mentally disabled person may not be the subject of research unless permission is obtained from the person's guardian. For purposes of these rules a guardian cannot be associated in any way with the research or the investigator(s). If the mentally disabled person is a ward of the state or any other agency, institution or entity, a person associated with the entity cannot be a guardian for purposes of these rules.

The parent of a mentally disabled person below the age of 18 is presumed to be the person's guardian. If the mentally disabled person is older than 18, the parent is not automatically the guardian. If the subjects are mentally disabled adults who have not formally had legal guardians appointed for them, the researcher should propose a procedure for securing permission from a competent adult acting solely in the interests of the mentally disabled person. This procedure must be consistent with federal, state, and local law.

Information that must be provided in requests for assent and permission and documentation of informed consent: Mentally disabled subjects and the competent adults acting on their behalf must be given the same information that is generally required when informed consent for participation in research is sought, and their permission and assent must be documented in writing. The general requirements are described on pp. 18-22. The assent form for the mentally disabled subjects should, of course, be written in language appropriate to their level of understanding.

In circumstances in which the CPHS/IRB may waive or alter the usual requirements for securing and documenting informed consent when the subjects are competent adults (refer to pp. 20-21), the CPHS/IRB may waive or alter the requirements for seeking permission and assent when subjects are mentally disabled.

PREGNANT WOMEN AND FETUSES

Pregnancy encompasses the period of time from confirmation of implantation (as evidenced by missed menses or a medically acceptable test) until expulsion or extraction of the fetus. Fetus means the product of conception, from the time of implantation until a determination is made, following expulsion or extraction, that it is viable.

Activities Directed Toward Pregnant Women

No pregnant woman may be involved in a research activity unless a) the risk to the fetus is minimal, or b) the purpose of the activity is to meet the health needs of the mother and the fetus will be placed at risk only to the minimum extent necessary to meet such needs.

Additional Consent Requirements

Research activity permitted above may be conducted only after fully informing the mother and father of any possible impact on the fetus and obtaining informed consent from the legally competent mother and father. Consent by the father need not be secured if:

- a. the purpose of the study is to meet the health needs of the mother;
- b. the identity or whereabouts of the father cannot be reasonably ascertained;
- c. the father is not reasonably available;
- d. the pregnancy resulted from rape.

Research Directly Involving Fetuses

Any research directly involving fetuses requires consultation with the CPHS/IRB.

PRISONERS

Prisoner means any individual involuntarily confined or detained in a penal institution. The term applies to those sentenced to such an institution, those detained in other facilities as alternatives to prosecution, and those detained pending arraignment, trial, or sentencing.

Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. Prisoners may be convicted felons, or may be untried persons who are detained pending judicial action, for example, arraignment or trial.

Common examples of the application of the regulatory definition of prisoner are as follows:

* Individuals who are detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration are prisoners; however, individuals who are receiving non-residential court-ordered substance abuse treatment and are residing in the community are not prisoners.

* Individuals with psychiatric illnesses who have been committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration are prisoners; however, individuals who have been voluntarily admitted to an institution for treatment of a psychiatric illness, or who have been civilly committed to nonpenal institutions for treatment because their illness makes them a danger to themselves or others, are not prisoners.

* Parolees who are detained in a treatment center as a condition of parole are prisoners; however, persons living in the community and sentenced to community-supervised monitoring, including parolees, are not prisoners.

* Probationers and individuals wearing monitoring devices are generally not considered to be prisoners; however, situations of this kind frequently require an analysis of the particular circumstances of the planned subject population. Institutions may consult with OHRP when questions arise about research involving these populations.

Prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary decision whether or not to participate as subjects in research. Additional safeguards are required, therefore, when prisoners are proposed as subjects. NOTE: The CPHS/IRB needs to be notified and a new protocol will need to be submitted for review if currently enrolled subjects in a non-prisoner project become incarcerated. Additional information regarding the new regulation is on the Internet (<http://hhs.gov/ohrp/humansubjects/guidance/prisoner.htm>).

CPHS/IRB Membership Regarding Research with Prisoners

A majority of the CPHS/IRB shall have no association with the prison(s) involved. At least one member of the CPHS/IRB shall be a prisoner or prisoner representative, with appropriate background and experience. If the research is reviewed by more than one IRB, only one need have a prisoner representative.

Types of Research Permitted

When using prisoners as subjects, only the following types of research are allowable:

- Study of possible causes, effects, or processes of incarceration or of criminal behavior;
- Study of prisons as institutional structures or of prisoners as incarcerated persons;
- Study of conditions particularly affecting prisoners as a class, including research on relevant social and psychological problems such as alcoholism, drug addiction, and sexual assault;
- Study of practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the prisoner subjects.

In all cases, the research is to present no more than minimal risk and inconvenience to subjects. For research in the latter two categories above, consultation with the CPHS/IRB is necessary to determine possible need for approval by experts in penology medicine and ethics. Any proposed biomedical research requires consultation with the CPHS/IRB.

Funded Research

The institution responsible for conducting research involving prisoners that is supported by DHHS shall certify to the Secretary through the Office of Human Research Protections (OHRP) that the IRB has made the seven findings required under the regulations (45 CFR 46.305(a)). The institution must send to OHRP a certification letter to this effect, which should also include the name and address of the institution and specifically identify the research protocol in question and any relevant DHHS grant application or protocol. DHHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing to the institution on behalf of the Secretary under 45 CFR 46.306(a)(2).

Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one. The term "research proposal" includes the IRB-approved protocol, any relevant HHS grant application or proposal, any IRB application forms required by the IRB, and any other information requested or required by the IRB to be considered during initial IRB review.

