

# **Texas A&M University-Texarkana**

## **Human Research Protection Program**

### **Standard Operating Procedures**



**Developed: May 18, 2014  
(adapted from UNC-Chapel Hill)  
Encompasses changes to comply  
with the 2018 Requirements as part  
of the Revised Common Rule.**

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## DEFINITIONS

**Adverse event** is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), 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.

**Affiliated** refers to an IRB member who is employed by Texas A&M University-Texarkana or has a dependent relationship with the University that might influence her/his objectivity. Individuals who have retired from the University are still considered to be affiliated.

**Allegation of noncompliance** is an unproven assertion of noncompliance with federal regulations or University or IRB policies.

**Assent** means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. [45 CFR 46.402(b)].

**Certification** means the official notification by the University to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance. [45 CFR 46.102(j)].

**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. [45 CFR 46.402(a)].

**Clinical investigation in the context of FDA regulations** (not all clinical research is subject to Food and Drug Administration (FDA) jurisdiction) means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the Food, Drug and Cosmetic Act, or is not subject to requirements for prior submission to the FDA under these sections of the Act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions regarding nonclinical laboratory studies. [21 CFR 50.3(c)].

**Closure** refers to the ending of a study by anyone other than the IRB (e.g., sponsor or the PI).

**Continuing noncompliance** is a pattern of noncompliance that indicates an unwillingness to comply or a lack of knowledge that may adversely affect the rights and welfare of participants or may place participants at an increased risk of harm. Examples of continuing noncompliance include: repeated instances of allowing a study to expire; repeated failure to respond to IRB inquiries or requests for documentation; repeated failure to respond to and resolve any study contingencies; or repeated instances of failures to respond to IRB inquiries and contingencies.

**Covered Entity** is the term that the Health Insurance Portability and Accountability Act (HIPAA) regulations use to describe the businesses in the health care industry that are subject to HIPAA regulations. Specifically, covered entities are health plans, health care clearinghouses and health care providers who transmit any health information in electronic form in connection with the following transactions: health care claims or encounter information, health care payment and remittance advice, coordination of benefits, health care claim status, enrollment or disenrollment or eligibility information regarding health plans, health plan premium payments, referral certification and authorization, first report of injury, or health claims attachments.

**Emergency use** means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. [21 CFR 56.102(d)]

**Engaged in Research:** An institution becomes "engaged" in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d),(f)]. For additional guidance and examples, see the Office for Human Research Protections website ([www.hhs.gov/ohrp](http://www.hhs.gov/ohrp)).

**Family member** means any one of the following legally competent persons: Spouse; parents; children (including adopted children); brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship. [21 CFR 50.3(m)].

**Fetus** means the product of conception from the time of implantation (as evidenced by any of the presumptive signs of pregnancy, such as missed menses, or a medically acceptable pregnancy test), until a determination is made, following expulsion or extraction of the fetus, that it is viable. [45 CFR 46.203(c)].

**Neonate** means a newborn.

**Viable** as it pertains to neonates means being able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. The Secretary of the Department of Health and Human Services (DHHS) may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a fetus is viable for purposes of this subpart. If a fetus is viable after delivery, it is a premature infant. [45 CFR 46.203(d)].

**Nonviable neonate** means a neonate ex utero which, although living, is not viable. [45 CFR 46.203(e)].

**Dead fetus** means a neonate ex utero which exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached). [45 CFR 46.203(f)].

**Financial interest related to the research** means financial interest in the sponsor, product or service being tested, or competitor of the sponsor or product or service being tested.

**Guardian** means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. A guardian also means an individual who is authorized to consent on behalf of a child to participate in research [45 CFR 46.402(e)] [21 CFR 50.3(s)].

**Honest Broker** The term "honest broker" is frequently used in connection with tissue repositories, and refers to someone who has a defined role whereby he/she maintains access to all identifying information on samples in the repository, but provides only de-identified tissue samples to the researchers. In order for the tissue repository to facilitate follow on research, the researchers typically need to access non-identifying information that is linked to the tissues (e.g., stage of disease, age of the tissue donor, proximity to date of surgery, etc.). The role of "honest broker" protects the tissue donors from any risks associated with the use of their private information and it allows the end-users (researchers who obtain de-identified tissue) to (i) conduct research that does not constitute human subject research, thereby allowing the research to proceed without the need for an IRB approval or approval of an exemption request; and (ii) to conduct research without needing to obtain a specific informed consent or authorization, provided that all requirements of the Honest Broker system are met.

**Human participant** [See Human Subject]

**Human cells, tissues, or cellular or tissue-based products (HCT/P's)** means articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Examples of HCT/P's include, but are not limited to, bone, ligament, skin, cornea, hematopoietic stem cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and



semen or other reproductive tissue. The following articles are not considered HCT/P's: (i) Vascularized human organs for transplantation; (ii) Whole blood or blood components or blood derivative products subject to listing under parts 607 and 207 of this chapter, respectively; (iii) Secreted or extracted human products, such as milk, collagen, and cell factors; except that semen is considered an HCT/P; (iv) Minimally manipulated bone marrow for homologous use and not combined with a drug or a device (except for a sterilizing, preserving, or storage agent, if the addition of the agent does not raise new clinical safety concerns with respect to the bone marrow); (v) Ancillary products used in the manufacture of HCT/P; (vi) Cells, tissues, and organs derived from animals other than humans; (vii) In vitro diagnostic products as defined in § 809.3(a) of this chapter; and (viii) Human dura mater and human heart valve allografts. [21 CFR 1271.3(d)].

**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. [45 CFR 46.102(f)] The FDA defines a human subject as “an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may either be a healthy human or patient.” [21 CFR 50.3(g)].

**Human subject research** encompasses DHHS definitions of “human subject” and “research” and FDA definitions of “human subject” and “research.”

**Immediate Family** includes the individual's spouse and dependent children. “Spouse” includes a person with whom one lives together in the same residence and with whom one shares responsibility for each other's welfare and shares financial obligations.

**Institution** means any public or private entity or agency (including federal, State, and other agencies). [45 CFR 46.102(b)]. 21 CFR 50.3(h) and 21 CFR 56.102(f) are the same as above with the additional sentence: “The word facility as used in section 520(g) of the act is deemed to be synonymous with the term institution for purposes of this part.”

**Institutional Review Board (IRB)** means the Texas A&M University-Texarkana committee formally designated by the University to review, to approve the initiation of, and to conduct periodic review of, research involving human subjects. The primary purpose of such review is to protect the rights and welfare of the human subjects.

**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. [45 CFR 46.102(h)]. 21 CFR 56.102(m) is the same except that the term “clinical investigation” is used in lieu of “research.”

**Intervention and interaction** includes both physical procedures by which data are gathered (e.g., 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. [45 CFR 46.102(f)].

**Investigational device** means a device, including a transitional device that is the object of an investigation. [21 CFR 812.3(g)].

**Investigator** means an individual who actually conducts research or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

**In vitro fertilization** means any fertilization of human ova which occurs outside the body of a female, either through admixture of donor human sperm and ova or by any other means. [45 CFR 46.203(g)]

**Legally Authorized Representative (LAR)** 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. [21 CFR 50.3(l)].

**Minimal risk** (for human subjects other than prisoners) 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. [21 CFR 50.3(k), 21 CFR 56.102(i), 45 CFR 46.102(i)].

**Minimal risk** (for human subjects who are prisoners) 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. [45 CFR 46.303(d)].

**Minors** are children who have not reached the age of majority.

**Neonate** means a newborn.

**Viable as it pertains to neonates** means being able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. The Secretary of DHHS may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a fetus is viable for purposes of this subpart. If a fetus is viable after delivery, it is a premature infant. [45 CFR 46.203(d)].

**Nonviable neonate** means a neonate ex utero which, although living, is not viable. [45 CFR 46.203(e)].

**Noncompliance** is a failure to follow applicable federal regulations, the requirements or determinations of the IRB, or University policy.

**Parent** means a child's biological or adoptive parent. [45 CFR 46.402(d)].

**Permission** means the agreement of parent(s) or guardian to the participation of their child or ward in research. [45 CFR 46.402(c)].

**Pregnancy** encompasses the period of time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until expulsion or extraction of the fetus. [45 CFR 46.203(b)].

**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. [45 CFR 46.303(c)].

**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 (e.g., 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. [45 CFR 46.102(f)]

**Protected Health Information (PHI):** HIPAA defines protected health information (PHI) as individually identifiable health condition, health care and health care payment information, including the demographic data that is a potential identifier of the individual, maintained in the records of "covered entities" for treatment, payment and healthcare operations purposes. (See definition of "covered entity" above. Most health care providers and health plans and health care clearinghouses are covered entities). PHI does not include individually identifiable health information in personnel records or education records covered by the Family Educational Rights and Privacy Act (FERPA).

**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. [45 CFR 46.102(d)].

**Serious Adverse Event (SAE)** is one which is fatal or life threatening; results in significant or persistent disability; requires or prolongs hospitalization; results in a congenital anomaly/birth defect; or represents other significant hazards or potentially serious harm to research subjects or others. [See also “Adverse Event”]

**Serious noncompliance** is noncompliance that adversely affects the rights and welfare of participants, places participants at increased risk of harm or willfully violates policies and procedures.

**Sponsor** is an entity external to the University that is providing support for a University research project pursuant to terms and conditions in an agreement between the sponsor and the University. With respect to FDA regulations, “sponsor” means the person or entity that has responsibility for fulfillment of FDA requirements for a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving, a subject under the immediate direction of another individual. An entity other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators. [21 CFR 50.3(e) and 21 CFR 56.102(j)].

**Sponsor-investigator** (with respect to FDA regulations) means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, for example, corporation or agency. [21 CFR 50.3(f)]. 21 CFR 56.102(k) is the same as above with the additional sentence: “The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.”

**Suspension** refers to the IRB’s temporary or permanent withdrawal of approval for some or all research activities. Suspended research remains under the jurisdiction of the IRB.

**Test article** means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Food, Drug and Cosmetic Act or under sections 351 and 354-360F of the Public Health Service Act. [21 CFR 50.3(j) and 21 CFR 56.102(l)].

**Termination** refers to permanent withdrawal of approval by the IRB for all research activities. Terminated research no longer undergoes continuing review.

**Transitional devices** are devices that were regulated as drugs prior to May 28, 1976, the date the Medical Device Amendments were signed into law. Any device that was approved by the New Drug Application process is now governed by the Premarket approval (PMA) regulations.

**Unanticipated Problem (UP)** refers to any incident, experience, or outcome that is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; is related or possibly related to a subject’s participation in the research; *and* suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

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<b>SOP Introduction</b>	
Current Version Date:	9/30/2014

The Office of Research and Sponsored Projects (ORSP) is responsible for ethical and regulatory oversight of research at Texas A&M University-Texarkana that involves human subjects, regardless of funding source. The ORSP administers, supports, and guides the work of the Institutional Review Board (IRB) and all related activities. Any research involving human subjects proposed by faculty, staff, or students must be reviewed and approved by an IRB before research may begin, and before related grants may be funded. ORSP and the IRB are critical components of the coordinated Human Research Protection Program, which serves to protect the rights and welfare of human subjects. All components of this program must work together to ensure institutional compliance with ethical principles and regulatory requirements.

It is the policy of Texas A&M University-Texarkana that all research involving human subjects should be conducted under equivalent levels of protections as those afforded by the federal regulations that govern this area, regardless of source of funding. This includes the requirement that all research must be reviewed and approved or determined exempt by an institutional review board (IRB) prior to the involvement of human subjects, with attention to informed consent and other protections.

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#### **Charter Statement for the Institutional Review Boards**

(1) There shall exist a Committee at Texas A&M University-Texarkana which shall serve as IRB in accordance with 45 CFR 46, 21 CFR 50 and 56, and other federal regulations. The IRB shall provide expert and timely review and oversight of the human research protection program at the University. The IRB shall be registered with the federal Office for Human Research Protections (OHRP).

(2) The IRB shall be guided by and act in a manner consistent with the ethical principles contained in the "Belmont Report." The IRB shall also be guided by relevant published ethical and professional standards of the various disciplines and professions represented among the faculty who conduct research with human participants.

(3) The IRB shall receive all protocols in which the use of human subjects in research is proposed, regardless of the source of funding for such protocols. The IRB shall review and have the authority to approve, require modifications to secure approval or, disapprove research conducted by the University; to suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that had been associated with unexpected harm to participants; and to observe or have a third party observe the consent process and the conduct of the research. The IRB shall exercise these authorities as it deems appropriate, consistent with the various federal regulations and University policies that govern its work. No research with human subjects shall take place at the Texas A&M University-Texarkana without the prior approval of the IRB.

(4) The judgments of the IRB shall be final. There shall be no appeal of substantive decisions of the IRB to any other authority. Appeal on procedural matters may be heard by the Vice President of Academic and Student Affairs who shall have the authority to require the IRB to reconsider a protocol if there is reason to believe the IRB did not follow its established procedures or acted in violation of federal regulations or University policy.

(5) With the approval of the University Institutional Official for Human Subjects, the IRB may enter into agreements with other institutions to serve as the IRB of record for some or all of the human subject protocols originating within such other institutions. With the approval of the Office of

Graduate Studies and Research, the IRB may enter into agreements with other institutions to allow an IRB at another institution to serve as the IRB of record for a project conducted collaboratively between the University and the other institution, so long as the other institution has a valid federal wide assurance of compliance and the other IRB is registered with OHRP.

(6) The IRB shall provide standard procedures for investigators to follow and standard forms for investigators to use in applying for approval of protocols to any of the IRBs and shall adopt and publish Standard Operating Procedures, consistent with applicable federal regulations and University policies, to govern their activities.

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### **Mission Statement for the Human Research Protection Program**

Texas A&M University-Texarkana is committed to developing and sharing information that benefits humans across the globe. An important part of that commitment to knowledge is research of the highest quality on all aspects of the health and behavior of people, and such research is only possible through the participation of humans as research subjects.

Human subjects are partners and participants in research and a precious resource to the University. At A&M University-Texarkana, human subjects research is a privilege, not a right. Consistent with that philosophy, it is the mission of the A&M-Texarkana Human Research Protection Program to provide that:

1. the rights and welfare of human subjects are paramount in the research process;
2. the highest standards of ethical conduct are employed in all human subjects research;
3. research investigators are properly trained in the ethical and regulatory aspects of research with human subjects;
4. research investigators deal honestly and fairly with human subjects, informing them fully of procedures to be followed, and the risks and benefits of participating in research; and
5. research using human subjects at TAMUT conforms with all applicable local, state and federal laws and regulations and the officially adopted policies of the University.

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### **Purpose of the Standard Operating Procedures (SOPs)**

This document has been authored to assist members of the University community in fulfilling the stated mission of the Human Research Protection Program (HRPP). This document is intended for the use of the IRB at Texas A&M University-Texarkana. It is directed to the IRB Chair and members, the staff of ORSP and other affiliated persons and includes policies and procedures applicable to these persons in their capacities with the IRB. These SOPs focus on specific areas when an unequivocal statement can be made and on broader issues when there are a variety of approaches to a situation. We recognize that due to the complex nature of the work in ORSP, these SOPs cannot address all possible contingencies or issues. It is expected that when issues arise that are not covered in these SOPs, they will be resolved through discussion with a variety institution personnel. It is further recognized that there will be case-specific departures from these SOPs.

Investigator concerns about human research protection at Texas A&M University-Texarkana can be reported through several routes as described in subsequent chapters. These may or may not result in changes to the SOPs.

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## Process for Revising and Approving SOPs

The SOPs are reviewed at least annually by ORSP administration for accuracy and completeness. Any ORSP personnel can question SOPs and/or suggest changes at any time. Other changes may be prompted by external sources, e.g., in response new federal guidance. These proposed changes are reviewed by the ORSP administration, and SOPs revised when warranted.

Final approval of the SOPs, either new or revised, requires review and signature of the (a) Dean of the ORSP, (b) Vice President of Academic and Student Affairs, (c) Chair of IRB, (d) University President. The latter has been designated as Institutional Official, with authority to bind the University and delegate authorities to the IRB. Each revised SOP will supersede all previously-approved versions, and will be effective on the date of the most recent signature.

Once finalized, the changes are reviewed at a regularly scheduled IRB meeting and with other relevant parties.

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## Revision History

Revision 1 August 1, 2019

**Overall:** Document was converted from PDF to Word, cleaned up, and revised to make more readable. Major changes to the below sections to bring the SOPs into compliance with the Revised Common Rule, which went into effect January 21, 2019.

**Section 15:** Exemption categories were merged and added so that there are now three additional exemption categories:

- Benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording of the subject with prospective agreement.
- Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use (broad consent required).
- Secondary research involving the use of identifiable private information or identifiable biospecimens (broad consent required).

Also, Section 15 now provides for a new process for studies that include identifiable information or biospecimens, but that are otherwise exempt from continuing review. This provision is called "Limited IRB Review," and allows these studies to be reviewed initially but no longer requires continuing review.

**Section 17:** Continuing Review is no longer needed for Expedited review studies, unless the IRB determines otherwise. Exempt studies under limited review do not need continuing review, as is already the case for other exempt studies.

**Section 26:** Changed include processes specific to biospecimens, as well as specifications for presentation of the Informed Consent information. There were also additional criteria for waivers of consent, and an ability to eliminate informed consent under certain conditions for screening, recruiting, or eligibility determinations.

**Section 35:** A new section specifying the process and conditions for Broad Consent.

Revision 2 August 16, 2022

**Overall:** Due to the University's organizational change, The Office of Research and Graduate Studies (ORGS) was changed into The Office of Research and Sponsored Projects (ORSP). The change was updated in the document.

**Section 4.2:** A valid CITI training certificate as IRB reviewer is required for the IRB committee members during their term.

**Section 6:** The previous requirement for paper record keeping was replaced by an encrypted digital backup stored on the TAMUT campus.

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SOP Title:	<b>Ethical and Regulatory Mandates for the Protection of Human Research Subjects</b>		
SOP Number:	1.0	Current Version Date:	9/30/14

The regulation of human subjects research by the U.S. Department of Health and Human Services (DHHS) is codified in 45 CFR 46. Because Subpart A of 45 CFR 46 has been adopted for human subjects research by many federal agencies, it is known as the “Common Rule.” The Common Rule requires that every institution performing federally- supported human subjects research file an assurance of protection for human subjects. In addition to complying with the requirements of DHHS, Texas A&M University-Texarkana (TAMUT) complies with applicable federal regulations and policies of other agencies. These include, but are not limited to the Food and Drug Administration (FDA), Department of Defense (DOD), Department of Navy (DON), National Science Foundation (NSF), Public Health Service (PHS), Environmental Protection Agency (EPA), Department of Education (DOEd), Department of Energy (DOE), and Department of Justice (DOJ).

TAMUT maintains a Federalwide Assurance (FWA) of compliance, approved by the Office for Human Research Protections (OHRP), for the protection of human subjects in research. Pursuant to the FWA, human subjects research should conform to the guidance documents described below:

#### 1.1 The Belmont Report

The Belmont Report elucidates three ethical principles that should guide research:

- Respect for persons (applied by obtaining informed consent, respecting privacy and confidentiality, and affording additional protections for vulnerable populations);
- Beneficence (applied by weighing risks and benefits);
- Justice (applied by the equitable selection of subjects)

The Belmont Report is attached to this document. (See Appendix A)

#### 1.2 45 CFR 46

This regulation, published by DHHS, codifies basic human subject protection measures. 45 CFR 46 is attached to this document. (See Appendix B)

#### 1.3 21 CFR 50 and 21 CFR 56

These FDA regulations also codify basic human research protection measures and are largely congruent with 45 CFR 46, with some differences that pertain to FDA-regulated research. 21 CFR 50 and 21 CFR 56 are attached to this document. (See Appendices C and D)

#### 1.4 Assurance and IRB registration process

TAMUT, as an institution involved in behavioral research, should have in place a set of principles and guidelines that govern the University, its faculty, and staff, in the discharge of its responsibilities for protecting the rights and welfare of human subjects taking part in research conducted at, or sponsored by, the institution, regardless of the source of funding. Assurances applicable to federally supported or conducted research must, at a minimum, contain such a statement of principles, which may include an appropriate existing code, declaration, and/or statement of ethical principles as formulated by the institution. *The Belmont Report* serves as such a document for TAMUT. The *IRB Standards Operating Procedure* represents the written procedures and guidelines provided for in TAMUT’s FWA.



## 1.5 Research Subject to the US Department of Education Regulations

The following special considerations apply to all research involving human subjects supported or conducted by the U.S. Department of Education. These considerations are in addition to those found in 45 CFR 46 Subparts A-D.

- All instructional material--including teachers' manuals, films, tapes, or other supplementary instructional material--which will be used in connection with any research or experimentation program or project must be available for inspection by the parents or guardians of the children engaged in such research.
- "Research" or "experimentation program" or "project" means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.
- "Children" are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

### 1.5.1 Research Subject to the Family Educational Rights and Privacy Act (FERPA)

The Family Educational Rights and Privacy Act (FERPA) protects the privacy of student education records. (See SOP 22.6.2 for policy).

### 1.5.2 Research Subject to the Protection of Pupil Rights Amendment

In order to comply with the Protection of Pupil Rights Amendment (34 CFR 98.4), the following must be in place as applicable, and the investigator must document for the IRB that for research projects directly funded by the U.S. Department of Education, no student will be required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:

- Political affiliations or beliefs of the student or the student's parent.
- Mental or psychological problems of the student or the student's family.
- Sex behavior or attitudes.
- Illegal, anti-social, self-incriminating, or demeaning behavior. Critical appraisals of other individuals with whom respondents have close family relationships.
- Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.
- Religious practices, affiliations, or beliefs of the student or student's parent.
- Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).

*Prior consent* means prior consent of the student, if the student is an adult or emancipated minor; or prior written consent of the parent or guardian, if the student is an un-emancipated minor.

### 1.5.3 Research Conducted in a School Receiving U.S. Department of Education Funding (34 CFR 98, 99)

For research not directly funded by the U.S. Department of Education but conducted in a school that receives funding from the U.S. Department of Education, the research protocol must include provisions, as applicable, to ensure:

- The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student. Such access must be made available within a reasonable period of time after the request is made by the parent.
- The protection of student privacy and data confidentiality in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items):
  - Political affiliations or beliefs of the student or the student's parent.
  - Mental or psychological problems of the student or the student's family.
  - Sex behavior or attitudes.
  - Illegal, anti-social, self-incriminating, or demeaning behavior.
  - Critical appraisals of other individuals with whom respondents have close family relationships.
  - Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.
  - Religious practices, affiliations, or beliefs of the student or the student's parent.
  - Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).
- The right of a parent of a student to have reasonable access to inspect any instructional material used as part of the educational curriculum for the student. The procedures for granting such a request must be described.
- The school has adopted a policy in conjunction with parents regarding:
  - Administration of physical examinations or screenings that the school or agency may administer to a student.
  - The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.
  - The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student.
  - Any applicable procedures for granting a request by a parent for reasonable access to such instrument within a reasonable period of time after the request is received.

#### 1.6 Research Subject to U.S. Environmental Protection Agency Regulations

Environmental Protection Agency (EPA) policy requires that researchers submit IRB determinations and approval to the EPA human subjects research review official for final review and approval before the research can begin.

For research not conducted or supported by any federal agency that has requirements for protecting human research subjects and for which the intention of the research is submission to the EPA, the EPA requirements for protecting human research subjects apply.

All covered human research conducted or supported by Environmental Protection Agency (EPA) must be compliant with [40 CFR 26](#) and [EPA Order 1000.17 Change A1](#). 40 CFR 26 includes EPA-specific additional protections and prohibitions for children, pregnant women and fetuses, and nursing women in research conducted or supported by the Agency at Subparts B-D. It also contains regulations for third-party human research for pesticides and rules for data use, compliance oversight, and other matters. EPA Order 1000.17 Change A1 requires that all human subjects research conducted by EPA be reviewed and approved by the EPA Human Subjects Research Review Official (HSRRO) as compliant with 40 CFR 26, or be determined to be exempt research, before the research begins. This requirement is in addition to IRB review and approval, and it occurs subsequent to it as the final step before the research commences.

- Subpart B of the regulations prohibits intentional exposure research, under all circumstances, in children and women who are pregnant or nursing. The ban is categorical and is not based on a risk-benefit ratio, including prospect of direct benefit.
- Subpart C establishes rules for studies that involve pregnant women (and thus their fetuses) participating in observational research. Research of this nature can be conducted when there is direct benefit to the woman or the fetus. However, in the absence of direct benefit, if the risk is no greater than minimal to the fetus and the research is important for biomedical knowledge which cannot be obtained in any other manner, the research is permissible.
- Subpart D establishes rules for studies that involve children participating in observational research. Research of this nature can be conducted on children as long as it involves no more than minimal risk. Research that involves greater than minimal risk can only be conducted when there is direct benefit to the subject. There is no provision in the EPA rule for the conduct of research when there is greater than minimal risk and no direct benefit to the child.

Unlike the regulations adopted by the Department of Health & Human Services, EPA's regulations:

- Do not further regulate research involving prisoners, beyond those additional protections found in the Common Rule.
- Define a child as someone less than 18 years of age (whereas HHS regulations defer to state or local law).
- Contain no exceptions to the rule prohibiting intentional exposure research involving children, nursing women, and pregnant women and fetuses
- Do not recognize a category of research on children involving "a minor increase over minimal risk."
- Have no provisions for "research not otherwise approvable" for children, nursing infants, or fetuses.
- The IRB is permitted to approve observational research involving children that does not involve greater than minimal risk 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 40 CFR 26.406.
- The IRB is permitted to approve observational research involving children that involves greater than minimal risk but presents the prospect of direct benefit to the individual subjects if the IRB finds and documents that:
  - The intervention or procedure holds out the prospect of direct benefit to the individual subject or is likely to contribute to the subject's well-being.
  - 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.
  - Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 40 CFR 26.406.

## 1.7 Research Subject to U.S. Department of Energy Regulations

For research supported by the U.S. Department of Energy (DOE) or subject to DOE regulations, DOE-specific regulations apply. These regulations will be added. Contact the IRB Chair for more details.

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SOP Title:	<b>Roles in the Protection of Human Research Subjects at Texas A&amp;M University-Texarkana</b>		
SOP Number:	2.0	Current Version Date:	5/18/14

## 2.1 The Institutional Official

The Institutional Official at TAMUT, as designated by the President is the Dean of the Office of Research and Sponsored Projects.

It is the responsibility of the Institutional Official to oversee the University's compliance with federal regulations pertinent to human subjects research. The official document pledging this responsibility the FWA, is approved by OHRP at DHHS. The Institutional Official shall be responsible for all required institutional reports to sponsors and federal agencies.

The FWA requires the development and adoption of policies and procedures for conducting human subject research and the appointment of an institutional official to oversee this process.

The Office of Research and Sponsored Projects maintains ultimate responsibility for considering complaints or concerns about the Human Research Protection Program (see also SOP 12.7)

As part of the FWA process, an institution is asked to identify a "Human Protections Administrator" (HPA) to serve as the primary institutional contact person for OHRP. The University has designated the Dean of GSR to be the University's HPA.

The ORSP holds regular meetings of the administrative staff and IRB Chairs to monitor and improve operational processes. The goals of these meetings are to measure and improve the effectiveness, quality, and compliance with organizational policies and procedures and applicable federal, State, and local laws of the HRPP. ORSP also provides a program of ongoing monitoring and auditing of record keeping as well as the conduct of the research under the aegis of Quality Improvement (QI).

The goals of the QI program are to keep ORSP staff and investigators attentive to applicable regulations and University policies as well as to correct procedural errors to achieve ORSP's goal of maintaining protections for subjects enrolled in research.

## 2.2 Institutional Review Board (IRB)

The IRB is established by the University and fall under the aegis of TAMUT. The IRB is an appropriately constituted group that the University has designated to review and monitor research involving human subjects. The IRB shall receive all protocols in which the use of human subjects in research is proposed, regardless of the source of funding for such protocols.

The IRB shall review and have the authority to approve, require modifications to secure approval or, disapprove research conducted by the University; to suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that had been associated with unexpected harm to participants; and to observe or have a third party observe the consent process and the conduct of the research. The IRB shall exercise these authorities as it deems appropriate, consistent with the various federal

regulations and University policies that govern its work. No research with human subjects shall take place at TAMUT without the prior approval of IRB.

The University's IRB contains professionals with expertise required for the review of the University's widely varied human subjects research studies.

