TEXAS WOMAN'S UNIVERSITY

Institutional Review Board Procedures

Federalwide Assurance # FWA00000178

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INTRODUCTION

It is the policy of Texas Woman's University (TWU) that all research conducted by any TWU faculty member, staff member, or student using human subjects must have prior approval from a TWU Institutional Review Board (IRB) before the research is initiated (see *TWU Policy 1.15 Human Subjects Research)*. The TWU IRBs on each campus (Denton – IRB #00000829, Dallas – IRB #00000844, and Houston – IRB #00000845) review and approve research involving human subjects. The IRBs operate under Federalwide Assurance # FWA 00000178 issued by the U.S. Department of Health and Human Services (DHHS).

ROLES AND RESPONSIBILITIES

Responsibilities of TWU Researchers

All TWU faculty members, staff members, or students conducting research using human subjects must have prior approval from a TWU IRB before the research can begin.

Responsibilities of the IRB

The TWU IRB is responsible for providing independent review and oversight of research involving human participants. The IRB is an administrative body established to protect the rights and welfare of human participants in research activities conducted under the auspices of the institution with which it is affiliated. The IRB has the authority to approve, require modification of, or disapprove all research activities that fall within its jurisdiction, as specified by federal regulations and local institutional policy. The fundamental responsibilities of the IRB include determining the risks and potential benefits of investigations, ascertaining the appropriateness of the methods used to obtain consent, and protecting the rights and welfare of the individuals involved.

The IRB is responsible for providing written notification of its findings and actions including approval or disapproval of protocols and written reminders of renewal dates to investigators. The IRB is also responsible for providing written reports of its findings and actions to the Provost. The reports are delivered to the Office of the Provost on a monthly basis.

Responsibilities of the Provost (Authorized Institutional Official)

The Provost, as the Authorized Institutional Official, is authorized to act for the University and, on behalf of the University, obligates TWU to the Terms of the Federalwide Assurance (FWA). The Provost is the point of responsibility for the oversight of research and IRB functions.

Responsibilities of the Assistant Provost for Promotion of Research & Sponsored Programs

The Assistant Provost for Promotion of Research & Sponsored Programs, as the Human Protections Administrator, serves as primary point of contact with the Office for Human Research Protections (OHRP) for questions related to TWU's FWA or other matters that may arise.

Responsibilities of the Director of Operations, Research & Sponsored Programs

The Director of Operations creates procedures to maintain and track compliance for the IRBs,

assists with planning and implementing programs of education and training for researchers, and maintains database and other electronic processes for the operation of the IRBs. The Director of Operations may assume the duties of the Assistant Provost for Promotion of Research & Sponsored Programs in his/her absence.

Responsibilities of the IRB Chair

The IRB Chair presides over regular meetings of the IRB and reviews applications and other documents in accordance with the *Code of Federal Regulations (45 CFR 46).* The Chair conveys the decisions of the IRB via written notifications.

Responsibilities of the IRB Co-Chair

The Co-Chair assists with the duties of the Chair, assumes the duties of the Chair in his/her absence, including presiding over meetings when Chair is unable to attend.

Responsibilities of the ORSP Staff

ORSP staff members serve in an administrative capacity for the IRBs. Staff members act at the direction of the IRBs by providing support and clerical services but are not authorized to participate in IRB decisions.

Responsibilities of the Principal Investigator (PI)

- The PI(s) must be a TWU faculty member, staff member, or student.
- PIs have the primary responsibility for protecting the rights and welfare of human research subjects and are responsible for complying with all applicable provisions of their institution's FWA.
- PIs are expected to be knowledgeable about the requirements of the DHHS regulations, applicable state law, their institution's FWA, and institutional policies and procedures for the protection of human subjects.
- PIs are responsible for conducting their research according to the IRB-approved protocol and complying with all IRB determinations.
- PIs are responsible for obtaining and documenting the informed consent of each subject or each subject's legally authorized representative, unless the IRB has waived these requirements.
- PIs are responsible for ensuring that each potential subject understands the nature of the research and participation.
- PIs are responsible for providing a copy of the IRB-approved informed consent document to each subject or the subject's legally authorized representative at the time of consent, unless the IRB has specifically waived this requirement. All signed consent documents are to be retained for at least 3 years after the completion of the research and according to institutional policy
- PIs are responsible for promptly reporting proposed changes in previously approved human subject research activities to the IRB. The proposed changes may not be initiated without

prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects.

- PIs are responsible for reporting progress of approved research to the IRB as often as, and in the manner, prescribed by the IRB.
- PIs are responsible for promptly reporting to the IRB any unanticipated problems involving risks to subjects or others or any serious or continuing non-compliance with the DHHS regulations or determination of the IRB.

Responsibilities of the Institution

Research covered by this policy that has been approved by the IRB may be subject to further appropriate review and approval or disapproval by the Provost. However, the Provost may not approve the research if it has not been approved by the IRB.

REQUIRED HUMAN SUBJECTS TRAINING

All individuals (including but not limited to PIs, research assistants, faculty advisors, and staff) conducting research with human subjects are required to successfully complete approved training in the protection of human research participants. A link to online training options is available at http://www.twu.edu/research/irb.html. A current training certificate (no more than 3 years old) must be on file for all research team members before an exemption, approval, or extension can be granted. This required training applies to all levels of review: Exempt, Expedited, and Full Review studies. For dual review studies or studies using the Institutional Authorization Agreement (IAA), the training requirements will apply to TWU research team members only.

A Confidentiality Agreement Form may be signed in lieu of the required training by individuals who have access to identifiable information but are not part of the research team and will not have direct contact with subjects. Individuals who transcribe interviews, type surveys results, or translate written documents fall into this category. Signed Confidentiality Agreement Forms must be submitted to the IRB prior to the individual's gaining access to the identifiable data.

IRB GUIDELINES

IRB Membership

The IRB shall have at least five members. The IRB shall be sufficiently qualified through the experience, expertise, and diversity of its members, including race, gender, cultural background, and sensitivity to community attitudes. In addition to the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable laws, and standards of professional conduct and practice. The IRB shall include persons knowledgeable in these areas. The IRB shall also include persons knowledgeable in working with individuals in vulnerable populations such as children, prisoners, pregnant women, and persons with physical and/or mental disabilities.

In addition to possessing the professional competence necessary to review specific research activities, the IRB membership will possess the following attributes.

- The IRB will be composed of both male and female members.
- The IRB will be composed of members representing more than one profession.
- The IRB will include at least one member who is not otherwise affiliated with the institution. **Unaffiliated member** means an IRB member who has no affiliation with the University except as a member of the IRB. Persons retired from the University or those who have family members (spouse, parent, children) employed by the University are not considered unaffiliated**.**
- The IRB will include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.
- The IRB will not permit a member to participate in the initial or continuing review of any project in which that member has a conflicting interest, except to provide information as requested by the IRB.
- The IRB may invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.
- IRB members are appointed or re-appointed annually by the Provost. IRB members will receive a letter of appointment or reappointment annually.

Member Appointments and Terms

The Assistant Provost for Promotion of Research & Sponsored Programs, in consultation with the IRB Chair and members of the IRB, will solicit nominations and names from the Faculty Senate committee volunteer list to fill vacant positions on the IRB. Candidates need not have specific qualifications. Candidates may be sought for expertise or to meet federal IRB composition requirements. All nominees are subject to approval by the Provost.

IRB members serve initial three-year terms. Members who are adequately performing required duties may be reappointed for unlimited one-year terms. IRB duties include regular attendance at convened meetings, timely review of assigned IRB applications, and submission of current CV and training certificates. All reappointments are subject to approval by the Provost.

The IRB Chair serves a three-year term and may be appointed for a subsequent two-year term. IRB terms begin in the fall semester. Members are encouraged to serve as Co-Chair before assuming the role of Chair. Duties of the IRB Chair consist of presiding over regular meetings of the IRB and reviewing applications and other documents in accordance with *45 CFR 46*. The Co-Chair assists with the duties of the Chair and presides over meetings in the Chair's absence. The Co-Chair serves a one-year term.

Members who are unable to attend meetings for extended periods of time must inform the Chair in writing. Replacements may be appointed. Members may be removed by the Chair or the Assistant Provost for Promotion of Research & Sponsored Programs for poor attendance or failure to complete required duties.

A current roster of IRB members including degrees, employment information, or position at TWU must be on file with OHRP. Changes in IRB membership shall be reported to the OHRP, DHHS, or any successor office within 90 days of the change.

CATEGORIES OF REVIEW

Exempt Review

Exempt Review applications may be submitted for studies that (a) involve no foreseeable risks to the subjects; (b) do not involve a sensitive subject; or (c) do not involve minors (see below for exception). Exempt studies include research conducted in educational settings involving normal curriculum (even if minors are involved), and research conducted using archival data, provided that the information collected is anonymous (i.e., no names or other identifying information were collected or recorded). The TWU IRB Chair (not the applicant or faculty advisor) determines, based on federal guidelines, whether a project is **Exempt from further IRB review**. Exempt applications will be reviewed by one IRB member (usually the Chair).

The Exempt Application form and instructions can be found on the IRB page of the ORSP website. Exempt Review does not apply when the research activities may expose the subjects to physical or psychological discomfort beyond levels encountered in daily life. A listing of federally approved exemptions is provided below.

- Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as research on regular and special education instructional strategies, or research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- Research involving the use of educational tests (i.e., cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and any disclosure of the human subjects' responses outside 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.
- Research involving the use of educational tests (i.e., cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph(2) of *45 CFR 46 Subpart A*, if: the human subjects are elected or appointed public officials or candidates for public office; or federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- 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 investigators in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which are designed to study, evaluate, or otherwise

examine: public benefit or service programs; procedures for obtaining benefits or services under those programs; possible changes in or alternatives to those programs or procedures; or possible changes in methods or levels of payment for benefits or services under those programs.

- Taste and food quality evaluation and consumer acceptance studies, if wholesome foods without additives are consumed or 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 Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Expedited Review

Expedited reviews are carried out by the IRB Chair or one or more (generally three) experienced members designated by the Chair. Reviewers are designated based on expertise in disciplines of studies and on a rotating basis when possible. Expedited protocol applications are sent to designated reviewers as soon as they are received by the IRB. In conducting expedited reviews, the IRB member(s) may exercise all of the authorities of the IRB except that they may not disapprove the research. A research activity may be disapproved only after review by the convened IRB in accordance with the non-expedited procedure set forth in *45 CFR 46.108(b).* Outcomes of expedited reviews are included in monthly activity reports to the IRB.