Additional Considerations

When using prisoners as subjects the following additional concerns must be addressed:

- Selection of subjects within the prison is to be fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless providing justification otherwise, control subjects must be selected randomly from an appropriate population of prisoners.
- Any advantages accruing a prisoner subject, when compared to standard prison conditions, are not to be of such magnitude as to impair the prisoner's ability to weigh appropriately the risks of research participation in the limited choice environment of prison.
- The risks involved should be commensurate with risks that would be accepted by non-prisoner volunteers.
- Adequate evidence exists that parole boards will not take into account a prisoner's participation or non-participation in research and prisoners are informed in advance that participation or non-participation in the research will have no effect on parole decisions.
- Information must be provided to prisoners in language they can understand.
- An adolescent (e.g., age 14) detained in a juvenile detention facility is a prisoner.
- Where the CPHS/IRB finds there may be a need for follow-up examination or care of subjects after participation, adequate provision is made, taking into account the lengths of subjects' sentences, and subjects are informed.
- The guidelines apply whenever any human subject in a research project subject to 45 CFR part 46 becomes a prisoner at any time during the study.
- If a subject becomes a prisoner after enrollment in research, the investigator should report this situation to the Office for Protection of Human Subjects immediately (541) 346-3106. If the investigator wishes to have the prisoner subject continue to participate in the research, all research interactions and interventions with and obtaining identifiable private information about, the now-incarcerated prisoner-subject must cease until all requirements for research involving prisoners have been satisfied with respect to the relevant protocol.
- The exempt review categories do not apply to research involving subjects.
- The definition of minimal risk for research involving prisoners differs from the definition of minimal risk in subpart A of 45 CFR 46. See 45 CFR 46. 102(i). For research involving prisoners, the definition of minimal risk requires reference to physical or psychological harm, as opposed to harm or discomfort, to risks normally encountered in the daily lives, or routine medical, dental or psychological examination of healthy persons.

Definition of Minimal Risk in Prisoner Research (45CFR 46.303(d)): "Minimal risk" is the probability and magnitude of **physical or psychological** harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of **healthy persons**.

IX. SPECIAL TOPICS

RECRUITMENT

Voluntariness begins with recruitment. Potential subjects must not feel that they have been coerced into participating, nor must they fear the loss of some benefit to which they are otherwise entitled if they choose not to participate (such as on-going support by a social agency).

Special care must be taken if the person doing the recruiting is a person who is in a position of authority (such as a teacher recruiting his or her own students) or makes decisions about the provision of services (such as a director of a training clinic). It is the investigator's responsibility to ensure that a person's decision to participate or not will have no other effect on an existing relationship.

Guidelines for Research Using Classroom Subjects

Students in University of Oregon classes are occasionally asked to participate in research. In such cases, the researcher should ask the instructor to give her/his permission to use class time to conduct a study. Because students in classrooms comprise a captive audience, care should be taken to respect their rights as subjects and as students.

If participation as a subject is part of the academic work of a student, it must not be a coercive requirement, and informed consent, if appropriate, must be obtained. Alternate means of receiving credit if a student chooses not to participate or chooses to withdraw during the course of the study should be provided.

To assure that students feel free to refuse to participate without concern that the evaluation of their classroom performance will be affected, the instructor should not be present during any research activities. Furthermore, the instructor should not be informed nor be aware of who participates.

When investigators wish to audio record or video record university classes, students have the right to refuse participation. At the same time, students should not be penalized by losing significant classroom instruction in the event they decide not to be recorded. The following procedures should be used:

- The investigator must notify students in advance that the class session will be recorded;
- Recording must be stopped long enough before the end of the class to allow students to ask questions without appearing on the recording;
- Students must be given a full explanation of the project after the recording and given the option to arrange for deletion of their participation on the recording.

Because research involves time that would otherwise be used for instructional activities, departments may wish to promulgate policies with regard to classroom research. The CPHS/IRB recognizes that participating in research and receiving information about the research may be instructionally relevant.

Recruiting Clients of Social Service Agencies, Schools, and Other Institutions

The researcher shall not ask institutions to directly identify potential subjects for a research study. Rather, the investigator shall ask an intermediary (doctor, case worker, school administrator) to first approach potential subjects (or their guardians, as appropriate) and inform them about the research. If a potential subject agrees to participate, the intermediary should provide her/him with the information necessary to contact the researcher, in such a way that the institution is unaware whether the subject chooses to participate in the research. The intermediary should not obtain consent from potential subjects.

The researcher shall not ask institutions to release records or anecdotal information either for the purposes of identifying subjects, or for examination by the investigator, unless this information is public. An investigator wishing to examine records must first obtain permission of the subject via an intermediary. If a potential subject agrees to release his or her records, the intermediary should provide the information necessary to contact the researcher. This provision does not apply to records with all identifiers removed (see p. 12, exemption 4). **NOTE: Approval from participating institutions (e.g., schools, agencies) must be on file with OPHS prior to recruitment.**

Advertising for Subjects

If advertising for subjects, investigators must follow these guidelines: a) Information must not be misleading to subjects, especially when a study will involve vulnerable populations; b) Include the name and address of the investigator, the purpose of the research and eligibility criteria for participation as subjects, a clear description of any benefits and/or risks of participating, the affiliation of the researcher, the location of the research, and whom to contact for further information; c) If a drug or device is to be used in the research, no claim should be made as to its superiority, safety or effectiveness. A copy of the advertisement must be included with the protocol.

PROTOCOLS USING MAGNETIC RESONANCE IMAGING (MRI)

Researchers must contact the director of the Lewis Center for Neuroimaging in Straub Hall to obtain specific requirements regarding the use of the machine and the specific language that is required in all informed consent forms that involve the use of the MRI. The completed protocol with the appropriate template informed consent form language must be submitted to the CPHS/IRB for review and approval before research can be initiated. The following general information must be included in the informed consent form:

- The Magnetic Resonance Imaging (MRI) equipment consists of a fast switching gradient coil accessory system (field strength of 3 Tesla). The Lewis Center for Neuroimaging is located in Straub Hall on the University of Oregon campus. This study will not require any invasive procedure.*

- *The total time of your involvement is expected to be ___ minutes, with about ___ of that time spent at the magnet.*
- *All testing carried out with the magnet will be conducted by a trained technician.*
- *There are some possible risks for participants if metal objects are drawn to the magnet while a participant is within or near the bore. Accordingly, you will be asked to leave all jewelry and metal objects outside of the testing area. No loose metal objects will be allowed near the magnet.*
- *The use of the MRI is not more than minimal risk. (However, the standard medical compensation and liability clauses may be required depending on the activities and population included in specific projects - see p. 19.)*