### 2.3 Principal Investigator (PI)

The principal investigator is the individual responsible for the conduct of research, and, as such, must personally conduct or supervise the research. The PI is responsible for ensuring that the research study is accurately and completely submitted for IRB review; that IRB approval is obtained prior to initiation of research or before making any changes or additions to the research; that the IRB is informed of new information (e.g., from study sponsor) or changes to information previously presented to the IRB, and work with the IRB to determine if and how new information should be communicated to subjects; that progress reports are submitted to the IRB as required; that all non-compliance is reported to the IRB; and that all unanticipated problems or serious adverse events involving risk to human subjects are reported to the IRB. These responsibilities extend to research determined by ORSP to be exempt. The PI has the ethical obligation to protect the rights and welfare of participants in exempt studies as well as in studies that are subject to continuing IRB review. The PI is also responsible for ensuring that all members of the research team comply with the findings, determinations, and requirements of the IRB, including adequate performance of the informed consent process. These requirements apply in all forms of human subject research, even those determined to qualify for exemption.

The PI is responsible for ensuring that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space. The PI is also responsible for ensuring that research staff are qualified (e.g., including, but not limited to, appropriate training, education, expertise, credentials and, when relevant, privileges) to perform procedures assigned to them during the study.

The role of PI implies administrative and fiscal responsibility as well as sufficient expertise for the research study and, as such, should be filled by a faculty member or a non-faculty employee unless approved in advance. For IRB communication purposes, a trainee/student may be listed as PI. However, a faculty advisor must be identified, who holds ultimate responsibility for ensuring that this project complies with all University, regulatory, and fiscal requirements.

### 2.4 Research team members

Every member of the research team is responsible for protecting human subjects in accordance with the guidelines specified in SOP 1.0, reporting all non-compliance to the IRB, and for complying with all IRB findings, determinations and requirements. Team members must complete human subject research training.

### 2.5 Other University reviewers

In addition to TAMUT IRB review, TAMUT human subjects research studies may be reviewed by other University committees and individuals charged with responsibility for evaluation of specific component research compliance issues.

The factual information, evaluations and recommendations of these research review units may be very useful to the IRB's consideration of the rights and welfare of human subjects within the context of the specific TAMUT research study. IRB staff may return an application to the PI if relevant reviews have not been initiated or completed prior to IRB review.

The TAMUT IRB retains final responsibility and authority to approve each TAMUT research study that involves human subjects.

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SOP Title:	<b>IRB Purpose, Responsibility and Authority</b>		
SOP Number:	3.0	Current Version Date:	9/30/14

### 3.1 Scope and purpose

The purpose of the TAMUT IRB is to protect the rights and welfare of human research subjects. To achieve this, the IRB must: (1) advise investigators in designing research projects in a manner that minimizes potential harm to human subjects, (2) review all planned research involving human subjects prior to initiation of the research, (3) approve research that meets established criteria for protection of human subjects, and (4) monitor approved research to ascertain that human subjects are indeed protected.

The IRB also informs and assists TAMUT and its researchers regarding ethical and procedural issues related to the participation of human subjects in research; facilitates compliance with relevant regulations of the United States government; and provides a framework suitable for continued support by government agencies, private foundations and industry for research involving human subjects at TAMUT.

### 3.2 IRB responsibilities and authority

All human subjects research carried out at TAMUT or under its auspices must be reviewed and approved or determined exempt by the IRB prior to the involvement of human subjects in research.

The TAMUT IRB reviews human subjects research: (1) sponsored by the University; (2) conducted by or under the direction of any employee or agent of the University in connection with his or her institutional responsibilities; (3) conducted by or under the direction of any employee or agent of the University using any property or facility of the University; or (4) involving the use of TAMUT non-public information to identify or contact human subjects.

The IRB must conduct initial and continuing reviews of research and report the findings and actions to the investigator and the institution. These reviews include: the review of all research involving human subjects at a convened meeting of the IRB (except research classified as exempt or evaluated in expedited review); the approval of research with the concurrence of the majority of IRB members; the evaluation of proposed changes in approved research protocols; and, the determination of whether any project requires verification from sources other than the investigator that no material changes have occurred since previous IRB review. In addition:

- The IRB has responsibility for reviewing all research that involves human subjects including the determination that research is exempt from further review under 45 CFR 46 101 (see Appendix B).
- The IRB has responsibility for oversight of all human subjects research that is not exempt from IRB review;
- The IRB must protect the rights and welfare of subjects according to 45 CFR 46 (Appendix B), 21 CFR 50 (Appendix C), and 21 CFR 56 (Appendix D), as applicable.



- The IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities;
- The 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 and the Institutional Official. The Institutional Official shall be responsible for all required institutional reports to sponsors and federal agencies.
- The IRB must report to the Institutional Official unanticipated problems involving risks to subjects and others or serious or continuing noncompliance by investigators. The Institutional Official shall be responsible for all required institutional reports to sponsors and federal agencies.
- The IRB decision to disapprove, suspend, or terminate a project may not be reversed by any officer or agency of TAMUT, state government or federal government. However, University officials may in certain cases, decide that a research study may not be conducted despite IRB approval.
- The IRB has the authority to observe or have third parties observe the consent process and the conduct of the research.
- Any attempt to unduly influence the IRB shall be reported to the IRB Chair, Dean of Graduate Studies and Research. These individuals will confer and determine the appropriate course(s) of action, which may include written communication, meeting with senior University leadership or referral to the Office of University Counsel.

### 3.3 Agreements to provide IRB review of research conducted by collaborating external investigators

Occasionally TAMUT may be asked to provide IRB review for investigators who are affiliated neither with TAMUT nor with another institution that has an IRB. Circumstances in which this arrangement might be considered would typically involve a study based at TAMUT in which the external investigator is collaborating. IRB oversight would not customarily be extended to research by external investigators in which TAMUT is not otherwise engaged; however, this arrangement may be considered in select circumstances.

All requests for TAMUT to serve as the IRB of record for an external investigator should be referred to the ORSP Compliance Coordinator. This referral should include an "Individual Investigator Agreement" based on the TAMUT approved template (See Appendix L). In most instances this agreement will apply to a single research project; less often, to a defined group of studies involving the external investigator. The Dean of ORSP, in consultation with the IRB, will determine whether the University will agree to extend IRB oversight to the external investigator. If the decision is that TAMUT will provide IRB oversight for the investigator, the Dean of ORSP has the authority to execute the agreement

documenting this arrangement. Copies of this documentation will be returned to the investigator, the responsible IRB, and ORSP files.

#### 3.4 Agreements for reliance on IRBs between collaborating institutions

On some occasions when two or more FWA institutions are engaged in the same research study, it may be appropriate for one institution to rely on the IRB of another for review and continuing oversight of that research. Circumstances in which this arrangement might be considered would typically involve studies primarily based at one institution, with somewhat peripheral involvement by investigators at the other. In effect, this constitutes a deferral of the right of review by the institution with lesser involvement, which retains responsibility for ensuring compliance with all IRB requirements.

An “IRB Authorization Agreement” is the form of agreement executed between the institutions to document this delegation of IRB oversight (See Appendix L). TAMUT may be either the institution deferring to another institution or the institution to which the IRB review is delegated. All requests for such delegations should be referred to the ORSP Compliance Coordinator. The Dean of the ORSP, in consultation with the IRB, will determine whether the University will agree to the deferral. If the decision is to agree to the IRB delegation, the Dean of ORSP has the authority to execute the agreement. Copies of this agreement will be filed with the IRB accepting responsibility for ongoing oversight, the IRB deferring, and the ORSP at TAMUT.

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SOP Title:	<b>IRB Membership</b>		
SOP Number:	4.0	Current Version Date:	9/30/14

#### 4.1 IRB membership requirements

The 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 not be comprised of members who are all males or all females or who all represent a single profession. The IRB shall have at least one member who represents the perspective of research subjects. The 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 (See Definitions for further information on “affiliation”). The unaffiliated member, the member representing the perspective of research subjects, and the non-scientific member may be the same person or they may be represented by two or three different persons.

Additionally, the IRB shall include at least one member who is not a scientist. 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.

The standards described above represent *minimum* requirements which the TAMUT IRB typically exceeds. In many instances, the IRB will have ten or more members with varied expertise and specialization in order to meet the research review requirements of the IRB. Appropriate size of the IRB will be determined by the board itself in consultation with the Dean of ORSP. Membership on each IRB is reviewed annually and as needed by the IRB Chair and the Dean of ORSP.

When a protocol involving a prisoner is reviewed, the IRB must include at least one member with appropriate background and experience to serve as an advocate for the prisoner population. Unless this individual is required for review of non-prisoner research, she/he may be noted on the roster to be counted for quorum only when s/he is conducting a review. A majority of the IRB members, exclusive of the prisoner representative, must have no association with the prison involved, apart from their membership on the IRB.

When the IRB reviews research involving children the IRB must include either a committee member or a consultant with expertise relevant to the participation of children in the study. In addition, IRBs that routinely review research including drugs, devices or medical interventions must include at least two physicians on their roster. Similarly, when the IRB reviews social/behavioral research, the IRB must include at least two social scientists on their roster.

IRB membership is recorded on a roster that is submitted to the federal Office for Human Research Protections (OHRP).

#### 4.2 Appointment of members

The Institutional Official appoints members to the IRB after consultation with the appropriate University administrators.

Prospective members will typically be identified by the IRB Chair and staff, who should review the nature and demands of IRB service with the candidate. If the candidate is willing to serve, they and/or the IRB Chair will review the proposed service with the relevant unit head (for TAMUT employees). For prospective members who are unaffiliated with TAMUT, recommendations may be solicited from a variety of sources and their memberships are vetted in a similar manner. If the unit supports said service, a recommendation should be submitted by the IRB Chair with any supporting information, CV, etc. These recommendations and materials will be forwarded to the Dean of ORSP, who will review with the IRB Chair and prepare the official letter of appointment to be signed by the Institutional Official.

No individual with competing business interests can serve as a member of the IRB or be involved in carrying out day-to-day operations of the review process. (see also SOP 4.12 and University COI policy)

IRB members are appointed for a three-year term which may be renewed, unless otherwise specified.

A valid CITI training certificate as IRB reviewer is required for the IRB committee members during their term.

The performance of IRB members is reviewed annually by the Dean of ORSP and the Chair of the IRB and results provided back to members at a minimum of every three years or more frequently if needed. Factors evaluated include attendance at convened meetings, adequacy of reviews, contribution to discussion, etc.

#### 4.3 Appointment of the chair

The President appoints the IRB Chair based upon the recommendation of the Dean of ORSP in consultation with the outgoing IRB Chair and the prospective Chair's unit head, dean or director, as appropriate. Though ultimate approval rests with the President, no appointment should be made without the agreement of the relevant unit head, dean or director.

Typically, but not necessarily, the IRB Chair is selected from among sitting members of the IRB. The Chair should ideally be an individual with credibility and standing in the institution to command respect among the research community and the IRB, and one who is committed to the protection of human subjects in research. IRB Chairs are appointed for three-year terms which may be renewed.

The performance of IRB Chairs is reviewed annually and feedback provided by the Dean of ORSP.

#### 4.4 Alternate members

Alternate members are appointed to the IRB according to the same procedures that apply to members. Additionally, alternate members are appointed to serve only for named members or roles of the IRB and therefore cannot serve as an "at large" alternate for absent members.

#### 4.5 Non-voting members

The Chair may, at his/her discretion, recruit non-voting members from among the academic or administrative staff of TAMUT, whose presence at the meetings of the IRB would aid the IRB in conducting its duties. Non-voting members are appointed to the IRB according to the same procedures that apply to voting members. These members may take part in all meetings of the IRB, participate in the discussions, and make recommendations, but they may not vote on the decisions. Non-voting members are not included in determining or establishing a quorum at the meetings.

IRB meeting minutes reflect the presence of non-voting members.

#### 4.6 Termination of appointment

Appointment to the IRB may be terminated before the expiration of the three-year term. The Institutional Official may remove an IRB member if the University Administration, determines that the member fails to perform his or her duties as a member.

When an IRB member leaves the TAMUT area, or is otherwise unable to serve, this would ordinarily result in a termination of the IRB appointment. The appointment may be retained if all parties agree that it should continue. It is appropriate to give sufficient advance notice so that a replacement can be found.

#### 4.7 Consultants

The TAMUT IRB may, at the discretion of the Chair or its members, invite individuals with competence in special areas and no conflict of interest with the study to assist in the review of issues that require expertise beyond or in addition to that available on the IRB.

Consultants are selected because they have expertise in specialized areas needed in the review of a protocol that is otherwise not available on the IRB committee. The IRB Chair and/or primary reviewer identifies the proposed consultant based on personal knowledge or based on other sources of input and contact the prospective consultant to request the needed assistance. Consultants may be drawn from faculty from TAMUT, or from outside the University.

Consultants are asked to disclose any relevant conflicts of interest. In the event of a conflict an alternate consultant will be selected. Once the consultant has agreed to assist and has signed a confidentiality agreement, the IRB staff will send the necessary materials for review.

Consultants may provide their comments in writing to the IRB or present their comments in person at the relevant meeting. Consultants will be excluded from discussion except to provide information requested by the IRB. These individuals will leave the meeting room for the discussion and may not vote with the IRB. Consultants are not included in determining or establishing a quorum at the meetings. Review by a consultant is noted in the committee minutes.

#### 4.8 Confidentiality agreement

Upon appointment to the IRB or attendance at an IRB meeting, members (voting or otherwise), consultants, guests, and/or staff will sign the confidentiality agreement. (See Appendix G). See SOP 11.4.7 for information regarding attendance by guests.

#### 4.9 Orientation and training of IRB members

Once a new member has been identified as a potential member to the IRB, he or she may wish to attend a meeting as an observer in order to learn about the workings of the IRB.

Orientation of new members should include an introductory session covering history, ethical principles in the Belmont Report and regulatory requirements for IRB review. This will be followed by an informational session on practical matters with the IRB staff and Chair. The new member will also receive a binder of reference materials, the IRB member handbook, and access to the journal *IRB: Ethics and Human Research* and other published guidance.

Typically, new members of the IRB attend several meetings before being assigned primary reviewer responsibility.

#### 4.10 Liability coverage for IRB members

IRB members function as employees or agents of TAMUT. As such their actions are covered by the TAMUT liability coverage.

IRB members who are unaffiliated with the University (sometimes referred to as “community members”) are also covered by this same liability coverage when performing within the course and scope of their IRB service.

#### 4.11 IRB Member conflict of interest

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.

An IRB member is considered to have a conflicting interest if the IRB member or anyone in the member's immediate family (see definitions):

1. Serves as an investigator or has any involvement in the design, conduct, or reporting of the research
2. Has any ownership interest, stock options, or other financial interest related to the research (see definitions). However, for the purposes of IRB review, members may participate if the interest in question meets three tests:
  - <\$5,000 when aggregated for immediate family
  - Publicly traded on a stock exchange
  - Value will not be affected by the outcome of the research
3. Receives any compensation related to the research. However, for the purposes of IRB review, members may participate if the compensation in question meets two tests:
  - <\$5,000 in the past year when aggregated for immediate family
  - Amount will not be affected by the outcome of the research
4. Has a proprietary interest related to the research including, but not limited to, a patent, trademark, copyright, or licensing agreement
5. Has any board or executive relationship related to the research, regardless of compensation
6. Or any other reason for which an IRB member believes that he/she cannot objectively review the research

IRB members are reminded of these policies at the beginning of each meeting, and instructed to recuse themselves at the time of discussion of any protocol with which they have a conflict of interest, as described above. The recusal is noted on the minutes; this documentation may indicate that the “member was recused for conflict of interest,” without specifying any additional reasons, details or dollar amounts.

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SOP Title:	<b>IRB Administrative Support</b>		
SOP Number:	5.0	Current Version Date:	9/30/14

The IRB staff support the function of the IRB at the direction and under the supervision of the Dean of ORSP who reports to the Vice President of Academic and Student Services. The Dean of ORSP is responsible for directing and overseeing all IRB support functions and operations; training, supervising and evaluating IRB staff; and developing and implementing procedures to effect efficient document flow and maintenance of all IRB records.

#### 5.1 Education and training of ORSP staff

Staff members will initially receive the same orientation as IRB members with an introductory session and orientation to IRB and office procedures. Further training is provided by working in close interaction with fellow staff members.

Staff members should be provided with continuing education opportunities, and resources should be made available for them to attend regional or national human research protection meetings, as deemed appropriate by the Dean of ORSP.

ORSP staff members should have a variety of informative resources available to them. These might include the journal *IRB: Ethics and Human Research*, the textbook *Institutional Review Board: Management and Function*, and similar references.

#### 5.2 Quality improvement

The internal audit program for in-line monitoring of processes, practices and outcomes to improve quality and ensure completeness, consistency, accuracy and timeliness of communication and documentation across the IRB processes and functions will be implemented by the Dean of ORSP utilizing periodic compliance review, directed audits and quality assurance reviews.

These audits and reviews will include evaluation of a sampling of memos, agendas, minutes and approval documents to ensure that appropriate findings are made and correctly recorded for all research studies. Over time this sampling should have the desired effect of standardizing practices across all IRB processes and functions.

Concerns for directed audits may include performance of review of memos, agendas, minutes and approval documents to ensure that appropriate findings are made and correctly recorded for all research studies, the IRB Committee, an external source (e.g., investigator, study coordinator, or sponsor), or an internal source (e.g., administration, IRB Chair, or ORSP staff).

#### 5.3 Evaluation of resources

At least annually, but more often when warranted, the resources available to and needed for the Human Research Protection Program are evaluated. These resources include, but are not limited to: space, personnel, continuing education, legal counsel, conflict of interest, Quality Improvement, and community outreach. Metrics are tracked on a routine basis to assess workload for staff and IRB committees, and adjustments made where warranted. For example, the entire workload volume is assessed at the end of each calendar year, for analysis of trends in number and type of submissions, turnaround time, and workload per staff. Similar data are used to assess trends in workload of the IRB committee and length of convened meetings.

Adjustments in staffing and committees are made when these metrics reflect substantial increases (or decreases) in workload. Physical space for staff and convened meetings are monitored continuously; changes are made to enhance the efficiency of the unit's work efforts. The educational needs of staff and IRB members are identified through informal and formal feedback and are addressed both in regular meetings of ORSP as well as through staff attendance at regional and national meetings. These assessments and metrics are initially gathered through the ORSP, and then shared with relevant parties.

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SOP Title:	<b>IRB Record Requirements</b>		
SOP Number:	6.0	Current Version Date:	9/30/14

## 6.1 IRB documentation

The IRB shall prepare and maintain adequate documentation of the IRB activities listed below in digital format.

- 6.1.1 Copies of all IRB application materials that have been reviewed by the IRB including the initial application, funding proposals, master protocols, consent documents (including DHHS-approved sample consent documents and protocols, when they exist), and data collection and subject recruitment materials, as relevant. Also to be included are scientific evaluations, if any, of the application, approved consent documents, progress reports submitted by investigators, reports of injuries to subjects, and statements of significant new findings provided to human subjects. In order to allow a reconstruction of a complete history of IRB actions related to the review and approval of the protocol, IRB records shall include copies of the Investigator brochure (if any) and data and safety monitoring reports (if any).
- For studies reviewed by the expedited procedure, IRB records shall contain the justification for using expedited review and actions taken by the reviewer.
  - For studies determined to be exempt, IRB records shall contain the justification for the exempt determination.
- 6.1.2 Records of continuing review activities including any activity occurring after initial approval. These may include the frequency for the next continuing review, modifications, renewals, and reports of unanticipated problems or adverse events.
- 6.1.3 Copies of all correspondence, including substantive email, between the IRB and the investigators.
- 6.1.4 A roster of IRB members that includes, but is not limited to the following: name; earned degrees; representative capacities; scientific/nonscientific status; affiliation status (whether the member or an immediate family member of the member was affiliated with the organization); indications of experience (such as board certifications and licenses) sufficient to describe each member's chief anticipated contributions to IRB deliberations; employment or other relationship between each member and the University. The IRB roster includes voting members, both regular and alternate, as well as the member or class of members for whom each alternate member can substitute.
- 6.1.5 Copies of the minutes of all convened IRB meetings (see SOP 7.0 Meeting minutes)
- 6.1.6 Written procedures (represented by this SOP document) that 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. Regulatory and other findings will be communicated to the investigator in the approval letter and to the IRB in the meeting minutes.

- 6.1.7 Written procedures (represented by this SOP document) 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; (ii) any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (iii) any suspension or termination of IRB approval.

## 6.2 IRB record retention requirements

The study-specific records detailed in SOP 6.1.1-6.1.3 above relating to research that is conducted shall be retained for at least 3 years after completion of the research. If a protocol is closed without enrolling participants, IRB records are maintained at least three years after study closure.

Records detailed in SOP 6.1.4-6.1.7 above shall be retained for at least three years following their last effective date, but may be retained indefinitely. Specific details for electronic file dispositions are found at the above referenced policy. Upon expiration of their retention period, IRB records must be destroyed in accord with University policies and procedures for destruction of confidential records.

For studies that the IRB has exempted from continuing review, study-specific records shall be retained for at least three years after the exemption is granted. Every three years following the grant of the exemption the IRB will inquire about the current status of the project from the PI until the investigator reports that the study is complete (see also SOP 15.0).

Authorized persons shall be able to access records for inspection and copying at reasonable times and in a reasonable manner. Investigators may be required to follow different record retention policies depending on research sponsorship.

## 6.3 Public Records request

Some of this documentation may be subject to public access under the Texas Public Records Act. The Office of Communications should be consulted when a public records request is received.

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SOP Title:	<b>Meeting Minutes</b>		
SOP Number:	7.0	Current Version Date:	9/30/14

IRB Meeting Minutes should be in sufficient detail to show the following:

- 7.1 Attendance at the meetings
  - date and time meeting starts and ends
  - names of members present
  - names of members absent
  - names of alternates attending in lieu of specified absent members
  - names of consultants present
  - names of investigators present
  - names of guests present
- 7.2 Documentation of actions taken outside of convened meetings
 

Documentation that exemptions granted and expedited reviews conducted outside the convened meeting were reported to IRB members. The information provided to members should include, at a minimum, the title, PI of each study and a brief summary of expedited actions. This information may be filed as an attachment to the agenda
- 7.3 Actions taken by the IRB
  - 7.3.1 Actions taken by the IRB at a convened meeting as well as the vote on these actions including the number of members voting for, against, and abstaining, and (if applicable) notation that any members with a conflict of interest (identified by name) were recused and were absent for the discussion and vote;
  - 7.3.2 The approval period for projects approved by the IRB. In specifying an approval period of less than one year, the IRB may define the period either with a time interval or a research milestone. The minutes should clearly reflect any determination requiring a review more frequently than annually. The IRB minutes may state that all approval periods are one year unless otherwise noted.
  - 7.3.3 The basis for requiring changes in or disapproving research; (see SOP 7.4 below)
  - 7.3.4 For each application in which changes are stipulated by the IRB, a determination of whether the changes represent minor modifications that do not require verification by the convened IRB, or whether they are significant, requiring convened IRB review; and,
  - 7.3.5 A written summary of the discussion of controverted issues and their resolution.
- 7.4 IRB findings and determinations
 

The following are required findings and determinations, and must be noted in the minutes with reference to the appropriate federal regulations. Justification for these findings may be found in the IRB application or related correspondence with the investigator.

- 7.4.1 Determination of the level of risk for human subjects in the research study. Determination of level of risk can be documented in the minutes by a single entry if it is stated that all studies were determined to have a certain level of risk unless otherwise specifically noted.
- 7.4.2 Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document.
- 7.4.3 Justification for waiver or alteration of informed consent; [45 CFR 46.116(c) and (d)]
- 7.4.4 Justification for the waiver of the requirement for written documentation of consent; [45 CFR 46.117]
- 7.4.5 Justification for approval of research involving pregnant women, human fetuses and neonates; [45 CFR 46.204-205]
- 7.4.6 Justification for approval of research involving prisoners; [45 CFR 46.306]
- 7.4.7 Justification for approval of research involving children; [45 CFR 46.404-407]
- 7.4.8 Justification for approval of research planned for an emergency setting [21 CFR 50.24]; and
- 7.4.9 Special protections warranted in specific research projects for groups of subjects who 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.
- 7.4.10 Rationale for significant risk/non-significant risk determination for studies involving investigational devices. [21 CFR 312]

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SOP Title:	<b>Determination if an Activity Constitutes Human Research Subject to TAMUT IRB Review</b>		
SOP Number:	8.0	Current Version Date:	9/30/14

The IRB has been charged with the responsibility for reviewing and monitoring human subjects research conducted under the aegis of TAMUT. Therefore, the first question with respect to IRB review of a project is a determination of whether the project fits this definition. In light of the mission to protect human subjects, the IRB should err on the side of review when the determination is not clear. An application to gather the information necessary to support this determination is provided by the IRB. This determination involves a multi-step process, including an assessment of whether an activity constitutes research, and then if human subjects are involved. The results of this determination will be communicated in writing to the investigator. The definitions of “research” and “human subjects” for this purpose are derived from federal research regulations. The criteria for “under the aegis of TAMUT” have been determined by the campus and may extend beyond what is required by federal regulations.

#### 8.1 Is it research?

DHHS regulations define *research* as “a systematic investigation, including development, testing, and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR 46.102(d)). FDA regulations define clinical investigation as “any experiment that involves a test article and one or more human subjects” as described in 21 CFR 50.3 (see Definitions for further details). Activities that meet either definition constitute research for the purposes of TAMUT policy.

As described in the Belmont Report, “...the term ‘research’ designates an activity designed to test a hypothesis [and] permit conclusions to be drawn...” Research is usually described in a formal protocol that sets forth an objective and a set of procedures to reach that objective.”

Thus, a key aspect of research is that there be a systematic design in advance, generally utilizing a scientific approach or protocol, for the defined purpose of contributing to generalizable knowledge. “Generalizable knowledge” means that (1) conclusions are drawn from particular instances, and (2) the information from the investigation is to be disseminated. “Systematic investigation” means the implementation of rule-based methods, specified in the investigation plan, that are repeated with multiple participants in a consistent manner across the participants. Alternatively, the method may be implemented according to specified rules with a single participant for certain types of investigations.

Research can encompass a wide variety of activities, including: experiments, observational studies, surveys, tests, and recordings. Studies assigned an Investigational New Drug (IND) number or an Investigational Device Exemption (IDE) by the FDA are by definition research that requires IRB review. (21 CFR 56.103)

“Research” generally does not include such operational activities as: defined practice activities in public health, medicine, psychology, and social work (e.g., routine outbreak investigations and disease monitoring in public health); studies for internal management purposes such as program evaluation, quality assurance, quality improvement, fiscal or program audits, or marketing studies. It generally does not include journalism or political polls. However, some of these activities may include or

constitute research in circumstances where there is clear advance intent to contribute to generalizable knowledge with a scientific protocol. Intent to publish is one possible indication of intent to contribute to generalizable knowledge.

## 8.2 Does it involve human subjects?

A human subject is defined by Federal Regulations as “a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.” (45 CFR 46.102(f)). The FDA defines a human subject as “an individual on whom or on whose specimen a device is used” (21 CFR 812.3) or “an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may either be a healthy human or patient.” (21 CFR 50.3 (g))

“Identifiable private information” includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation is taking place,” (such as a public restroom) “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 health care record).” (45 CFR 46.102(f)). Although there is no definition of “identifiable” information in the Common Rule, HIPAA provides a list of 18 identifiers, the removal of which renders a data set de-identified for the purpose of determining if a human subject is involved. (See Appendix M)

Intervention includes physical procedures, manipulations of the subject or subject's environment for research purposes. Interaction includes communication between the investigator and the subject. This includes face- to-face, mail and phone interaction as well as any other mode of communication.

Private information includes observation of behavior when an individual can reasonably expect that no observation is taking place, or information for specific purposes (such as a health care record) that individuals can reasonably expect will not be made public. Thus, approaches involving only existing records or human specimens or observations may still constitute human subjects research requiring IRB approval. The IRB will make this determination. Simple observational studies of public behavior (including television and internet chat rooms) do not involve human subjects as defined, because there is no intervention or interaction and the behavior is not private. Also, studies based on data collected for non-research purposes may not constitute human subjects research if individual identity is not identifiable. Examples include programmatic data such as service statistics, school attendance data, crime statistics, or election returns. Studies based on data that are individually identifiable data but also are publicly available may not constitute human subjects research [45 CFR 46.101(b)(4)]; however, the term “publicly available” is intended to refer to record sets that are readily available to the broad public, such as death certificates.