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 categories listed in the *Federal Register (63 FR 60364-60367)* may be reviewed by the IRB through the expedited review procedure as authorized by *45 CFR 46.110* and *21 CFR 56.110*. Expedited review procedures may also be used to review minor changes in previously approved research during the period (one year or less) for which approval is authorized.

Expedited reviews must fulfill all the requirements of review found at *45 CFR 46.111 and subparts B, C, and D*, if applicable. Requirements for informed consent (or for altering or waiving the requirement for informed consent) apply regardless of whether research is reviewed by the convened IRB or under an expedited procedure.

The *Federal Register* lists all categories of research that can be reviewed using Expedited Review procedures (see *Appendix D* for the complete list or go to http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm). The list includes, but is not limited to, certain minimal risk clinical studies of drugs and medical devices, collection of blood samples that meet certain criteria, collection of data through noninvasive procedures, and research involving materials such as data, documents, records, or specimens collected solely for non-research purposes.

Full Review

Full Review applications must be submitted for studies that: (a) involve more than just minimal risks to the subjects; (b) involve a sensitive topic; or (c) involve minors unless exempt under federal policies. Full Review application packets including the protocol, consent documents, recruitment materials, and data collection materials are distributed to all IRB members prior to

meetings. Full Review applications are reviewed at convened meetings with a majority of members present, including at least one member with concerns in nonscientific areas.

The IRB Chair may designate primary reviewer(s) as needed to manage the volume of applications. Primary reviewers are designated by the Chair on a rotating basis. The role of a primary reviewer is to review application materials in detail and submit written recommendations to the committee for discussion on changes or clarifications necessary to approve a protocol.

Dual Review

There are two ways to handle studies conducted with other institutions: 1) implementation of an Institutional Authorization Agreement (IAA), and 2) the dual review process. Unless an IAA is put in place, TWU requires that studies conducted at offsite institutions that require approval by the offsite institution's IRB also be reviewed and approved by the TWU IRB using the dual review process. (Refer to Research Conducted at Non-TWU Sites that Requires Approval by a Non-TWU IRB section for more detail regarding the IAA).

Consent documents must meet TWU standards. The goal would be to have one consent form for the study which informs the subject about his or her rights, the purpose of the study, the procedures, potential risks and benefits of participation, and identify each institution and their role. The TWU IRB may exercise some flexibility in determining the specifics of the consent and may take into consideration the roles of the various institutions and researchers.

An offsite-approved protocol is reviewed by TWU with the purpose of protecting the rights and welfare of study participants and in light of the fact that it has been approved by another IRB.

- The researcher's initial step after discerning that offsite IRB review is required is to review the requirements of both institutions in order to develop a single consent document that meets the standards of both. This step is critical in minimizing delays and preventing resubmissions.
- All offsite-approved protocols must be submitted for review at the level approved by the offsite IRB and will be reviewed as follows:
  - Full Review Studies will be reviewed at a fully convened meeting. The TWU IRB Chair will designate a primary reviewer who possesses expertise in the study discipline as well as dual review procedures.
  - Expedited Studies will be reviewed by the TWU IRB Chair or one reviewer designated by the Chair.
  - Exempt Studies will be reviewed by the IRB Chair or Co-Chair.
- Dual review applications must include a completed Dual Review Application form, the completed offsite IRB application with all associated materials (including the consent form), the offsite IRB approval letter, and any additional administrative requirements as determined by TWU policy. The Dual Review Application will also include the researcher's role in the study, name and role of the offsite PI, and offsite IRB contact information.
- Dual review studies are subject to the same TWU IRB guidelines, reporting requirements, and deadlines as regular IRB applications. The TWU IRB is authorized to approve,

disapprove, upgrade review levels, terminate, or suspend any study submitted for review regardless of the method of submission.

IRB OPERATIONS AND FUNCTIONS

IRB Functions

The function of the IRB is to review and approve, require modifications in, or disapprove all research activities with human subjects. The IRB will notify investigators and appropriate University administrators, in writing, of decisions to approve, require modifications in, or disapprove proposed research activities. When the IRB disapproves research activities, the written notification will include the reasons for the decision and offer investigators the opportunity to respond in person or in writing.

The IRB may identify studies that require interim verification that no material changes have occurred since previous IRB reviews. Selection of projects to be reviewed may be random or may be based on investigator history, or project complexity. Sources other than investigators such as study participants, faculty advisors of student PIs, or faculty members' supervisors may be used in this process.

The IRB requires that all human subjects be given all relevant information about the research activities as part of the informed consent process. The IRB may require that additional information be provided to research subjects when the IRB determines that the information would meaningfully add to the protection of the rights and welfare of the subjects. The IRB will require documentation of informed consent or may waive documentation of informed consent in accordance with these procedures (see *General Requirements for Obtaining Informed Consent* for details of the informed consent process). The IRB has the authority to observe or have a third party observe the informed consent process and the research.

Convened Meetings

The IRBs meet according to meeting schedules and submission deadlines posted on the IRB website under the individual campus sections. The IRB may cancel scheduled meetings if there are no items that require review.

A quorum at a convened IRB meeting shall consist of more than one-half of the total membership including at least one member with a non-scientific focus. A voting majority of members at a convened meeting shall consist of more than one-half of the members present.

The IRB Chair may abstain from voting in a convened meeting unless necessary to make a quorum or to break a tie vote. IRB members may abstain from voting by personal choice. Members who have a conflict of interest in a study shall recuse themselves from voting and leave the room to eliminate any chance of influencing the procedure. Conflicts of interest may include but are not limited to: conflicts of interest as defined by University policies and review of protocols in which an IRB member is the principal investigator, a research team member, or a faculty advisor.

Adequate minutes of all meetings and the monthly activity reports, which provide the results of reviews of all research protocols submitted to the IRB, are sent to IRB members. Monthly

activity reports are also sent to the Provost. Minutes and the monthly activity reports are maintained in the IRB Offices on the Denton and Houston campuses. The monthly activity report including the outcomes of Exempt and/or Expedited reviews, adverse events on active projects, and annual extension requests will be approved, modified, or disapproved by a majority of members present.

The IRB may conduct convened meetings by telephone or video conference as long as members have received copies of all documents to be reviewed, a majority is present, and discussion occurs in real time. All members must be connected simultaneously for teleconferences or video conferences. “Telephone polling" (in which IRB members are contacted individually) does not qualify as a convened meeting.

Investigators may be asked to attend or may request to attend relevant portions of IRB meetings when the need exists to clarify research procedures or to answer questions regarding applications. Students may also be granted permission to attend IRB meetings for educational purposes.

Criteria for Review

The IRB reviews each protocol to determine that the following requirements are met:

- Risks to participants are minimized.
- Risks to participants are reasonable in relation to anticipated benefits, if any, to participants and the importance of the knowledge that may reasonably be expected to result. The IRB considers only those risks and benefits that may result from the research, and not risks or benefits that would likely result even if persons did not participate in the research.
- Selection of participants is equitable. When considering the selection of participants, the IRB will be particularly cognizant of the purpose and setting of research involving vulnerable populations.
- Informed consent will be sought from all prospective participants or the participants’ legally authorized representatives in accordance with and as required by *45 CFR 46.116*.
- Informed consent will be appropriately documented in accordance with, and to the extent required by, *45 CFR 46.116.*
- The research plan makes adequate provision for monitoring the data collected to ensure the safety of participants as deemed appropriate by the IRB.
- Adequate safeguards are provided to protect the privacy of participants and to maintain the confidentiality of data as deemed appropriate by the IRB.

Adverse Events or Unanticipated Problems

An *adverse event* is any untoward or unfavorable occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject’s participation in the research, **whether or not considered related to the subject’s participation in the research**. Adverse events encompass both physical and psychological harms (see *Definitions*).

An *unanticipated problem* is any incident, experience, adverse event, or outcome that meets all

of the following criteria: unexpected given the described procedures, informed consent, and population characteristics; related or possibly related to participation in the research; suggests that subjects are placed at greater risk than previously known (see *Definitions*).

Adverse events and unanticipated problems are not mutually exclusive. An adverse event is not necessarily an unanticipated problem and vice versa. The IRB makes the final determination on categories of incidents.

- TWU investigators shall verbally report adverse events or unanticipated problems to the IRB within two (2) working days of knowledge of the incident and shall submit an IRB Incident Report Form to the IRB Office within five (5) working days. If the Incident Report Form is incomplete when initially submitted, a completed report form must be submitted to the IRB before the close of the study.
- The IRB Incident Report Form shall include at a minimum: name of PI, title of research project, award information (if applicable), a detailed description of the incident, a detailed description of actions or plans to address the incident, and the outcome.
- When reviewing reports of unanticipated problems and adverse events, the IRB shall consider whether the affected research protocol continues to satisfy the requirements for IRB approval, whether risks to participants continue to be minimized and reasonable in relation to the anticipated benefits to the participants, and the importance of the knowledge that may be reasonably expected to result.
- The IRB Chair may call an emergency meeting of the IRB or suspend research activities if necessary to prevent immediate threat to the safety and well-being of research subjects. Notification of suspensions or terminations will include the rationale for the IRB's action and will be sent by the IRB to investigators, faculty advisors of student investigators, the academic unit administrator, appropriate institutional officials, and the funding agency head if applicable.
- The IRB is authorized to require additional information from the investigator and/or require any modifications necessary to ensure the safety and wellbeing of research subjects and ensure that such incidents will not happen again, either with the investigator or the protocol in question. Changes to a research study proposed by the investigator in response to an unanticipated problem must be reviewed and approved by the Chair or Co-Chair before being implemented, except when necessary to eliminate apparent immediate hazards to participants. If the changes are determined by the Chair or Co-Chair to be more than minor, the changes must be reviewed and approved by the convened IRB.

Reporting Requirements

The IRB shall promptly report unanticipated problems or incidents to the Assistant Provost for Promotion of Research & Sponsored Programs. ORSP shall prepare required reports to the Provost, OHRP and the supporting agency head. The time frame for reporting will be based on the nature and severity of the incident and be in accordance with applicable *45 CFR 46* regulations or the OHRP Guidance on Reporting Incidents to OHRP (**http://www.hhs.gov/ohrp/compliance/reports/**).