INFORMED CONSENT AND ABUSE REPORTING REQUIREMENTS

Child Abuse Reporting Requirements

According to ORS 419B.010, "Any public or private official having reasonable cause to believe that any child with whom the official comes into contact has suffered abuse or that any person with whom the official comes in contact has abused a child shall immediately report or cause a report to be made..." to the Department of Human Services/Child Welfare Program of the State of Oregon. Public or private officials include:

- Physicians, interns, residents, chiropractors, dentists, optometrists, licensed practical or registered nurses, naturopathic physicians.
- School employees.
- Certified provider of foster care, or an employee thereof.
- Registered or certified child care provider.
- Employees of the Department of Human Services, State Commission on Children and Families, Child Care Division of the Employment Department, the Oregon Youth Authority, a county health department, a community mental health and developmental disabilities program, a county juvenile department, a licensed child-care agency or an alcohol and drug treatment program.
- Peace officers, firefighters, emergency medical technicians.
- Attorneys, court appointed special advocates.
- Psychologists, clergy members, licensed clinical social workers, licensed professional counselors, licensed marriage and family therapists.

If the research requires subjects in these professions to respond to questions about suspected sexual abuse in the children they observe, the respondents must be informed about the possible legal ramifications of their answers. The following language is suggested for use in the informed consent form:

The questions you will be asked include information regarding child abuse. According to Oregon Revised Statute 419B.010, all public or private officials are required to report any "reasonable cause to believe that any child...has suffered abuse." In the unlikely event that your responses to the child abuse items were disclosed and there was evidence that you did not appropriately report child abuse, you could be subject to a fine not exceeding \$1,000.

Abuse of Elderly Persons

According to ORS 124.060, "Any public or private official having reasonable cause to believe that any person 65 years of age or older with whom the official comes into contact while acting in an official capacity, has suffered abuse, or that any person with whom the official comes in contact while acting in official capacity has abused a person 65 years of age or older shall report or cause a report to be made..." to the Senior and Disabled Services Division or to a law enforcement agency within the county where the person making the report is at the time of contact.

Definitions of abuse means one or more of the following:

- Any physical injury caused by other than accidental means, or which appears to be at variance with the explanation given of the injury.
- Neglect which leads to physical harm through withholding of services necessary to maintain health and well-being.

- Abandonment, including desertion or willful forsaking of an elderly person or the withdrawal or neglect of duties and obligations owed an elderly person by a caretaker or other person.
- Willful infliction of physical pain or injury.

Public or private officials include:

- Physician, naturopathic physician, osteopathic physician, chiropractor or podiatric physician and surgeon, including any intern or resident.
- Licensed practical nurse, registered nurse, nurse's aide, home health aide or employee of an in-home health service.
- Employee of the Department of Human Services, county health department or community mental health and developmental disabilities program.
- Peace officer.
- Clergyman.
- Licensed clinical social worker.
- Physical, speech or occupational therapists.
- Senior center employee.
- Information and referral or outreach worker.
- Licensed professional counselor or licensed marriage family therapist.
- Any public official who comes in contact with elderly persons in the performance of the official's official duties.

Abuse Reporting for Mentally Ill or Developmentally Disabled Persons who Receive Services from a Community Program or Facility (ORS 430.735 to 430.765)

According to ORS 430.737, the mandatory reporting policy states “that for the purpose of preventing abuse and safeguarding and enhancing the welfare of adults who are mentally ill or developmentally disabled, it is necessary and in the public interest to require mandatory reports and investigations of allegedly abused mentally ill and developmentally disabled adults.”

The definition of “Adult” means a person who is mentally ill or developmentally disabled, who is 18 years of age or older and receives services from a community program or facility.

Any public or private official who has reasonable cause to believe that any adult with whom the official comes in contact while acting in an official capacity, has suffered abuse, or that any person with whom the official comes in contact while acting in an official capacity has abused an adult shall report or cause a report to be made as required to Department of Human Services or a law enforcement agency within the county where the person making the report is at the time of contact.

Adult Abuse Definitions:

- Any death caused by other than accidental or natural means or occurring in unusual circumstances;
- Any physical injury caused by other than accidental means, or that appears to be at variance with the explanation given of the injury;
- Willful infliction of physical pain or injury;
- Sexual harassment or exploitation including, but not limited to, any sexual contact between an employee of a community facility or community program, or provider, or other caregiver and the adult. For situations other than those involving an employee, provider, or other caregiver and an adult, sexual harassment or exploitation means unwelcome verbal or physical sexual contact including requests for sexual favors and other verbal or physical conduct directed toward the adult;
- Abuse may also include:
- Failure to act/neglect that leads to or is in imminent danger of causing physical injury, through negligent omission, treatment, or maltreatment of an adult, including but not limited to failure by a provider or staff to provide an adult with adequate food, clothing, shelter, medical care, supervision, or through condoning or permitting abuse of an adult by any other person. However, no person shall be deemed neglected or abused for the sole reason that he or she voluntarily relies on treatment through prayer alone in lieu of

medical treatment;

- Verbal mistreatment by subjecting an adult to the use of derogatory names, phrases, profanity, ridicule, harassment, coercion or intimidation and threatening injury or withholding of services or supports, including implied or direct threat of termination of services;
- Placing restrictions on a resident's freedom of movement by seclusion in a locked room under any condition. Restriction to an area of the residence or restricting access to ordinarily accessible areas of the residence is not allowed, unless arranged for and agreed to on the Individual's Support Plan or Personal Care Plan;
- Using physical restraints without a written physician's order, or as part of an Individual Support Plan, unless a resident's actions present an imminent danger to himself/herself or others, and only until appropriate action is taken by medical, emergency, or police personnel;
- Financial exploitation which may include, but is not limited to, unauthorized rate increases, staff borrowing from or loaning money to residents, witnessing wills in which the caregiver is beneficiary, adding caregiver's name to resident's bank accounts or other personal property without approval of the individual or his/her guardian and the ISP team or PCP; and
- Inappropriately expending a resident's personal funds, theft of a resident's personal funds, using a resident's personal funds for staff's own benefit, commingling resident's funds with caregiver or other resident's funds, or the caregiver becoming guardian or conservator

INTERNATIONAL RESEARCH

Research in foreign countries also presents special concerns regarding the rights and welfare of human subjects. In general, the CPHS/IRB accepts the standards of the location in which the research is taking place; unless those standards grossly violate the basic principles of ethical human subjects research. In addition, the following issues apply to international human subject research:

- All materials, including consent forms must have English language translations included with the protocol.
- Documentation of permission from local authorities and/or research visa are generally required before approval can be granted.