## 8.3 Is it conducted under the aegis of TAMUT?

In the interest of protecting human subjects participating in research that is either under University aegis or would appear to be under University control, human subjects research that meets any of the following criteria will be subject to TAMUT IRB review and monitoring:

- The research is sponsored by TAMUT
- The research is conducted or directed by any employee or trainee of the University in connection with his or her TAMUT responsibilities
- The research involves access to any property or facility of TAMUT other than access to open spaces on the University campus that are readily available to the public at large

- The research involves the use of non-public information in the custody of TAMUT to identify or contact human research subjects or prospective subjects

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SOP Title:	<b>Applications for IRB Review</b>		
SOP Number:	9.0	Current Version Date:	9/30/14

### 9.1 New studies

All applications submitted for IRB review are screened for complete documentation before reviewed. ORSP provides application forms for new studies through its website. A complete submission for IRB review includes, when applicable:

- 1) TAMUT IRB Initial Application Form including reports of prior investigations that provide relevant information to this review
- 2) written protocol (e.g., master protocol)
- 3) consent and assent document(s), including any DHHS-approved sample consent documents
- 4) fact or information sheets
- 5) recruitment materials
- 6) questionnaires, focus group guides, scripts or other means to collect data
- 7) other materials specific to the proposed study (e.g., grant application, investigator's brochure, sponsor correspondence with a regulatory agency)
- 8) HIPAA Authorization addendum to the consent document
- 9) documentation of review from PI's program (e.g., Psychology) and Dean of PI's College
- 10) addendum for multi-site studies where TAMUT is the lead coordinating center
- 11) data use agreements

The IRBs retain the discretion to accept materials prepared for review in another IRB's format.

### 9.2 Amendments or modifications

Amendments or modifications are changes to a previously approved study. Amendments or modifications are reviewed in the same way a new study is reviewed, which may be by the convened IRB or by expedited review, depending on how the changes affect the protocol. For more information on amendments or modifications see SOP 16.0.

### 9.3 Continuing review for renewal

All non-exempt research involving human subjects requires continuing IRB review at intervals appropriate to the degree of risk, but at least once per year. For information on continuing review see SOP 17.0.

### 9.4 Process at ORSP

The ORSP in consultation with the IRB Chair will conduct an initial screening of all applications for completeness (according to the criteria listed in 9.1 above) and make a preliminary determination of the type of review to be conducted. If the application is incomplete or otherwise not fully prepared for review it may be returned to the investigator or a request made for necessary changes or to provide additional information. ORSP may contact the investigator by phone or letter requesting clarification of protocol issues or



revisions in consent document(s) prior to referral to the IRB. All applications are assigned a study number in the IRB database; this number remains with the study in the IRB records. As soon as the initial entry of study information has been completed, the investigator receives an email noting the study number and that the IRB review of the submitted materials has commenced.

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SOP Title:	<b>Determination of Type of Review</b>		
SOP Number:	10.0	Current Version Date:	9/30/14

### 10.1 Levels of IRB review

The three levels of review described below correspond to the level of potential risk of harm to human subjects within the proposed research study.

#### 10.1.1 Convened IRB review

For a detailed description of this level of review, see SOP 11.0 Review by Convened IRB, and SOP 12.0, Actions Following Review.

#### 10.1.2 Expedited IRB review

For a detailed description of this level of review, see SOP 13.1 Expedited Review, and SOP 14.0 Actions Following Expedited Review.

#### 10.1.3 Exempt from continuing IRB review

For a detailed description of this level of review, see SOP 15.0 Exemption from Continuing IRB Review

### 10.2 Determination of review type

In order to determine the type of review necessary, the IRB Chair will screen the application and make determinations as to whether the project constitutes human subjects research and, if so, the type of review required. All applications are assigned to be reviewed at a convened meeting unless (1) they meet the criteria for expedited review listed in SOP 13.0, (2) they meet the criteria for exemption listed in SOP 15.0, or (3) they are deemed not to be human subjects research.

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SOP Title:	<b>Review by Convened IRB</b>		
SOP Number:	11.0	Current Version Date:	9/30/14

### 11.1 Projects requiring review by convened IRB

Any study involving greater than minimal risk requires review by the convened IRB. Examples of studies that *may* involve greater than minimal risk:

- Studies involving vulnerable populations. Clinical intervention studies that randomly assign human subjects to alternative experimental or placebo groups
- Studies involving sensitive information connected to personal identifiers

### 11.2 Scheduling of meetings

The IRB sets its own meeting schedule, but generally each meets once a month on a regularly scheduled day with meeting frequency determined by workload.

Scheduled meetings may be cancelled by the Chair due to a) insufficient number of applications requiring review at a convened meeting, b) inability to secure a quorum for attendance, or c) other reasons as may arise that make a scheduled meeting unnecessary or otherwise inappropriate.

The IRB should have a mechanism in place to notify members of meetings.

### 11.3 Assignment of reviewers

The TAMUT IRB uses a primary reviewer system in which one or more members are assigned to lead the review and present the protocol for discussion at the convened meeting. Primary reviewers will be assigned in advance of the meeting by the IRB Chair or staff. The IRB Chair or staff will evaluate each protocol and assign a primary reviewer with appropriate scientific expertise to conduct an in-depth review of the protocol.

When the IRB reviews research that involves participants likely to be vulnerable to coercion or undue influence, the IRB Chair will evaluate each application and ensure that at least one IRB member knowledgeable about or experienced in working with such participants would be present at the meeting.

When there is not appropriate scientific/scholarly or representational expertise available on a specific committee, the application will be assigned to another meeting.

### 11.4 Materials

#### 11.4.1 Primary reviewers

Primary reviewers must receive the full packet of materials described in SOP 9.0 at least one week prior to a convened meeting. Their review should take into consideration all of the factors described in SOP 24.0.

Additionally, primary reviewers should receive a checklist that will help guide the review and presentation of protocols at the meeting (See Appendix Q).

#### 11.4.2 Other reviewers

At least one week prior to a convened meeting, all IRB members should be provided with detailed materials describing the research so that each member will be able to discuss the protocol at the meeting. At a minimum, the IRB members other than the primary reviewer(s) must receive a copy of the consent documents and the IRB application summarizing the protocol in sufficient detail to support the review. In addition, the complete documentation should be available to all members for their review, both before and at the meeting. If the IRB prefers, all materials may be distributed to each member.

#### 11.4.3 Agenda

All members should receive an agenda for the meeting that includes a list of protocols under review as well as the title, PI and a brief summary of the studies that have been expedited since the last convened IRB meeting.

#### 11.4.4 Minutes of previous meeting

All members should receive a copy of the minutes from the previous meeting of the IRB.

### 11.5 Conduct of the meeting

#### 11.5.1 Role of the Chair

The Chair leads the meeting of the convened IRB. This includes calling the meeting to order, leading the IRB through the agenda, and calling for motions and votes. The Chair should ensure that all members have an opportunity to express their opinions and concerns on the research under review. For the purpose of establishing a quorum for a meeting the Chair is counted as any other regular member.

#### 11.5.2 Role of primary reviewers

The primary reviewers for a given research protocol should make an evaluation of the protocol before the convened IRB meets and should present the protocol during the meeting. This presentation should include an overview of the project and the identification of major issues arising in the project.

#### 11.5.3 Voting

In order for research to be approved, it shall receive the approval of a majority of the members present at the meeting. The voting process proceeds as follows: The Chair may entertain a motion (which usually comes from a primary reviewer) and a second that the IRB take a certain action regarding a given protocol. The actions the IRB may take are as follows: approval, approval with stipulated changes, deferral, or disapproval. For a thorough discussion of these options, see SOP 12.0, Actions Following Review by the Convened IRB. After a motion has been made and seconded, there should be an opportunity for discussion before a vote is taken. Those members physically present for the vote should be recorded as either voting for, against, or abstaining. Members who are recused from the vote (e.g. due to conflict of interest) should physically leave the room, are not counted in the aforementioned tally, and should be identified by name in the minutes

A quorum is defined as a majority (more than half) of the voting members including at least one member whose primary concerns are in

nonscientific areas. It is expected that convened meetings will also include the presence of at least one unaffiliated member and at least one member who represents the general perspective of subjects. In many cases these three roles will be satisfied by the same member; when not, the general attendance of the unaffiliated member and the member who represents the perspective of subjects will be assessed through documentation in the minutes (the expectation is attendance at a minimum of 10 of 12 meetings per year).

Protocol approval requires the approval of a majority of the members present. The meeting may not start absent a quorum, and if the quorum is lost during the meeting for any reason, no votes may be taken. If required members (e.g. non-scientific) leave the room and quorum is lost, votes cannot be taken until the quorum is restored, even if half of the members are still present. It is the responsibility of the IRB staff and chair at that meeting to determine the presence of a quorum, including any special representation required for particular reviews.

The IRB may include alternates for specific board members. This enables IRB members to share the workload associated with membership. However, if a member and his or her alternate are both present at the same meeting, only one may vote on each protocol. In addition, only one member will count toward the quorum needed for full committee actions.

Given the importance of having a quorum for an IRB to conduct business, it is vital that a member inform the IRB staff as far in advance as possible if he or she will be unable to attend a particular meeting. While not required by the regulations, it is expected that the unaffiliated member(s) and the member(s) representing the perspective of participants will attend the majority of convened meetings.

#### 11.5.4 Open meetings

The meetings of the TAMUT IRB is not subject to Texas "Open Meeting" laws because the TAMUT IRB does not constitute a "public body" within the meaning of the Open Meeting laws and pursuant to the relevant guidelines issued by the TAMUT Office of the President.

#### 11.5.5 Recusal of members with a conflict of interest

When an IRB member has a conflict of interest (see SOP 4.12 Member conflict of interest) that requires him/her to recuse himself/herself from discussion of and voting on a particular protocol, that member should leave the meeting room for the duration of the discussion and vote, except as requested to address questions raised by other members. If the member's recusal causes a loss of quorum, the vote should be postponed to another meeting. For this reason, IRB members should notify the chair prior to the meeting if they have a conflict of interest related to a specific protocol slated for review at the meeting, and every effort should be made to ensure adequate members in attendance.

#### 11.5.6 Attendance by investigators

Investigators may be invited and encouraged to attend the portion of the IRB meeting at which their protocol is discussed. The investigator may answer questions raised by the IRB. The investigator should not be present for the final deliberation and vote on his or her protocol.

#### 11.5.7 Attendance by guests

The IRB may permit guests to attend a meeting, for example, in order for them to learn about the IRB process. Members should be alerted to the presence of guests and their reason for attending. Guests should sign the confidentiality agreement prior to the start of their attendance at the meeting.

#### 11.6 Teleconferencing/videoconferencing

In some cases, teleconferencing and/or videoconferencing may be necessary in order to have a quorum for a meeting, or to ensure that a protocol is reviewed by someone with a proper level of expertise. When the IRB makes use of this technology, all other normal meeting requirements apply. Additionally, whenever teleconferencing and/or videoconferencing is used, special care must be taken to ensure the security of the data transmissions so that the privacy of researchers and IRB members is protected.

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SOP Title:	<b>IRB Actions Following Review by the Convened IRB</b>		
SOP Number:	12.0	Current Version Date:	9/30/14

### 12.1 Approval of research

In the case of an approval with no changes, the research may proceed once the PI receives written documentation of IRB approval. Unless otherwise specified, the approval period for research approved without changes is one year from the date of the meeting at which approval was granted (see SOP 17.1).

### 12.2 Stipulated minor changes or clarifications required prior to approval

The IRB may determine that a study may be approved with stipulated minor changes or clarifications. Minor changes are those changes that do not involve potential for increased risk or decreased benefit to the human subjects. Some examples of minor changes are: changes in contact information or identity of non-key research personnel, changes in the study title, and changes in the consent form that reflect the minor changes listed earlier.

For minor changes, the IRB Chair or a voting IRB member(s) designated by the Chair must ensure that the PI makes the appropriate changes to the research protocol. Such changes must be clearly delineated at the convened meeting so that subsequent review requires simple verification of concurrence. The research may proceed after the required changes are verified and the designated reviewer approves the protocol.

The Chair, the primary reviewers, or a subcommittee may be assigned responsibility for reviewing the changes to ensure that the stipulated changes are appropriately addressed. The application receives final approval when all required changes have been submitted and approved.

Unless otherwise specified, the approval period for research for which minor changes were stipulated is one year from the date of the last convened meeting at which the protocol was reviewed.

### 12.3 Deferral

The term “deferral” is used to describe the situation in which an IRB determines that substantive changes must be made before approval may be granted. The PI’s response, including any amended materials, must be reviewed by the convened IRB.

Subject to IRB discretion, a proposal may be withdrawn if the PI does not respond to a deferral within a reasonable amount of time. If the investigator wishes to conduct a study that has been withdrawn, he/she must submit a new application, incorporating comments from the prior IRB review.

Unless otherwise specified, the approval period for research protocols that are deferred is one year from the date of the last convened meeting at which approval was granted or minor changes were stipulated.

### 12.4 Disapproval

If the IRB determines that the research cannot be conducted at TAMUT or by employees or agents of the University or otherwise under the auspices of the University, the project, as proposed, is disapproved and may not go forward.

Disapproval usually indicates that a proposal requires major changes not likely to be feasible without a complete reassessment of the protocol by the investigator and/or sponsor.

#### 12.5 Suspension or termination of research study by IRB

Suspension refers to the IRB's temporary withdrawal of approval for some or all research activities. Suspended research remains under continuing review.

Termination refers to permanent withdrawal of approval of all research activities. Terminated research no longer undergoes continuing review.

The Chair of the IRB may suspend a study at any time if it is determined that the study requires further review or evaluation by the convened IRB. This determination may be made due to an adverse event, noncompliance or other danger to human subjects. The study may be suspended in whole or in part (e.g., enrollment of new subjects only), as appropriate to the circumstances. Once a study has been suspended, the convened IRB should review the study and either requires changes to the protocol, allow the study to restart, or terminate the study.

Though the Chair may temporarily suspend a study, only the convened IRB can make that suspension permanent.

When a study is suspended or terminated for cause, the IRB must notify the Dean of ORSP. The Dean of ORSP is responsible for all required reports to federal agencies. (See SOP 36.0)

When a suspension or termination involves the withdrawal of current subjects from a research protocol, the IRB should consider alternatives that protect subjects currently enrolled to ensure that harm is not incurred from such withdrawal. Such considerations may include possible transfer of subjects to another investigator, arrangement of clinical care outside the research, continuation of some research activities under the supervision of an independent monitor, permitting follow-up of subjects for safety reasons, or notifying current participants of the suspension or termination if it is determined that such information might relate to their willingness to continue to take part in the research.

Investigators should also be reminded to continue reporting any adverse events or outcomes to the IRB and the sponsor, as required, while the study is suspended or terminated.

#### 12.6 Notification of IRB actions

The IRB sends written notification of actions taken to the PI. There is no regulatory requirement that IRB approval documents be signed, and TAMUT policy does not require signatures on such documents. Approval documents are generated electronically by a password-protected IRB information system, with access limited to authorized IRB personnel. Internal tracking and audit procedures are used to verify that only those authorized personnel generate approval documents.

Summaries of actions taken will be provided to the Dean of ORSP and the Vice president of Academic and Student Affairs in the form of meeting minutes. If revisions to new and continuing human subjects applications are required, correspondence is sent to the investigator detailing requests for revisions, clarification, or additional information as well as information regarding continuing review.

Notification of approvals, terminations and suspensions will be provided to individual offices when appropriate.

#### 12.7 Appeal of IRB decisions

Investigators may appeal IRB requirements for specific changes in the protocol and/or consent document(s) in writing. At the IRB's discretion, the PI may be invited to the



IRB meeting at which his or her appeal will be considered.

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 and/or in writing. An appeal of a disapproved research project must be reviewed at a convened meeting.

Other University officials may, in certain cases, decide that a research study may not be conducted despite IRB approval. One example could be a circumstance in which a certain project or area of research is deemed to be inappropriate or under-funded. In the case of a decision by the IRB to disapprove, suspend, or terminate a project, only the Dean of ORSP may request that the IRB reevaluate a project because of procedural questions related to the IRB review. However, the IRB decision to disapprove, suspend, or terminate a project may not be reversed by any officer or agency of TAMUT, State government or federal government.

In the event that an investigator has concerns about the human research protection program beyond a specific IRB review result, she/he may contact the Dean of ORSP.

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SOP Title:	<b>Expedited Review of Research</b>		
SOP Number:	13.0	Current Version Date:	9/30/14

### 13.1 Expedited review

An IRB may use an expedited review procedure to review some or all of the research appearing in a list of categories published in the Federal Register (see also below) and found by the reviewer(s) to involve no more than minimal risk or minor changes in previously approved research during the period (of one year or less) for which approval is authorized. Expedited review will be conducted with the same depth and rigor as convened meeting reviews; the only difference is the number of reviewers.

Under an expedited review procedure, the review may be carried out by the IRB Chair or by one or more experienced reviewers designated by the Chair from among members of the IRB. An experienced reviewer is a member who, in the opinion of the Chair, has both the training and experience to review the research in question. Generally, the relevant IRB Chair will conduct the expedited review, with other members designated as reviewers on a protocol-by-protocol basis. As with convened meeting reviews, IRB members and ad hoc consultants with a conflict of interest should be recused from conducting expedited reviews. The IRB should keep members advised of research proposals that have been approved by expedited review by providing members with the title of the study, the PI and a brief summary of each expedited protocol. The minutes will include documentation that this information was provided.

For initial or continuing review, the reviewer will determine and document the following:

- The research presents no more than minimal risk to subjects.
- The identification of the subjects or their responses will not reasonably place them at risk of criminal or civil liability or be damaging to their 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.
- The research is not classified.
- The category or categories of research allowing review using the expedited procedure.

For each expedited study review, the IRB files must contain documentation showing the review and action taken by the IRB Chair or designated reviewer and any findings required under 45 CFR 46 or 21 CFR 50 or 56. The expedited review checklist used by reviewer(s) should be included in the IRB file.

### 13.2 Types of research eligible for expedited review

A protocol must meet one of the following categories to qualify for an expedited review. However, research matching one of these categories is not guaranteed to be reviewed via expedited review, e.g., in situations where the reviewer cannot approve the research as it is proposed, with or without modification, or where the investigator will not agree with requested modification.

- Category 1 Research on drugs for which an investigational new drug application IND (21 CFR 312) is not required or research on medical devices for which a) an investigational device exemption IDE application (21 CFR 812) is not required or b) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
- Category 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, amounts drawn may not exceed 550 ml in an 8-week period and no more than 2 times per week; or (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml/kg in a 8-week period and collection may not occur more frequently than 2 times per week.
- Category 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 the 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 unstimulate 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.
- Category 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, the tomography, 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.
-

- Category 5 Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research 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.)
- Category 6 Collection of data from voice, video, digital, or image recordings made for research purposes.
- Category 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.)
- Category 8 Continuing review of research previously approved by the convened IRB (a) where the research is permanently closed to the enrollment of new subjects, and all subjects have completed all research-related interventions, and 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 and report writing.
- Category 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.
- 13.3 Materials available to expedited reviewer
- Expedited reviewers will have access to all application materials including, as relevant, completed application including conflict of interest information, master protocol, consent documents, data collection instruments and recruitment materials.
- 13.4 Identification of expedited reviewers
- IRB records will include completed reviewer checklists which identify the expedited reviewers.

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SOP Title:	<b>IRB Actions Following Expedited Review</b>		
SOP Number:	14.0	Current Version Date:	9/30/14

#### 14.1 Approval of research

In the case of an approval with no changes, the research may proceed once the PI receives written documentation of IRB approval.

Unless otherwise specified, the approval period for research approved without changes is one year from the date of the approval letter sent by the IRB.

#### 14.2 Stipulated changes required prior to approval

The Chair or designated reviewer may determine that the research may be approved after minor changes or clarifications are made. Questions and issues should be communicated to the investigator in writing. The written response from the investigator should be reviewed by the IRB Chair or voting IRB member(s) designated by the Chair, to ensure that the investigator has made the appropriate changes. The application receives final approval when all required changes have been submitted and approved.

If expedited review raises questions of a substantive nature, the protocol may be referred for review by the convened IRB.

Unless otherwise specified, the approval period for research approved after minor stipulations is one year from the date of the approval letter sent by the IRB.

#### 14.3 Suspension or termination of research study by IRB

The Chair of the IRB or the convened IRB may suspend a study at any time if it is determined that the study requires further review or evaluation. This determination may be made due to an adverse event, noncompliance or other danger to human subjects. If the PI wishes to continue the study, continued the convened IRB should review the study and either require changes to the protocol, allow the study to restart, or terminate the study.

Though the Chair may suspend a study, only the convened IRB can make the decision to terminate a study. See SOP 12.0, IRB Actions Following Review by the Convened IRB.

#### 14.4 Limitation on disapproval following expedited review

In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. Minor changes to previously approved research may, however, be disapproved through expedited review. A research activity may be disapproved only after review 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.

#### 14.5 Notification of IRB actions

The IRB sends written notification of actions taken to the PI. There is no regulatory requirement that IRB approval documents be signed, and TAMUT policy does not require signatures on such documents. Approval documents are generated electronically by a password-protected IRB information system, with access limited to

authorized IRB personnel. Internal tracking and audit procedures are used to verify that only those authorized personnel generate approval documents.

Summaries of actions taken will be provided to the Dean of ORSP and the Vice President of Academic and Student Services in the form of meeting minutes. If revisions to new and continuing human subjects applications are required, correspondence is sent to the investigator detailing requests for revisions, clarification, or additional information as well as information regarding continuing review.

Notification of approvals, terminations and suspensions will be provided to individual offices when appropriate.

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SOP Title:	<b>Exemption from Continuing IRB Review</b>		
SOP Number:	15.0	Current Version Date:	8/01/19

### 15.1 Exemption

The ORSP may determine that a human subjects research project is exempt from IRB review, if regulatory criteria for exemption are met. Applications for exemption should be submitted to ORSP, and will undergo confirmatory review similar to that for determinations that a given activity is Not Human Subjects Research (NHSR). Studies that are determined to be exempt can still raise ethical concerns, and these should be considered. These potential areas of concern include methods of recruitment, communication with subjects, consent to participate in the exempt research, and use of the data. The ORSP is not required to exempt studies that appear to meet exemption criteria if they raise serious ethical concerns.

An investigator may not initiate research involving human subjects that the investigator believes is exempt until the investigator has received formal written concurrence of this exempt determination from the IRB. Changes to exempted studies that might change the exempt status must be reviewed by the IRB.

In some instances, changes to an exempted study may render it no longer exempt. Decision charts published by OHRP may assist the IRB in determining level of IRB review needed: <http://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html>

Per OHRP guidelines, institutions retain the option under their FWAs not to claim the exemptions provided in the regulations, choosing instead to require IRB review of all research involving human intervention/interaction or identifiable private information.

If information comes to the attention of the IRB suggesting that there are factors increasing the sensitivity and/or potential risk to human subjects in research that otherwise would appear to qualify for exemption under the criteria listed below, the IRB may, in its own sole judgment, deem the protocol to be subject to expedited or convened IRB review.

15.2 Records of exemption actions will be maintained in accordance with SOP 6.2.

15.3 Categories for exemption from continuing review

Research activities involving other human subjects may be exempted from IRB review if the only involvement of human subjects fits within one or more of the following categories (45 CFR 46.101(b)):

Category 1 Research conducted in established or commonly accepted educational settings, involving normal educational practices that are not likely to adversely impact either students opportunity to learn required educational content or the assessment of educators who provide instruction, 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.

Category 2 Research that is limited to the use of educational tests, survey procedures, interview procedures or observations of public behavior unless:

- (i) Information obtained is recorded in such a manner that human subjects cannot be identified, directly or through identifiers linked to the subjects;
- (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, educational

- advancement, or reputation; or
- (iii) Research not involving children and where the information obtained is recorded by the investigator in such a manner that the identity of the human subjects **can** readily be ascertained, directly or through identifiers linked to the subjects, **and** an IRB conducts a limited IRB review (see SOP 15.7).

**Note: For research involving children (subpart D)**, exemptions (i) and (ii) above **only** apply to research that involves (a) educational tests or (b) survey or interview procedures or observations of public behavior when the investigator does not participate in the activities being observed or interact directly with the children. [45 CFR 46.104(b)(3) as modified by Subpart D 45 CFR 46.401(b)]

Category 3 Research with adults involving collection of information (verbal, written, or audiovisual recording) in conjunction with **benign behavioral interventions** (i.e., research that is brief in duration, painless, harmless, not physically invasive, not likely to have a significant adverse lasting effect on the subjects), and who prospectively agree to the intervention and, if at least one of the following criteria are met:

- (i) information obtained is recorded in such a manner that human subjects cannot be identified, directly or through identifiers linked to the subjects;
- (ii) any disclosure of the human subject's responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation; or
- (iii) the information obtained is recorded by the investigator in such a manner that the identity of the human subjects **can** readily be ascertained, directly or through identifiers linked to the subjects, **and** an IRB conducts a limited IRB review (see SOP 15.7).

Category 4 Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following apply:

- (i) these sources are publicly available and/or
- (ii) 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; and/or
- (iii) Investigator's use is regulated under HIPAA as "health care operations" or "research" [45 CFR 164.501] , or "public health activities and purposes" [45 CFR 164.512(b)], and/or
- (iv) Research is conducted by, or on behalf of, a federal agency using data collected or generated by the government for non-research purposes, and the information is protected by federal privacy standards

Category 5 Research and demonstration projects conducted by or subject to approval of a federal agency and designed to study, evaluate or otherwise examine some aspect of (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. Additionally, the following criteria **must** be satisfied for an exemption to be granted (OPRR Guidance):

- (1) The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).
- (2) The research is conducted pursuant to specific federal statutory authority.
- (3) There is no statutory requirement that an IRB review the research.
- (4) The research does not involve significant physical invasions or intrusions upon the privacy of participants.

The IRB reviewer should consult with the federal agency regarding the above additional considerations.



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

Category 7. Storage or maintenance of identifiable private information or identifiable biospecimens for secondary research for which broad consent and limited IRB review is required (see SOP 15.7).

Category 8: Secondary research using identifiable private information or identifiable biospecimens for which broad consent and limited IRB review is required (see SOP 15.7).

#### 15.4 Broad consent for secondary research

Broad consent applies to the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens, and it allows information and biospecimens to be stored and used for unspecified future research that is in contrast with consent for a specific study. It should be used: (i) Optional use; (ii) allows subjects a means to exercise their autonomy in deciding whether or not to allow secondary research use of their identifiable materials; (iii) Includes a defined set of elements that cannot be omitted or altered (iv) when declined, IRB cannot waive informed and consent tracking mechanism is need.

#### 15.5. Prisoner Research

These exemption categories do not apply to research involving prisoners except for research aimed at involving a broader subject population that only incidentally includes prisoners. They also do not apply to FDA-regulated research with the exception of category 6.

#### 15.6 Identification of exemption reviewer(s)

IRB records will include the name of reviewer(s) of the application.

#### 15.7 Limited Review.

Limited IRB review is a process that allows research whose sole risk is breaches of privacy and confidentiality to be reviewed as Exempt rather than Expedited.

Continuing review is **not** required for research approved as Exempt with limited review. The limited IRB review process may be done either via the expedited review mechanism, that is, by the Chair or an experienced IRB member designated by the Chair, or by the convened IRB.

Limited review is always required for exemption Category 7 and 8. It is required for exemption Category 2 and 3 in the following circumstances:

- (a) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, AND
- (b) Any disclosure of the human subjects' responses outside the research would reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.

Limited review does not require an IRB to consider all of the IRB approval criteria in §46.111. In limited IRB review, the IRB must determine that certain conditions, as specified below, are met.

- 15.7.1 For purposes of conducting the limited IRB review under exempt categories 2(iii), 3(iii), and 8, IRB approval should satisfy the criteria at 45 CFR 46.111(a)(7): "When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data." Pending further guidance from OHRP, the

following criteria should be considered in the limited review:

- The extent to which identifiable private information is or has been de-identified and the risk that such de-identified information can be re-identified;
- The use of the information;
  
- The extent to which the information will be shared or transferred to a third party or otherwise disclosed or released;
- The likely retention period or life of the information;
- The security controls that are in place to protect the confidentiality and integrity of the information; and
- The potential risk of harm to individuals should the information be lost, stolen, compromised, or otherwise used in a way contrary to the contours of the research under the exemption.

For exemption category 8, limited review **also** requires the IRB determine that the proposed secondary research is within the scope of the broad consent.