Reports to OHRP, supporting agency heads, and the Provost on unanticipated problems shall

include: name of the institution, name of PI, title of the research project, award information (if applicable), a detailed description of the incident, actions TWU is taking or plans to take to address the problem (e.g., protocol revision, suspension of participant enrollment, termination of research).

Noncompliance

Noncompliance is the failure to comply with federal or state regulations, TWU policies and procedures governing research with human subjects, or requirements of the IRB. Categories of noncompliance are *minor noncompliance*, *serious noncompliance*, and *continuing noncompliance.* The safety and wellbeing of research participants shall be the primary concern when addressing acts of noncompliance.

All institutional members, research participants, and others are encouraged to report observed or suspected noncompliance. Noncompliance may also be discovered through documents such as new applications, reviews, or adverse event reports as well as through processes such as internal audits, mass emails, or research presentations.

Reports of noncompliance should be made to the IRB. The recipient of the noncompliance report will immediately notify the IRB Chair. The IRB Chair, or another IRB committee member designated by the Chair, will review the report and associated information. If the reviewer determines that the report is unsubstantiated, no further action will be taken. If the reviewer determines that the report is substantiated, the IRB Chair or designee will make a determination of minor noncompliance, serious noncompliance, or continuing noncompliance; and the Assistant Provost for Promotion of Research & Sponsored Programs will be notified.

The IRB Chair may call an emergency meeting of the IRB or suspend research activities if necessary to prevent immediate threat to the safety and well-being of research subjects. Notification of suspensions or terminations will include the rationale for the IRB's action and will be sent by the IRB to investigators, faculty advisors of student investigators, the academic unit administrator, Dean, other appropriate institutional officials as the IRB deems necessary, and the funding agency head if applicable.

<u>Minor Noncompliance</u>

Minor noncompliance is a deviation from procedures that does not increase risks to research participants, compromise participants' rights or welfare, or affect the integrity of the research/data or the IRB process. Examples may include but are not limited to:

- Lapses in continuing IRB approval *****
- Failure to obtain exempt determination before exempt research is conducted;
- Initiation of research on protocols pending IRB approval;
- Minor changes in or deviations from an approved protocol;
- Deviations from an approved consent procedure; and
- Administrative errors.

* Protocols expire automatically when IRB approval lapses. Investigators will be notified of the approval lapse, given 30 days to submit an extension request, and informed that recruitment and data collection must cease immediately. If the extension request is not received within the

30-day period, the protocol will be closed and a new IRB application must be submitted if the investigator wishes to continue with the study. Lapses in IRB approval are considered minor noncompliance providing that all research activities have ceased. Research activities conducted during a lapse in IRB approval are considered serious noncompliance and will be reported according to DHHS regulations.

Minor noncompliance may be addressed by a notification letter from the IRB Chair to the investigator that includes the nature of the noncompliance, a corrective action plan, and a time frame for completion. Copies of notification letters may be sent to faculty advisors, academic unit administrators, Deans, Dean of the Graduate School, and other entities as deemed necessary by the IRB. Failure to respond to notification letters may be considered by the IRB to be either serious or continuing noncompliance.

Serious Noncompliance

Serious noncompliance is an act or omission that has the potential to increase risk to research participants, compromise participants' rights or welfare, or affect the integrity of the research/data or IRB process. Examples may include but are not limited to:

- Failure to obtain IRB approval on expedited or full review studies before starting research;
- Continuing research activities after IRB notification that approval has expired;
- Failure to notify the IRB of changes in approved procedures, scope/intent of the study;
- Failure to monitor data to ensure safety of participants;
- Failure to report serious unanticipated problem involving risks to participants or others, including adverse events;
- Failure to adequately protect participant privacy and confidentiality of data;
- Failure to obtain informed consent;
- Failure to protect vulnerable participants from coercion or undue influence;
- Failure to recruit participants according to IRB approved protocol;
- Failure to conduct research according to the IRB approved protocol; and
- Failure to maintain complete records of informed consent.

Continuing Noncompliance

Continuing noncompliance is noncompliance that has been previously reported, or a pattern of ongoing activities that indicate a lack of understanding of human subjects protection requirements that may affect research participants or the validity of the research and suggest the potential for future noncompliance without intervention. Examples may include but are not limited to:

- Repeated failure to provide or review progress reports resulting in lapses of IRB approval;
- Inadequate oversight of ongoing research; and
- Failure to respond to or resolve previous allegations or findings of noncompliance.

The IRB Chair, or one or more members designated by the Chair, shall investigate reports of serious or continuing noncompliance based on information gathered with the assistance of ORSP. The IRB will notify the investigator, the investigator's direct supervisor (for faculty / staff research), and faculty advisor (for student research) of the initiation of an investigation. The IRB Chair or designee shall report findings and recommendations to the full IRB at a convened

meeting. The investigator may be required to attend this IRB meeting. The following documents, as applicable, will be sent to IRB members prior to the meeting at which the report of noncompliance is reviewed:

- Initial report of noncompliance;
- Written reports of findings and recommendations by the reviewing members;
- Any other reports generated during the investigation;
- Copies of most recently approved documents including application, protocol, consent documents, and any other relevant documents;
- Minutes of meetings in which the protocol was discussed;
- Any correspondence from the investigator; and
- Reports of any interviews conducted.

The IRB will review the information and decide if serious or continuing noncompliance has occurred. If it is determined that serious or continuing noncompliance has occurred, the IRB will list remedial actions to be taken. These actions may include but are not limited to:

- Require modification of the research protocol;
- Require modification of the information that must be disclosed in a consent form;
- Require that current study participants be notified of the noncompliance when such information may affect willingness to continue participation;
- Require re-consent of all participants;
- Modify the continuing review schedule;
- Monitor research activities;
- Monitor the consent process;
- Suspend research activities until corrective actions are implemented;
- Terminate the research; and
- Other actions necessary to protect the study subjects.

If the IRB determines that serious or continuing noncompliance occurred, the IRB will notify the investigator and list any remedial actions and a timeframe for completion of such actions. A copy of this notification will be sent to the following:

- Provost
- Academic Unit Administrators;
- Investigator's Dean;
- Dean of Graduate School;
- Research Advisor; and
- Assistant Provost for Promotion of Research & Sponsored Programs.

If the IRB determines that no serious or continuing noncompliance occurred, the IRB will notify the investigator, the investigator's direct supervisor (for faculty / staff research), and faculty advisor (for student research).

Reporting Requirements

ORSP shall prepare required reports to the Provost, OHRP and the supporting agency head. The

time frame for reporting will be based on the nature and severity of the incident and be in accordance with applicable *45 CFR 46* regulations or the OHRP Guidance on Reporting Incidents to OHRP (**http://www.hhs.gov/ohrp/compliance/reports/**).

Reports to OHRP, supporting agency heads, and the Provost on serious or continuing noncompliance shall include: name of the institution, name of PI, title of the research project, federal award information (if applicable), a detailed description of the incident, actions TWU is taking or plans to take to address the problem (e.g., protocol revision, suspension of participant enrollment, termination of research).

The Provost and/or Dean may take disciplinary action against the investigator for violation of University policies and regulations.

Appeal

PIs may appeal IRB decisions regarding serious or continuing noncompliance by submitting a brief summary outlining the reasons for the appeal to IRB. PIs who appeal such decisions must attend the convened IRB meeting in which the appeal is reviewed.

Suspension or Termination of Approval

The IRB has the authority to suspend or terminate approval of research that is not conducted in accordance with IRB requirements or is associated with unexpected serious harm to participants, adverse events, unanticipated problems, or serious or continuing noncompliance Researchers must not recruit participants, enroll participants, or collect data in any form when research studies have been suspended or terminated. Data collected during periods of suspension or termination must be discarded and may not be used in any capacity for research projects.

Any suspension or termination of approval will include a statement of the reasons for the IRB's action and will be reported promptly to investigators, faculty advisors of student investigators, the academic unit administrators, the Provost, OHRP, and the funding agency head.

Continuing Protocol Reviews

All research protocols approved by the IRB as Expedited or Full Reviews shall be reviewed periodically. Intervals between consecutive reviews may not exceed 12 months. The interval between consecutive reviews may be less than twelve months if the IRB determines more frequent reviews are needed. The IRB Chair can approve extensions of expedited reviews or extension requests for full review studies where only data analysis is being done (subject recruitment and data collection are no longer taking place).

Review of Research for Sponsored Projects

Proposals for federal funding involving human subject research must be reviewed in conjunction with standard IRB review procedures. Research & Sponsored Programs may also require that proposals for non-federal funding be reviewed by the IRB to comply with funding agency requirements or as necessary to maintain the protection of human subjects in research taking into consideration the size of the award, complexity of the project, experience-level and history of investigator, etc. If review of the proposal is required, all sections of the proposal that

address human subject research methodology will be provided to the IRB for review at the award stage. The proposal information will be reviewed by the IRB chair or their designee to assure consistency with the approved IRB protocol. The Office of Research & Sponsored Programs will assist the principal investigator and the IRB to assure that the IRB completes the review.

Review of Research by Other Institutional Compliance Committees

Investigators must inform the IRB if, in addition to IRB approval, the research must be reviewed and approved by other institutional compliance committees such as the Radiation Safety committee or the Institutional Biosafety Committee (IBC).

Research at TWU by Investigators from Other Institutions

Researchers who are not affiliated with TWU may recruit TWU faculty members, staff members, or students as participants if approval has been granted by another IRB. Although such studies do not require the involvement of the TWU IRB, approval by instructors, academic unit administrators, or deans may be necessary. Faculty members or administrators who approve such studies should verify that the research protocol has received IRB approval.

Research Conducted at Non-TWU Sites that Requires Approval by a Non-TWU IRB

Studies conducted at offsite institutions may require approval by the offsite institution's IRB. TWU requires that studies also be reviewed and approved by the TWU IRB (dual review). Under certain circumstances, TWU may enter into an agreement that authorizes an offsite IRB to serve as the IRB of record. Such agreements must be approved by the signatory officials of both institutions (see *IRB Authorization Agreement*).