TRANSPORTATION OF RESEARCH SUBJECTS

Subjects shall not be transported by employees/researchers in a personal/private vehicle. If subjects need to be transported by a researcher, a State vehicle must be used and the request must be submitted through your departmental travel coordinator. If subjects need to be transported as part of the research activities, they can be reimbursed for bus/cab fare or their driver could be reimbursed for mileage for the use of a car.

COMPENSATION FOR PARTICIPATION IN RESEARCH

If financial compensation is offered for participation in research, a pro-rated payment system should be used whenever possible. For example, when subjects choose to withdraw from participation early, they should receive a portion of the payment relative to the time spent participating.

The use of a drawing is permitted as a form of compensation. Subjects must be informed of the estimated probability of winning in the consent form. The issue of undue inducement to participate based upon the value of the drawing will be determined during the review process (i.e., a study with small costs/risks should have correspondingly small compensation).

If students will be awarded academic/extra credit for research participation, the amount and type of credit as well as any required conditions should be clearly stated in the consent form. Alternate academic/extra credit options must be available for students who do not wish to participate and students must be informed that they may complete alternatives to receive the same credit in the consent form. OPHS may require a copy of the class syllabus describing the academic and research extra credit options.

INVESTIGATIONAL DRUGS/DEVICES REVIEW

The Food and Drug Administration regulations governing the use of investigational drugs and devices in research with human subjects require the review of such research by the CPHS/IRB. The CPHS/IRB determines whether the drug or device is of significant risk or non-significant risk (Significant risk devices are considered to support or sustain life or are of substantial importance in diagnosing, curing, or treating disease, such as artificial hearts, intrauterine devices, or hemodialysis systems). An "investigational device exemption" (IDE) exempts sponsors or investigators temporarily during the period of investigation from certain parts of the regulations. OPHS will make the appropriate certification to funding agencies when an investigational new drug or device is proposed in the research.

CLASSROOM INITIATED RESEARCH OR TRAINING PROJECTS INVOLVING HUMAN SUBJECTS

Student research conducted purely for instructional purposes as part of course work at the University of Oregon is generally not reviewed by the CPHS/IRB. If, however, there is a possibility that the data will be published, presented at conferences or maintained for later use, the project should be approved by the CPHS/IRB prior to human subjects recruitment/involvement. The Committee is unable to give *post facto* approval.

Even though some classroom initiated research is not reviewed for risk by the CPHS/IRB, it is important that instructors and students discuss the guidelines and ethics for protection of research subjects and incorporate these into their methodology. Particular emphasis should be placed on:

1. Developing an awareness of the types of risks subjects may be exposed to in various types of research projects, i.e., psychological, social, physical, economic, legal, etc.
2. Obtaining voluntary informed consent to participate in a way that truly informs subjects of the purpose and potential risks and benefits of the research.
3. Protection of the privacy and confidentiality of the subjects.
4. Management of potential risks to subjects.
5. Identification of benefit to be derived from participation in the research.
6. A risk/benefit analysis for all populations, with special consideration of vulnerable populations (children, pregnant women, fetuses, mentally disabled, institutionalized persons, prisoners, etc.).
7. Recommended Reading: The Belmont Report Ethical Principles and Guidelines for the Protection of Human Subjects of Research, April 18, 1979. The document is available on the web (<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>). Student researchers are encouraged to complete the UO's training program. The program is available online via the Office for Protection of Human Subjects website (<http://humansubjects.uoregon.edu/citiprogram.htm>).

REGULATIONS FOR RESEARCH WITH HUMAN SUBJECTS UNDER HIPAA

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) is a federal law that has several provisions affecting research that involves health information from human research participants. The Act includes a Privacy Rule that restricts disclosure of protected health information (PHI) for individuals, and the Rule is effective for research projects on April 14, 2003. If your research includes accessing PHI from health care providers as part of your data collection activities, you will need to use a HIPAA compliant authorization form to obtain permission to access subjects' health information. A sample authorization form is attached with six required elements. The new authorization for release of records form for research projects must be approved by the Office for Protection of Human Subjects.

Researchers must comply with the new rules if they are currently accessing or may want to access protected health information on individual research subjects from "covered entities" (includes doctors, hospitals, mental health providers, billing services, and insurance carriers), whether obtaining PHI directly from those covered entities or through a collaborator on the project who accesses PHI for the project. The Privacy Rule under HIPAA requires legal descriptions in the consent form and in the "authorization for release of records form" for each research subject. HIPAA does not remove any of the requirements of informed consent set forth in the other federal regulations.

Medical information that research participants self-report for research projects is not considered PHI because a covered entity (includes doctors, hospitals, mental health providers, and insurance carriers, etc.) is not collecting the information. Answers given on health history questionnaires and intake forms are not considered PHI. HIPAA guidelines may affect research projects that include recruitment procedures that identify subjects through covered entities in which the names of patients are released to researchers (i.e., names are considered PHI).

HIPAA Definitions

Authorization: an agreement between the covered entity and the participant to use specific PHI for specific purposes. The authorization must specifically describe the PHI being collected, who is collecting the information, to whom it will be released, why it is being released it, how long the authorization is in effect, and it must be signed and dated by the participant.

Covered entity: a health plan, a health care clearinghouse, or a health care provider who transmits any protected health information in electronic form. A health care provider becomes a "covered entity" only if it transmits health information in electronic form in connect with a "HIPAA transaction." A "HIPAA transaction" is the electronic transmission of information "to carry out financial or administrative activities related to health care." Examples include the following: First report of injury, counseling, physical assessments, providing medical devices or equipment, health care claims, coordination of benefits.