15.7.2 For Exemption category 7, the IRB need only to make the following determinations, as required by §46.104(d)(7):

(i) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of §46.116(a)(1)-(4), (a)(6), and (d);

(ii) Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with §46.117; and

(iii) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

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SOP Title:	<b>Modifications to Previously Approved Research</b>		
SOP Number:	16.0	Current Version Date:	9/30/14

### 16.1 Modifications to approved protocols

A modification is a change to previously approved research. IRB review and approval is required before investigators can modify research protocols, except when necessary to eliminate apparent immediate hazards to the subjects. Any proposed change to a previously approved project must be submitted as an amendment to that project and may be reviewed by the expedited review procedure (see SOP 13.0) or by the convened IRB (see SOP 11.0), depending on the Chair's assessment of associated risk. Minor changes in previously approved research may be approved by expedited review. Minor changes are those that do not involve procedures that increase risk more than minimally or add procedures that would make the protocol ineligible for initial review using the expedited procedure, such as procedures that involve exposure to ionizing radiation. Minor changes to previously approved research may be disapproved through expedited review.

Modifications that might increase the risk to human subjects in a study or otherwise represent a substantive change should be reviewed by the convened IRB. If an amendment requires convened IRB review, at least one primary reviewer is assigned and the amendment is reviewed by the IRB, as described for initial or continuing review. Substantive modifications should also receive adequate scientific/scholarly review prior to or in conjunction with IRB review (see SOP 24.2).

If the modification involves any new findings, the IRB will determine whether the new findings may be related to participants' willingness to continue participation and should be provided to participants.

If a modification in the previously approved research is needed to eliminate immediate hazard(s) to subjects the investigator should make the necessary change. Within five (5) business days of making the change the investigator should describe the change using the modification form, which will be reviewed by the IRB Chair to determine if a change in risk has occurred in the research and if further changes are warranted.

Decision charts published by OHRP may assist the IRB in determining level of IRB review needed: <http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html>

Modifications should be submitted to the IRB using the form provided at the ORSP website.

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SOP Title:	<b>Continuing Review for Renewal</b>		
SOP Number:	17.0	Current Version Date:	8/01/19

### 17.1 Continuing review

The 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. Unless it is determined that review is needed more often than annually (SOP 17.2), the expiration date of a protocol's approval is 364 days from the initial approval or last renewal. This means that a study approval expires at midnight on the expiration date. The information system used by OHRE automates these calculations and accounts for leap years.

IRB continuing review responsibilities include reviewing reports of any unanticipated problems that involve risk to research subjects or others. This information may be gathered through investigator or sponsor reports, by third party observations, or by IRB inquiries. Continuing review is allowed to stop only when the research is permanently closed to the enrollment of new subjects, all participants have completed all research-related intervention or activities, and collection and active analysis of private identifiable information has been completed.

For more on reporting of adverse event/unanticipated problem, see SOP 19.0.

Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:

- Research eligible for expedited review in accordance with SOP 13.0.
- Research reviewed by the IRB in accordance with the limited IRB review described in SOP 15.3, Categories 2, 3, 7, & 8 [eCFR §46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8)].
- Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
  - Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
  - Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

### 17.2 Criteria for requiring review more often than annually

Intervals for continuing review, in the absence of problems, are often set to a default of one year. However, the IRB may determine that more frequent intervals are appropriate. The IRB shall consider the following factors in determining the criteria for studies requiring more frequent review:

- Nature, probability and magnitude of anticipated risks to subjects;
- Likely medical or psychological condition of the proposed subjects;
- Overall qualifications of the PI and other members of the research team;
- Specific experience of the PI and other members of the research team in conducting similar research;
- Nature and frequency of adverse events observed in similar research at this and other facilities;
- Vulnerability of the population being studied (this should be understood to include unfamiliarity with the language used on consent forms and other printed matter intended for subjects in the study);
- Other factors the IRB deems relevant.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a research milestone, e.g., number of subjects enrolled. The minutes should clearly reflect any determination requiring a review more frequently than annually.

### 17.3 Reminders

When a research project is due for continuing review, a written reminder is sent from the IRB to the PI approximately 60 days before the expiration date. Another reminder is sent approximately 30 days prior to the expiration date. If an application for renewal is not received from the PI by the expiration date, then the IRB will send an expiration notice to the PI. Copies of all reminders and expiration notices are kept in the IRB records.

### 17.4 Submission of applications for continuing review

At least 45 days in advance of the protocol expiration, a Continuing Review Application or Progress Report Form must be submitted to the ORSP. For studies that do not require Continuing Review, the Progress Report will be used to request a revised project end date. All researchers are required to submit a Study Closure Application when the study is closed.

The ORSP provides a form for the submission of continuing review materials. When an application for continuing review is received, the packet is checked by the ORSP for completeness, logged in, and given to the IRB Chair or his/her designee for review and determination as to whether review at a convened meeting (see SOP 11.0) or expedited review (see SOP 13.0) is indicated.

The application for continuing review will include a progress report in which the PI describes the number of subjects enrolled, any problems that occurred during the prior approval period, and any changes being requested as a part of the current renewal. The progress report will also confirm if the current consent documents remain accurate and complete.

### 17.5 IRB processes unique to continuing review

Research approved previously by expedited review is considered eligible for expedited review at the time of its regular continuing review if during the course of the study, the risks of the study have not increased. Projects that were initially reviewed by the convened IRB continue to receive the same type of review unless the IRB determines that the study meets the criteria for expedited review as described in Category 8 or 9 in SOP 13.0.

The IRB will also determine, as part of continuing review, whether any new findings (e.g., published reports, information from sponsor) that may be related to participants' willingness to continue participation should be provided to participants.

The IRB will also determine, as part of continuing review, if the protocol requires verification from sources other than the investigator that no material changes have occurred since previous IRB review.

Investigators are notified in writing of the decision of the IRB and any changes required. Final approval is not granted until all required changes have been made and submitted for review and approval.

### 17.6 Lapsed Study

A lapsed study is one for which the approval period has expired prior to the renewal of approval by the IRB. Once a study has lapsed:

- Notification must be sent to the PI ordering that all study-related measures must immediately cease except those necessary for welfare of the human subjects;
- No new subjects may be enrolled;

- If the PI desires to continue a study that has lapsed for more than three months, then the PI must submit a new application for re-review by the IRB, and must wait for IRB approval before resuming research under the protocol. If the PI submits the materials for continuing review within three months following the expiration date, the IRB may conduct continuing review and reactivate the protocol. This reactivation establishes a new approval period that is not retroactive to the prior date of expiration.
- For studies where subjects are receiving treatment or other intervention that may raise safety concerns if withdrawn, the investigator may request in writing that currently enrolled subjects continue with study activities. The IRB will consider the request in light of the medical condition of the subject (if any), the nature of the treatment or intervention, and the impact of withdrawal of the subject from the study. If the IRB finds that it is in the best interest of currently enrolled subjects to continue their involvement in the research, their participation may continue. Continuation of study activities in such circumstances should only be considered by the IRB if there is clear intent for the study to continue and an application for renewal is in progress.

#### 17.7 Observation of consent process or research activities

The IRB shall have authority to observe or have a third party observe the consent process and the research. This observation might be prompted by subject complaints, concerns about the conduct of a particular research study, the performance of a particular research team, or because the study was selected for random audit.

Observation may be conducted by IRB members or staff or by others designated to conduct audits as a part of their responsibilities. Such observation would typically be initiated by the Dean of ORSP and/or the IRB Chair who will designate the observers, selected based on the particular circumstances.

When appropriate, the observation shall include determination of whether any project requires verification from sources other than the investigator that no material changes have occurred since previous IRB review.

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SOP Title:	<b>Study Completion, Closure or Termination</b>		
SOP Number:	18.0	Current Version Date:	9/30/14

Research studies can be deemed completed for a number of reasons, each requiring a different degree of IRB involvement. In some cases, the IRB must perform in a supervisory or disciplinary fashion and require that a study be ended. More often, however, the investigator or sponsor will close the study and the IRB's role will be more passive, receiving study completion documents and archiving the records for the study.

#### 18.1 Voluntary completion by investigators

By submitting a notice of completion, the researcher confirms that the study is finished and that researchers have no further interaction with subjects or their data in ways that would require ongoing IRB approval. Once the IRB receives and accepts the notice of completion, the researcher is no longer required to submit for continuing review for renewal. If the investigator wishes to enroll new subjects for the study, or otherwise engage human subjects in research, he/she must reactivate the protocol with the IRB. Therefore, an investigator should only close a study when the research is permanently closed to the enrollment of new subjects, all participants have completed all research-related intervention or activities, and collection and active analysis of private identifiable information has been completed. A study will not invariably be considered completed when it is closed to accrual, as research-related procedures may still be continuing. The IRB, in consultation with the PI, may consider closing a study when active data analysis and publication pursuant to the approved study has ceased, even if the investigator retains records that may identify individual subjects. Additional research projects using data acquired in the approved study may constitute new human subjects research studies subject to separate IRB review.

#### 18.2 Termination of a study by the IRB

In cases of Serious Adverse Events (SAEs) or Unanticipated Problems (UPs) (see SOP 19.0), researcher noncompliance (see SOP 22.0 below), or protocol violations (see SOP 23.0 below), the IRB may decide to suspend a study to ensure subject safety. All notices of study suspension (suspension in whole or in part) should be copied to the Dean of ORSP. If the study is sponsored, the ORSP will be responsible for notifying the funding agency as appropriate. Once a study has been suspended, in whole or in part, an investigation of the problem prompting suspension of the study is initiated by the IRB and coordinated by ORSP. Upon completion of the investigation, the convened IRB may decide that a study should be terminated. Following the vote of the IRB to terminate a study and the evaluation of any appeals made by the PI, the study will be classified as inactive.

Though the Chair may suspend a study, pending IRB review, only the convened IRB may vote to terminate a study.

See also SOP 12.0, IRB Actions Following Review by the Convened IRB.

The Institutional Official is responsible for all required reporting of suspension or terminations by the IRB to the appropriate federal agencies. This reporting would generally be coordinated through the ORSP. (See 34.0)

### 18.3 Expiration of approval period

The approval of a study expires at midnight on the expiration date.

Once the approval period for a given study has expired prior to the renewal of approval by the IRB, it is considered a lapsed study and all research-related procedures must halt, except where doing so would jeopardize the welfare of the human subjects. (See 17.6 above)

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SOP Title:	<b>Reporting of Unanticipated Problems and Adverse Events to the IRB</b>		
SOP Number:	19.0	Current Version Date:	9/30/14

Federal regulations require investigators to report to the IRB any unanticipated problems involving risks to subjects or others. There has historically been confusion about what needs to be reported. Therefore, it is important to delineate the definitions that inform reporting requirements. In particular, it is important to understand the difference between “adverse events” and “unanticipated problems” because many adverse events are not reportable. OHRP and FDA have issued guidance that clarifies what should be reported to the IRB, and TAMUT policy is based on this guidance. This federal guidance clarifies that investigators need only report unanticipated problems. Adverse events that are not unanticipated problems are not required to be reported to the IRB. (See Appendix T).

## 19.1 Definitions

19.1.1 According to federal guidance, “unanticipated problems involving risks to subjects or others” or “Unanticipated Problem” (UP) refers to any incident, experience, or outcome that:

- is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- is related or possibly related to a subject’s participation in the research; and
- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

Note that for TAMUT reporting purposes an event that satisfies the first two criteria will be considered reportable. See SOP 19.4 for additional information.

19.1.2 “Adverse event” or “adverse experience” (AE) is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), 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 and occur most frequently in the context of biomedical research, although they can occur in the context of social and behavioral research.

19.1.2.1 “Internal adverse event” is an adverse event experienced by subjects enrolled by the investigator(s) at TAMUT or at a site for which TAMUT IRB has oversight.

19.1.2.2 “External adverse event” is an adverse event experienced by subjects enrolled by investigators at other (“outside”) institutions engaged in a multi-site clinical trial.

- 19.1.3 “Serious Adverse Event” (SAE) is any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria:
- results in death;
  - is life-threatening (places the subject at immediate risk of death from the event as it occurred);
  - requires inpatient hospitalization or prolonged hospitalization;
  - results in a persistent or significant disability/incapacity;
  - results in a congenital anomaly/birth defect; or
  - any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).
- 19.1.4 “Unexpected Adverse Event” as defined by the FDA, is any adverse event, the specificity or severity of which is not consistent with the current Investigator Brochure; or, if an Investigator Brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended.
- 19.1.5 “Possibly related to the research” refers to the reasonable possibility that the adverse event, incident, experience or outcome may have been associated with the procedures involved in the research (modified from the definition of associated with use of the drug in FDA regulations at 21 CFR 312.32(a)).
- 19.1.6 “Related to the research” refers to an incident, experience or outcome that is likely to have resulted from participating in the research study.
- 19.1.7 “Data Safety Monitoring Plan” (DSMP) is a plan written to ensure that the relevant data are collected and assessed to monitor subject safety within a study. Part of the DSMP may be the establishment of a Data and Safety Monitoring Board (DSMB), also called a “Data Monitoring Committee” (DMC), but this is not necessarily required for every DSMP. Ongoing review of the data by an independent individual or committee assures the investigator(s) that the study can continue without jeopardizing patient safety. Monitoring activities should be conducted by experts in the disciplines needed to interpret the data and ensure patient safety and should be external to (independent from) the study.

The IRB’s evaluation of the DSMP should include:

- Reporting mechanisms
- Frequency of monitoring regarding time or number of subjects

- Specific data to be monitored
- Procedures for analysis and interpretation of the data
- Actions at defined events or end points
- Procedures for communication from the data monitor to the IRB and sites

DSMBs for multi-site studies are responsible for forwarding summary reports of adverse events to each IRB involved in the study.

## 19.2 Deciding if an event meets the criteria for Unanticipated Problem

### 19.2.1 Is it unexpected?

An event is unexpected if it occurs in one or more subjects or others participating in a research protocol, and the event's nature, severity or frequency is not consistent with either:

- The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or
- The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

### 19.2.2 Is it related or possibly related to a subject's participation in the research?

Events that qualify as relative to, or possibly related to the research, may involve one or more of the following:

- The procedures involved in the research;
- An underlying disease, disorder, or condition of the subject;
- Other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject.

In general, events that are determined to be at least partially caused by the procedures in a study would be considered related to participation in the research, whereas events determined to be solely caused by the subject's condition or state of illness or other circumstances clearly outside of the study would be considered unrelated to participation in the research.

### 19.2.3 Does it suggest that the research places subjects or others at greater risk of harm than was previously known or recognized?

Adverse events that are unexpected, related or possibly related to participation in research, and serious are the most important subset of adverse events representing unanticipated problems, because such events always suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized. These events warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects.

Other adverse events that are unexpected and related or possibly related to participation in the research, but not serious, would also be unanticipated problems if they suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized. These events should also be reported, for consideration of changes or corrective actions.

### 19.3 Differentiating between an Unanticipated Problem and an Adverse Event

By definition, an “unanticipated problem” is unexpected, whereas an “adverse event” may be anticipated or unanticipated. Additionally, an unanticipated problem may involve the increased risk of harm—whether or not any actual harm occurred. In order to decide which events or circumstances constitute an unanticipated problem, it is important to bear in mind the following:

- Not all Adverse Events are Unanticipated Problems. Only a small subset of “adverse events” occurring in FDA-regulated clinical trials and other types of studies constitute unanticipated problems and therefore must be reported promptly to the IRB. Many events that are required to be reported to the sponsor or federal agency are not unanticipated problems.
- An unanticipated problem may not be an Adverse Event. It is possible for an event that does not involve actual physical, psychological, social, or economic harm to a research subject or another person nevertheless to constitute an unanticipated problem that must be reported to the IRB. This is the case if the event places subjects or others at increased or different risk of harm, regardless of whether actual harm has occurred.

There are other types of incidents, experiences and outcomes that occur during the conduct of human subjects research that represent unanticipated problems but are not considered adverse events. Some unanticipated problems involve social or economic harm instead of the physical or psychological harm associated with adverse events. In other cases, unanticipated problems place subjects or others at risk of harm, but no harm occurs. For example, an investigator conducting behavioral research collects individually identifiable sensitive information about illicit drug use and other illegal behaviors by surveying college students. The data are stored on a laptop computer without encryption, and the laptop computer is stolen from the investigator’s car on the way home from work. This is an unanticipated problem that must be reported because the incident was (a) unexpected (i.e., the investigators did not anticipate the theft); (b) related to participation in the research; and (c) placed the subjects at a greater risk of psychological and social harm from the breach in confidentiality of the study data than was previously known or recognized.

Examples of unanticipated problems that should be reported to the IRB, even though they are not adverse events, include:

- Publication in the literature, safety monitoring report, interim result, or other finding that indicates an unexpected change to the risk/benefit ratio of the research;
- Breach in confidentiality resulting from a disclosure of confidential information or from lost or stolen confidential information, that may involve risk to that individual or others;
- Complaint of a participant or family member that indicates an unanticipated risk;

- Laboratory or medication errors that may involve potential risk to that individual or others;
- Change in FDA labeling because of adverse consequences or withdrawal from marketing of a drug, device, or biologic used in a research protocol;
- Disqualification or suspension of investigators;
- Accidental or unintentional change to the IRB-approved protocol that involves risks or has the potential to recur;
- Deviation from the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant
- Any deviation from the IRB-approved protocol that increases the risk or affects the participant's rights, safety, or welfare.

#### 19.4 Required Reporting of Unanticipated Problems

Reporting is required of all unanticipated problems, including those which may occur after the participant has completed or has withdrawn from the study, including after study closure. This reporting is carried out through completion of an online form found at the ORSP website.

Expectations for reporting include:

- Any Unanticipated Problem involving risks to subjects or others which occurred at a site for which TAMUTIRB has oversight. For TAMUT purposes, a reportable UP is any incident, experience or outcome that is unexpected and related or possibly related to the research (the first two criteria in 19.1). Upon review of the unexpected and related/possibly related event, the IRB will make the final determination as to whether the event places the subjects at greater risk than previously recognized (the third criterion in 19.1).
- Any event occurring at TAMUT or other location, whether or not TAMUT IRB has direct oversight responsibility, in which a determination has been made by the FDA, research sponsor, coordinating center, DSMB/DMC or other centralized monitoring group that the event meets the three criteria for an Unanticipated Problem involving risks to subjects or others (see 19.1.1).
- For adverse events that were determined to be UPs (as defined above, under 19.1.1), a summary should be submitted to the IRB at the time of continuing review. This summary should reflect the aggregate analysis described above with a commentary on risk-benefit analysis. Do not simply list events.

#### 19.5 Timing of Unanticipated Problem (UP) Reports

Unanticipated Problems that are serious adverse events should be reported to the IRB within one (1) week of the investigator becoming aware of the event.

Any other Unanticipated Problem should be reported to the IRB within two (2) weeks of the investigator becoming aware of the problem.

If the Unanticipated Problem Report cannot be completed in its entirety within the required time period, a preliminary report should be submitted. The Unanticipated Problem Report should be amended once the event is resolved and/or more information becomes available.

#### 19.6 Handling non-reportable adverse events and IND safety reports

Individual IND safety reports from external sites are generally not reportable to the IRB because their implications for the study cannot be understood. External events should not be reported to the IRB unless accompanied by an aggregate analysis that establishes their significance and a corrective action plan that addresses the problem. All individual AE and IND Safety Reports shall be maintained by the Investigator.

Reports from a DSMB/DMC or other independent safety monitoring group should be provided to the IRB on a regular basis, generally at least as often as the study undergoes continuing review. Reports should include findings from adverse event reports and recommendations derived from data and safety monitoring.

#### 19.7 Additional Reporting Responsibilities

It is the Investigator's responsibility to make all required reports of unanticipated problems or adverse events to the FDA and/or sponsor. Because the TAMUT IRB does not require the reporting of many adverse events, this does not obviate the investigator's contractual relationships with sponsors or the FDA.

#### 19.8 IRB and Institutional Responsibilities

The chair or designee(s) of the TAMUT IRB will review all reports of unanticipated problems. If a reported event poses serious risk to subject safety, the chair or designated subcommittee may immediately suspend the study. In most cases, the IRB will review a corrective action plan with the PI in order to resolve the immediate scenario and prevent future occurrences.

Any unanticipated problem involving more than minimal risk(s) to participants or others will be reviewed by the convened IRB. For unanticipated problems referred to the convened IRB, all members will receive the application and consent form, where relevant, and materials describing the unanticipated problem as well as any correspondence with the investigator to date.

The IRB has the authority to suspend or terminate IRB approval of protocols that are found to pose unanticipated or heightened risk. Other actions taken by the IRB may include but are not limited to modification of the research protocol; (ii) modification of the information disclosed during the consent process; (iii) additional information provided to past participants; (iv) notification of current participants, which is required when such information might relate to participants' willingness to continue to take part in the research; (v) requirement that current participants re-consent to participation; (vi) modification of the continuing review schedule; (vii) monitoring of the research; (viii) monitoring of the consent; (ix) obtaining more information pending a final decision; (x) referral to other organizational entities (e.g., Office of University Counsel, Office of Research Compliance, Institutional Official); and/or (xi) requirements for additional training for investigators and/or research staff. Determinations from the convened IRB meeting are documented in the minutes.

The Institutional Official is responsible for all required reporting of unanticipated problems involving risks to subjects or others and the resulting IRB actions to the appropriate federal agencies. This reporting would generally be coordinated through the ORSP. (See SOP 36.0).

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SOP Title:	<b>Allegations of Noncompliance, Subject Complaints and Other Concerns</b>		
SOP Number:	20.0	Current Version Date:	9/30/14

20.1 Information regarding noncompliance, subject complaints and other concerns.

Information regarding noncompliance in human subject studies may come to the attention of the IRB through several pathways. These include information contained in new applications, continuing reviews, adverse event reports, and reports from collaborators, employees, or subjects.

20.2 IRB investigations of noncompliance, subject complaints and other concerns

The Chair of IRB reviews allegations of noncompliance or subject complaints. The Chair makes a determination as to whether the alleged practices appear to (1) cause injury or any other unanticipated problems involving risks to subjects or others, or (2) constitute serious or continuing noncompliance with the approved protocol, IRB determinations or federal regulations. In such cases, the Chair shall suspend the study procedures pending a timely investigation, and shall immediately notify the principal investigator, ORSP Compliance Coordinator. When appropriate, others may also be notified, including the relevant dean, department chair or program director, the Office of University Counsel, or others with a role in the given situation. Investigations by the IRB focus on the protection of study subjects. In cases that involve allegations of scientific misconduct, the Chair shall contact the Office of University Counsel for further action. Inquiries or investigations into scientific misconduct do not preclude IRB review and actions.

The following are recommended procedures for resolving alleged noncompliance:

20.2.1 Chronological sequence

- When made aware of a potential problem, ORSP staff compiles file information and presents concerns to the IRB Chair.
- The Chair determines whether to pursue the matter with the PI via telephone call, e-mail, paper memo, or in person. The purpose of such contact is fact-finding, i.e., to determine whether a problem exists and if so, its magnitude and significance relative to the rights and welfare of human subjects.
- When the initial inquiry does not result in resolution of the matter, a meeting with the PI may be scheduled.
- The IRB Chair will determine whether the noncompliance requires additional review at a convened IRB meeting. All serious or continuing noncompliance will be reviewed by the convened IRB.
- For allegations that are referred to the convened IRB, all members will receive the application and consent form, where relevant, and materials describing the allegation of noncompliance and any investigation to date.
- The IRB has the authority to suspend or terminate IRB approval of protocols that are found to pose unanticipated or heightened risk or are out of compliance with institutional policies and procedures, state laws, and/or federal regulations. Other actions taken by the IRB may include

but are not limited to modification of the research protocol; (ii) modification of the information disclosed during the consent process; (iii) additional information provided to past participants; (iv) notification of current participants, which is required when such information might relate to participants' willingness to continue to take part in the research; (v) requirement that current participants re-consent to participation; (vi) modification of the continuing review schedule; (vii) monitoring of the research; (viii) monitoring of the consent; (ix) obtaining more information pending a final decision; (x) referral to other organizational entities (e.g., Office of University Counsel, Office of Research Compliance, Institutional Official); (xi) compliance audits; (xii), requirements for additional training for investigators and/or research staff; (xiii) letters of reprimand, and (xiv) restrictions on serving as an investigator on human subjects protocols.

- Determinations from the convened IRB meeting are documented in the minutes.
- In cases where the IRB determines that the allegations, complaints or concerns are unwarranted or resolved, relevant parties should be notified.
- If the IRB takes action regarding the noncompliance, the IRB sends written notification of these actions to the PI, ORSP and relevant others. To the extent that any action includes suspension or termination in cases of externally funded programs, the Institutional Official will communicate with the relevant sponsors.
- If the allegations of noncompliance come from a subject complaint, the complaint should be acknowledged and the subject informed of the steps taken, as appropriate. Depending on the circumstances, this correspondence will come from the IRB, the PI or other designated individual.
- The Dean of ORSP is responsible for all required reporting of noncompliance and the resulting IRB actions to the appropriate federal agencies. This reporting would generally be coordinated through the ORSP. (See SOP 36.0)

#### 20.2.2 General guidance

- Care should be taken to maintain confidentiality when leaving messages for the PI via voice mail or with secretarial and support staff. Similar care should be exercised when leaving messages for research subjects.
- The Chair should document in writing for the IRB files the outcome of any and all communications and discussions. Such documentation should be factual and objective and should include timelines for resolution (e.g., meeting dates, response deadlines). ORSP should also maintain copies of all written correspondence between the IRB and the PI or any research subjects.

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SOP Title:	<b>Protocol Violations, Deviations and Exceptions</b>		
SOP Number:	21.0	Current Version Date:	9/30/14

Protocol violations, deviations and exceptions occur when there is a variance between the protocol that has been reviewed and approved by the IRB and the actual performance within the research study. A protocol violation may rise to the level of noncompliance (see SOP 22.0, Allegations of Noncompliance, Subject Complaints and Other Concerns). If any member of the research team or any other knowledgeable individual obtains information concerning violations, deviations or exceptions, he or she is obligated to report this information to the IRB.

## 21.1 Protocol violations

A violation is defined as a variance from the approved study protocol that:

- Has harmed or increased the risk of harm to one or more research participants.
- Has damaged the scientific integrity of the data collected for the study.
- Results from willful or knowing misconduct on the part of the investigator(s).
- Demonstrates serious or continuing noncompliance with federal regulations, State laws, or University policies.

Some examples of protocol violations are:

- Proceeding with the protocol before obtaining final IRB approval.
- Failing to follow the established criteria or procedures that were approved by the IRB.
- Adding, removing or modifying a research instrument (or adding to an existing instrument) in a survey study without prior IRB approval unless the changes are within a range of anticipated potential changes specified as acceptable within the IRB approval.
- Implementing any change in the protocol without IRB approval.

### 21.1.1 IRB notification and response in case of protocol violations

When the IRB receives notification of a protocol violation, the violation should be reviewed by the Chair. Depending on the circumstances, the violation may be presented at a meeting of the convened IRB. A serious violation (e.g., one that affects subject safety) may prompt the Chair to suspend the study pending IRB review of the violation(s). Correspondence about serious violations should be copied to the ORSP, and others as relevant. Violations should be reported within one (1) week of the investigator becoming aware of the event using the same online mechanism used to report Unanticipated Problems and Adverse Events (See 19.0)

## 21.2 Protocol deviations

A deviation is defined as a variance from the approved study protocol that:

- Is generally noted or recognized after it occurs.
  - Has no substantive effect on the risks to research participants.

- Has no substantive effect on the scientific integrity of the research plan or the value of the data collected.
- Did not result from willful or knowing misconduct on the part of the investigator(s).

Some examples of protocol deviations are:

- Performing a planned procedure on a different timetable than previously specified in the research protocol because of an unforeseen disruption such as a subject's vacation.
- A mechanical failure such as a recording device malfunction.

#### 23.2.1 IRB notification and response in case of protocol deviations

Deviations should be tracked by the investigator and reported to any sponsor or data and safety monitoring committee in accordance with their policies. Deviations should be summarized and reported to the IRB at the time of continuing review.

#### 21.3 Single patient/subject exceptions

When an investigator anticipates a one-time, intentional action that departs from an IRB approved protocol, he or she may request a one-time exception from the IRB. An example would include enrollment of a single subject who does not meet all eligibility criteria for a study, but the investigator and sponsor have agreed this subject should be enrolled.

Under these circumstances the investigator should request this exception by submitting a modification form; the IRB approval should note that this modification applies to one subject only and not to the study as a whole.