Regardless of the approval method, consent documents must meet TWU requirements. The goal in all circumstances is a single consent form that explains the roles of each institution and fairly and completely represents the decisions of each IRB involved.

<u>Dual Review</u>

An offsite-approved protocol is reviewed by TWU with the purpose of protecting the rights and welfare of study participants and in light of the fact that it has been approved by another IRB. (Refer to Categories of Review for more detail regarding the Dual Review process.)

<u>Institutional Authorization Agreement (IAA)</u>

An IRB IAA is a written agreement prescribed by OHRP that describes the obligations of both parties when one relies on the other for IRB review and continuing oversight of one or more human subject research projects. IAAs must be signed by the signatory officials of each institution.

Each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy.

An IAA must include descriptions of the regulatory requirements for each party and must be in compliance with the procedures of the TWU IRB.

Researchers must contact the Assistant Provost for Promotion of Research & Sponsored Programs if they wish to initiate an IAA with an external study site. The Assistant Provost for Promotion of Research & Sponsored Programs, in conjunction with the IRB Chair, will determine if an IAA is appropriate and, if so, will initiate the agreement process. The researcher may be required to provide information on the offsite IRB including but not limited to: application forms, consent form requirements and/or templates, review processes, and the institution's FWA.

The offsite institution must have an approved FWA on file with the OHRP and must meet the requirements set forth by TWU as the deferring IRB. If the research project in question involves Federal funding, the sponsoring agency must be informed of and approve the IAA. With or without the existence of an IAA, if Federal funding is involved, the other institution needs to have or obtain a FWA. The designated (offsite) IRB will report serious or continuing non-compliance, unanticipated problems involving risks to subjects or others, and/or suspensions or terminations of IRB approved research related to the TWU FWA to OHRP and other oversight agencies as appropriate.

The IAA shall, at a minimum, include:

- Procedures for communication between TWU and the Offsite IRB;
- Procedures for notification of findings, actions (terminations, suspensions), adverse events, or unanticipated problems to TWU;
- A provision stating that, if the Offsite Institution fails to notify TWU as stated above, TWU shall have the right to immediately terminate the agreement and request any study related documents associated with the TWU investigator's role in the study;
- A description of each institution's engagement in the research activity;
- Provisions that ensure that consent documents meet TWU requirements;
- The effective date and term of the agreement; and
- TWU shall retain ultimate authority and responsibility for the protection of human subjects enrolled in research conducted under its auspices regardless of the venue of IRB review.

Documents that must be provided to TWU by the researcher if an IAA is executed:

- IRB approval letter;
- Application documents including the FWA number and the IRB number of the offsite institution;
- Approved consent documents;
- Reports including, but not limited to, progress reports, extension reports, adverse event reports, and final reports;

- Protocol modifications; and
- Any correspondence between the researcher and the offsite IRB.

TWU may require additional review of research covered by an IAA and may impose additional administrative requirements as determined by TWU policy. The TWU IRB reserves the right to upgrade any review based on risk.

EVALUATION OF RISK

The IRB shall evaluate potential risks on a case-by-case basis and be sensitive to possible harms. If a research activity will expose individuals to risk, the IRB must be assured that:

- The rights and welfare of the individuals are adequately protected;
- The methods used to obtain informed consent are adequate and appropriate;
- The risks to individuals are outweighed by the potential benefits to individuals or society or by the importance of the knowledge to be gained;
- Study personnel are qualified to conduct the study, including any specialized procedures or testing; and
- Adequate provisions for “debriefing” or post-investigation explanations are included in studies involving deception or incomplete disclosure.

The IRB may call qualified consultants to serve as non-voting members when participants will be recruited from vulnerable populations such as prisoners, children, pregnant women, or persons with physical and/or mental disabilities. The IRB may also refer investigators to consultants for assessment of the potential risks and benefits of the proposed research. The IRB Chair will contact the University's General Counsel when the IRB believes that a legal opinion is needed. Individuals are considered to be at risk if they may be exposed to physical, psychological, social, or economic harm.

Physical Harms

Research involving physical activities or medical interventions can expose participants to pain, discomfort, physical injury, injury from invasive medical procedures, or harm from possible side effects of drugs. These adverse effects are considered "risks" for purposes of IRB review. Research designed to measure the effects of therapeutic or diagnostic procedures applied in the course of caring for an illness may not entail any significant risks beyond those presented by medically indicated interventions. Research designed to evaluate new drugs or procedures may present more than minimal risk, and, on occasion, can cause serious or disabling injuries.

Psychological Harms

Participation in research may result in undesired changes in thought processes and emotion (e.g., episodes of depression, confusion, or hallucination resulting from drugs, feelings of stress,

guilt, and loss of self-esteem). Stress, feelings of guilt, or embarrassment may arise from thinking or talking about one's own behavior or attitudes on sensitive topics such as drug use, sexuality, selfishness, or violence. Psychological harm can also occur when the environment of the participant is manipulated, when studies involve any form of deception, and when studies involve invasion of privacy.

Social Harms

Some invasions of privacy and breaches of confidentiality may result in embarrassment within one's business or social group, in loss of employment, or in criminal prosecution. Areas of particular sensitivity are information regarding alcohol or drug abuse, mental illness, illegal activities, and sexual behavior. Some social and behavioral research may yield information that could label or stigmatize participants. Confidentiality safeguards must be strong in these instances. Breaches of confidentiality can adversely affect present or future employment, eligibility for insurance, political campaigns, and standing in the community. A researcher's plans to contact such individuals for follow-up studies should be reviewed with care.

Economic Harms

Participation in research may also result in actual monetary losses to individuals such as transportation expenses, childcare expenses, and time off work. Any anticipated costs to research participants should be described in detail during the consent process.

GENERAL REQUIREMENTS FOR OBTAINING INFORMED CONSENT

Except as provided elsewhere in this policy, investigators may not involve a human being as a participant in research covered by this policy unless the investigator has obtained the legally effective informed consent of the participant or the participant's legally authorized representative. Investigators may seek such consent only under circumstances that provide the prospective participant or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the participant or the representative shall be in language understandable to the participant or the representative. The consent process may not involve the use of exculpatory language through which the participant or representative is made to waive or appear to waive any of the participant's legal rights, or releases or appears to release the investigator, sponsor, institution, or agents from liability for negligence.

Basic Elements of Informed Consent

When seeking informed consent, the following information must be provided to all participants.

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- A description of any reasonably foreseeable risks or discomforts to the participant;
- A description of any benefits to the participant or to others which may reasonably be

expected from the research;

- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant;
- A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained;
- For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- Contact information for answers to pertinent questions about the research and research participants' rights, and contact information in the event of a research-related injury to the participant; and
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
- The following disclaimer statements must be included on all consent forms.

  Confidentiality will be protected to the extent allowed by law.

  The researchers will try to prevent any problem that could happen because of this research. You should let the researchers know at once if there is a problem and they will help you. However, TWU does not provide medical services or financial assistance for injuries that might happen because you are taking part in this research.

When appropriate, any of the following additional elements of informed consent may be required by the IRB.

- A statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or fetus, if the participant is or may become pregnant) which are currently unforeseeable;
- 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 a 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; and

- The approximate number of participants involved in the study.

Documentation of Informed Consent

Informed consent must be documented by the use of an IRB approved written consent form that contains all of the required elements of informed consent and has been signed by the participant or the participant's legally authorized representative. Participants must be provided with a copy of the consent forms.

Consent forms that have been approved by the IRB contain the official approval stamp indicating the date of approval. Stamped consent forms are sent to investigators with their IRB approval letters. Investigators are prohibited from using any other form without the prior approval of the IRB.

The IRB may waive the requirement for investigators to obtain signed, written informed consent from participants, if the IRB makes one of the following determinations:

- The only record linking participants to the research would be the consent document and the primary risk would be potential harm resulting from a breach of confidentiality.

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

SPECIAL CATEGORIES OF RESEARCH

Research Involving Vulnerable Populations

Children

The IRB shall review research with children as participants and shall approve only research which satisfies the conditions set forth in *Subpart D of 45 CFR Part 46*.

The *CFR* provides that educational and social research with children as participants may be considered Exempt and may not require signed informed consent (see *Exempt Review*). Expedited and Full Review research studies involving children require signed informed consent from parents or legal guardians.

The IRB, in accordance with *45 CFR Part 46.405*, may approve studies with children that involve greater than minimal risk if the risk is justified by the anticipated benefit to the subjects, the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches, and adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

Research projects with children that involve greater than minimal risk but are likely to yield generalizable knowledge about the subject's disorder or condition may be approved by the IRB if the risk represents a minor increase over minimal risk; the intervention presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations; the intervention is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and adequate

provisions are made for soliciting assent of the children and permission of their parents or guardians. These requirements are in accordance with *45 CFR Part 46.406*.

The IRB shall determine that adequate provisions are made for soliciting the assent of the children when, in the judgment of the IRB, the children are capable of providing assent. In determining whether children are capable of assenting, the IRB will take into account the ages, maturity, and psychological states of the children involved. This judgment may be made for all children involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived.

The IRB shall determine that adequate provisions are made for soliciting the permission of each child's parents or guardian in accordance with *45 CFR 46.408*. The IRB may waive the consent requirements provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

The IRB shall require appointment of an advocate for each child who is a ward of the state or any other agency, institution, or entity, in addition to any other individual acting on behalf of the child as guardian or in *loco parentis*. One individual may serve as advocate for more than one child. The advocate shall be an individual 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 in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

<u>Prisoners</u>

As prisoners may be under constraints due to their incarceration, which could impact their ability to make truly voluntary and un-coerced decisions whether or not to participate as participants in research, the IRB is obligated to provide additional safeguards for the protection of prisoners involved in research activities.

The *CFR* mandates that the majority of IRB members have no association with the prisons involved in research (apart from IRB membership) and that at least one member of the IRB must be a prisoner or have the appropriate background to serve as a prisoner representative.

The selection of research participants must be fair to all prisoners and immune from arbitrary intervention by prison authorities, parole boards, or other prisoners. The risks involved in this research must be commensurate with risks that would be accepted by non-prisoner volunteers. The information must be presented in language that is understandable to the prison population. The benefits of the research must not be of such a magnitude that they impair the ability of prisoners to weigh the risks of the research given the limited choice environment of

the prison. Adequate assurance must be provided to the IRB that parole boards will not consider prisoners' decisions about participation in research in making decisions regarding parole. All prisoners must be clearly informed, in advance, that participation in the research will have no effect on their parole. Where the IRB finds a need for any sort of follow-up procedures following participation, adequate provisions for prisoners must be made, taking into account varying lengths of prisoners' sentences, in order to inform prisoner participants of the follow-up.