Protected Health Information (PHI): includes 18 categories of individually identifiable health information, which is created or received by a covered entity, transmitted or maintained in any form or medium, including paper records. Such information relates to the past, present, or future physical health, mental health or condition of an individual. PHI either identifies or could be used to identify the individual. Health information which includes any of the following identifiers is considered PHI and is subject to the regulations contained in the privacy rule:

Name	Address
Names of relatives	Names of employers
E-mail address	Fax number
Telephone number	Birth date
Finger or voice prints	Photographic images
Social security number	Internet protocol (IP) address
Any vehicle or device serial number	Medical record number
Health plan beneficiary number	Account number
Certificate/license number	Web URL
Any other unique or identifying number, characteristic, or code	

Improper disclosure or use of PHI without a signed release for that purpose can result in very large fines and up to 10 years imprisonment of the individual researcher (e.g., Civil Penalties - \$100 up to \$25,000/person/year).

HIPAA FAQs

Q. Who is affected by HIPAA?

A. All researchers (faculty, staff, or students) at the University of Oregon who access protected health information (PHI) preceding or during the conduct of their research must comply with HIPAA regulations. Researchers must use an authorization form that includes specific HIPAA requirements. Some health care providers may require the use of their authorization form. The specific requirements for a valid authorization are:

1. Description of personal health information (PHI) to be used
2. Who may use or disclose the information
3. Who may receive the information
4. Description of each purpose to whom the covered entity may disclose PHI
5. Expiration date or event (must indicate date or state "None")
6. Individual's signature and date
7. Right to revoke authorization
8. Right to refuse to sign authorization
9. Re-disclosures not protected
10. Individual given a copy of the authorization
11. Authorization must be written in plain language

Authorization may need to be retained for six years. Subjects have the right to revoke the authorization.

Q. Does the receipt of PHI from a covered entity enforce the HIPAA Privacy Rule requirements on researchers?

A. The "covered entity" has to comply with HIPAA regulations prior to transferring the PHI to another organization, but it is the receipt and possession of the PHI that will impose HIPAA requirements on researchers. This will affect recruitment procedures for studies involving patient referrals. For example, if a physician gives the UO researcher a list of patient names that meet the enrollment criteria, the physician has released PHI (names being one of the 18 criteria). However, if prospective participants contact the UO researcher as a result of information given to them by their physician about the study, PHI will not have been shared and HIPAA will not apply.

Q. Does HIPAA require that authorization and consent language used prior to April 14, 2003, be changed and new consent/authorizations be obtained?

A. No. The language must be used in any authorizations signed after April 14. If an investigator is actively enrolling subjects and will continue to do so after April 14, the authorization must be obtained by the date of enrollment. The key is the date the authorization is signed. If, for instance, you have a five-year study beginning in April but subjects recruited for the project do not sign the authorization/consent form until after April 14, 2003, HIPAA language must be used. All subjects enrolled in research prior to April 14, 2003, are grandfathered in if they have completed an informed consent form. However, any subjects consented or re-consented after April 14, 2003, under a new or an existing University of Oregon approved protocol, must complete both a new informed consent form and an authorization form for the release of health information.

Q. Does HIPAA only apply to electronic data?

A. No. Initially the Privacy Rule referred only to electronic data and thus there is some confusion about this issue. HIPAA applies to all use and disclosure of private health information whether it is paper, oral, or electronic. An elevator conversation could easily be the cause of a HIPAA violation.

GENETIC RESEARCH AND COMPLIANCE WITH STATE LAW

The Oregon Legislature enacted Genetic Privacy laws in response to concern about genetic privacy in the areas of insurance, employment and research (ORS 192.533). The laws were amended in 2003. Genetic research can be of two kinds: either anonymous research (or research otherwise exempt from Institutional Review Board approval), or non-exempt research. Any researcher, who proposes to conduct genetic research, including anonymous research, must submit the research to an IRB for a determination that the research is anonymous or

approval of non-exempt research (OAR 333-025-0120(1)).

Anonymous or Exempt Research

The law generally requires informed consent to obtain genetic information, subject to certain exceptions. One of the exceptions is for anonymous genetic research, which research requires notification to or consent from the research subject. The statute defines anonymous research as:

...scientific or medical genetic research conducted in such a manner that any DNA sample or genetic information used in the research is unidentified (ORS 192.531(1)).

Subsequent statutes direct the Department of Human Services to adopt rules to implement a notification requirement for anonymous research subjects. Anonymous research must be determined by an Institutional Review Board to be exempt from review requirements.

The administrative rule provides this more expansive definition of anonymous research:

...scientific or medical research conducted in such a manner that the identity of an individual who has provided a sample, or the identity of an individual from whom genetic information has been obtained or the identity of the individual's blood relatives, cannot be determined. "Anonymous research" does not include research conducted in such a manner that the identity of such an individual, or the identity of the individual's blood relatives, can be determined by use of a code, encryption key or other means of linking the information to a specific individual (OAR 333-025-0100(1)).

Under the Administrative Rules, the researcher must demonstrate that the research subject was notified that anonymous research might take place in the future and, at the time of notification, did not request that the sample be withheld from the anonymous research. "Notification" is defined as a written statement in plain language, either before or after the sample is obtained, that the sample may be used for anonymous research. Multiple notifications are permitted, but at least one notification is required. Any notification must include a general description of the type of sample intended to be used, a general explanation of the meaning of anonymous research, and an opportunity for the subject to withhold the sample from the anonymous research (OAR 333-025-0120(3 & 4)).

Non-exempt Research

The statute requires researchers conducting non-exempt research to obtain informed consent of the individual research subject or his or her representative. The consent must comply with statutory requirements and the Department of Human Services rules must adopt rules conforming to the Federal Policy for the Protection of Human Subjects, 45 C.F.R. 46, particularly addressing the operation and appointment of Institutional Review Boards, which Boards must register with DHS pursuant to DHS rule.

If the research anticipates coded or identified or identifiable DNA samples or genetic information, the statute imposes additional requirements. Coded is defined in the statute as:

...identifiable only through the use of a system of encryption that links a DNA sample or genetic information to an individual or the individual's blood relative. A coded DNA sample or genetic information is supplied by a repository to an investigator with a system of encryption (ORS 192.531(5)).