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SOP Title:	<b>IRB Evaluation Criteria</b>		
SOP Number:	22.0	Current Version Date:	9/30/14

Whether by expedited or convened committee review, the IRB should apply the following criteria when reviewing a research study.

#### 22.1 Risk of harm

“Minimal risk” (for human subjects other than prisoners) 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.  
[21CFR50.3(k), 21CFR56.102(i), 45CFR46.102(i)]

Risk should be considered in terms of both severity and probability, and should not be understood to include only physical risk, though such risks are important to consider. In reviewing a study, the IRB should also evaluate emotional, psychological, financial, and legal (civil or criminal) risks, potential insurability risks, as well as risks to professional or community standing. For example, in conducting a drug use survey, respondents could face severe penalties in the workplace or in their community if confidentiality were breached even though the survey does not present a physical or psychological risk.

Risks to subjects must be minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and whenever appropriate, rely on procedures already being performed on the subjects for diagnostic or treatment purposes.

Risks to subjects must be reasonable in relation to anticipated benefits, if any, to subjects. Additionally, the subject must be given knowledge of risks and benefits 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 or procedures 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 (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

The IRB should be guided by the principles of The Belmont Report (See Appendix A) in assessing risks to research subjects.

#### 22.2 Benefit, including assessment of scientific/scholarly merit

The benefits of research fall into two major categories: benefits to subjects and benefits to society. Frequently, the research subjects are undergoing treatment, diagnosis, or examination for an illness or abnormal condition. This kind of research often involves evaluation of a procedure that may benefit the subjects by ameliorating their conditions or providing a better understanding of their disorders. Patients and healthy individuals may also agree to participate in research that is either not related to any illnesses they might have or that is related to their conditions but not designed to provide any diagnostic or therapeutic benefit. Such research is designed principally to increase our understanding and store of knowledge about human physiology and behavior. Research that has no immediate therapeutic intent may, nonetheless, benefit society as a whole. These benefits take the form of increased knowledge,

improved safety, technological advances, and better health. The IRB should assure that the anticipated benefits to research subjects and the knowledge researchers expect to gain are clearly identified.

In considering the possible benefit to be derived from a particular study, the IRB should examine both direct benefit to potential participants in the study (as may be the case in a drug study) as well as the long term societal benefits (i.e., generalizable knowledge) that the study may make possible.

Remuneration or an incentive to participate in the study should not be considered a benefit to subjects.

The IRB is also charged with evaluating the scholarly merit of a project. Such an evaluation entails a peer-review of the research proposal and its likelihood of producing results that are both unique and significant in a given field of study. Depending on the status of the applicant (trainee versus non-trainee) and the employing department of the PI, pre-IRB scientific review includes those conducted by faculty advisors (trainees) and department chairs as well as those conducted by "local pre-IRB review committees.

Researchers who submit proposals deemed lacking in scholarly merit should be given feedback that will help the researcher to better define the scholarly significance of his/her project before resubmitting the proposal to the IRB.

### 22.3 Selection of subjects

In accordance with Belmont Report principles, both the burdens and benefits of research should be distributed equitably. Selection of subjects is one important means of ensuring this equity. 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. Additionally, it 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. For more information, see SOP 25.0 Recruitment.

### 22.4 Review and documentation of informed consent

Unless specifically waived by the IRB, informed consent must be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46 and 21 CFR 50. See the discussion of informed consent below in SOP 28.0, Informed Consent. The IRB reserves the right to observe the informed consent process in any study under its purview.

### 22.5 Safety monitoring

When appropriate, the research plan should make adequate provision for monitoring the data collected to ensure the safety of subjects. (See 19.6 which refers to Data and Safety Monitoring Plans)

### 22.6 Privacy of subjects and confidentiality of data

There should be adequate administrative, procedural, and technical provisions to protect the privacy of subjects and to maintain the confidentiality of data. The assessment of adequacy should include consideration of the sensitivity of the data. Although there are some specific state and federal regulations governing privacy of some specific types of records (e.g., HIPAA, FERPA, state health care records privacy laws), privacy and confidentiality protections for human subjects do not derive

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merely from governmental regulation. They are also integral to the ethical principle of “respect for persons” as enunciated in The Belmont Report.

Additional guidance is available in the University’s “Information Security Policy and Standards” and the NIH Data Sharing Policy and Implementation Guidance, available at [http://grants.nih.gov/grants/policy/data\\_sharing/index.htm](http://grants.nih.gov/grants/policy/data_sharing/index.htm). The investigator is responsible for maintaining the confidentiality of research data for as long as the investigator is in possession of such data.

#### 22.6.1 HIPAA

If human subjects research creates or uses individually identifiable health information that is “Protected Health Information” as defined by the Health Insurance Portability and Accountability Act (“HIPAA”), the research use of that protected health information may require additional IRB review and documentation (see SOP 29.0 HIPAA and IRB Review).

#### 22.6.2 FERPA

The Family Educational Rights and Privacy Act (FERPA) protects the privacy of student education records. The term “education records” includes any information that directly relates to a student and is maintained by an educational institution. In general, FERPA provides that, with certain exceptions, information from a student’s education records may not be released to others, including those within the same educational institution, without the student’s or parent’s prior written consent. If the student is over 18 or enrolled in college, the student must give the consent. If the student is under 18 and not enrolled in college, the consent must come from his or her parent. For a FERPA consent to be effective, it must:

- be in writing;
- signed and dated by the student or parent (as applicable);
- specify the records that may be disclosed;
- state the purpose of the disclosure; and
- identify the party to whom the records may be released.

Notably, FERPA does not apply to schools that do not receive funds under a program of the U.S. Department of Education (e.g., certain private or parochial schools).

Note that health records pertaining to students, which are created and maintained by an educational institution (e.g., Campus Health Services; school nurses) are covered by FERPA rather than the Health Insurance Portability and Accountability Act (HIPAA). Accordingly, educational institutions must observe the restrictions and requirements of FERPA, including obtaining a valid FERPA consent (described above) or meeting a relevant exception (described below), before such records may be released.

In the research context, information from education records may be released, without the student’s or parent’s consent, to organizations conducting studies for, or on behalf of, educational agencies or institutions, but only if the study is: (1) for developing, validating, or

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administering [academic] predictive tests; (2) to administer student aid programs; or (3) to improve instruction. In order to qualify for this exception, the study must be conducted in such a way that parents and students may not be personally identified by anyone other than those working on the study, and the identifying information must be destroyed when it is no longer needed for the study's purposes. If the study at issue involves the University's data, there must be a written agreement between the University and the organization conducting the study. That agreement must:

- specify the purpose, scope and duration of the study or studies, and the information to be disclosed;
- require that the organization use personally identifiable information from education records only to meet the purpose or purposes of the study as spelled out in the agreement;
- require the organization to conduct the study in such a way that there is no personal identification of parents and students by anyone other than representatives of the organization who have legitimate interests;
- require the organization to return to the University or destroy the personally identifiable information when it is no longer needed for purposes of the study; and
- specify the time period within which the organization must either return or destroy the personally identifiable information.

More generally, information from education records may be released without the student's or parent's consent where the information released is de-identified. Even if a student's name or other common identifiers (e.g., date of birth, address) have been removed, the educational institution must still consider whether a reasonable person in the community could use the released information to identify a student with reasonable certainty. If so, then the information does not qualify as "de-identified" and may not be released without a valid consent.

Directory information publicly maintained by an educational institution may also be released without the student's or parent's consent, provided that the student or parent (as applicable) has not opted out of directory information disclosures. Researchers must check to confirm that a student has not opted out before accessing or disclosing directory information absent written consent. Researchers can verify whether a student has opted out of directory information disclosures by checking the relevant, publicly-available directory (e.g., the University's online directory) or asking the appropriate administrative office of the educational institution (e.g., the Office of the University Registrar).

Questions about FERPA and permissible uses of education records may be directed to the Office of University Counsel.

### 22.6.3 Certificates of Confidentiality

The Public Health Service Act at 301(d), 42 U.S.C. 241(d) authorizes DHHS agencies to issue Certificates of Confidentiality in response to an application submitted to the agency by the investigator. Certificates of

Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for human subjects. The Certificate of Confidentiality is intended to allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. This protection is not limited to federally supported research.

Certificates of Confidentiality have not been extensively tested in the courts and thus cannot be relied upon as an absolute guarantee of protection. The agency granting the Certificate of Confidentiality may require specific related language in the informed consent document. More information is available from DHHS program officers and from the following website: <http://grants.nih.gov/grants/policy/coc>

#### 22.6.4 Limits on Confidentiality: Reporting Requirements

A principal investigator or other researcher may encounter in a research participant a dependency, abuse or neglect situation, or a specific disease condition that is required to be reported to a State or local official. Such reporting requirements should be disclosed to subjects in the informed consent process. Generally, these reporting requirements are related to whether the participant is within a protected category—based on age or mental or physical condition—or if the condition may threaten the public health. (See Appendix H)

#### 22.6.5 Limits of Confidentiality: NIH Data Sharing Policy

Starting with the October 1, 2003, receipt date, investigators submitting an NIH application seeking \$500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why data sharing is not possible. In cases where human subjects' privacy precludes or limits data sharing, that explanation will be required in the NIH application. The NIH Data Sharing Policy and Implementation Guidance, is available at [http://grants.nih.gov/grants/policy/data\\_sharing/data\\_sharing\\_guidance.htm](http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm)

#### 22.6.6 Limits of Confidentiality: Subpoenas

All subpoenas for research data should be referred immediately to the Office of University Counsel for assistance.

#### 22.6.7 Limits of Confidentiality: The Shelby Amendment

The Shelby Amendment (Public Law 105-277 signed October 21, 1998) provides that if federally supported research results are used by the federal government in developing "an agency action that has the force and effect of law", then the federal agency may be required to obtain the research data and make it available if requested under the Freedom of Information Act (FOIA, 5 U.S.C. 552(a)(4)(A)). The extent and format of research data that must be shared is not specified in the Shelby Amendment. In some instances it has been narrowly interpreted to be limited to published data specifically cited in the promulgation of federal regulations. Seek assistance from the Office of University Counsel regarding any request for research data under the Shelby Amendment.

#### 22.7 Additional safeguards for vulnerable subjects

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 must be

included in the study to protect the rights and welfare of these subjects. (See SOP 32.0 Special Topics: Research Subject Groups)

#### 22.8 Continuing review for renewal

The IRB should determine which studies require review more than annually in evaluating a proposal based on the degree of risk. These criteria can be found in 17.2.

#### 22.9 Recruitment and payment

The IRB must consider the appropriateness of the methods for identifying, recruiting and compensating subjects and potential research subjects.

For more information, see SOP 25.0 Recruitment and SOP 26.0 Recruitment Incentives.

#### 22.10 Compensation for injury

TAMUT will negotiate liability coverage with the sponsor of the research study on a case-by-case basis. The IRB shall require that subjects are provided with accurate information about the availability of compensation and/or treatment for injury that is a result of participation in the research study.

#### 22.11 Reviews of scientific proposal or contractual statement of work

IRB review shall include review of any supporting documents (e.g., master protocols from outside sponsors, federal grant applications, and statements of work) for congruence with the application approved by the IRB.

#### 22.12 Human research ethics training and database

All faculty, staff, students, and other personnel who are engaged in the design, conduct, or analysis of human subjects research that is conducted under the aegis of TAMUT, regardless of the source of funding, are required to complete human subjects research protection education. Unless alternative training has been approved by the IRB, all personnel who will come in contact with human subjects or their identifiable data must complete the IRB-approved training.

Under limited circumstances, the IRB may approve an alternative human subjects training program to satisfy these requirements. A modified training package may also be acceptable for support personnel who have a very defined and limited role with respect to their interaction with human participants, such as telephone interviewers or data entry clerks. In these situations, the lead investigator(s) would typically assume responsibility for training their staff.

Some research projects involve collaborators external to TAMUT. Any collaborators or subcontractors who have contact with human participants or their data are expected to complete training in human research ethics. If the collaborators work in a setting where they are not already subject to institutional training requirements (e.g., private practices, public schools, or community hospitals without an IRB), they should fulfill TAMUT requirements as described above. If, however, the collaborating investigators come from another university or organization where they have already completed training required by their home institution, the IRB may recognize that training.



- 22.12.1 Documentation that all research team members have completed required education in human subjects research protection

ORSP maintains a database documenting investigators' completion of required research ethics training. The database is available at: [http://cfx3.research.unc.edu/training\\_comp/](http://cfx3.research.unc.edu/training_comp/)

Prior to IRB approval of the research study, the IRB will verify that all personnel who come in contact with human subjects or their identifiable data have completed IRB approved training and are entered in the aforementioned database.

- 22.12.2 Human subjects research ethics training for unaffiliated investigators

When the TAMUT IRB is serving as the IRB of record for investigators who are not faculty, staff, or students of TAMUT when they conduct human subjects research, they are nevertheless subject to all of the usual human protection requirements, including TAMUT training requirements. When the University is involved in collaborative research with an investigator from another FWA institution, their subcontract with that institution should require that the local institution will train each researcher involved with the project and will document that training. Such researchers will not be entered into the Research Ethics Training Database at TAMUT. If the investigator is not covered by an FWA IRB, he or she must complete TAMUT human subjects ethics training as described in SOP 24.12 and be entered into the Research Ethics Training Database at TAMUT.

The University may recognize training completed in satisfaction of requirements at other FWA institutions.

When research approved by the TAMUT IRB is conducted with staff members in a foreign country or members for whom TAMUT human subjects ethics training is impractical or inappropriate, the PI or other ethics certified researcher may provide training based on a training package developed in consultation with the IRB.

## 22.13 Knowledge of the local research context

IRBs have a responsibility to obtain sufficient knowledge of the local context to satisfy ethical and regulatory requirements that local factors are taken into consideration before research is approved. This responsibility endures regardless of the IRB's geographic location relative to the site where research will be conducted. It is particularly critical where the research involves greater than minimal risk to subjects or vulnerable categories of subjects. There are several ways to obtain this knowledge, depending on the nature of the proposed research and the location. While direct, firsthand knowledge on the part of IRB members may be the ideal situation, it is recognized that this will not always be practical. The following options take this into account. Note that this is not intended as an all-inclusive or restrictive list of options, but as a general approach to obtaining site-specific information, with higher levels of risk warranting more extensive efforts to assess local context.

- Where the research involves minimal risk to subjects, the IRB may obtain necessary information about the local research context through written materials or discussions with appropriate consultants. In some cases, investigators or their on-site collaborators may be able to provide sufficient insight to the IRB.

- Where the research involves greater than minimal risk, but there is no intervention with subjects and the principal risk is limited to the potential harm resulting from a breach of confidentiality (e.g., studies that collect extremely sensitive data), the IRB may obtain necessary information about the local research context through written materials or discussions with appropriate consultants. The IRB and investigators should give special attention to provisions to protect the privacy of subjects and maintain the confidentiality of data.
- Where the research involves greater than minimal risk to subjects and there will be direct interventions or interactions with subjects, the IRB should obtain necessary information about the local research context through one or more of the following mechanisms or through other mechanisms deemed appropriate for the proposed research and the local research context:
  - (a) Personal knowledge of the local research context on the part of one or more IRB members, through direct experience with the research site, its subject populations, and its surrounding community.
  - (b) Participation by one or more appropriate consultants in convened meetings of the IRB, or prior written review by such consultants. Such consultant(s) should have personal knowledge of the local research context, through direct experience with the research site, its subject populations, and its surrounding community.
  - (c) Input from a local IRB or other review body that is familiar with the research site in question. This scenario may also raise questions as to whether one or both IRBs is/are willing to rely on the review of the other (see SOPs 3.4 and 30.10).
  - (d) Systematic, reciprocal, and documented interchange between the IRB and elements of the local research context. Such interchange could include (i) periodic visits to the research site by one or more IRB members in order to obtain and maintain knowledge of the local research context; (ii) periodic discussion with appropriate consultants knowledgeable about the local research context; (iii) regular interaction with one or more designated institutional liaisons; and (iv) review of relevant written materials.

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SOP Title:	<b>Recruitment</b>		
SOP Number:	23.0	Current Version Date:	9/30/14

### 23.1 Advertisements

The IRB and investigators should be cognizant that advertising for subjects is often the first step in the informed consent process. When advertising is to be used, the IRB must review the information contained in the advertisement, as well as the mode of its communication, to determine whether the procedure for recruiting subjects affords adequate protection. IRB review is necessary to ensure that the information is not misleading to subjects.

Any advertisement to recruit subjects should state clearly that the project is a “research study,” and may include, where appropriate:

- The purpose of the research, and, in summary form, the eligibility criteria that will be used to admit subjects into the study;
- A straightforward and truthful description of the incentives to the subject for participation in the study (e.g., payment);
- The location of the research and the person to contact for further information; and
- The time or other commitment required of the participants

Advertisements should not:

- State or imply a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the protocol;
- Include exculpatory language; or
- Emphasize the payment or the amount to be paid, by such means as larger or bold type.

If a study involves investigational drugs or devices, no claims should be made, either explicitly or implicitly, that the drug or device is safe or effective for the purposes under investigation, or that the drug or device is in any way equivalent or superior to any other drug or device. Such representation would not only be misleading to subjects, but also would violate FDA regulations concerning the promotion of investigational drugs and investigational devices. The FDA specifically discourages the use of terms such as “new treatment,” “new medication” or “new drug” without explaining that the test article is investigational and that its effectiveness has not been proven.

### 23.2 Direct solicitation

Generally, researchers at TAMUT may not solicit by direct appeal to students, employees or trainees in that researcher’s department or class in an effort to recruit subjects for a study. Such direct and targeted solicitation (which should be distinguished from the dissemination of information such as is done in mass distribution emails) takes place within a power dynamic that could be construed as coercive by the potential subjects being solicited. The IRB should evaluate the proposed method of recruitment as it would be applied to students, employees or trainees to make sure that recruitment materials are not presented in a manner that could suggest that their decision regarding research participation could have an effect

on their relationship with instructors, mentors or employers. See also SOP 32.9 Employees, students or trainees as research subjects.

Describing opportunities to participate in research to individuals in a subject pool (for example, students registered for classes at TAMUT that require participation in human subjects research or an alternative activity, or healthy volunteers or patients who have enrolled in research registries) is not considered inappropriate since the prospective subject's inclusion in the subject pool implies his/her desire to be apprised of such opportunities. Creation and use of such pools or registries must be reviewed by the IRB.

#### 23.2.1 "Dear Colleague" Letters

The use of "Dear Colleague" letters intended to solicit the help of professional peers in recruiting subjects should be reviewed by the IRB and will be considered on a case-by-case basis.

#### 23.3 Requests from outside researchers to solicit on the TAMUT campus

When non-University researchers wish to solicit human subjects on the TAMUT campus, it should first be determined if this recruitment activity will engage the University in the research (e.g., involve University personnel to access records or potential subjects), (see SOP 8.0) and if the investigators have approval from an external IRB. Following that it may or may not be necessary to enlist the support of a TAMUT sponsor, depending on the nature of the research and what is involved. For example, the IRB may under some circumstances require that a local collaborator be designated when the targeted populations are TAMUT students. On the other hand, when direct access for recruiting may be gained publicly, e.g., faculty lists from the TAMUT website, the IRB may determine that a local collaborator is not required.

Even when further IRB oversight is not required, external researchers may still need to obtain approval from various "gatekeepers" who are responsible for the target population or facility (e.g., student affairs offices, deans' offices, dorm supervisors).

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SOP Title:	<b>Recruitment Incentives</b>		
SOP Number:	24.0	Current Version Date:	9/30/14

#### 24.1 Payments to research study subjects

Subjects may be paid for their participation in research. However, the IRB should review the amount and type of payment and the proposed method of disbursement in the context of the proposed subject population to assure that undue influence is avoided. Rewards such as course credit or goods with local monetary value should be considered to be forms of payment to study participants.

Problems with undue influence might occur, for example, if the entire payment were to be contingent upon completion of a longitudinal study or if the payment were unusually large. The appropriate level of payment is contingent upon a variety of factors, including: the amount of inconvenience or time associated with participation, local economic and cultural factors, the socioeconomic status of prospective subjects and any other circumstance that may affect subjects' ability to make a decision regarding their participation in the study.

Payment should not depend on the degree of risk or amount of discomfort associated with participation.

FDA-regulated research may not include compensation for participation in a trial that involves a coupon offered by a sponsor for a discount on purchasing the product once it has been approved for marketing.

#### 24.2 Finders fees, enrollment bonuses, etc.

To minimize inappropriate financial incentives in human subjects research, TAMUT research may not include payments of incentives for achievement of enrollment target numbers or meeting enrollment accrual timelines ("enrollment bonuses"). Also prohibited are finder's or referral fees to colleagues who may identify or refer eligible subjects to a research study (e.g., a general practitioner sending patients to a specialist conducting a study).

Additionally, University employees may not accept gifts, payments or in-kind support (including but not limited to financial payments, gift certificates, books, conference attendance and payment of travel expenses) as inducements for performance in TAMUT research other than as expressly included in budgeted project costs in a contract between the University and the research sponsor.

#### 24.3 Lotteries, raffles and door prizes

Occasionally, investigators who are not in a position to offer equal compensation to each research subject propose to substitute a drawing as an incentive. For example, an investigator with only \$200 to compensate 100 subjects might propose a drawing for two \$100 prizes rather than paying each subject \$2.00. University research projects may not include distribution of prizes to the research subjects via chances purchased by the human subjects or obtained by them in exchange for something of value (e.g., money, human tissues, or blood samples). The terms used for these purchased chance distributions include "lottery" and "raffle." The prohibition is pursuant to state law and university policy.

A prize distributed by chance where the chance is obtained merely by attendance at an event (sometimes called a “door prize”) and not by the payment of any fee, donation or other consideration is not prohibited by law or university policy.

Regardless of the terminology used, university research generally should not include distribution of incentives to human subjects by chance. This method may represent coercion or undue influence if the incentive is sufficiently valuable. Additionally, the distribution of incentives via chance represents an unequal distribution of the incentive and may be unfair to subjects who will ultimately receive nothing. Generally, rather than conducting a drawing, researchers should provide equitable incentives to each subject, even if such a practice diminishes the value of the incentive. However, use of incentives structured as described above for “door prizes” may be considered by the IRB on a case-by-case basis for research studies of minimal risk and brief duration if the proposed incentives do not have potential for coercion or undue influence and clearly are not distributed in exchange for valuable consideration such as blood or tissue samples or significant time and effort in research participation. The IRB should consult with the Office of University Counsel prior to approval of any incentive distributed by chance.

If such an incentive is approved for a given study, consent form language describing the incentive should avoid terms like “lottery” or “raffle.” Acceptable terminology might include a reference to a “drawing based on chance in which each subject has equal odds of receiving [the incentive].”

#### 24.4 Collection of Social Security Numbers for Research Purposes

Introduction:

There are occasions within the research setting when an investigator either needs to or is required to collect the social security number (SSN) of a subject. Most often, the SSN is collected as required by law, to comply with Internal Revenue Service (IRS) reporting requirements. Less often, the SSN may be collected as a unique identifier to help match research datasets.

Definitions:

**Social Security Number (SSN)** – SSN refers to the unique nine-digit number assigned by the United States government to individuals. For the purposes of this policy, this also applies to the use of 4 or more digits of the SSN when accompanied by place and date of birth. This policy also applies to circumstances where an individual subject (e.g., a worker who is not a US resident) has an Individual Tax Identification Number (ITIN) in lieu of an SSN.

Personal Identifying Information (PII) consists of:

- 1) Social security or employer taxpayer identification numbers (EIN)
- 2) Driver’s license (unless appearing in a law enforcement record), state identification card, or passport numbers.
- 3) Checking account numbers.
- 4) Savings account numbers.
- 5) Credit card numbers.
- 6) Debit card numbers.
- 7) Personal Identification (PIN) codes, which are numeric and/or alphabetical codes assigned to the cardholder of a financial transaction card (FTC) by the issuer to permit authorized electronic use of that FTC.

- 8) Digital signatures.
- 9) Any other numbers or information that can be used to access a person's financial resources.
- 10) Biometric data
- 11) Fingerprints
- 12) Passwords

Conditions for use of SSN in research:

SSNs collected for research must be relevant to the purpose for which they are collected and shall not be collected until and unless the need for the SSN has been clearly documented and approved by the IRB. When collecting the SSN, the investigator is required to provide a statement of the purpose or purposes for which the SSN is being collected and used. The SSN may not be used for any purpose other than the purpose stated.

#### 24.4.1 IRB responsibilities

Review and Approval of Proposed Use:

The IRB has been designated to serve in lieu of the Social Security Number Management and Advisory Committee to review and approve collection of SSNs and/or PII when required within the context of a research project.

The IRB may approve such collection for the following purposes:

1. Tax identification and other purposes mandated by federal or State laws. Per university policy, investigators are required to collect and report SSN and related information (as described below) when total payment(s) to an individual research subject will exceed \$200 per calendar year.
2. Use as a unique identifier for a national registry or database where there is potential for duplicate registration and no other means of unique identification exists.
3. Matching existing records or specimens to those contained in another data set (SSNs should be destroyed prior to data analysis).

Collection of the SSN may NOT be approved for:

- 1) Use as an identifier when other means of unique identification would suffice.
- 2) Labeling of stored biological specimens.
- 3) Convenience.
- 4) An identifier to facilitate future contact with subjects.

IRB Documentation:

The IRB will document the justification for collection of the SSN and whether disclosure of the SSN is voluntary or required for participation in the research.

#### 24.4.2 Investigator responsibilities

Mechanisms for Processing Payments to Subjects

Researchers should be aware that the method used to compensate subjects may have an impact on the need to collect SSN. For amounts that will total less than \$200 per calendar year, investigators are not required to collect SSN if payments are made using a cash advance

approach (e.g., gift cards or “petty cash” accounts). However, SSN must be collected for checks of any amount issued through the Accounts Payable system, even if that amount does not reach the \$200 threshold because the university system requires the SSN in order to “cut checks.” Investigators are also reminded that the IRS requires SSN to be collected and reported for payments of any amount to research subjects who are university employees.

#### SSN Collection Forms:

Investigators should use a form to collect and store SSN. The form must state the purpose of collection and the planned use(s) of the SSN. It must also clarify whether disclosure of the SSN is voluntary or required for participation in the research or required solely for tax identification. If the SSN is required solely for tax identification, the subject must be informed that (s)he has the right to renounce any research payment and consequently would not be required to disclose the SSN in order to participate in the research study. SSNs should be segregated on a separate page from the consent form or worded in a manner that permits easy redaction of the SSN. Investigators should use the appropriate [SSN Collection Form](#) provided by the IRB (on ORSP [Forms page](#) under Consent) as a consent form addendum that will be approved and stamped by the IRB via the review process. There are separate templates when the [SSN is collected for tax identification purposes](#) or when the [SSN is used as a unique identifier to match datasets](#).

#### Submit for IRB Approval:

If investigators know they will be required to collect SSN (e.g., because payments to subjects will exceed the stated threshold amounts) they should address this in the IRB application and attach the [SSN Collection Form](#) provided as a template. The IRB will review the justification for collecting the SSN. It may also happen that the IRB identifies a previously-unrecognized need for collecting the SSN while reviewing the study, in which case the investigator will be instructed accordingly. Submissions that occur after the initial review should be submitted as a Modification, as with any change to an approved protocol.

#### Storage and Disposition of Forms after SSN Collection:

Investigators are expected to collect and store signed forms using appropriate security measures. For participants who have been paid a total of more than \$200.00 within a calendar year, the investigator should forward the *name, address and SSN of recipients*, with the dollar amount paid, to [Material & Disbursement Services](#) (M&DS) at the end of that calendar year. *No study-related information* is required by M&DS, which should alleviate concerns about identities being linked to potentially-sensitive research topics by others outside the research team. M&DS will file necessary tax forms with the IRS and the individual (e.g., 1099-Misc). If total payments to a participant do not exceed the threshold of \$200 by the end of the calendar year, the SSN forms should be destroyed (e.g., shredded), unless payments will continue and might reach that amount in subsequent years.

#### Confidentiality:

SSNs and PII must be maintained utilizing proper security measures to protect the information. Proper security measures include, for example, locked file cabinets in locked offices, password-protected electronic files,



and encryption. An investigator or any other member of the research team may not intentionally communicate or otherwise make available to the general public a person's SSN or other PII.

Breach of Confidentiality:

In the event of a security breach, as defined by the University's "[Protocol for Responding to Security Breaches of Certain Identifying Information](#)," the Office of University Counsel, and other University offices as appropriate, must be notified immediately.