Biomedical and behavioral research involving prisoners as research participants may be conducted only if (a) the above requirements have been met; and (b) the proposed research is solely for the following purposes:

- Possible causes, effects, and processes of criminal behavior or incarceration, with no more than minimal risk and inconvenience to participants;

- Prisons, as institutional structures, or prisoners, as incarcerated persons, with no more than minimal risk and inconvenience to participants;

- Conditions particularly impacting prisoners as a group, in that certain conditions are more prevalent in prisons than elsewhere (e.g., hepatitis, alcohol/drug addiction, sexual assaults), following consultation with appropriate experts and published notice in the *Federal Register*;

- Practices with the intent and reasonable probability of improving the health or well-being of participants. Where prisoners are to be assigned to control groups in which they may not benefit from the research, consultation with appropriate experts and published notice in the *Federal Register* are required.

Except as provided above, biomedical or behavioral research will not involve prisoners as research participants.

Pregnant Women, Fetuses, and Neonates

Research involving pregnant women, human fetuses, and neonates (i.e., newborns) is expected to present a reasonable opportunity to further the understanding, prevention, or alleviation of serious problems impacting the health or welfare of these populations. Research involving pregnant women, fetuses, and neonates is generally expected to hold out the prospect of direct benefit. If no such prospect of direct benefit is available, then the risk must be minimal and the purpose of the research must be the development of important biomedical knowledge that cannot be obtained by any other means. For pregnant women and fetuses, any risks associated with the research will be the least possible for achieving the objectives of the research. For neonates, no risks may be added as a result of the research. Researchers will not: (1) offer any form of inducement to terminate a pregnancy; (2) determine the timing, method, or procedure used to terminate a pregnancy; or (3) determine the viability of a neonate. Researchers conducting studies with these populations must follow sound ethical principles and follow all appropriate provisions regarding informed consent.

Non-English Speaking

45 CFR 46 requires that informed consent information be presented in language understandable to the participant. Thus participants should be presented with consent documents and other research-related documents (such as questionnaires or cover letters) written in a language understandable to them. Any verbal explanation of the consent or research procedures should be presented in a language understandable to the participant. The IRB must receive all translated versions of the written documents as a condition of approval.

PIs assure the IRB by submission of the application that any translated documents are accurate. The IRB, at their discretion, may request additional information regarding translated documents. Translators involved only in translation of written documents are not required to fulfill the training requirement.

Studies Involving Deception

The validity of data in some studies can be potentially compromised if participants are fully informed of the purpose of the study. Studies that propose to mislead participants or use deception cannot violate the rights and welfare of participants. Studies that involve deception must include procedures for debriefing participants immediately following or within a reasonable period of time after completion of the study. Debriefings must include descriptions of the deception, the purpose of the deception, and the necessity of the deception as it relates to the purpose of the research.

Course-related Activities/Class Projects

The IRB is only required to review student course-related activities and projects that meet the Federal definitions of research and human subject, or "engaged in research." If there is a possibility that researchers may use data for research purposes, IRB approval is required prior to initiation of the project. Class projects conducted by students in which data are gathered strictly for educational purposes do not require IRB approval. More detail is provided below to distinguish between research and educational purposes.

Research is defined in *45 CFR 46.102(d)* as "…a systematic investigation, including research development, testing and evaluation, designed to contribute to generalizable knowledge." A human subject is defined in *45 CFR 46.102(f)* as "a living individual about whom an investigator conducting research obtains either data through intervention/interaction with the individual or Identifiable private information…(i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information)."

The TWU IRB generally does not review course-related/educational activities designed specifically for the following:

- Educational or teaching purposes in which information about human subjects is collected as part of a class exercise or assignment and the data are not used outside the classroom. Example: Instruction on research methods and techniques.
- A project that involves the replication of an experiment with known results and is not designed to develop or contribute to generalizable knowledge.

Despite the fact that the applicable activities do not require IRB review, course instructors and students are still ethically obligated to provide full disclosure in all recruitment and data collection efforts. This disclosure includes, but is not limited to, the following:

- Notice that the study is for a class project intended for educational purposes only. Subject recruitment materials should not advertise the project as "research" if the definition of research is not met and the study is intended for educational purposes only.
- Informing participants of all risks associated with the study.
- Information regarding how, when, and where the data will be used.

The TWU IRB would review and approve projects, before they begin, where the activity falls within the definition of research such as:

- Class-related research that involves the testing or confirmation of a hypothesis and involves the collection of private identifiable data about living individuals or the collection of data about living individuals through interaction or intervention with those individuals.
- Class-related research which may result in publication or presentation findings from their course-related research.
- Directed or Independent Research Projects (e.g., honors projects, graduate theses, dissertations and professional papers) that employ systematic data collection with the intent to contribute to generalizable knowledge.

Oral Histories

A decision whether oral history or other activities solely consisting of open-ended qualitative type interviews are subject to the policies and regulations outlined in an institution's Federalwide Assurance (FWA) and HHS regulations for the protection of human research subjects (*45 CFR 46*) is based on the prospective intent of the PI and the definition of "research" under HHS regulations at *45 CFR 46.102(d)*: "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

The following activities would require IRB review:

- An activity that involves a prospective research plan which incorporates data collection, including qualitative data, and data analysis to answer a research question and the activity is designed to draw general conclusions (i.e., knowledge gained from a study maybe applied to populations outside of the specific study population), inform policy, or generalize findings.

  Example: An open-ended interview of surviving Gulf War veterans to document their experiences and to draw conclusions about their experiences, inform policy, or generalize findings would require IRB review and approval.

- An activity designed to create archives for the purpose of providing a resource for others to do research. Since the intent of the archive is to create a repository of information for other

investigators to conduct research as define by *45 CFR 46*, the creation of such an archive would constitute research under *45 CFR 46*.

Example: Open-ended interviews are conducted with surviving Negro League Baseball players in order to create an archive for future research. The creation of such an archive would constitute research under *45 CFR 46* since the intent is to collect data for future research.

The following activities would NOT require IRB review:

Oral history activities, such as open-ended interviews, that only document a specific historical event or the experiences of individuals without intent to draw conclusions or generalize findings would not constitute "research" as defined by *45 CFR 46*.

Example: An oral history video recording of interviews with Holocaust survivors is created for viewing in the Holocaust Museum. The creation of the video take does not intend to draw conclusions, inform policy, or generalize findings. The sole purpose is to create a historical record of specific personal events and experiences related to the Holocaust and provide a venue for Holocaust survivors to tell their story.

Studies Involving the Use of Drawings for Prizes as Incentives for Participation in Research

Lotteries are considered "gambling" under the Texas Penal Code, which is an illegal activity. The Texas Penal Code (Sec. 47.01 et seq.) defines a lottery as "any scheme or procedure whereby one or more prizes are distributed by chance among persons who have paid or promised consideration for a chance to win anything of value, whether such a scheme is called a pool, lottery, raffle, gift, gift enterprise, sale, policy game, or some other name."

The Attorney General stated in JC-0174 (2000) that "if the 'payment' required of a lottery participant is not monetary in nature, then such a 'payment' needs to involve a 'substantial expenditure of time and effort' before it would constitute 'consideration' under the gambling law."

Given the above parameters, the key question for researchers who want to use drawings as incentives for research participation is whether the subject's participation requires a substantial amount of time and effort. Researchers should ensure that no conditions are imposed for enrollment. This means that everyone is eligible for the drawing upon providing consent to participate in the study. If the researcher wants to impose a condition (e.g., completion of the survey) before entry is granted to the subject, then the IRB (with legal counsel if needed) will need to make the determination as to whether or not the condition(s) involve a "substantial expenditure of time and effort" on behalf of the subject.

The determination of "substantial time and effort" is made on a case-by-case basis and considers various factors such as the time involvement of the subject, if return visits are required, what is asked of the subject (e.g., survey completion, blood draw), etc.

Health Insurance Portability and Accountability Act of 1996 (HIPAA)

Research that involves health and health-related information may be subject to the privacy standards for protected health information as established by the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Researchers who gather health-related data and are responsible for the storage and destruction of such data are expected to comply with HIPAA guidelines as well as all other required privacy standards.

INITIAL REVIEW OF RESEARCH

Submission of Application

Applications and instructions for each level of review are on the IRB webpage at http://www.twu.edu/research/irb.asp. The separate instructions include submission requirements in addition to instructions for completing the application. Applications are entered into the IRB database by IRB staff at the time they are received and are tracked in the database until they are closed.

Applications submitted by faculty PIs require approval from the academic unit administrator. The faculty member certifies that he/she accepts primary responsibility for all aspects of the research project. The academic unit administrator certifies that he/she has read, reviewed, and approved the content of the application.

Applications submitted by students require approval from the faculty advisor and the academic unit administrator. The student certifies that he/she accepts primary responsibility for all aspects of the research project. The faculty advisor and academic unit administrator certify that they have read, reviewed, and approved the application. Incomplete applications or applications containing unclear information may delay the review and approval process.

IRB submission forms are revised as necessary to improve the process or to meet University and Federal regulations. Revisions are approved by the IRBs prior to implementation.

Possible Actions

The IRB may take one of three actions regarding proposed protocols: approve, request changes, or disapprove.

- ***Approve:*** Permission has been granted to proceed with the research as proposed.

- ***Request changes:*** Specific changes must be made before the protocols can be approved. The IRB determines whether required changes will be reviewed by the IRB, an *ad hoc* committee of the IRB (i.e., the Chair and two other IRB members), or the Chair. Investigators are notified of required revisions immediately following the review of the study. The notification includes specific instructions for implementing and documenting the required changes. Required revisions must be received by the IRB within six months of the notification or the protocol file will be closed.

- ***Disapprove:*** The IRB has determined that the rights and welfare of research participants cannot be adequately protected as the protocol is designed. Decisions for disapproval go to

the full IRB for consideration. The IRB shall notify investigators and the institution in writing of its decision to disapprove proposed research activity. The written notification shall include a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

Approved Protocols

Notification letters signed by the IRB Chair (or Co-Chair in the absence of the Chair) are sent to PIs when protocols have been approved.