"Identifiable," "Identified" and "Identifier" are all separately defined in the statute. Their general meaning is that there is data capable of linking the individual or a blood relative to the DNA sample, and include names, telephone numbers, social security or driver's license numbers and fingerprints (ORS 192.531(15), (16) and (17)).

If the genetic research is coded, the research subject must grant informed consent for the specific research project or genetic research generally. The research must be approved by an IRB after disclosure to the board by the researcher of the risks of coding. Approval of the IRB does not need to take any particular form, so long as the IRB is fully informed in the course of the researcher's presentation and approves the protocol with the clear understanding that coding is an element of the research. The code must not be derived from individual identifiers, must be kept securely and separately from the DNA samples and genetic information, and must not be accessible to the investigator unless specifically approved by the IRB. The data must be stored securely in electronic files or by

other means with access limited to necessary personnel. The data must also be limited to elements required for analysis and meet the criteria for a “limited data set” (45 C.F.R. 164.514 (e)). Finally, the investigator must be a party to the data use agreement. An agreement into which a “covered entity” enters with the recipient (e.g., researcher) of a limited data set that establishes the ways in which the limited data set may be used and how it will be protected (45 C.F.R. 164.514 (e)).

The Administrative Rules enacted by DHS to implement the statutes on Genetic Privacy require all genetic research, whether anonymous, exempt or otherwise, to be submitted to an IRB for explicit approval or explicit determination that the research is exempt. The researcher is responsible for obtaining informed consent for non-exempt genetic research and for assuring the IRB that the requirements of the genetic research rules have been met. If the genetic information or biological sample is obtained after June 25, 2001, it may only be used by the researcher with the specific informed consent of the research subject.

Specific informed consent for genetic research is defined in the administrative rule as:

The individual or the individual’s representative has consented to the use of that individual’s DNA sample or genetic information for genetic research or for a specified genetic research project (OAR 333-025-0100(21)).

Recontact of Research Subject

The statute and rules also addresses recontact of research subjects. The statute prohibits recontact of a subject based on coded information. The rule requires the subject be notified of the specific circumstances under which recontact can occur in the original consent process. Any recontact option, whether part of the original protocol or a later application, must be approved by the IRB. However, if recontact was not contemplated during the original consent process, the researcher must seek separate IRB approval for recontact. The threshold for permissible recontact is extremely high. Such approval must assure three conditions: that the findings are scientifically valid and confirmed (e.g., the DNA was analyzed by a CLIA approved facility); that they have significant implications for the subject’s or public’s health, AND; that a course of action to ameliorate or treat the subject’s or the public’s health concerns be readily available. Additionally, the researcher is required to determine and adhere to the expressed wishes and desires of the research subject in relation to disclosure of genetic information to that individual. Finally, if research results are disclosed to a subject, appropriate medical advice and referral must be provided (OAR 333-025-0130).

Retention, Inspection and Disclosure of Genetic Information

Retention of genetic information obtained for research is addressed in the statute. Genetic information obtained for anonymous research conducted after notification or with consent as discussed above may be retained. Genetic information obtained for non-exempt research may be retained with the authorization of the individual research subject. Genetic information obtained for non-exempt research should be destroyed promptly upon the completion of a non-exempt research project or withdrawal of the individual from the project, unless the research subject has directed otherwise by informed consent. An individual may inspect, request correction of and obtain genetic information from his or her records, if that information is coded, identified, or identifiable (ORS 192.537).

The general rule is that disclosure of genetic information is not allowed and cannot be compelled, unless specifically authorized by the tested individual in a consent form prescribed by DHS rules (ORS 192.539(1)(d)). This would suggest that, for research purposes where a repository was being developed or genetic information was going to be stored, an informed consent form approved by an IRB would need to be supplemented with the DHS consent form in order to disclose the genetic information to the repository.

Remedies

The statute grants a private right of action for violation of the statutes on genetic privacy. Violation of an individual’s rights in genetic information, retention, or destruction of that information or failure to follow DHS procedures for IRBs can result in penalties ranging from \$100 for inadvertent violation to \$25,000 for a knowing violation. Violation of the informed consent or disclosure requirements can result in penalties ranging from \$1000

for an inadvertent violation to \$250,000 for a knowing violation. Affirmative defenses to such claims include prompt corrective action (ORS 192.541).

RADIOLOGY DEVICES

Investigators who wish to enroll human subjects in research that results in the absorption of ionizing radiation (e.g., x-rays, DEXA scanner, etc.) are required to obtain written approvals from two committees and a State agency before the research is initiated. The two committees are the Radiation Safety Committee, the Committee for the Protection of Human Subjects (CPHS/IRB), and the State of Oregon Radiation Protection Services, X-ray Program.

Researchers who plan to use the DEXA scanner operated by the Department of Human Physiology at the University of Oregon need to contact John Halliwill, Ph.D. (halliwil@uoregon.edu or 541-346-5425) for permission and review the document entitled, *Radiation Safety and Institutional Review Board Application Guidelines*.

All research with human subjects requires prior review and approval by the CPHS/IRB. Research involving x-rays requires a Full Review by the CPHS/IRB. While the CPHS/IRB determines whether research is performed in a manner that protects the rights and welfare of human subjects by conducting a risk/benefit analysis of the study, the Radiation Safety Committee reviews the science of the radiation dose absorbed and also performs an additional risk assessment particular to the use of radiation and exposure of an individual for the purpose of healing arts screening (i.e., research purposes). Normally, a medical need for an x-ray is determined and proper prescription authorized by a physician licensed to practice the healing arts in Oregon.

As part of the review process by the Committees, an evaluation by a qualified expert of the X-ray system(s) to be used in the screening program is required. The evaluation by the qualified expert shall show that such system(s) do satisfy all requirements of Oregon Administrative Rules for deliberate exposures.

The protocol needs to include the following information: (NOTE: The information can be submitted as a separate memo that addresses the concerns.)