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SOP Title:	<b>Investigator Conflict of Interest</b>		
SOP Number:	25.0	Current Version Date:	9/30/14

#### 25.1 Investigator conflict of interest: Internal disclosure requirements

The university requires submission of a project-specific conflict of interest disclosure by members of the research team associated with new and renewing research projects. All researchers also are required to disclose changes in external affiliations that may give rise to a potential conflict of interest. In addition the IRB application directs all members of the study team to file Conflict of Interest (COI) disclosures. These disclosure requirements apply to any researchers and research staff who are subject to TAMUT policies; personnel subject to their home institution's COI policies (e.g., EPA, other universities) are not required to submit separate disclosures through the TAMUT COI office. Non-TAMUT study personnel may be required to submit documentation of compliance with their home institution's COI policies. This may be accomplished through the agreement indicating reliance on the TAMUT IRB. Non-TAMUT study personnel who are not subject to a home institution's policies are expected to comply with TAMUT policies.

#### 25.2 Investigator conflict of interest: University review coordination with IRB

When an individual first submits a human subjects research study to the IRB or Sponsored program office for review, the electronic system automatically creates Conflict of Interest (COI) disclosures in the COI system ([coi.unc.edu](http://coi.unc.edu)) for all persons named on a human subjects research study or all investigators listed on a sponsored research project. These persons are notified by email of the requirement to complete their respective disclosures. Individuals can also self-submit a disclosure through the electronic system.

Upon completion of a disclosure by an investigator, the COI system programmatically evaluates that disclosure for a potential COI. If a potential COI is identified by the system, the disclosure is flagged for review and routed to the COI office. All persons named on a human subjects research study or investigators on a sponsored research project are also required to update their disclosures at least annually through an annual disclosure form.

When the COI Officer receives a COI disclosure disclosing a potential conflict of interest in the research, whether self-initiated, through the annual evaluation process, or through a project specific form, the COI Officer will conduct a preliminary review and provide appropriate information to the applicable school conflict of interest committee. In the case of human subject research, the TAMUT IRB is also notified of a pending conflict undergoing review.

The applicable university conflict of interest review committee will share any written evaluations of the conflict of interest and its resolution, including any conditions or management plans that are put in place regarding that conflict, with Dean or Director of the School and in the case of human subjects research, the IRB. Approval of a conflict of interest management plan by a University Conflict of Interest Committee does not obligate an IRB to approve a proposed human subjects research activity.

The TAMUT IRB retains the final authority as to whether human subjects research may in fact proceed.

### 25.3 Summary of University policy on conflict of interest in human subjects research

The primary goals of the conflict of interest policy are to prevent financial interests from adversely affecting the protection of participants, the integrity of the research, and the credibility of the human research protection program. It is university policy that individuals conducting human subjects research have a paramount responsibility to ensure that any conflicting interests of the researchers do not compromise the welfare and rights of those human subjects. The University's Policy on Conflicts of Interest and Commitment includes a rebuttable presumption that an investigator may not conduct human subjects research that is related to a significant financial interest of the investigator or the investigator's immediate family, except in compelling circumstances. Compelling circumstances are those facts that convince the reviewer that a covered individual who has a financial interest should be permitted to conduct human subjects research, taking into account the following factors:

- the nature of the research
- the nature and magnitude of the financial interest
- how closely the financial interest is related to the research
- the extent to which the interest may be affected by the research
- the degree of risk to the human subjects involved that is inherent in the research protocol
- the extent to which the investigator is uniquely qualified to perform a research study with important public benefit
- the extent to which the interest is amenable to effective oversight and management.

When the significant financial interest is directly related to the human subjects research and may be substantially affected by it, the risk is greatest and the bar must be high.

In instances where a conflict of interest involving human subjects research is allowed, it is essential that research subjects and other interested parties be informed of the conflict of interest. If an investigator is participating in a multi-center trial and has been allowed to conduct human subjects research while possessing a significant financial interest, that fact should be made known to the PI or sponsor by the coordinating center (confer with the Conflict of Interest Officer before disclosing specifics of any significant financial interest). Notification of research subjects falls within the purview of the applicable IRB, which will determine how the conflict of interest should be disclosed to the relevant human research subjects. This may include a description in the consent form of the conflict of interest.

### 25.4 Compensation from sponsors

To minimize inappropriate financial incentives in study sponsorship, project support in all University projects:

- Must be based on fair market value of services performed or actual cost;
- Must be expressly stated in a contract between the University and the research sponsor;

- May not be conditioned upon a particular research result or tied to successful research outcomes; and
- May not include payments or other incentives for achieving human subject enrollment target numbers or meeting target enrollment accrual timelines or identifying eligible human research subjects. [See 26.2 “Finders Fees”]

University employees may not accept gifts, payments, or in-kind support (including but not limited to financial payments, gift certificates, books, conference attendance and payment of travel expenses) as inducements for performance in a University Project other than as expressly included in budgeted project costs in a contract between the University and the research sponsor.

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SOP Title:	<b>Informed Consent</b>		
SOP Number:	26.0	Current Version Date:	8/01/2019

Informed consent is a process rather than merely a document. Any individual invited to participate in a research study should be given a description of the study that is clear and complete enough for the individual to judge whether she or he wants to participate. The informed consent process should be designed to provide potential subjects with readily understandable information in an amount and timing appropriate to the level of risk in participating. The circumstances of the consent process should minimize the possibility of coercion or undue influence.

The subject's consent must follow and not precede receipt of this information unless the IRB approves a waiver or alteration of informed consent (as in some behavioral research that would be compromised by full disclosure in advance). Consent must be obtained from each subject who is legally, mentally, and physically able to provide it unless waived by the IRB. Consent should be in writing unless the IRB finds that written documentation of informed consent may be waived. Consent forms and other informational documents should be written in simple language so as to be easily understood by persons with no technical background in the field.

No informed consent, whether oral or written, may include any exculpatory language through which the subject or the subject's authorized 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.

The standard expectation is that all subjects will sign a document containing all the elements of informed consent, as specified in the federal regulations and noted below. Some or all of the elements of consent, including signatures, may be waived under certain circumstances.

As stated in SOP 22.4, the IRB has the authority to observe or have a third party observe the consent process and the research (as allowed under 45 CFR 46.109(e)).

#### 26.1 Basic elements of informed consent

Unless the IRB approves exceptions, the following information must be provided to the subject when seeking informed consent:

- 26.1.1 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 that are experimental;
- 26.1.2 A description of any reasonably foreseeable risks or discomforts to the subject;
- 26.1.3 A description of any benefits to the subject or to others that may be reasonably expected from the research;
- 26.1.4 A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- 26.1.5 A statement describing the extent, if any, to which confidentiality of the records identifying the subject will be maintained; (see SOP 29.0 HIPPA and IRB Review and SOP 24.6 Privacy of Subjects and Confidentiality

of Data). For FDA-regulated research, this also includes a statement that notes the possibility that the FDA might inspect the records.

- 26.1.6 For research involving more than minimal risk, an explanation as to whether any compensation and/or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- 26.1.7 An explanation of whom to contact for answers to pertinent questions about the research and research subject's rights, and whom to contact in the event of a research related injury to the subject, if relevant. Typically, questions concerning a research project should be referred to the PI for that project, whereas questions concerning the rights of human subjects should be referred to the IRB.
- 26.1.8 A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
- 26.2 Additional elements of informed consent
- For some studies, one or more of the following elements or information may be appropriate and required by the IRB:
- 26.2.1 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) that are currently unforeseeable;
- 26.2.2 Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- 26.2.3 Any additional costs to the subject that may result from participation in the research;
- 26.2.4 The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject (particularly when potentially therapeutic experimental interventions are being administered and unscheduled cessation of the intervention may pose health risks to subjects);
- 26.2.5 A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject;
- 26.2.6 The approximate number of subjects involved in the study.
- 26.2.7 The amount and schedule of payments, if any.
- 26.2.8 When required by applicable regulation, the results of the research will be posted on [clinicaltrials.gov](http://clinicaltrials.gov).
- 26.2.9
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- When a subject withdraws from an FDA-regulated study, the data collected on the subject to the point of withdrawal remains part of the

study database and may not be removed. The consent document cannot give the subject the option of having data removed.

- A researcher may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
- The researcher must obtain the subject's consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.
- If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent. However, a researcher may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

### 26.3 Exceptions to informed consent requirements

An IRB may approve a consent procedure that does not include, or that 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:

26.3.1 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:

- public benefit of service programs; (45 CFR 46.116(c)(1)(i))
- procedures for obtaining benefits or services under those programs; (45 CFR 46.116(c)(1)(ii))
- possible changes in or alternatives to those programs or procedures; or (45 CFR 46.116(c)(1)(iii))
- possible changes in methods or levels of payment for benefits or services under those programs; and (45 CFR 46.116(c)(1)(iv))
- The research could not practicably be carried out without the waiver or alteration. (45 CFR 46.116(c)(2))

For research using protected health information (PHI), see SOP 29.3 for additional criteria for waiver or modification of the HIPAA requirement for written authorization.

### 26.4 Other exceptions to informed consent requirements 45 CFR 46.116(d)

An IRB may approve a consent procedure that does not include, or that 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:

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- 26.4.1 The research involves no more than minimal risk to the subjects;
- 26.4.2 The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- 26.4.3 The research could not practicably be carried out without the waiver or alteration;
- 26.4.4 Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

These exceptions do not apply to FDA-regulated research.

For research using PHI, see SOP 29.30 for additional criteria for waiver or modification of the HIPAA requirement for written authorization

## 26.5 Other information concerning informed consent

- 28.5.1 The informed consent requirements in this policy are not intended to preempt any applicable federal, State, or local laws that require additional information to be disclosed in order for informed consent to be legally effective.
- 28.5.2 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.

## 26.6 Short form consent procedures

There may be circumstances when a subject is unable to read the full consent document (e.g., when the subject is illiterate or does not speak the language in which the consent document is written). In most circumstances, the IRB expects that a translation of the full form will be provided. However, there may be times when there is no opportunity to prepare a long form in advance; in such cases, a short form may be used.

The short form is not to be used when a study team has simply failed to make provisions for translated versions of the consent document in commonly spoken languages in the recruitment area/population.

A short form is a written consent document stating that the required elements of informed consent 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. Under many circumstances the full consent form may serve as this written summary. Only the short form itself is to be signed and dated by the subject or the legally authorized representative. However, the witness shall sign (and date for FDA-regulated research) both the short form and a copy of the summary, and the person actually obtaining consent shall sign (and date for FDA-regulated research) a copy of the summary. A copy of the signed (and dated for FDA-regulated research) summary shall be given to the subject or the representative, in addition to a copy of the signed (and date for FDA-regulated research) and short form.

## 26.7 Waiver of written consent

The IRB may waive the requirement for the investigator to obtain a signed consent form in cases where circumstances warrant such a waiver. Such a waiver is allowable if:



- The consent document is the only link between the subject and the research and the principal risk of harm would come 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 [45 CFR 46.117 (d)(1)]
- The research presents no more than a minimal risk of harm to the subjects and involves no procedures for which written consent is normally required outside of the research context. [45 CFR 46.117 (d)(2)]

In lieu of a signed consent form, the IRB may require the investigator to provide subjects with a written statement regarding the research in the form of an information or fact sheet. This information will be reviewed by the IRB. The written statement should contain, at a minimum:

- A statement that the project involves research;
- A description of the level of involvement and amount of time expected from subjects;
- A description of the study
- A description of the risks and benefits to subjects;
- A statement describing the subject's rights;
- A description of the compensation to be provided to subjects;
- Contact information for both the investigator and the IRB.

Examples of circumstances in which a waiver of written consent may be considered include situations where the researcher plans to use an abbreviated consent process, as in recruiting passersby for a brief, minimal risk survey. Similarly, a waiver may be granted to allow researchers to obtain oral consent for a telephone survey. Finally, a waiver may also be granted if researchers want subjects to imply their consent by returning a survey via the mail or the internet. This last approach is especially useful in preserving the anonymity of the subjects surveyed. For research using PHI, see SOP 29.3 on the additional criteria for waiver or modification of the HIPAA requirement for written authorization

28.7.1 Waiver of written consent does not apply to FDA-regulated studies.

## 26.8 TAMUT consent form templates

In most cases the IRB requires that the Consent Form templates available via the Internet be used for all written consent form documents. This consent template contains all of the basic elements described above. For clarity and to assure timely processing by the IRB, the consent form should follow the guidelines described below.

The consent form and study fact sheet must be written at a level understandable to all potential participants and it must contain all information that would reasonably inform the subject's willingness to participate. In order to facilitate this requirement, the IRB will provide templates that reflect appropriate language for various subject populations. The consent form should be written in second person with "you" or "your child" consistently used to refer to the subject in all statements.

In most cases, the title of the project as listed on the consent form should be the same as the title listed on the application form, though the IRB may suggest or require modifications in the title under certain circumstances (e.g., in case the title would alert subjects to deception in the study or when the title may be too explicit regarding subject criteria such as a study of dysfunctional parents).

The date on which the consent form was prepared or modified should be indicated on the form so that revised forms can be easily distinguished from prior versions.

## 26.9 Assent by children

Except under specific circumstances, assent to participate in a study must be obtained from children who are capable of providing assent, which can be written, oral, or both. The IRB shall determine that adequate provisions are made for soliciting the assent of the children (this includes providing age specific language to the prospective subjects), 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 individually, 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 (such as in a study with therapeutic potential), 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 45 CFR 46.116.

When assent is a requirement, the IRB will determine whether assent is to be documented. When assent is to be documented, the IRB will review the process to be used.

### 26.9.1 Special issues in consent involving older children

Principal investigators are required to seek the consent of a child's parent or guardian before enrolling a child in a study and beginning treatment and/or conducting research. Texas statutes do not address consent for research; however, IRBs and investigators should be aware that under Texas state law, a child can consent to medical treatment when he/she is emancipated or when the services are for the "prevention, diagnosis and treatment of (i) venereal disease and other diseases reportable under Texas law (ii) pregnancy, (iii) abuse of controlled substances or alcohol, and (iv) emotional disturbance."

In certain cases, limited to those described below, the assent of children may, by itself, represent informed consent. Most children, however, must assent in tandem with parental permission. The special circumstances, which will be reviewed on a case-by-case basis by the IRB, include:

- Minors emancipated via court petition. Pregnancy or parenthood does not automatically emancipate a minor (See Appendix K). For children who are pregnant, assent and permission will be obtained in accordance with the regulations;
- University students under the age of 18;
- Minors who are legally married;
- Minors serving in the armed forces of the United States; or

- International subjects (investigators and IRBs should consider local laws and customs in evaluating the majority status of international subjects)

It is sufficient for researchers to use a verbal statement to confirm a child is indeed emancipated. A confirmation of such a claim can be done in a similar way to the verification of individuals who claim to be married or over the age of 18. For example, a researcher, keeping in mind that under Texas law a child is not eligible to be emancipated by a court until he or she is 16 years or older, could ask the child his/her age and how long he/she has been emancipated. This age restriction does not apply to married children, who are considered emancipated by virtue of being married regardless of age. A researcher could also simply ask about the process the child went through to get emancipated (i.e., see if the child talks about going to court).

Investigators and IRBs should consult with the Office of University Counsel if there are questions regarding legal issues related to guardianship and/or the age for consent.

#### 26.10 Parental permission

Unless otherwise provided by State law, or unless this requirement is waived by the IRB pursuant to 45 CFR 46.408(c), the permission of the parent or legal guardian is required in order for children to participate in research.

Where research is approved under 45 CFR 46.404 or 46.405 (see SOP 35.3), the IRB may find that permission of one parent is considered sufficient for the child's participation.

Where research is approved under 45 CFR 46.406 or 46.407 (See SOP 35.3), permission is to be obtained from both parents 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.

Per 45 CFR 46.408(c), in addition to the normal waiver requirements, the IRB may waive the parental permission requirement if the research is not FDA-regulated *and* it determines that a research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects. This waiver might apply to studies involving neglected or abused children, or older adolescents presenting in medical situations wherein a parental consent requirement might deter the child from seeking needed care (e.g., seeking care at a sexually transmitted disease clinic). If parental permission is waived, the IRB must be sure that an appropriate mechanism for protecting the child is substituted. The choice of an appropriate mechanism would depend on the nature and purpose of activities in the protocol, the risk and benefit to the subject, and their age, maturity, status, and condition.

##### 26.10.1 Durability of Parental Permission

Generally, if a subject whose participation was provided through parental permission reaches the age of majority or becomes legally emancipated during the period of his or her active study participation involving contact with study investigators, the informed consent of that subject should be required for continued participation in the study. The IRB may waive this requirement for informed consent if the criteria for such a waiver are met. See SOPs 28.3, 28.4 and 28.7 above.

## 26.11 Surrogate consent for subjects who are decisionally impaired

### 26.11.1 What is Decisional Impairment?

In the absence of a specific legal or medical finding to the contrary, the individual subject must be presumed to have decision-making power for himself/herself and must give consent, informed to the best ability of the research team. If there is any doubt as to the subject's capacity to consent, the investigator and the IRB should consider the need for independent assessment of capacity (e.g., psychiatric consult). If the subject does not have decisional capacity and the IRB has approved enrollment via surrogate consent, consent should be obtained from the highest available surrogate representative as described below.

There is an important distinction between the legal meaning of the term "incompetent" and our broader use of the term "decisionally impaired." Decisionally impaired persons are those who, due to a psychiatric, organic, developmental or other disorder or situation that affects cognitive or emotional functions, are unable to exercise independent decision making. "Incompetence" is a finding of a court of law that results in the appointment of a legally authorized representative for the individual judged incompetent by the court (see "court appointed guardian" below). Persons who have been judged "incompetent" in a court of law are only a subset of the larger group of persons who may be decisionally impaired.

Decisional impairment in a human research subject may be determined by a court finding of incompetence, by a physician's determination, or by a reasonable determination by the investigator or an independent consultant that the surrounding circumstances indicate that the individual is not able to exercise competent judgment about her/his personal risks and benefits in research participation. If a determination of decisional impairment is not confirmed by a court or physician, but only suspected, then consent should be obtained from both the subject and the appropriate representative.

### 26.11.2 Who can act as a legally authorized representative (LAR) for a decisionally impaired research subject in Texas?

As is the case for most states, Texas does not have State legal statutes that specifically address research enrollment. In accordance with federal regulations and guidance from the ORSP, TAMUT has established that the informed consent laws applicable to clinical care in Texas will be followed to determine who would be considered an acceptable LAR for purposes of providing surrogate consent for decisionally impaired subjects in studies conducted in Texas. Although the statute is specific to medical care, it may reasonably be applied to research participation as well.

In the case of an adult subject who lacks the capacity to consent, the LAR of the subject will be determined by taking the following individuals in this order of priority:

(1) **Court-appointed legal guardian** (except to the extent any appointed health care agent has authority, unless the health care agent's authority has been suspended by a court order) is a court appointed guardian granted "general" guardianship or "guardian of the person" may provide surrogate consent for all activities of the individual; therefore, this guardian may provide surrogate consent for research participation of the individual.

(2) A **health care power of attorney (HCPOA)** is a health care agent pursuant to the execution of health care power of attorney document. A HCPOA document (to the extent of authority granted) grants the agent power to make health care decisions for the individual following a physician's determination that the individual lacks adequate capacity to make her/his own health care decisions. Therefore, if such a physician determination has been made, the agent under an HCPOA may provide surrogate consent for research participation; to the extent this does not contradict the written HCPOA.

(3) A **durable general power of attorney** grants the agent whatever authority is specified in the power of attorney document and is referred to as an attorney-in-fact. Where the power of attorney includes a specific provision stating that it shall survive any period of incapacity or mental incompetence of the principal it is considered a "durable" power of attorney, and the person holding power of attorney may provide surrogate consent for research participation unless the research participation includes an activity expressly excluded from the power of attorney. NOTE that a general power of attorney is only valid when registered with the register of deeds in either the county named in the power of attorney or the county in which the principal resides. Before relying on the decision of a person holding a general power of attorney, investigators should require proof that the power of attorney has been registered and should examine the document to ensure that it expressly survives any period of incapacity or mental incompetence of the principal. For assistance with these determinations, please contact the Office of University Counsel.

Where there is both a valid HCPOA and a valid general power of attorney, the person holding the HCPOA has priority over the person holding the general power of attorney in making decisions regarding participation in human subjects research.

(4) In the event that there is neither a court appointed guardian nor an agent under a durable general power of attorney or HCPOA, surrogate consent for research may be given, as long as there is no evidence to the contrary, by the **other individuals listed below**, in order of priority. When surrogate consent will be sought from one of these individuals, in the absence of a legal designation, their authority would be no broader (and may be more limited) than that of a duly appointed health care agent:

(4a) The subject's spouse;

(4b) A majority of the subject's reasonably available parents and adult children;

(4c) A majority of the subject's reasonably available adult siblings; or

(4d) Another individual with an established relationship with the subject who is acting in good faith on behalf of the subject and can reliably convey the subject's wishes.

If there is any doubt as to which individual is the legally appropriate authorized representative for the subject, the Office of University Counsel must be contacted.

NOTE: In the case of designations (1), (2) or (3) above, the investigator should obtain a copy of the court order, HCPOA, or durable power of attorney and should maintain the copy with the research records as documentation of the authority of the surrogate decision maker.

Beyond the categories described above, others may not give surrogate consent for research enrollment. Institutional custodians or caretakers are not legally authorized representatives in the absence of a specific court appointment granting them guardianship (see above).

#### ADDITIONAL NOTES:

- While the presumption is that primary consent under these circumstances (i.e., decisional impairment) will be obtained from the LAR, there may be occasions when it is possible to seek the assent of the subjects, in addition to consent of the LAR. The IRB will determine whether assent of the participants is a requirement, and if so, whether the plan for assent is adequate.
- IRBs and investigators should seek guidance from the Office of University Counsel if there are questions about legal authorization for surrogate consent in specific situations.
- See SOP 32.5 for more information on IRB review of research involving decisionally impaired persons in research, and limits on this participation. For emergency research scenarios, see SOP 20.0, Emergency Use of a Test Article and SOP 21.0 Exceptions from Informed Consent Requirements for Emergency Research.”
- The foregoing applies to studies in Texas. For studies that will be conducted in other states or countries, the investigator will be expected to determine local requirements for legally authorized representatives in consultation with the Office of University Counsel.

#### 26.12 Obtaining consent from non-English speaking subjects

Researchers should take great care when they obtain informed consent from individuals who do not speak English or whose understanding of the language is limited. Researchers should be fluent in the subject’s language or an interpreter should be available during the consent process and throughout the subject’s participation as needed. Consent forms should be prepared in the language understandable to potential subjects. For more information, see SOP 28.13 below.

When performing research using non-English speaking subjects, the use of short form consent documents should *only* be used when unexpected circumstances arise and there is not sufficient time to prepare a full consent form translation. The short form should not be used as a convenient way to circumvent translation of the full consent form. See SOP 28.6 for more information.

While the use of non-English speaking subjects presents a unique set of challenges for the researcher, care must be taken not to exclude non-English speaking subjects from research that may yield potential benefits.

#### 26.13 Translation and informed consent

Attention should be paid to both oral interpretation and written translation in the informed consent process.

##### 26.13.1 Oral interpretation

Oral interpretation should be performed by a qualified individual who is not a family member of the prospective subject. The individual performing the interpretation should be available for ongoing communication between subjects and investigators.

#### 26.13.2 Written translation

Written translation of informed consent documents should be performed by a qualified individual. Though there is no standard definition of what constitutes a “qualified individual,” the investigator should demonstrate due diligence in obtaining an adequate translation of the informed consent documents from an individual whose qualifications would appear adequate to a reasonable person. Back translations to English may be one method for validating the accuracy of the translation; however, back translations are not always sensitive to dialect and idiom.

#### 26.14 Consent for use of stored samples and genetic testing

In general, all anticipated uses of collected samples of human tissues, body fluids, or biological products should be carefully delineated in the *Procedures* section of the consent form. Issues to be addressed might include the specific information to be obtained, whether the information may be of value to the subject, whether and how that information will be disclosed or made available to the human subject and whether genetic counseling will be available at the subject’s option.

26.14.1 If specimens are to be collected and stored for as yet unspecified purposes (genetic testing or otherwise), this should be addressed in the *Procedures* section of the consent form or in an addendum. The IRB will provide templates addressing these issues. Whether these templates must be included as an addendum to the consent form depends on the study. Generally, in cases where the primary purpose of the study is to store specimens, then the addendum is unnecessary. The addendum is required when specimen storage is adjunct to the main purpose of the study.

The consent form and process for maintaining human specimens in a repository for future research uses must inform the subjects explicitly about the unspecified possible future use of the specimens and related personal information. The consent process should consider the following:

- The sample will be stored and possibly used in future research studies.
- A description of any personal information about the specimen source that will be maintained (this may or may not include identifiers).
- If no personal identifiers will be used for labeling the stored samples, i.e., if it is impossible for the sample to be linked with the subject, the consent form should so state.
- If personal identifiers are to be used that will allow future matching of the subject to the collected sample, the consent form should describe how they will be used, how privacy and confidentiality will be protected, and whether and under what circumstances identifying information would be disclosed.
- Future research using the samples will be reviewed by the IRB prior to additional use of the samples

- Whether and how researchers may contact individuals whose specimens are in the repository
- A statement about any potential commercialization and that there are no plans for subjects to share in financial proceeds that may accrue from products derived from the specimens.
- Whether, how, and under what circumstance results from research studies using the specimens would be communicated to the subjects and, where relevant, to their family members).
- If specimens are individually identifiable, how the specimens and associated data may be withdrawn from the repository. If the specimens are not individually identifiable, a statement that they may not be withdrawn for that reason. Specimens that have already been used and the data derived from their use cannot generally be withdrawn.

#### 26.15 Consent for inclusion in research registry

A research registry is a database of potential research subjects who have signaled their willingness to participate in research studies. Subjects must consent to inclusion in the registry. However, researchers may use a staged consent process in which preliminary consent is granted by subjects when they are included in the registry and additional consent is obtained when those subjects participate in a study.

#### 26.16 Disposition of consent documents

As noted above, participants or their Legally Authorized Representative (LAR) must sign and date the consent form prior to participating in the study, unless this documentation is waived by the IRB. A copy of the signed consent form (photocopy or duplicate signed original) shall be given to the person signing the form. An original signed consent form should be retained in the investigator's files.

#### 26.17 Stamped copies of consent forms

All consent forms following the standard template will receive the IRB approval stamp that includes the current approval period. The IRB may require that copies signed by participants include a stamp of approval.

#### 26.18 Research consent forms in health care records

An informed consent document for research participation is not a health care document and ordinarily would not be included in a health care record. Similarly, other forms of information about research interventions that are not health care would not ordinarily be included in an individual's health care record.

However, some clinical research includes health care. Additionally, information about some research interventions, whether or not treatment-related, may be relevant to a health care provider's diagnosis and treatment decisions about the individual. For example, it may be important for a health care provider not associated with the research study to know that a patient is receiving drugs or interventions as part of a research protocol. In these circumstances, it may be appropriate for the consent form to be included in the health care record.

At the time of the review, the IRB, in consultation with the PI, should make a determination as to the appropriateness of including the consent form in the health care record. Conversely, there may be circumstances where it is inappropriate to include the consent form in a subject's health care record, and specific mechanisms should be in place to exclude research information from the health care record (e.g., when research participation is not relevant to ongoing health care but might disclose



sensitive personal information such as sexual preferences). If the decision is made to include the consent form in the health care record, then the informed consent and HIPAA authorization for the study should state that this information will be placed in the health care record.

In determining whether research participation records will be placed in the health care record, IRBs and investigators should consider several points. Although protection of the subject's health and safety by providing research participation information to a health care provider is an appropriate concern, there are also other human subjects welfare issues to be considered, particularly privacy and confidentiality. Some human subjects will not want information about their research participation to be shared with their healthcare provider for a variety of reasons including personal privacy or the concern that the information may be transmitted to a health insurer or employer. These are the very privacy and confidentiality concerns that underlie the HIPAA regulations giving patients the right to know what is in their health care record and to control disclosure of their PHI from the health care record.

#### 26.19 Record retention of informed consent forms

As with all protocol related materials, a copy of the approved consent documents (not the signed consent forms themselves) should be retained by the IRB for a minimum of three (3) years following the end of the study. For more information on storage of records, see IRB records requirements.