Copies of the approval letter are sent to:

- PIs;
- PI's Department;
- Faculty advisors when PIs are students; and
- Graduate School, when PIs are graduate students.

Copies of IRB approval letters may be required with external funding proposals involving research with human subjects.

Researchers must submit copies of signed consent forms to the IRB upon completion of projects or be granted an exception by the IRB for this requirement. Original signed consent forms should be retained by the investigator. Consent forms placed on file with the IRB will be handled with the confidentiality of the subjects in mind.

Graduate students who have conducted research as required by degree plans will be cleared to graduate only when all signed documents are received by the IRB and the Graduate School has been notified.

Disapproved Protocols

PIs are notified in writing by the Chair when protocols have been disapproved by the IRB. The IRB will work closely with PIs to modify aspects of protocols that are cause for concern. PIs may resubmit protocols that incorporate the required changes. PIs may appeal decisions of the IRB by submitting a brief summary outlining the reasons for the appeal. PIs who appeal decisions must attend the convened IRB meeting in which the appeal is reviewed.

INTERIM REVIEW PROCEDURES

Review of Proposed Changes in Research Projects

Researchers are required to promptly report proposed changes in research activities to the IRB. Such changes during the period for which IRB approval has already been given may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the participant. The requirement for prompt reporting is stated in both the initial approval letter and the extension letter, is included in IRB training, and is stated on the IRB website.

Researchers must complete the *IRB Modification Request Form* found on the IRB website at http://www.twu.edu/research/irb-denton.asp to propose changes in a research activity.

Changes to previously approved and exempted research are reviewed by the IRB Chair or by one or more experienced reviewers designated by the Chair from among members of the IRB. Except in the instance of a change of principal investigator, modifications for the sole purpose of adding or removing a research team member(s) may be administratively reviewed and processed by the IRB staff. In reviewing the request for modifications, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. These authorities include referral to a convened IRB meeting if more than minimal risks are involved (*46 CFR part 103(b)(4)*). When a modification to an exempt study is approved, the closed date of the protocol will be changed to reflect the date of the most recent modification.

Continuing Review of Research

Continuing review of research will be conducted at intervals appropriate to the degree of risk, but not less than once per year. Extension requests must be reviewed prior to the anniversary date of the last approval. Full review anniversaries are the date of the full IRB approval. The anniversary for expedited studies is the date of the approval letter signed by the IRB Chair. The IRB may determine the frequency of continuing review of protocols based on an investigator's IRB history including past and current violations, the level of risk, the vulnerability of the participant population, the use of deception, the complexity of the project, or any other concern. The IRB may take the same actions on continuing reviews as those taken on initial applications. Investigators are notified of required revisions to an extension request immediately following the review of the request.

PIs are notified of renewal dates and the requirement to submit requests for extensions or requests to close IRB files at least 30 days prior to the anniversary date of the last approval. Extension requests on expedited review studies should be submitted prior to the expiration date and will be reviewed by one member of the IRB. Extension requests on full review studies are reviewed at fully convened IRB meetings and therefore should be submitted both prior to the expiration and prior to the next scheduled IRB meeting. IRB meeting schedules are on the IRB website at http://www.twu.edu/research/irb.asp.

Extension requests must include the number of participants accrued, a summary of unanticipated problems and/or adverse events, participant complaints, withdrawals, and a summary of amendments and modifications since the last review. Current consent documents must be attached to the extension (see *Minor Noncompliance* for procedures on lapses of IRB approval).

CLOSEOUT OF IRB PROTOCOL

Exempt studies are closed at the time that an exemption is granted. Investigators who have received approval for an expedited or full-review study must submit a request to close their file when approved research projects are completed. Close file requests should be submitted prior to the expiration date of the study. A protocol file must also be closed when the investigator is no longer at the University unless a modification is approved to change the investigator on a study. Any exception allowing an investigator no longer affiliated with TWU to maintain an active IRB approval must be approved by the appropriate Dean and Assistant Provost for

Promotion of Research & Sponsored Programs. The close file request must include the number of participants accrued, a summary of unanticipated problems and/or adverse events, participant complaints, withdrawals, and a summary of amendments and modifications since the last review.

Researchers must submit copies of signed consent forms to the IRB upon completion of projects or be granted an exception by the IRB for this requirement. Original signed consent forms should be retained by the investigator. Consent forms placed on file with the IRB will be handled with the confidentiality of the subjects in mind.

Graduate students who have conducted research as required by degree plans will be cleared to graduate when all signed documents are received by the IRB and the Graduate School has been notified.

IRB RECORDS

The IRB will prepare and maintain adequate documentation of IRB activities, including the following.

- Copies of all research proposals reviewed, scientific evaluations that accompany proposals, approved informed consent documents, progress reports, and reports of adverse events / unanticipated problems;
- Minutes of IRB meetings in sufficient detail to show attendance at the meetings; actions taken by the IRB; votes on these actions including the number of members voting for, against, and abstaining; the basis for required changes in or disapproval of research; and summaries of the discussion of controverted issues and their resolution;
- Records of continuing review activities;
- Copies of all correspondence between the IRB and the investigators;
- List of IRB members and copies of their vitas;
- Written procedures for the IRB; and
- Statements of significant new findings provided to participants.

The records maintained by the IRB will be retained for at least four years from the file closed date. All records will be accessible for inspection and duplication by authorized representatives of the DHHS at reasonable times and in a reasonable manner.

APPENDICES

APPENDIX A: DEFINITIONS

Adverse Events

An *adverse event* is any untoward or unfavorable occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms.

- ***Internal adverse events****:* adverse events experienced by subjects enrolled by an investigator at TWU whether as a part of a multi-center study or solely as a TWU study.
- ***External adverse events****:* adverse events experienced by subjects enrolled by investigators at other institutions engaged in a multi-center study in which TWU is participating.

Certification

Certification is the official notification to sponsoring agencies and to the TWU Graduate School, by the IRB, that research projects or activities involving human subjects have been reviewed and approved by the IRB in accordance with these guidelines.

Exempt Review Applications

Activities that do not depart materially from events encountered in ordinary daily life may be determined by the IRB to be *Exempt* from further review by the IRB. However, cases in which these ordinary activities may impose physical or psychological discomfort (beyond levels encountered in daily life), harassment, invasion of privacy, a threat to the subjects' dignity, or other foreseeable risks will require a Full or Expedited Review (see *Exempt Review Applications* section for detailed criteria).

Expedited Review Applications

Expedited applications are submitted for studies that (a) involve minimal risks to the subjects; (b) do not involve sensitive topics; or (c) do not use minors except in certain circumstances. Expedited studies include research using questionnaires, surveys, and interviews that are not anonymous (i.e., the subjects can be identified) (see *Expedited Review Applications* section for detailed criteria).

Full Review Applications

Full Review applications must be submitted for studies that (a) involve more than just minimal risks to the subjects; (b) involve a sensitive topic; or (c) involve minors unless exempt under federal policies. Full review applications are reviewed at a convened meeting at which a majority of the membership of the IRB is present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting (see *Full Review Applications* section for detailed criteria).

Human Subjects in Research

Human subjects in research are living individuals about whom investigators (professionals or students) conducting research obtain (1) data through intervention or interaction with individuals, or (2) identifiable private information. Identifiable private information includes any acquired information via self-report, behavior, or observation in which the identity of research subjects is or may readily be ascertained by the investigators or be associated with the information.

Informed Consent

Informed Consent is a person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence.

Minimal Risk

Minimal risk means that 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.

Noncompliance

Noncompliance is the failure to comply with federal or state regulations, TWU policies and procedures governing research with human subjects, or requirements of the IRB.

- ***Minor Noncompliance*** is a deviation from procedures that does not increase risks to research participants, compromise participants' rights or welfare, or affect the integrity of the research/data or the IRB process.
- ***Serious Noncompliance*** is an act or omission that has the potential to increase risk to research participants, compromise participants' rights or welfare, or affect the integrity of the research/data or IRB process.
- ***Continuing Noncompliance*** is noncompliance that has been previously reported, or a pattern of ongoing activities that indicate a lack of understanding of human subjects protection requirements that may affect research participants or the validity of the research and suggest the potential for future noncompliance without intervention.

Principal Investigator (PI)

The *Principal Investigator (PI)* has primary responsibility for the research project. The PI may be a TWU faculty member, staff member, or student, depending on the nature of the project. All research in which a student is the PI must be supervised by a TWU faculty advisor with a current appointment.

Protocol

Protocol is the description of research or related projects presented to the IRB for review.

Research projects may encompass several individual investigations using related techniques or common themes. The proposed projects must be presented in sufficient detail to enable the IRB to determine whether adequate provisions have been made for the protection of the subjects' rights and welfare.

Research

Research is a systematic investigation designed to test hypotheses, evaluate programs, draw conclusions, or contribute to generalizable knowledge. Research is usually described in a formal protocol that sets forth objectives and a set of procedures designed to reach those objectives.

Research Team

The research team is made up of investigators who are individuals performing various tasks related to the conduct of human subjects research activities, such as obtaining informed consent from subjects, interacting with subjects, and communicating with the IRB. Such tasks could include:

- obtaining information about living individuals by intervening or interacting with them for research purposes;
- obtaining identifiable private information about living individuals for research purposes;
- obtaining the voluntary informed consent of individuals to be subjects in research; and
- studying, interpreting, or analyzing identifiable private information or data for research purposes.

Research team members can include physicians, scientists, nurses, administrative staff, teachers, and students, among others. In every human subjects research study, all research teams members have certain responsibilities regarding the ethical treatment of human subjects.

Risk

The OHRP IRB Guidebook defines *risk* as the probability of harm or injury occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. The risks to which research subjects may be exposed have been classified as physical, psychological, social, and economic [Levine (1986), p. 42]. The determination of such risk is a matter of sound professional judgment and responsibility by the IRB as well as the investigators (see *Evaluation of Risk* section for further detail).

Unanticipated Problems

An *unanticipated problem* is any incident, experience, adverse event, or outcome that meets all of the following criteria: unexpected given the described procedures, informed consent, and population characteristics; related or possibly related to participation in the research; suggests that subjects are placed at greater risk than previously known.