6. Name and address of the applicant and, where applicable, the names and addresses of agents within the state (include address information on the cover page of the application);
2. Diseases or conditions for which the X-ray examinations are to be used in diagnoses;
3. A detailed description of the X-ray examinations proposed in the screening program;
4. Description of the population to be examined in the screening program, i.e., age, sex, physical conditions, and other appropriate information;
5. An evaluation of any known alternate methods not involving ionizing radiation which could achieve the goals of the screening program and why these methods are not used instead of the X-ray examinations;
6. A description of the diagnostic film quality control program;
- 7..A copy of the technique chart for the X-ray examination procedures to be used;
8. The qualifications of each individual who will be operating the X-ray system(s);
9. The qualifications of the individual who will be supervising the operators of the X-ray system(s). The extent of supervision and the method of work performance evaluation shall be specified;
10. The name and address of the individual who will interpret the radiograph(s);
11. A description of the procedures to be used in advising the individuals screened and their private practitioners of the healing arts of the results of the screening procedure and any further medical needs indicated;
12. A description of the procedures for the retention or disposition of the radiographs and other records pertaining to the X-ray examinations.

The following language needs to be included in consent forms for projects involving radiation exposure for research purposes. The IRB may require a comparison with background radiation levels. Please use the following statement UNLESS otherwise instructed by the Radiation Safety Committee or the CPHS/IRB:

This research study involves exposure to radiation from (example/name of procedure: DEXA PRODIGY spine or femur scan, DEXA PRODIGY whole body scan, etc.). This radiation exposure is not necessary for your medical care and is for research purposes only. While no radiation dose has been determined to be entirely safe, the amount to which you will be exposed in this study is not known to cause health problems. (List any reasons subjects

may be excluded. For example, women who are currently pregnant.)

DATA SAFETY MONITORING PLAN (DSMP)/DATA SAFETY MONITORING BOARD (DSMB)

In June of 1998, NIH issued a policy stating that research centers in NIH should have a system for the appropriate oversight and monitoring of the conduct of clinical trials to ensure the safety of participants and the validity and integrity of the data for all NIH-supported or conducted clinical trials. According to this policy proposals submitted after October 2000, a data and safety monitoring is required for all types of clinical trials, including physiologic and toxicity studies (Phase I); efficacy studies ((Phase II); efficacy, effectiveness and comparative trials (Phase III); etc. It includes all types of intervention studies whether medication or non-medication (e.g., behavioral, prevention, diagnostic) trials. Monitoring should be correspond with the study risks. NIH Investigators must submit a monitoring plan for Phase I and Phase II clinical trials as part of the human subjects application.

For the purpose of these guidelines, a clinical trial is a prospective study to test the effect of a biomedical or behavioral intervention in human subjects. It includes medications, herbal/nutritional supplements, physical interventions, behavioral interventions, prevention trials, and/or diagnostic tools that affect the outcome of the study participants. Grants that include multiple clinical trials must submit a DSM plan to NIDA prior to initiation of each new trial. Initial funding of a grant and continuation of funding will be contingent on the Institute's acceptance of the DSM plans.

In addition to the DSM plan, a Data and Safety Monitoring Board (DSMB) is generally required for Phase III clinical trials. For earlier medication trials (Phase I or II) and some behavioral clinical trials, a DSMB may be appropriate if the study has multiple clinical sites, is blinded, tests a high-risk intervention, or is conducted in vulnerable populations. Generally, Phase III trials involve larger numbers of subjects, but size is not a specific criterion for this designation.

The purpose of the DSMB is to monitor the safety of the interventions and the validity and integrity of the data from clinical trials that require a DSMB. The decision to establish a DSMB corresponds with the level of risk and/or the number of treatment sites participating in the study. A DSMB may be required by the grantee's institution, but the ultimate decision rests with the sponsoring Institute. In conducting its reviews and making recommendations, the DSMB works to assure that the safety of study subjects is protected while the scientific goals of the study are being met. In monitoring the data and safety of the trial, The DSMB may recommend continuation of the trial, modifications to the trial, or termination of the trial in the event of overwhelmingly significant efficacy difference between groups or unacceptable adverse events.

The detailed DSM plan should include:

Summary of the protocol

- * Brief description of the protocol (Study design)
- * Primary and secondary outcome measures
- * Inclusion/exclusion criteria
- * Power calculation and sample size

Trial Management

- * List of participating enrolling clinics or data collection centers
- * Projected timetable
- * Target population distribution (e.g, women, minorities, etc)

Data Management and Analysis

- * Data acquisition and transmission
- * Data entry methods
- * Data analysis plan

- * Data security

Quality Assurance

- * Procedures in place to ensure the validity and integrity of the data
- * Procedures to guarantee the accuracy and completeness of the data, during data collection, entry, transmission, and analysis.

Regulatory Issues

- * Reporting of SAEs
 - o Medication trials: to the IRB, NIDA, and, as applicable to the FDA.
 - o Non-medication trials: to the IRB and NIDA.
- * Reporting of IRB actions to NIDA
- * Report of changes or amendments to the protocol
- * Trial stopping rules
- * Disclosure of any conflict of interest in the DSM

Trial Safety

- * Potential risks and benefits for participants
- * Collection and reporting of AEs and SAEs
- * Management of SAEs or other study risks
- * Safety reviews
- * Training of personnel

Trial Efficacy

- * Plans for Interim Analysis of efficacy data

DSM Plan Administration

- * Responsibility for data and safety monitoring
 - o Persons responsible for monitoring the trial
- * Frequency of DSM
 - o How often are the data reviewed in the course of the trial?
- * Content of DSM report
 - o Brief description of the trial
 - o Baseline sociodemographic characteristics
 - o Retention and disposition of study participants
 - o Q.A. Issues
 - o Regulatory Issues
 - o AEs
 - o SAEs
 - o Efficacy

If applicable, DSM Board Plan

- * Members and affiliation
- * Frequency of meetings
- * Conflict of interest
- * Protection of confidentiality
- * Monitoring activities (initial and ongoing study review)
- * Communication plan to IRB, NIDA, and FDA (if applicable)

OTHER COMPLIANCE ISSUES

State and local laws may exist which govern the use of special populations, existing data or documents, or other activities in research. The University has other committees which must review protocols involving the use of animals, radiation, and biological or chemical hazards. Investigators should attach documentation to the protocol that the relevant approvals have been obtained, as applicable.