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SOP Title:	<b>HIPAA and IRB Review</b>		
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“HIPAA” refers to the Health Insurance Portability and Accountability Act of 1996. HIPAA regulations apply to health care providers, insurers and clearinghouses. HIPAA’s privacy regulations afford privacy protections for individually identifiable health care and demographic information (this includes nonmedical information such as addresses) that has been obtained in the course of health care treatment, payment or operations. This individually identifiable information is called “protected health information” (“PHI”). For a definition of “Protected Health Information” see the Definitions section of these SOPs. HIPAA’s privacy requirements are additional to other ethical and regulatory protections for human research subjects and do not supersede them.

The application of the HIPAA privacy regulations to research occurs at the interface of research with health care – i.e., when researchers access and use PHI held by health care providers, insurers or clearinghouses. The HIPAA access and use rules are based on the purpose for accessing and using the PHI. A clinician who also is an investigator may create PHI in the course of providing health care services to a patient and may also wish to use this patient’s PHI in a research study. The rules for the clinician’s access to and use of the PHI for treatment purposes are different from the rules for that same clinician’s access to and use of the same PHI for research. When both treatment and research are occurring simultaneously in a study, it is very important to comply with all appropriate regulations for each of these separate purposes/functions as required by law.

Research use of PHI requires an explicit written authorization except under the following circumstances:

- The individually identifiable health information is not PHI (as defined by HIPAA), because it was not generated in the course of the provision of health care services by a health care provider, health plan, or health care clearinghouse and does not flow from the researcher into a medical record or other record related to health care treatment, payment or health care operations; Examples of this would be (a) personal health information provided directly by the research subject to the researcher and put into a research record but not flowing from the researcher into any medical record of that individual, or (b) physical or physiological measurements of an individual made by a researcher in a nonclinical setting and entered by the researcher into a research database but not flowing from the researcher into a medical record; or
- The IRB has approved a waiver of authorization; or
- The PHI is no longer PHI governed by HIPAA because it has been “deidentified” by being stripped of all 18 identifiers specified by HIPAA (See Appendix M) before the data are provided to the researcher; or
- The PHI data are converted to a “limited data set” as defined by HIPAA before the data are provided to the researcher, and the use of the “limited data set” is governed by a data use agreement that includes the HIPAA-required provisions; or
- The research is limited to decedents;

Note that while decedents are not included in the Common Rule definition of “human subjects,” the disclosure of their PHI by a covered entity is subject to HIPAA requirements as further described in the TAMUT HIPAA and Research Policy; or

- The research is limited to a “review preparatory to research.”

Note that TAMUT policy is that use of the “review preparatory to research” option under HIPAA (a) is limited to preparation of a research protocol or assessment of feasibility of performing a specific research protocol; and (b) does not permit recording or copying any PHI; and (c) may not be used to prescreen patients as part of the recruitment process. Such a review may be utilized only to determine the existence of potential research subjects and not to identify them or to permit a more comprehensive review of the medical record – nor may such PHI leave the health care facility during the course of the review. See below for more discussion. Once there is intent to recruit pursuant to a formulated protocol, then the research activity is sufficiently well prepared to require IRB approval. See the TAMUT HIPAA and Research Policy.

The health care provider, insurer or clearinghouse is responsible for HIPAA compliance in providing access or disclosure of PHI in its custody. HIPAA requires that a health care provider, insurer or clearinghouse permit access to PHI for research purposes only in accord with HIPAA’s requirements for the transaction. The TAMUT IRB has been designated to function as the Privacy Board when required by HIPAA for the use of PHI in research. Therefore, the IRB will review and approve the following HIPAA documentation for TAMUT research studies:

- Review and approval of all authorization documents used by University researchers in the informed consent process for University research.
- Review and approval of all waivers of authorization, including limited waivers of authorization, for access, use and/or disclosure of PHI for University research purposes.

The IRB’s review and approval of these HIPAA documents is within the performance of the IRB’s broader responsibilities for the protection of human research participants, including privacy and confidentiality protections beyond those required by HIPAA. Several questions in the IRB application are relevant to HIPAA but are also applicable to all studies, not just those using PHI subject to HIPAA. The IRB does not serve as the Privacy Board when HIPAA applies beyond the scope of research studies. (See SOP 29.1)

As explained above, researchers generally must obtain written authorization for the use of PHI from the human subjects who’s PHI will be included in a study. This is a separate regulatory requirement from the requirement for informed consent. The authorization document must include all elements defined in HIPAA and described in the TAMUT HIPAA and Research policy. The authorization document would generally be executed as a separate document from the informed consent document; however, the IRB has the discretion to accept a HIPAA-compliant authorization that has been incorporated into the informed consent document except with respect to authorization for the access, use or disclosure of psychotherapy notes for research. For the access, use, or disclosure of psychotherapy notes, the HIPAA authorization and the informed consent must be executed as separate documents. The TAMUT IRB provides access to a HIPAA-compliant authorization template for the researcher to customize for the research study and submit with the application for IRB review and approval.

#### 27.1 Procedure for signing an authorization

Adults: A competent individual, 18 years of age or older, should always sign the authorization to use or disclose his/her PHI. A person is competent if he/she has the general ability to understand the concept of release of his/her medical information. If the patient is not conscious, coherent or not competent for other reasons, a legally authorized representative must sign the authorization.

Minors: Any parent or legal guardian may sign an authorization for a minor child in his/her legal custody. Note that HIPAA does not require a child’s assent for access to PHI. The individual must be provided with a copy of the signed authorization.

#### 27.2 HIPAA waiver of authorization:

In some circumstances, authorizations for research use of PHI may be waived by the IRB, provided that the IRB determines and documents its finding that the HIPAA authorization waiver criteria, listed below, are satisfied. These waiver criteria are in addition to the criteria for waiver of research consent requirements under 45 CFR 46.116, although some of the waiver criteria overlap. A request for a waiver of authorization must be completed by the researcher and submitted to the IRB for prior review and approval. The IRB shall maintain documentation of the request and its approval. This request may be combined with a waiver of informed consent for research.

HIPAA authorization waiver criteria:

The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals, based on the presence of at least the following elements:

- An adequate plan to protect the identifiers from improper use and disclosure; and
- An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
- Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of PHI would be permitted by the federal HIPPA policy; and
- The research could not practicably be conducted without the waiver; and
- The research could not practicably be conducted without access to and use of the PHI.

Uses or disclosures of PHI made pursuant to a waiver are subject to the “minimum necessary” rules (see University Policy, the “Minimum Necessary” Standard for Accessing, Disclosing and Requesting Protected Health Information (PHI)).

### 27.3 Limited Waiver of Authorization solely for the purpose of prescreening, contacting and/or recruiting potential research participants

In addition to the scenarios that would support a waiver of authorization for the full study activity, there is the potential need to grant a limited waiver of authorization solely for the purpose of prescreening, contacting and/or recruiting potential research participants. The waiver is “limited” in that it is temporary and will be followed by full authorization, when applicable. An example of a scenario in which a limited waiver may be appropriate is if a researcher needs to review health care records to make recruitment contacts. Since a researcher cannot practicably obtain a potential research participant’s authorization for review of PHI in advance of contacting the potential participant, the IRB may issue a limited waiver of authorization permitting specified access and use of the minimum necessary PHI solely for prescreening and recruitment contact pursuant to an approved protocol.

IRB approval of a limited waiver of authorization will be in accord with the criteria for a waiver of authorization as applied to the limited portion of study activity to which the waiver will apply, e.g., to prescreening, contact and recruitment procedures described in the protocol and IRB application.

Physicians and other health care professionals who have a direct treatment relationship with an individual may review that individual’s PHI for eligibility with respect to a research protocol and may initiate a discussion with the individual about

potential participation as a research subject in a protocol relevant to the treatment relationship. This limited scenario of health care-patient conversation prior to any actual research enrollment does not require an authorization or a waiver of authorization.

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SOP Title:	<b>Special Topics: Research Design and Context</b>		
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Some of the scenarios described below may be eligible for exemption, but the IRB should be cognizant of the challenges and issues inherent in these types of research.

### 28.1 Research in educational settings

Research conducted in established or commonly accepted educational settings that involve normal educational practices as well as research involving the use of educational tests, survey procedures, interview procedures, or the observation of public behavior is eligible for exemption from the Common Rule. However, such research sometimes raises special concerns to which the IRB must be especially attentive. One example of such a concern is the “two-hat” problem in which a researcher is also an instructor with potential coercive power or undue influence over students who are also potential research subjects. Such a situation does not automatically disqualify a project from exemption, but the IRB should be cognizant of the problems such an arrangement might create. Furthermore, even if the research is exempt, the investigator has an ethical obligation to ensure that students’ rights and welfare are respected. When educational institutions become engaged in the actual conduct of research, they are required to file an assurance in accordance with 45 CFR 46.103(a).

### 28.2 Trainees as investigators

The PI is the person who will personally conduct or supervise the research study. Under most circumstances, this will be a faculty member. For IRB communication purposes, a trainee/student may be listed as PI. However, a faculty advisor must be identified, who holds ultimate responsibility for ensuring that this project complies with all University, regulatory, and fiscal requirements.

If a trainee investigator is listed as PI, the faculty supervisor remains responsible for appropriate supervision of study compliance with all research ethical and regulatory requirements, including those related to human subjects protection.

Trainee investigators are students, postdoctoral employees, or fellows who have a significant, even primary, research responsibility for a protocol submitted to the IRB. These trainee investigators may conduct the majority of the research for a given protocol, but do not have ultimate administrative and fiscal responsibility for the project. Primary responsibility for protecting the rights and welfare of human subjects in research performed by trainees rests with the faculty member supervising the trainee investigator. This faculty member must be identified in materials submitted to the IRB for review of the project. Faculty who assign or supervise research conducted by trainees or staff have an obligation to consider carefully whether those individuals are qualified to safeguard adequately the rights and welfare of subjects (See Appendix E).

### 28.3 Trainee or student projects involving human subjects research

#### 28.3.1 Student or trainee honors projects, theses and dissertations

Student or trainee research projects in the form of directed or independent research, such as theses, dissertations and honors research projects, are

generally research intended to contribute to generalizable knowledge. When they involve human subjects, these projects require IRB review, as with any human subject research (See Appendix E).

### 28.3.2 Student or trainee human subjects projects (class projects)

Class human subject research projects (not for thesis or dissertation) are often designed primarily to educate students in research techniques or issues, without an expectation of contributing to generalizable knowledge. However, since the lines between educational goals and research are sometimes difficult to demarcate, and class projects may still (either directly or through data about them) involve living persons, class projects may expose individual subjects to the same risks as research intended for broader purposes. Furthermore, since a major goal of a class project should be to educate students in the process of human subjects research, instructors should make every effort to make the research process as realistic as possible. For more information, including examples, see Appendix E.

### 28.3.3 Training of student researchers

Trainees must complete the human research education training required for all University research team members, or a tailored package deemed appropriate by the IRB, in consultation with the instructor. Instructors should actively instruct the students in the application of ethical principles and regulations as they apply to the class project, including, but not limited to, respect for persons as it translates into informed consent, courtesy, avoidance of unnecessary discomfort, and protection of privacy.

## 28.4 Pilot studies

Pilot studies may represent complex research even though they may be conducted as preludes to more expansive studies. Therefore, pilot studies must be reviewed by the IRB.

## 28.5 Oral history as a type of humanities or social science research

The goals of oral historians, represented by standard practice in the discipline, may at times seem to be at variance with the principles underlying the protection of human subjects. Oral historians generally wish to create documents that allow individuals to be identified with their actions and accomplishments. They may wish to archive individually identifiable records indefinitely and make those identifiable records available to other historians in the future. As a result, the IRB should approach protocols involving oral history with special attention to four distinct issues.

- Description of the protocol: As in most qualitative research, the historian may have only a general outline of the topics to be covered in a wide-ranging interview, and the list of questions to be asked may grow or shrink as circumstances dictate. The historian may not know, in advance of an interview, the level of knowledge the subject possesses about the events of interest. The IRB should focus primarily on the purposes of the interview, the more general types of information likely to be elicited, the risks to subjects who may disclose certain types of information, and the roles played by the various respondents in the events being studied.
- Consent: Many oral history protocols may be eligible for a waiver of written documentation of informed consent. This is especially true in cases where the events described were, or are, controversial, involve

illegal behavior, or involve events that may portray powerful or influential members of a society in a negative light.

- Use of pseudonyms by respondents to identify themselves or other actors: Oral historians generally do not wish to have subjects use pseudonyms or to have them use pseudonyms to describe other actors in the events being described, but may agree to such devices under circumstances that would otherwise place individuals at risk or where the protection of identities is necessary in order to obtain the data. Related to this issue is the level of quotation allowed in research reports. Protection of subjects may suggest allowing full attribution to the named source, attribution only to a pseudonym or anonymous source, or quotation only by “role” in the events portrayed.
- Disposition of audio or videotapes: There are generally four options for the disposition of oral history tapes: permanently archived (in a library or similar collection); retained indefinitely by the scholar; returned to the respondent; or, destroyed by a date fixed in advance.

## 28.6 Qualitative research

Qualitative studies, which may involve such methods as participant observation, case studies, unstructured interviews, focus groups and various other descriptive techniques, raise special issues for the IRB. Qualitative research investigators usually have a well-articulated plan for their research, often have one or more reasonably specific hypotheses to be tested, and can describe in general terms the techniques they intend to employ. However, they may undertake research projects with the full expectation that techniques will be developed in the course of research, used on the basis of opportunity, and modified as events and experiences suggest are necessary for the success of the project. As a result, qualitative research investigators may present a research protocol that does not fit the usual model contemplated by federal human subject regulations for research, if those regulations are narrowly interpreted.

Reviewing qualitative research projects requires flexibility on the part of the IRB and is facilitated by a willingness to waive some of the elements of informed consent and approve methods of consent that are culturally appropriate. If the study protocol approved by the IRB is intended to encompass development of one or more research instruments, it may also be necessary to give relatively wide professional latitude to scientists in the application of approved methods so that an investigator does not need to come back to the IRB repeatedly for approval of changes that would be considered normal and routine under the circumstances. However, the IRB should make clear to the investigator that any significant changes, including all changes that could increase risk for the human subjects (for example, the addition of a new topic in a survey), must be approved in advance by the IRB. Finally, the IRB may need to consider an informed consent process that is multi-layered and takes place over time as the research develops and the investigator is better able to articulate both areas of further interest and the methods being employed for studying them. Whatever flexibility the IRB decides is appropriate in the specific research context, that determination must include adequate protection for the welfare and rights of the human subjects in that specific context.

## 28.7 Survey research

The IRB should pay particular attention to the following issues in survey research:

- Possibility of undue influence in administration of the survey;



- Possibility of deductive disclosure based on demographic information garnered from subjects (subject confidentiality and privacy must be protected);
- The setting of the survey and the issues raised by such a setting; and
- The mode of obtaining consent, especially when implied consent is to be used. Surveys may often involve a waiver of written consent, and in these instances, attention should be paid to the oral presentation of required elements of consent (e.g., review of phone script for telephone surveys).

#### 28.8 Research involving radiation

Studies involving the use of radiation, such as those requiring patients to be X-rayed, are not eligible for expedited review, even if all of the other procedures in the study have been deemed to pose no more than minimal risk.

#### 28.9 Research using existing data and materials

Each separate human subjects research study requires IRB review and approval of the specific proposed study, regardless of whether the data set or research materials have been previously compiled.

Research involving the use of data meeting any one of the conditions below is not considered human subjects research and does not require approval by the IRB:

- Data on decedents;
- Data that have been stripped of all identifiers that could link that data to living persons; (See Appendix M for further information on individual identifiability of data.)
- Data coded in such a way that the present investigators cannot identify individual subjects (e.g., access to linkage codes is prohibited through an agreement with the custodian).

Under federal regulations, research utilizing only the types of data described above is not considered human subjects research and need not be approved by the IRB, although IRB review may be needed to make this determination.

Research involving the use of data meeting one of the conditions below is eligible for IRB exemption from continuing review:

- if the sources of data are publicly available; (45 CFR 46.101(b)(4))
- 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. (45 CFR 46.101(b)(4))

When existing data sets contain identifiable private information about living individuals and these sets are not publicly available, IRB review and approval is required before research can proceed. The IRB must determine whether the information can be used without obtaining additional informed consent. As such, the IRB should first examine the conditions of informed consent under which the data were originally obtained. It may be that the proposed research is permissible under the conditions under which the data were obtained, including contracts, informed consent or a HIPAA authorization.

If this is not the case, the IRB should consider whether it is appropriate to waive the informed consent requirements in accordance with 45 CFR 46.116(d). In

many cases, a waiver of consent will be appropriate. In other cases, the IRB may determine that the research can only proceed if the investigator obtains data with codes and identifiers removed in such a way as to preclude the investigator or the source maintaining the data set from establishing subjects' identities. If the proposed data set includes PHI the IRB must determine whether the original HIPPA authorization will cover the use of the data, whether the IRB can waive authorization or whether additional consent/authorization is required.

Prospective studies using materials (e.g., data, documents, records, specimens) that will be collected for some purpose unrelated to the research do not qualify for exemption. The IRB may use expedited procedures to review research that proposes to use materials (e.g., data, documents, records, specimens) that will be collected in the future for non-research purposes.

The IRB review should include review of the terms and conditions under which the data or materials were originally obtained and released to the investigator. The purpose of this review is to make sure that the proposed new use is not incongruent with original purposes, permissions, or approvals. (See SOP 29.0 HIPPA and IRB Review)

#### 28.9.1 Creation of biospecimen repositories

IRB review of a research proposal using human specimens for research purposes must include a determination of whether the proposed research use constitutes human subjects research or qualifies for an exemption. If there are any questions regarding potential biosafety issues and related regulations, the investigator should contact the Department of Environment, Health and Safety for guidance.

If the IRB determines that the proposed human specimen use constitutes a human subjects research project, and if the research project will create a human specimen collection that will not be destroyed upon completion of the immediate research study, then the collection must be presumed to constitute a human specimen repository maintained for possible future research projects. The IRB review of the proposal for research that will create the human specimen repository must include review of the following components: (a) collection of the human specimens (creation of the human specimen repository); (b) maintenance and management of the human specimen repository; and (c) access to human specimen material in the repository for use in specific research studies; and (d) destruction or disposal of the specimens, as detailed below.

(a) The collection phase of the project involves issues familiar to IRBs in individual research studies that do not create repositories, although human specimen collection involves special concerns. For example, depending on the sources and timing in obtaining human specimens, there may be sensitive recruitment procedure issues. The protocol should state whether the tissues will be screened for HIV, hepatitis or other diseases, and if so, to whom that information will be reported and what guidance will be provided to the human subject. Particular attention must be paid to informed consent for collection of human specimens to provide that in addition to all of the usual requirements for informed consent, it informs the human subjects explicitly about the use of the specimens and any related personal information. (See 28.14, Consent for use of stored samples and genetic testing.)

(b) With respect to maintenance and management of the repository, the protocol should state clearly what institution will be responsible for the specimen repository. The IRB should receive the investigator's assurance that there has been adequate planning for the institutional resources required to perform the operations described for the proposed lifespan of the repository including any promised privacy protections, an adequate contingency plan for any institutional transfers of custody of the repository and a plan for destruction of the specimens. (See SOP 28.14, Consent for use of stored specimens)

(c) The section of the protocol addressing transfers from the specimen repository to investigators for use in specific research studies must also be reviewed. This section should note whether actual specimens will be shared with investigators or only data obtained from the specimens. Furthermore, it should clarify whether the transfer/access protocol adequately provides for security and privacy protections and addresses any restrictions on uses that were promised in agreements for establishing the repository. The relevant agreements may include one or more of the following: informed consent, waiver of informed consent, authorization or waiver of authorization, and/or any contracts with sponsors or agencies for creation or management of the specimen repository.

IRB approval of access/transfer protocols should include review of an application form for requesting samples and/or data from the repository, an application procedure that includes documentation of required IRB approvals as well as elimination of potential recipients who do not provide adequate assurance of compliance with specimen transfer agreement, and a transfer agreement executed by the University.

If the access/transfer to material in the repository includes PHI, HIPAA regulations apply. For example, for a "limited data set" pursuant to HIPAA, a data use agreement must include terms specified in HIPAA for such agreements. (See also SOP 29.0 HIPAA and IRB Review)

(d) Investigators should make appropriate provisions for the disposal or destruction of specimens. These provisions should include procedures for maintaining the confidentiality of donors as well as for adhering to any guidelines related to the disposal of hazardous waste material.

#### 28.9.2 Data registries and databases (data bank)

If the research project under review is specifically intended to create a database that will contain individually identifiable data and will serve as an ongoing data resource for other researchers and other research projects, the IRB review of the proposal for creating the database should include all four of the database activities noted as (a), (b), (c) and (d) below. The level of detail should be appropriate to the size, complexity, sensitivity and anticipated pattern of use of the database. "Registry" is a term often applied to a large database of defined data elements that is designed to be updated and to support the ongoing exchange and use of data. Registries are sometimes created by a public authority. Regardless whether the database is called a registry, if it is created to serve as a data resource (herein referred to as a "data bank"), it must be consciously and appropriately managed. Useful guidance and links to helpful information on managing databases and data registries can be found at the NIH Data Sharing Policy and

Implementation Guidance site at  
[http://grants.nih.gov/grants/policy/data\\_sharing/](http://grants.nih.gov/grants/policy/data_sharing/)

The different activities in creating a data bank for future use are:

- (a) collection and use of the data for the immediate project;
  - (b) maintenance and management of the data bank;
  - (c) access to data in the data bank for use in future research studies;
  - (d) disposal or return of the data.
- (a) The collection phase of the project involves the issues familiar to IRBs in individual research studies; however, particular attention must be paid to the informed consent process to provide that in addition to all of the usual requirements for informed consent, human subjects are explicitly informed about and agree to the intended ongoing use of their information in the data bank.
- (b) With respect to maintenance and management of the data bank, the IRB should receive the investigator's assurance that there has been adequate planning for the institutional resources required to perform the operations described for the proposed lifespan of the data bank including any promised privacy protections, an adequate contingency plan for any institutional transfers of custody of the data bank and a plan for destruction or return of the data.
- (c) The section of the protocol addressing future disclosures from the data bank for other research studies must also be reviewed. The transfer/access protocol should provide adequately for security and privacy protections and address any restrictions on uses that were promised in agreements under which the data were originally obtained. These relevant agreements may include one or more of the following: informed consent, waiver of informed consent, authorization or waiver of authorization, data use agreement and/or any contracts with sponsors or agencies for creation or management of the data bank.

In accordance with OHRP guidance from August 2004, secondary use of data from de-identified sources may not constitute human subjects research that requires further IRB review. This does not apply to researchers who originally established the database or registry and continue to have access to ID codes.

IRB approval of access/transfer protocols should include review of the process for disclosing data from the data bank including an application form that documents required IRB approval and also including an institutionally approved data use or data transfer agreement. If PHI is involved, HIPAA regulations may apply. A data use agreement for a "limited data set" pursuant to HIPAA must include terms specified in HIPAA for such agreements. Even without HIPAA involvement, written agreements for data use or data transfer agreements generally include provisions addressing the following:

The data bank custodian will not release any identifiers to the investigator;

The recipient investigator will not attempt to recreate identifiers or to identify individuals or institutions who are the subject of the data or

individuals from whom the data were obtained.

The recipient investigator will use the data only for the purposes and research specified;

The agreement may include additional conditions imposed by the IRB as a condition of approval for creation of the data bank.

The recipient investigator is required to comply with IRB approval of the project for which current data access is sought.

The agreement generally includes requirements for disposal or return of the data by the recipient investigator.

(d) The IRB approved protocol for creation of the data bank must also address the anticipated lifespan of the data bank and the procedure(s) to be followed when it is dismantled, including appropriate confidentiality and privacy protections in the disposal of data.

## 28.10 Review involving data from voice, video, digital or image recordings

If researchers wish to utilize data from voice, video, digital or image recordings, they must take a variety of special precautions. First, the researcher must obtain appropriate permissions from subjects who will not have their anonymity protected due to the very nature of the data being collected. The information or fact sheet and/or informed consent document must explain the intended use of the voice, video or image data, the provisions being taken for the storage of the data, and the means and timeline planned for the destruction of these data. Because of these unique constraints, researchers must take great care in authoring protocols in which the use of voice, video and image data are planned.

Certain studies involve the collection of voice, video and image data for the purpose of creating an archive or registry that will preserve the data indefinitely. In such cases, researchers will not make provisions for the destruction of data, and they should take care to inform participants of the archival nature of the data gathering performed in such a study.

### 28.10.1 PhotoVoice

Some researchers use a method of qualitative data collection in which participants take photographs of some aspect(s) of their lives, environment, or community. The photographs are then used as a basis for group discussions and to elicit important qualitative information about the photographers' attitudes and beliefs. The degree of risk to subjects in such research depends, in part, on what is photographed. For example, this process may pose the risk of self-incrimination to subjects who photograph themselves taking part in certain activities.

From the perspective of the IRB, the "human subjects" in the research are the research participants who are taking the photographs and then presenting their interpretations in group or other data gathering sessions. If the photographers are minors, then written parental consent for their participation in the research is required, along with assent of the child participant.

Although the individuals whose photos are taken are not the subjects of the research, there may be legal requirements for obtaining permission for using their photographs. If the photographers take photos of other people, then written permission to use the photo should be obtained. If the person being photographed is a minor, then written permission to take the photo must be obtained from the child's

parent or guardian. Those being photographed must be informed about how their photo will be used, and whether they will have the opportunity to view the photo before making a final decision about its use. If the photographs will be publicly displayed, such as at a professional meeting or community gathering, or used in manuals or brochures or other publications, then written consent to take and display the photograph publicly is required. Researchers must have a method to link pictures with the signed permission forms.

#### 28.11 Research involving deception or withholding of information

Some research designs may require the withholding of information from human subjects. Research involving deception or withholding of information must be reviewed by the IRB with common sense and sensitivity. The withholding of information by researchers is different from the practice of deception, in which researchers provide false or misleading information to subjects. Studies involving deception need to be carefully reviewed by the IRB to ensure that the deception is justified through an examination of the risks and benefits of that deception.

Furthermore, the IRB should ensure that, when appropriate, the subjects will be debriefed. Before approving a study that involves deception, the IRB should determine that the subject population is suitable and that the deception involved in the study would not alter a subject's assessment of risk to himself/herself if he/she was aware of the deception at the time he/she agreed to participate.

28.11.1 Deception can only be permitted where the IRB finds and documents that waiver or alteration of the informed consent requirements is justified according to 45 CFR 46.116(d). The IRB must document that the following criteria have been satisfied:

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

#### 28.12 Research involving potentially addictive substances

With respect to cigarettes and alcoholic beverages, IRBs and researchers should be aware that under Texas law these substances may not be distributed to or used by minors.

When research involving potentially addictive substances is proposed, the IRB must consider the subjects' capacity to provide ongoing informed consent if judgment is diminished by exposure to the substances. There may also be unusual potential for coercion in some circumstance, for example if such research involves subjects that are institutionalized.

The IRB must also be sensitive to the ethical context of the research, in that there may be other ethical dilemmas associated with these studies if they involve the use of deception or include randomization. It is critical that the IRB focus on the considerations of risk and benefit of such research. For more information, see SOP 28.13.

In addition, research involving substances that may impair the judgment of subjects must include provisions for the safety of those subjects both within the research setting and if those subjects choose to withdraw from research while in an impaired state. For example, if a subject who is legally intoxicated should choose to withdraw from a study, he or she cannot be permitted to drive from the research setting.

Potential human subjects with a history of addiction or with direct access to the class of substances in their work environment should be excluded from studies using potentially addictive substance, unless the IRB makes a determination that there is a compelling reason for their inclusion and the study includes all appropriate safeguards to reduce the risk for these subjects.

#### 28.13 Genetic information in research

Research including genetic information about individuals is potentially sensitive and requires that investigators take great care in handling this information. The IRB should expect the investigator to describe in detail how individual privacy will be protected and how the confidentiality of obtained information will be maintained.

Additionally, the consent process should include explicit descriptions of the type and scope of genetic information that will be collected and used in the research project. The IRB and investigators should also consider when and how subjects will be informed of the results of genetic analysis and/or study conclusions, including outcomes not currently contemplated that may have personal implications (e.g., if a researcher discovers a gene linked to an incurable disease). Inevitably, such research decisions have implications for the confidentiality of identifiers linking subjects to their genetic data.

See also SOP 29.9, HIPPA and IRB Review, and SOP 32.8, Third Party Research Subjects.