APPENDIX B

BELMONT REPORT

The Belmont Report

Office of the Secretary

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

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

April 18, 1979

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

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

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a

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

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

Members of the Commission

Kenneth John Ryan, M.D., Chairman, Chief of Staff, Boston Hospital for Women.
Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University.
Robert E. Cooke, M.D., President, Medical College of Pennsylvania.
Dorothy I. Height, President, National Council of Negro Women, Inc.
Albert R. Jonsen, Ph.D., Associate Professor of Bioethics, University of California at San Francisco.
Patricia King, J.D., Associate Professor of Law, Georgetown University Law Center.
Karen Lebacqz, Ph.D., Associate Professor of Christian Ethics, Pacific School of Religion.
**** David W. Louisell, J.D., Professor of Law, University of California at Berkeley.*
Donald W. Seldin, M.D., Professor and Chairman, Department of Internal Medicine, University of Texas at Dallas.
****Eliot Stellar, Ph.D., Provost of the University and Professor of Physiological Psychology, University of Pennsylvania.*
**** Robert H. Turtle, LL.B., Attorney, VomBaur, Coburn, Simmons & Turtle, Washington, D.C.*

**** Deceased.*

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Ethical Principles & Guidelines for Research Involving Human Subjects

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

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

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

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

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Part A: Boundaries Between Practice & Research

A. Boundaries Between Practice and Research

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

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.(2) By contrast, the term "research' designates an

activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

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

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

Part B: Basic Ethical Principles

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence and justice.

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

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

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

while they are incapacitated.

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

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

2. Beneficence. -- Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: **(1)** do not harm and **(2)** maximize possible benefits and minimize possible harms.

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

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

The principle of beneficence often occupies a well-defined justifying role in many areas of

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

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

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

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures,

justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

Part C: Applications

C. Applications

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

1. Informed Consent. -- Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

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

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

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not

be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that **(1)** incomplete disclosure is truly necessary to accomplish the goals of the research, **(2)** there are no undisclosed risks to subjects that are more than minimal, and **(3)** there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

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

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may need to be made when comprehension is severely limited -- for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disable patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

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

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

Unjustifiable pressures usually occur when persons in positions of authority or commanding

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

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.

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(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.

National Institutes of Health
Bethesda, Maryland 20892

APPENDIX C

CODE OF FEDERAL REGULATIONS (CFR)

45 CFR 46

Code of Federal Regulations

TITLE 45
PUBLIC WELFARE

Department of Health and Human Services

PART 46
PROTECTION OF HUMAN SUBJECTS

* * *

Revised January 15, 2009
Effective July 14, 2009

SUBPART A—
Basic HHS Policy for Protection of Human Research Subjects

Sec.

SUBPART B—
Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

Sec.

SUBPART C— Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

Sec.

SUBPART D— Additional Protections for Children Involved as Subjects in Research

Sec.

Authority: 5 U.S.C. 301; 42 U.S.C. 289 (a).

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SUBPART E — Registration of Institutional Review Boards

Sec.

Editorial Note: The Department of Health and Human Services issued a notice of waiver regarding the requirements set forth in part 46, relating to protection of human subjects, as they pertain to demonstration projects, approved under section 1115 of the Social Security Act, which test the use of cost-sharing, such as deductibles, copayment and coinsurance, in the Medicaid program. For further information see 47 FR 9208, Mar. 4, 1982.

SUBPART A
Basic HHS Policy for Protection of Human Research Subjects

Authority: 5 U.S.C. 301; 42 U.S.C. 289; 42 U.S.C. 300v-1(b).

Source: 56 FR 28012, 28022, June 18, 1991, unless otherwise noted.

§46.101 To what does this policy apply?

(a) Except as provided in paragraph (b) of this section, this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the federal government outside the United States.

(1) Research that is conducted or supported by a federal department or agency, whether or not it is regulated as defined in §46.102(e), must comply with all sections of this policy.

(2) Research that is neither conducted nor supported by a federal department or agency but is subject to regulation as defined in §46.102(e) must be reviewed and approved, in compliance with §46.101, §46.102, and §46.107 through §46.117 of this policy, by an institutional review board (IRB) that operates in accordance with the pertinent requirements of this policy.

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such 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.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, 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 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 Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

(c) Department or agency heads retain final judgment as to whether a particular activity is covered by this policy.

(d) Department or agency heads may require that specific research activities or classes of research activities conducted, supported, or otherwise subject to regulation by the department or agency but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

(e) Compliance with this policy requires compliance with pertinent federal laws or regulations which provide additional protections for human subjects.

(f) This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

(g) This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections to human subjects of research.

h) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the FEDERAL REGISTER or will be otherwise published as provided in department or agency procedures.

(i) Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Human Research Protections, Department of Health and Human Services (HHS), or any successor office, and shall also publish them in the FEDERAL REGISTER or in such other manner as provided in department or agency procedures.[1]

[56 FR 28012, 28022, June 18, 1991; 56 FR 29756, June 28, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.102 Definitions.

(a) *Department or agency head* means the head of any federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.

(b) *Institution* means any public or private entity or agency (including federal, state, and other agencies).

(c) *Legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

(d) *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

(e) *Research subject to regulation*, and similar terms are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).

(f) *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.

(g) *IRB* means an institutional review board established in accord with and for the purposes expressed in this policy.

(h) *IRB approval* means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

(i) *Minimal risk* means that 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.

h) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the FEDERAL REGISTER or will be otherwise published as provided in department or agency procedures.

[1]Institutions with HHS-approved assurances on file will abide by provisions of Title 45 CFR part 46 subparts A-D. Some of the other departments and agencies have incorporated all provisions of Title 45 CFR part 46 into their policies and procedures as well. However, the exemptions at 45 CFR 46.101(b) do not apply to research involving prisoners, subpart C. The exemption at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

§46.103 Assuring compliance with this policy -- research conducted or supported by any Federal Department or Agency.

(a) Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy. In lieu of requiring submission of an assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, on file with the Office for Human Research Protections, HHS, or any successor office, and approved for federalwide use by that office. When the existence of an HHS-approved assurance is accepted in lieu of requiring submission of an assurance, reports (except certification) required by this policy to be made to department and agency heads shall also be made to the Office for Human Research Protections, HHS, or any successor office.

(b) Departments and agencies will conduct or support research covered by this policy only if the institution has an assurance approved as provided in this section, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB. Assurances applicable to federally supported or conducted research shall at a minimum include:

(1)A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to Federal regulation. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institution itself. This requirement does not preempt provisions of this policy applicable to department- or agency-supported or regulated research and need not be applicable to any research exempted or waived under §46.101(b) or (i).

(2)Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

(3)A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the department or agency head, unless in accord with §46.103(a) of this policy, the existence of an HHS-approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Human Research Protections, HHS, or any successor office.

(4)Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(5)Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

(c) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes.

(d) The department or agency head will evaluate all assurances submitted in accordance with this policy through such officers and employees of the department or agency and such experts or consultants engaged for this purpose as the department or agency head determines to be appropriate. The department or agency head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

(e) On the basis of this evaluation, the department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The department or agency head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval.

(f) Certification is required when the research is supported by a federal department or agency and not otherwise exempted or waived under §46.101(b) or (i). An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by §46.103 of this Policy has been reviewed and approved by the IRB. Such certification must be submitted with the application or proposal or by such later date as may be prescribed by the department or agency to which the application or proposal is submitted. Under no condition shall research covered by §46.103 of the Policy be supported prior to receipt of the certification that the research has been reviewed and approved by the IRB. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

[56 FR 28012, 28022, June 18, 1991; 56 FR 29756, June 28, 1991, as amended at 70 FR 36328, June 23, 2005]

§§46.104--46.106 [Reserved]

§46.107 IRB membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(f) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB

§46.108 IRB functions and operations.

In order to fulfill the requirements of this policy each IRB shall:

(a) Follow written procedures in the same detail as described in §46.103(b)(4) and, to the extent required by, §46.103(b)(5).

(b) Except when an expedited review procedure is used (see §46.110), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

§46.109 IRB review of research.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with §46.116. The IRB may require that information, in addition to that specifically mentioned in §46.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

(c) An IRB shall require documentation of informed consent or may waive documentation in accordance with §46.117.

(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(e) An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Secretary, HHS, has established, and published as a Notice in the FEDERAL REGISTER, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate, after consultation with other departments and agencies, through periodic republication by the Secretary, HHS, in the FEDERAL REGISTER. A copy of the list is available from the Office for Human Research Protections, HHS, or any successor office.

(b) An IRB may use the expedited review procedure to review either or both of the following:

(1) some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk,

(2) minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the nonexpedited procedure set forth in §46.108(b).

(c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.

(d) The department or agency head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.

[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.111 Criteria for IRB approval of research.

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

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

§46.112 Review by institution.

Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

§46.113 Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.114 Cooperative research.

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

§46.115 IRB records.

(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

(2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members in the same detail as described in §46.103(b)(3).

(6) Written procedures for the IRB in the same detail as described in §46.103(b)(4) and §46.103(b)(5).

(7) Statements of significant new findings provided to subjects, as required by §46.116(b)(5).

(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the department or agency at reasonable times and in a reasonable manner.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) 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; and

(6) The approximate number of subjects involved in the study.

(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

(1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit 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; and

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

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.117 Documentation of informed consent.

(a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

(b) Except as provided in paragraph (c) of this section, the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

(2) A short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

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

(2) That 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.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.118 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under §46.101(b) or (i), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the department or agency.

§46.119 Research undertaken without the intention of involving human subjects.

In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted, by the institution, to the department or agency, and final approval given to the proposed change by the department or agency.

§46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

(a) The department or agency head will evaluate all applications and proposals involving human subjects submitted to the department or agency through such officers and employees of the department or agency and such experts and consultants as the department or agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

(b) On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

§46.121 [Reserved]

§46.122 Use of Federal funds.

Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

§46.123 Early termination of research support: Evaluation of applications and proposals.

(a) The department or agency head may require that department or agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the department or agency head finds an institution has materially failed to comply with the terms of this policy.

(b) In making decisions about supporting or approving applications or proposals covered by this policy the department or agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension under paragraph (a) of this section and whether the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have, in the judgment of the department or agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to federal regulation).

§46.124 Conditions.

With respect to any research project or any class of research projects the department or agency head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects.