X. REFERENCES

45 CFR Part 46 Federal Policy for the Protection of Human Subjects

45 CFR 46.110 Protection of Human Subjects: Categories of Research That May be Reviewed by the Institutional Review Board (IRB) Through an Expedited Review Procedure (rev. November 9, 1998)

21 CFR Parts 50 and 56 Food and Drug Administration

University of Oregon, Federalwide Assurance

The Nuremberg Code of 1947--Trials of War Criminals Before the Nuremberg Military Tribunals, Vol. II, pp. 181-182: GPA 1949.

The Declaration of Helsinki: Recommendations Guiding Doctors in Clinical Research, Journal American Medical Association, 197 (II): 32, September 12, 1966. (Revised in 1975.)

Statement on the use of human subjects for research, American Journal of Mental Deficiency, 74(1):157, July, 1969.

Ethical Principles in the Conduct of Research with Human Participants, American Psychological Association, Inc., 1973.

Ethical Standards of Psychologists, American Psychological Association, Inc., 1979.

AMA Ethical Guidelines for Clinical Investigation, American Medical Association, November 20, 1966.

The Belmont Report--Ethical Principles and Guidelines for the Protection of Human Subjects of Research, The National Commission for the Protection of Human Subjects Biomedical and Behavioral Research, April 18, 1979.

OHRP Guidance on the Involvement of Prisoners in Research, Office for Human Research Protections, Department of Health and Human Services, May 23, 2003
(Source: <http://ohrp.osophs.dhhs.gov/prisoner.htm>)

Oregon Genetic Privacy Statutes (ORS 192.531 to 192.549), June 12, 2003. (<http://www.leg.state.or.us/ors>)

Oregon Administrative Rules on Genetic Privacy and Research (OAR 333-025-0100 to 333-025-0160), September 2002. (<http://arcweb.sos.state.or.us/banners/rules.htm>)

Amdur, R, and Bankert, E. Institutional Review Board: Management and Function, 2002, Jones and Bartlett Publishers.

APPENDIX A

The Belmont Report
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.

Table of Contents

Ethical Principles and Guidelines for Research Involving Human Subjects

A. Boundaries Between Practice and Research

B. Basic Ethical Principles

1. Respect for Persons

2. Beneficence

3. Justice

C. Applications

1. Informed Consent

2. Assessment of Risk and Benefits

3. Selection of Subjects

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.

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 disabled 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 arrayal 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.

XII. INDEX

- Abbreviations 4
- Abuse reporting requirements
 - child abuse 38
 - abuse of elderly persons 38
 - mentally ill or disabled persons 39
- Adverse events 10
- Anonymity 5, 22
- Appeal process 12
- Approval from participating institutions 37
- Belmont report 42
- Biomedical research
 - definition of 6
 - committee review 16
- Certification of IRB approval 7
 - continuation proposals 7
- Changes in approved procedures 10
- Children 28
 - assent 28
 - definition of 30
 - exempt research and 30
 - informed consent 31
 - permission from parent(s) or guardian 31
 - sample assent form 26
 - special considerations 30
 - wards of the state 31
- Classroom projects 7, 37
- Classroom subjects 37
- Compensation for participation
 - in research 22
- Conditional approval 12
- Confidentiality 5, 19
 - guidelines to ensure 19
 - legal conditions 25
 - loss of 19, 22
- Continuing projects 10
- Cooperative research 7
- CPHS/IRB
 - authority 9
 - calendar 12
 - definition of 6
 - determination of risk level by 9
 - membership regarding research with prisoners 35
 - subcommittees 12
- Criteria for approval 11
- Data safety monitoring plan/data safety monitoring board (DSMP/DSMB) 47
- Definitions 4, 30
- Disapproval of research 9
- Education requirement 11
- Exempt
 - exemption categories 13
 - review process 8
- Expedited
 - expedited review categories 14
 - review process 8
- Final report 10
- 45 CFR Part 46 4
- Full review
 - assignment to 16
 - review process 8
- Genetic Research 44
- Graduate clearance form 8
- HIPAA 42
- Human subjects 4
 - special subject populations 42
- Informed consent 6
 - additional elements 21
 - child abuse 38
 - definition of 6
 - documentation of 24
 - language 20
 - legal liability clause 22
 - medical compensation clause 22
 - required elements of 22
 - retaining documents 25
 - types of consent 25
 - types of forms 22
 - verbal consent 24
 - video recording and 27
 - waiver of 24
 - waiver of documentation 23
- International Research 40
- Investigational drugs/devices review 41
- Magnetic resonance spectroscopy 37
- Mentally disabled individuals 32
 - assent of 33
 - definition of 29
 - exempt research and 30
 - informed consent and 6, 30
 - permission from competent adults 33
 - special considerations 30
 - wards of the state 31
- Minimal risk 4
 - defining 4, 16
- Modifications 10
- OPHS (Office for Protection of Human Subjects)
 - authority to withhold funds 12
 - definition of 4
 - preliminary review by 8
- Other compliance issues 49

- Overview of process 7
- Passive parental consent in elementary and secondary settings 23
- Physical risk 5, 18
- Pregnant women and fetuses 34
 - consent 31
 - definition of 31
 - research activities and 31
- Prisoners 34
 - CPHS/IRB membership and 35
 - definition of 34
 - selection of subjects 36
 - types of research permitted with 41
- Protocol
 - definition of 6
 - protocol packet 8
- Psychological risk 5, 18, 29
- Psychological risk language 29
- Radiology devices 46
- Recruitment 36
 - advertising for subjects 37
 - clients of social service, schools, & other institutions 37
 - research using classroom subjects 37
- Reporting unanticipated problems and adverse events 10
- Research
 - classroom projects 7, 37
 - definition of 4
 - research using classroom subjects 37
 - review by the CPHS/IRB 7
- Retention of signed consent forms 25
- Risks to subjects 18
 - legal risks 19
 - loss of confidentiality 25
 - physical risks 5, 18
 - psychological risks 5, 18, 29
 - social/economic risks 19
- Social science and behavioral research
 - definition of 6
 - committee review 10
- Student research 8, 41
- Transportation of research subjects 40
- Verbal consent 24
- Video recording
 - consent agreement for 27
 - video recording university classes 37
 - written consent form elements 21