Subpart B

Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

Source: 66 FR 56778, Nov. 13, 2001, unless otherwise noted.

§46.201 To what do these regulations apply?

(a) Except as provided in paragraph (b) of this section, this subpart applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates conducted or supported by the Department of Health and Human Services (DHHS). This includes all research conducted in DHHS facilities by any person and all research conducted in any facility by DHHS employees.

(b) The exemptions at §46.101(b)(1) through (6) are applicable to this subpart.

(c) The provisions of §46.101(c) through (i) are applicable to this subpart. Reference to State or local laws in this subpart and in §46.101(f) is intended to include the laws of federally recognized American Indian and Alaska Native Tribal Governments.

(d) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§46.202 Definitions.

The definitions in §46.102 shall be applicable to this subpart as well. In addition, as used in this subpart:

(a) Dead fetus means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

(b) Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means.

(c) Fetus means the product of conception from implantation until delivery.

(d) Neonate means a newborn.

(e) Nonviable neonate means a neonate after delivery that, although living, is not viable.

(f) Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

(g) Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

(h) Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the FEDERAL REGISTER guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subparts A and D of this part.

§46.203 Duties of IRBs in connection with research involving pregnant women, fetuses, and neonates.

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart and the other subparts of this part.

§46.204 Research involving pregnant women or fetuses.

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

(a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

(b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

(c) Any risk is the least possible for achieving the objectives of the research;

(d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A of this part;

(e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

(f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

(g) For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;

(h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

(i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

(j) Individuals engaged in the research will have no part in determining the viability of a neonate.

§46.205 Research involving neonates.

(a) Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

(1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

(2) Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

(3) Individuals engaged in the research will have no part in determining the viability of a neonate.

(4) The requirements of paragraph (b) or (c) of this section have been met as applicable.

(b) Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:

(1) The IRB determines that:

(i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or

(ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

(2) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

(c) Nonviable neonates. After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

(1) Vital functions of the neonate will not be artificially maintained;

(2) The research will not terminate the heartbeat or respiration of the neonate;

(3) There will be no added risk to the neonate resulting from the research;

(4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

(5) The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

(d) Viable neonates. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of subparts A and D of this part.

§46.206 Research involving, after delivery, the placenta, the dead fetus or fetal material.

(a) Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

(b) If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.

§46.207 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

The Secretary will conduct or fund research that the IRB does not believe meets the requirements of §46.204 or §46.205 only if:

(a) The IRB finds that the research presents

a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and

(b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either:

(1) That the research in fact satisfies the conditions of §46.204, as applicable; or

(2) The following:

(i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;

(ii) The research will be conducted in accord with sound ethical principles; and

(iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

Subpart C

Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

Source: 43 FR 53655, Nov. 16, 1978, unless otherwise noted.

§46.301 Applicability.

(a) The regulations in this subpart are applicable to all biomedical and behavioral research conducted or supported by the Department of Health and Human Services involving prisoners as subjects.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will authorize research involving prisoners as subjects, to the extent such research is limited or barred by applicable State or local law.

(c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§46.302 Purpose.

Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research, it is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable.

§46.303 Definitions.

As used in this subpart:

(a) *Secretary* means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

(b) *DHHS* means the Department of Health and Human Services.

(c) *Prisoner* means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

(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.

§46.304 Composition of Institutional Review Boards where prisoners are involved.

In addition to satisfying the requirements in §46.107 of this part, an Institutional Review Board, carrying out responsibilities under this part with respect to research covered by this subpart, shall also meet the following specific requirements:

(a) A majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.

(b) At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement.

[43 FR 53655, Nov. 16, 1978, as amended at 46 FR 8366, Jan. 26, 1981]

§46.305 Additional duties of the Institutional Review Boards where prisoners are involved.

(a) In addition to all other responsibilities prescribed for Institutional Review Boards under this part, the Board shall review research covered by this subpart and approve such research only if it finds that:

(1) The research under review represents one of the categories of research permissible under §46.306(a)(2);

(2) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

(3) The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

(4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

(5) The information is presented in language which is understandable to the subject population;

(6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

(7) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

(b) The Board shall carry out such other duties as may be assigned by the Secretary.

(c) The institution shall certify to the Secre-

tary, in such form and manner as the Secretary may require, that the duties of the Board under this section have been fulfilled.

§46.306 Permitted research involving prisoners.

(a) Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:

(1) The institution responsible for the conduct of the research has certified to the Secretary that the Institutional Review Board has approved the research under §46.305 of this subpart; and

(2) In the judgment of the Secretary the proposed research involves solely the following:

(i) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

(ii) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

(iii) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research; or

(iv) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of the intent to approve such research.

(b) Except as provided in paragraph (a) of this section, biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

Subpart D

Additional Protections for Children Involved as Subjects in Research

Source: 48 FR 9818, March 8, 1983, unless otherwise noted.

§46.401 To what do these regulations apply?

(a) This subpart applies to all research involving children as subjects, conducted or supported by the Department of Health and Human Services.

(1) This includes research conducted by Department employees, except that each head of an Operating Division of the Department may adopt such nonsubstantive, procedural modifications as may be appropriate from an administrative standpoint.

(2) It also includes research conducted or supported by the Department of Health and Human Services outside the United States, but in appropriate circumstances, the Secretary may, under paragraph (i) of §46.101 of subpart A, waive the applicability of some or all of the requirements of these regulations for research of this type.

(b) Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at §46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.101 (b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

(c) The exceptions, additions, and provisions for waiver as they appear in paragraphs (c) through (i) of §46.101 of subpart A are applicable to this subpart.

[48 FR 9818, Mar.8, 1983; 56 FR 28032, June 18, 1991; 56 FR 29757, June 28, 1991.]

§46.402 Definitions.

The definitions in §46.102 of subpart A shall be applicable to this subpart as well. In addition, as used in this subpart:

(a) *Children* are 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.

(b) *Assent* means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

(c) *Permission* means the agreement of parent (s) or guardian to the participation of their child or ward in research.

(d) *Parent* means a child's biological or adoptive parent.

(e) *Guardian* means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

§46.403 IRB duties.

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart.

§46.404 Research not involving greater than minimal risk.

HHS will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §46.408.

§46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

HHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:

(a) The risk is justified by the anticipated benefit to the subjects;

(b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and

(c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §46.408.

§46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.

HHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

(a) The risk represents a minor increase over minimal risk;

(b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

(c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and

(d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in §46.408.

§46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

HHS will conduct or fund research that the IRB does not believe meets the requirements of §46.404, §46.405, or §46.406 only if:

(a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

(b) the Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:

(1) that the research in fact satisfies the conditions of §46.404, §46.405, or §46.406, as applicable, or (2) the following:

(i) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(ii) the research will be conducted in accordance with sound ethical principles;

(iii) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in §46.408.

§46.408 Requirements for permission by parents or guardians and for assent by children.

(a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.

(b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by §46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405. Where research is covered by §§46.406 and 46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

(c) In addition to the provisions for waiver contained in §46.116 of subpart A, if the IRB determines that 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 subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

(d) Permission by parents or guardians shall be documented in accordance with and to the extent required by §46.117 of subpart A.

(e) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

§46.409 Wards.

(a) Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if such 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 children involved as subjects are not wards.

(b) If the research is approved under paragraph (a) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual 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 in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

Subpart E

Registration of Institutional Review Boards

Source: 74 FR 2399, January 15, 2009, unless otherwise noted.

§46.501 What IRBs must be registered?

Each IRB that is designated by an institution under an assurance of compliance approved for federalwide use by the Office for Human Research Protections (OHRP) under §46.103(a) and that reviews research involving human subjects conducted or supported by the Department of Health and Human Services (HHS) must be registered with HHS. An individual authorized to act on behalf of the institution or organization operating the IRB must submit the registration information.

§46.502 What information must be provided when registering an IRB?

The following information must be provided to HHS when registering an IRB:

(a) The name, mailing address, and street address (if different from the mailing address) of the institution or organization operating the IRB(s); and the name, mailing address, phone number, facsimile number, and electronic mail address of the senior officer or head official of that institution or organization who is responsible for overseeing activities performed by the IRB.

(b) The name, mailing address, phone number, facsimile number, and electronic mail address of the contact person providing the registration information.

(c) The name, if any, assigned to the IRB by the institution or organization, and the IRB's mailing address, street address (if different from the mailing address), phone number, facsimile number, and electronic mail address.

(d) The name, phone number, and electronic mail address of the IRB chairperson.

(e)(1) The approximate numbers of:

(i) All active protocols; and

(ii) Active protocols conducted or supported by HHS.

(2) For purpose of this regulation, an ``active protocol'' is any protocol for which the IRB conducted an initial review or a continuing review at a convened meeting or under an expedited review procedure during the preceding twelve months.

(f) The approximate number of full-time equivalent positions devoted to the IRB's administrative activities.

§46.503 When must an IRB be registered?

An IRB must be registered before it can be designated under an assurance approved for federalwide use by OHRP under §46.103(a).

IRB registration becomes effective when reviewed and accepted by OHRP.

The registration will be effective for 3 years.

§46.504 How must an IRB be registered?

Each IRB must be registered electronically through http://ohrp.cit.nih.gov/efile unless an institution or organization lacks the ability to register its IRB(s) electronically. If an institution or organization lacks the ability to register an IRB electronically, it must send its IRB registration information in writing to OHRP.

§46.505 When must IRB registration information be renewed or updated?

(a) Each IRB must renew its registration every 3 years.

(b) The registration information for an IRB must be updated within 90 days after changes occur regarding the contact person who provided the IRB registration information or the IRB chairperson. The updated registration information must be submitted in accordance with §46.504.

(c) Any renewal or update that is submitted to, and accepted by, OHRP begins a new 3-year effective period.

(d) An institution's or organization's decision to disband a registered IRB which it is operating also must be reported to OHRP in writing within 30 days after permanent cessation of the IRB's review of HHS-conducted or -supported research.

APPENDIX D

CATEGORIES OF RESEARCH THAT MAY BE REVIEWED BY THE IRB THROUGH AN EXPEDITED REVIEW PROCEDURE

Federal Register: November 9, 1998 (Volume 63, Number 216)

[Page 60364-60367]

Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure[1]

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, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children[2], 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.)

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 behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the 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 of 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.

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[1] An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

[2] 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).

Source: 63 FR 60364-60367, November 9, 1998.