#### 28.14 Family history research

Family research typically involves obtaining information from one family member (called a proband) about other family members (third parties). For a detailed description of family history research, see SOP 32.8, Third Party Research Subjects.

##### 28.14.1 Recruitment of family members via family history research

In some cases, researchers may learn about potential subjects through family history research and wish to enroll a third party in a study. In such situations, the researcher must exercise extreme care in approaching a third party via a proband.

Under most circumstances researchers should ask the proband to discuss participation in the research study with his/her family member(s) before the researcher approaches those family members directly. Additionally, researchers should obtain consent directly from the family member(s) and not via the proband.

#### 28.15 Internet research

The vast amount of social and behavioral information potentially available on the Internet has made it an important tool for researchers wishing to study the dynamics of human interactions and their consequences in this virtual medium. Researchers can potentially collect data from widely dispersed populations at relatively low cost and in less time than similar efforts in the physical world. However, the problem of subject identification and verification can severely limit this potential. For example, researchers could unknowingly involve protected

populations or decisionally impaired subjects in the research study. There are also online data integrity issues.

Internet research protocols may involve research on the topic of the internet, research collecting data over the internet, observations of human behaviors on the internet, or some combination of these aspects. In evaluating studies utilizing the internet as a research tool, the IRB should ensure that investigators have a plan for:

- Obtaining and verifying informed consent if required, including parental permission and child assent; and
- Maintaining the promised degree of privacy of subjects and confidentiality of information through the use of appropriate security measures; and
- Ensuring appropriate online data collection method and data validation checks.

#### 28.16 Self-experimentation

Generally, researchers should not enroll themselves as subjects in a study that they are supervising. Such a practice presents obvious conflict of interest issues and a variety of other ethical and practical issues.

#### 28.17 Family members in research

While there is no absolute prohibition on an investigator enrolling family members in a study, due to the possibility of undue influence and a conflict of interest this typically should be avoided.

#### 28.18 Case studies

A case study is a report of treatment (including innovative treatment, e.g., surgery), and, as such, does not meet the Common Rule definition of research (a systematic investigation, including research development, testing and evaluation designed to develop or contribute to generalizable knowledge).

If any of the following is present, the activity is considered research rather than a case study if:

- There is a plan to perform the treatment on some individuals but not on others.
- Investigational drug(s) or device(s) are involved (off-label use of an approved drug or device for the sake of an individual patient does not constitute research).
- There is a clear intent before treating the patient to use systematically collected data that would not ordinarily be collected in the course of clinical practice in reporting and publishing the case study.
- There is intent to manipulate medications (even approved ones) to determine maximum effectiveness, or to test if they work consistently well.
- Extra tests are conducted for the sake of reportability.
- There is a protocol/study plan.
- Records or data sheets are maintained separate from clinical records (particularly with identifiers).
- The primary purpose is to answer a research question, not to



provide care.

- There is a possibility that the treatment might yield a case series if it is effective in others (e.g., testing a hypothesis).

Case studies may be published; the published report must be descriptive, not analytical.

Case studies that contain no PHI (i.e., health information paired with identifiers) do not need to be reviewed by the IRB or the HIPAA Privacy Board. Neither HIPAA Authorization nor a waiver of HIPAA authorization is required. Case studies that contain identifiers will be reviewed by the IRB, which will determine the need for authorization.

#### 28.19 Community Partnerships in Research

Increasingly research design involves members of the community under study in the design and implementation of this research. These approaches include community engaged research and community based participatory research (CBPR).

*Community-engaged research* encourages the participation and influence of nonacademic researchers in the search for new knowledge. Community members,

organizations, and researchers work together in all aspects of the research process. Community-engaged research is done with communities and not on communities.

This approach to research recognizes the strengths of the community and builds on those strengths.

Health-related research studies may develop new treatments or find ways to prevent disease, but it can take years before these treatments become available in most clinics, doctors' offices, or community health centers. This is especially true for research that involves disadvantaged communities. *Community-Based Participatory Research* (CBPR) actively involves the community in the research process. CBPR seeks to directly benefit the public in a process that:

- Is a collaborative approach that equitably includes community members, organizations, and researchers in all aspects of the research process.
- Enhances the understanding of a mutually shared area of public health interest.
- Puts findings into action to improve the health and well-being of community members.

In CBPR, community members are also involved in getting the word out about the research and promoting the use of the research findings. This involvement can help improve the quality of life and health care in the community by putting new knowledge in the hands of those who need such information in order to make changes.

These processes may present challenges for both researchers and IRBs, including whether the community partners are subjects, members of the research team or both; what training is required; how to manage conflicts of interest; when it is appropriate to establish community advisory boards; how to solicit their input in ongoing involvement; whether and what kind of collaborative agreements are required; and how/when to disseminate results. In many cases it will not be necessary or appropriate to apply the same policies and

requirements to community partners that are applied to University-based members of the research team. For example, it may be more appropriate for the principal investigator to provide training that is tailored to the role of community partners (e.g., church members, barbers, community advocates) than it is to require completion of the same online CITI modules that investigators complete.

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SOP Title:	<b>Special Topics: International Research</b>		
SOP Number:	29.0	Current Version Date:	9/30/14

IRB review of research studies that involve human subjects in other countries must include appropriate expertise for evaluation of the study in the context of the specific international setting(s) and study population(s).

In addition to the usual requirements for human subjects research, some issues particularly vital for IRB review for protection of human subjects in international populations are noted below. The questions listed below should not be understood as either prescriptive or exhaustive, but as guidance in assessing international research protocols.

#### 29.1 Human Subjects protection administration issues

- Training in ethical conduct of research should be carried out and documented as appropriate to the circumstances. For more information on this issue, see SOP 24.12.
- The IRB should determine whether an FWA is required for the local performance site, with the assistance of the ORSP Compliance Coordinator. See SOP 3.3 and 3.4.
- The IRB should determine whether privacy protections and data security measures and other standard protections for human subjects are practicable in the specific research setting.
- According to the NIH, when research takes place in a country with human subjects protection laws equivalent to or more stringent than those of the United States, researchers should conform to local law. Where local human subjects protections are less stringent, researchers should conform to United States law.
- The IRB and investigators have an obligation to be knowledgeable about the setting where the research is to be performed. This may include knowledge of customs, standards of care, and socio-economic conditions. See SOP 24.13. The IRB must confirm the qualifications of TAMUT researchers and research staff for conducting research in a foreign country through review of responses to questions in the IRB application that focus on cultural and situational study-specific issues and knowledge of investigator background and experience. In addition, the department approver must acknowledge the researcher's qualifications as part of the submission process.
- It should be determined whether a local IRB or other analogous review body exists. In some cases, it may be required to use the local IRB, if they have jurisdiction over the site where research will be performed (for example, the IRB for a collaborating investigator or a ministry for the entire country). In other cases, even where not required, the local IRB may be an appropriate source for local context and guidance. See SOP 24.13.

#### 29.2 Risk of harm

- The IRB should determine whether the study design anticipates and minimizes the political, social, economic and legal risks that are particular

to prospective human subjects or their communities in the particular country and subculture.

- The IRB should determine whether the risks of adverse events are likely to be different in this population than in the same research performed elsewhere.
- The IRB should determine whether adequate care is readily available for injuries sustained in the course of research.
- Complaints, non-compliance, and unanticipated problems involving risk to subjects or others will be handled as described in SOPs 19, 22 and 36.

### 29.3 Justice/Benefit

- The IRB should determine whether the study is responsive to the needs of the subject population and whether the benefits of the study will be available to this human subject population. In other words, researchers may not utilize a human subject population merely for their own convenience and without the prospect of benefit to that population. Consideration should be given to producing benefits for the population that will continue after the termination of the study.
- If the study includes an experimental health treatment intervention, the IRB should determine whether an established effective treatment exists and whether it is available to this subject population. Incorporation of a placebo arm for a study when an effective treatment exists is always a serious ethical issue, but scrutiny must be particularly intense when there are additional issues of potential vulnerability in the subject population. If it is determined that the research intervention is an effective treatment, the IRB must determine whether it will be available to the human subjects and the subject population following completion of the research study.

### 29.4 Understanding the protocol and consent process

- Group consent and individual consent: In some cultures, group consent by the family and/or the community may be an important adjunct or precursor to individual informed consent. It is important to keep in mind that although group consent may be appropriate and necessary, it is not a substitute for individual informed consent. The informed consent process should be designed to minimize the potential for coercion of the individual by the group.
- The IRB should determine how a child is defined within the local jurisdiction and whether local laws defining who is an adult differ from United States laws. The IRB must also specify how researchers are to document “legal age” for giving consent (e.g., this comes up often with research on adolescents and reproductive health issues).
- In addition to the obvious necessity of conducting the informed consent process in the local language, the IRB review should address whether there are special dialects that need to be included. Translation of the informed consent documents should be performed by a qualified translator. Interpretation of the informed consent dialogue should not be performed by a family member or other individual who has a personal relationship with the participant. For more information, see SOP 28.13.
- Literacy levels and diverse cultural experience may affect individuals in their ability to understand new concepts such as randomization, experiment versus treatment, and use of placebos. Thus, the IRB should

evaluate whether the language and concept level is appropriate. In some cases, supplementary materials such as diagrams, pictures, and tools to communicate the concept of “chance,” may be needed.

- In cases where subjects do not read and write, or when signing documents may be a violation of local norms or customs, researchers and the IRB should consider alternate methods of documenting consent. Thumbprints, marking an “x,” or an interviewer signing a statement attesting that oral consent was given by the subject are all possible modes of documenting consent in such cases.
- The question of compensation to the participant should also receive culturally-specific review. The investigator should provide clear evidence that the incentive is not excessive in the local context. Some comparison metric is needed when incentives are described (e.g., \$3 may seem small, but could be more than a day’s wage: thus, an investigator should describe the incentive relative to a day’s wage or cost of a meal, etc.).

#### 29.5 Researcher safety

While not an IRB issue per se, attention should be paid to research proposed to be conducted in dangerous areas, including countries on the US Department of State Travel Warnings and Consular Information Sheets. In particular, students may not be allowed to travel to these countries under University auspices. Specific concerns should be addressed with the Office of the Provost or the Office of University Counsel.

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SOP Title:	<b>Special Topics: Research Subject Groups</b>		
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FDA regulations and the Common Rule require IRBs to give special consideration to protecting the welfare of vulnerable subjects. At the same time, there are also requirements that members of specific populations be permitted or encouraged to become human research subjects to ensure that specific populations are adequately represented in research and have access to potential benefits of such research. For example, inclusion pressures may emerge from NIH grant programs that require applicants to address how underrepresented minorities will be included. The IRB is required to ensure that it has adequate board representation or the input of appropriate external consultants to consider specific kinds of research involving these vulnerable populations in a satisfactory manner.

#### 30.1 Elements to consider in research involving vulnerable subjects

- The methods of recruitment, selection and the inclusion/exclusion criteria should be considered by the IRB, as should informed consent, the confidentiality of data, and the willingness of the subjects to volunteer.
- Group characteristics such as economic, social, physical and environmental conditions should be considered to ensure that the research includes appropriate safeguards for the protection of vulnerable subjects.
- Applicable laws that bear on the decision-making abilities of potentially vulnerable populations should be considered.
- Research studies involving potentially vulnerable subject groups should have adequate procedures in place for assessing and ensuring subjects' capacity, understanding and their ability to participate in the consent process. In some cases, researchers should be expected to take additional measures to enhance the consent process for potentially vulnerable subjects.
- Whether or not additional safeguards are necessary to protect vulnerable subjects. Such safeguards could include IRB monitoring of the consent process or the creation of a waiting period between contact and enrollment to allow for family questions.

#### 30.2 Pregnant women, human fetuses and neonates

For further information see SOP 33.0, Research on Pregnant Women, Human Fetuses and Neonates.

#### 30.3 Prisoners

For information on the special considerations regarding research involving prisoners, see SOP 34.0, Research Involving Prisoners.

#### 30.4 Children

For further information on research involving children, see SOP 35.0, Research Involving Children.

#### 30.5 Decisionally impaired subjects

Decisionally impaired persons are those who have a diminished capacity for autonomous decision making due to a psychiatric, organic, developmental or other disorders that affect cognitive or emotional functions. "Incompetence" is a finding of a court of law and results in the appointment of a legally authorized representative for the individual judged incompetent by the court. While some decisionally impaired

persons may have been declared legally incompetent and may have a court-appointed legally authorized representative, this is not necessarily the case for all decisionally impaired persons

For definitions and guidance on who may serve as a legally authorized representative, see SOP 28.11 Surrogate Consent for Subjects Who are Decisionally Impaired.

Decisionally impaired persons may not be enrolled in research without the prior approval of the IRB. Such approval should be noted by the findings of the IRB and by the approval of a consent form with a signature line for a legally authorized representative.

Apart from the question of who may give legal permission for research participation by subjects who are decisionally impaired, there are many issues the IRB should consider in deciding whether to approve enrollment of decisionally impaired persons in a research study. These include:

1. Are decisionally impaired persons suitable subjects for the project? While the federal regulations do not specifically address additional protections for decisionally impaired subjects, it may be useful for the IRB to review proposed studies within the risk-benefit framework established for research involving children, as another vulnerable population lacking capacity for consent (i.e., Subpart D). Thus, enrollment of decisionally impaired subjects would generally be limited to categories of research that involve:
  1. no more than minimal risk (analogous to 45 CFR 46.404); or
  2. greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (~405); or
  3. a minor increase over minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge of vital importance for the understanding or amelioration of the subject's disorder or condition (~406).
2. What are the available alternatives to research participation? Is the risk-benefit balance at least as favorable as that presented by those alternatives?
3. If surrogate consent will be used, will assent of the subject also be required?
4. Are there circumstances under which a surrogate decision maker may enroll a decisionally impaired individual in the study over the individual's objection or resistance?
5. Can the consent process be structured to be appropriate and effective within the limits of the individual's decisional capacity?
6. Who will determine capacity of individual subjects to give consent? For example, the IRB might consider requiring an independent assessment by a trained professional from outside the research team (e.g., psychiatry consult service).

### 30.6 Research involving other potentially vulnerable adult subjects

The IRB should be sensitive to the vulnerability of subjects resulting from unique socioeconomic factors. For example, an offer of financial compensation for participation in research may be interpreted as exploitive when directed toward impoverished subjects.

Additionally, cultural factors may affect the ability of some subjects to give informed consent. For example, if a local leader has urged (or required) participation in research, prospective subjects may not feel free to opt out of the study.

Finally, the IRB should consider any individuals who are in the midst of a traumatic or emergency situation (e.g., someone experiencing the catastrophic loss of a family member or a home) or otherwise under emotional duress to be potentially vulnerable.

### 30.7 Research involving decedents

Decedents are not human research subjects under the Common Rule; however, research on decedents may create living third-party research subjects. See Third party research subjects below and also SOP 28.19, Family History Research. Additionally, HIPAA specifically addresses using the protected health information (PHI) of decedents for research purposes; see SOP 27.0, HIPAA and IRB Review.

### 30.8 Third party research subjects

Because the Common Rule defines a human subject as a living individual about whom an investigator obtains identifiable private information, the family members or others identified and described by the primary subject may be human subjects under the regulations if the investigators obtain identifiable private information about them. Third parties may become human subjects when researchers acquire private, factual information about those parties (as opposed to opinions of the primary subject about third parties).

In addition to considering the nature and volume of the information acquired by researchers about third parties, the IRB should:

- determine whether third party information is collected incidentally or deliberately;
- review the proposed uses of the third party information collected;
- consider the significance of the implications to be drawn from the third party information collected;
- evaluate the ability of the investigators to ensure that confidentiality is maintained for the third parties, which might include PIs recording the information in a manner that protects the identities of the third parties;
- consider the potential impact on the primary subject if a third party is classified as a human research subject.

Taking all of these considerations into account, IRBs should consider whether third parties are human subjects and, if so, determine whether their informed consent is required or can be waived according to 45 CFR 46.116(d).



### 30.9 Employees, students or trainees as research subjects

Employees, students and trainees of TAMUT may be vulnerable subjects, depending on the context of the specific research study proposed, because of the potential for perceived coercion in the student/trainee or employment relationship (regardless of the researcher's intentions). This is particularly the case if the research is being conducted by investigators in the employee's or student's department or in any situation in which (1) recruitment materials are presented in a manner that could appear to the potential subjects to be closely related to their individual student/trainee or employment relationships, and (2) a power differential and/or dependency relationship exists between the researcher and a prospective subject. If the proposed subjects are a part of the research team there may also be inherent conflicts of interest in their participation. Therefore, only in compelling circumstances will students or employees directly supervised by the researcher be allowed to participate in the research project. Compelling circumstances would be those in which (1) the participation of these individuals holds out reasonable likelihood of direct benefit to these subjects (e.g., treatment protocol for condition experienced by the employee, student or trainee) or (2) the risks to and vulnerabilities of these employees, students or trainees have been eliminated or have been minimized to the satisfaction of the human subjects. Particular attention should be paid to recruitment of students from subject pools mandated as a condition of course enrollment (See also SOP 23.0).

When reviewing any protocol that may seek to recruit human subjects from among the research entity's employee, student or trainee populations, the IRB's review should include consideration of the potential vulnerabilities of such subject groups in the context of the specific proposed study.

#### 30.9.1 Parental Permission for TAMUT Students in Minimal Risk Research

When research studies broadly recruit college students as subjects, it is likely that some students will be children as defined by the regulations. Under these circumstances, parental permission may not be a reasonable requirement to protect older adolescents/young adults who volunteer for minimal risk research. Unless there are mitigating circumstances, the IRB may routinely waive parental permission for minimal risk studies that enroll TAMUT students, some of whom may be younger than 18 years old. This determination should be made on a study-by-study basis, and findings documented in accordance with 45 CFR 46.408.

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SOP Title:	<b>Research Involving Pregnant Women, Human Fetuses and Neonates</b>		
SOP Number:	31.0	Current Version Date:	9/30/14

In addition to the general requirements for review of research by the IRB, prior research with animal subjects, and, if feasible, research with nonpregnant persons should form the basis of the risk/benefit assessment for fetal research. The proposed research should seek information not obtainable in any other way. If abortion is involved, the investigators may have no part in either the decision to abort or decisions about the timing or the method to be used; no change in the abortion procedure that would present more than minimal risk to the fetus or its mother can be introduced for research purposes. No monetary or other inducements (e.g., free care) may be offered to a woman to induce her to terminate her pregnancy for research purposes.

Pregnant women may be involved in several categories of research. IRB duties differ in each category, but the primary objectives are assessing: (1) whether the research holds out the prospect of direct benefit for the mother's health or for the fetus; and (2) the risks to the woman and to the fetus or infant. These requirements do not apply when the enrollment of pregnant women is entirely coincidental and bears no relationship to the research (e.g., a minimal risk survey of 1000 respondents and 1 happens to be pregnant).

### 31.1 Conditions required for pregnant women or fetuses to be involved in research

- 31.1.1 Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; (45 CFR 46.204(a))
- 31.1.2 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 that cannot be obtained by any other means; (45 CFR 46.204(b))
- 31.1.3 Any risk is the least possible for achieving the objectives of the research; (45 CFR 46.204(c))
- 31.1.4 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 in 45 CFR 46.204(d). See also SOP 28.0, Informed Consent.
- 31.1.5 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 accordance with the informed consent provisions. 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; (45 CFR 46.204(e)) (See SOP 28.0, informed consent)
- 31.1.6 Each individual providing consent under SOP 33.1.4 or 33.1.5 is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; (45 CFR 46.204(f))
  - 31.1.7 For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of SOP 35.0, Research Involving Children (45 CFR 46.204(g))
  - 31.1.8 No inducements, monetary or otherwise, will be offered to terminate a pregnancy; (45 CFR 46.204(h))
  - 31.1.9 Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; (45 CFR 46.204(i))
  - 31.1.10 Individuals engaged in the research will have no part in determining the viability of a neonate. (45 CFR 46.204(j))
- 31.2 Conditions required for neonates of uncertain viability and nonviable neonates to be involved in research
- 31.2.1 Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates; (45 CFR 46.205(a)(1))
  - 31.2.2 Each consenting individual under SOP 33.3 and 33.4 is fully informed regarding the reasonably foreseeable impact of the research on the neonate. (45 CFR 46.205(a)(2))
  - 31.2.3 Individuals engaged in the research will have no part in determining the viability of a neonate. (45 CFR 46.205(a)(3))
  - 31.2.4 The requirements of both SOP 33.3 and 33.4 have been met as applicable. (45 CFR 46.205(a)(4))

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SOP Title:	<b>Research Involving Prisoners</b>		
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### 32.1 Definition of research addressed in this section

A “prisoner” is 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 that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. [45 CFR 46.303(c)]

The regulations covering research involving prisoners apply not only to research that targets prisoners or the prison setting, but also to subjects who become incarcerated following their enrollment or subjects for whom their incarceration is coincidental with their research involvement, (e.g., a prisoner with cancer enrolled in a treatment-oriented study that involves no other prisoners).

### 32.2 Issues to be addressed in reviewing research involving prisoners

When a proposal proposes to enroll prisoners as a study population, the IRB should ascertain whether that population was chosen simply out of convenience to the investigator. Because the population is relatively stable and the life is routine, prisons have in the past seemed ideal environments in many ways for the conduct of certain types of research. Some procedures that would inconvenience free subjects are not a burden to prisoners. Since prison pay scales are notably lower than those in the free world, the cost of using prisoners as subjects may be less than using those who are not prisoners. And, unlike the general civilian population, they are all in one place. However, the nature of incarceration may conflict with the ethical principle of autonomy.

The primary issue surrounding the participation of prisoners in research is whether prisoners have a real choice regarding their participation in research, or whether their situation prohibits the exercise of free choice. A secondary issue is whether confidentiality of participation and of data can be adequately maintained in the prison. These issues must be evaluated by both the TAMUT IRB as well as the Texas Department of Correction (DOC), for studies that involve its prisoner population. The PI is responsible for communicating with the DOC prior to submission of an IRB application.

The circumstances common in prisons create environments in which the offer to participate in research may give rise to undue influence in favor of participation. The lack of control allowed prisoners and their desire to obtain the advantages offered to those who agree to participate may impair their ability to weigh fairly the risks and benefits involved in participation. An example of a situation potentially presenting undue influence may be one in which research participants are moved to special units where they are given additional medical care and where the living conditions may be better than those provided to the general prison population. Other rewards for participation, such as offering parole or a reduction in sentence, would likewise constitute an undue inducement. Even the opportunity to leave the prison cell and interact with people from outside the prison may act as an undue inducement to participate in research.

Another question is whether prisoner-subjects can ethically be paid for participation, and if so, how much? Where prisoners must earn money to purchase the means by which to maintain their health and personal hygiene, and one way to earn that money is by participating in research, the potential for undue influence also exists. In non-prison settings, paying subjects to participate in research is considered ethically acceptable, so long as it is commensurate with the time, effort or inconvenience involved. Paying prisoners the same amount that would be paid to non-prisoners may, however, be seen as unduly influential in a setting where inmates can earn only a small fraction of that amount for any other "work" activity. On the other hand, paying prisoners a fraction of what would be paid to non-prisoners can be seen as exploitive.

In addition to problems of undue inducement, the involvement of prisoners in research raises questions of burden and benefit. Prisoners should neither bear an unfair share of the burdens of participating in research, nor should they be excluded from its benefits, to the extent that voluntary participation is possible.

Minimal risk, as defined for studies involving prisoners, 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. In assessing risk to prisoners, the IRB should ensure that the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers. [45 CFR 46.303 (d)]

Confidentiality is extremely difficult to maintain in a prison environment. In prisons, people do not move about freely; the movements of prisoners are carefully tracked. When inmates are moved around (e.g., to go to a research appointment), everyone will know about it. Prison records, including health care records, are accessible to persons who in other settings would not have access to such personal information, thus compromising the security of confidential information.

Generally, research involving prisoners does not qualify for expedited review; however, in the event that such a research study does qualify for expedited review, a prisoner representative should be one of the designated reviewers. The exemptions under 45 CFR 46.101 do not apply to research involving prisoners.

#### 32.2.1 Research involving direct interaction with prisoners reviewed by the expedited procedure

- Research involving direct interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
  - The prisoner representative must concur with the determination that the research involves no greater than minimal risk.
  - The prisoner representative must review the research as a reviewer, designated by the chair, or as a consultant. The prisoner representative review may be as the sole reviewer or in addition to another reviewer, as appropriate.
  - Review of modifications and continuing review must use the same procedures for initial review outlined above, including the requirements related to the prisoner representative.

For research that does not involve direct interaction with prisoners (e.g., existing data, record review) reviewed by the expedited procedure:

- Research that does not involve direct interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that

the research involves no greater than minimal risk for the prison population being studied.

- Review by a prisoner representative is not required.
- The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair. Review of modifications and continuing review must use the same procedures as initial review.

### 32.3 Required findings

When an IRB is reviewing a protocol in which a prisoner is a subject, the IRB must make, in addition to other requirements under 45 CFR 46, subpart A, seven additional findings under 45 CFR 46.305(a), as follows:

- (1) the research under review represents one of the categories of research permissible under 45 CFR 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 non-prisoner 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 IRB 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 that 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 IRB 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.

#### 34.3.1 Meeting minutes and the IRB approval letter should verify the following statement:

This study was reviewed in accordance with all applicable regulations governing human subjects research found at 45 CFR 46 (Common Rule) and 45 CFR 164 (HIPAA). In approving this study the Committee found that the study meets all criteria at 45 CFR 46.305(a)(1)–(7).

If necessary include brief, protocol-specific explanations of the IRB's rationale for each finding.

### 32.4 Permitted research involving prisoners

For research conducted or supported by HHS to involve prisoners, two actions must occur:

(1) The institution engaged in the research must certify to the Secretary (through OHRP) that the IRB designated under its assurance of compliance has reviewed and approved the research under 45 CFR 46.305, and

(2) The Secretary (through OHRP) must determine that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2). The categories of permissible research are 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;

(Note that the definition of minimal risk for prisoner research at 45 CFR 46.303(d) differs from the definition of minimal risk for other research, contained in 45 CFR 46, subpart A, 45 CFR 46.102(i))

- (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 (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the Secretary's intent to approve such research; or
- (iv) research on practices, both innovative and accepted, that 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 that may not benefit from the research, the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the Secretary's intent to approve such research.
- (v) an additional fifth category of permissible research is provided by HHS Secretarial waiver for certain epidemiological research conducted or supported by HHS. The criteria for this category are that the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease. The institution still must review the research under subpart C and certify to OHRP that an appropriately constituted IRB has reviewed the proposal and made all other required findings under HHS regulations at [45 CFR 46.305\(a\)](#) and receive OHRP authorization prior to initiating any research involving prisoners. All of the other requirements of subpart C apply to research in this category.

34.4.1 Meeting minutes and the IRB approval letter should indicate which of the four categories of permissible research involving prisoners in 45 CFR 46.306(a)(2) is applicable to the research (i, ii, iii or iv), for example:.

The IRB determined that the study meets criteria at 46.306(a)(2)(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."

### 32.5 Certification of prisoner research

Institutions that conduct DHHS-supported research involving prisoners as human subjects must take several steps to certify that the research is permissible according to federal regulations. The institution must certify to OHRP that the IRB has made the seven findings required under 45 CFR 46 305(a), (see SOP 34.3 above), including the finding that the proposed research represents one of the permissible categories of research under 45 CFR 46 306(a)(2), (see SOP 34.4 above). The institution must send OHRP a certification letter to that effect which should include the name and address of the institution and specific identification of the research protocol including the relevant grant number. OHRP also encourages the institution to include the following information in its prisoner research certification letter:

- Title of the Protocol and PI name
- Purpose of the study
- OHRP Assurance number for Engaged Site
- IRB Registration number
- Title of DHHS Grant
- PI named on DHHS grant
- DHHS Grant Award Number
- DHHS Funding Agency Name
- Funding Agency Grants/Program Officer Name/Phone
- Site(s) Where Research Will be Conducted
- IRB for TAMUT Site Where Research Will be Conducted
- OHRP Assurance # for TAMUT
- Version of Consent Form
- Date of IRB Meeting where IRB approved findings for research to be certified to OHRP, including a brief chronology that encompasses the date of initial IRB review and date of Subpart C review.
- Reason for IRB Review (Choose most applicable from the following; edit as necessary)
  - a. Amendment to non-prison study in which subject(s) has become incarcerated and PI wishes to continue the subjects(s) participation in the study.
  - b. Non-prison study with at-risk population (e.g., probationers, substance abusers).
  - c. Non prison study, majority of study population are non-prisoners but PI seeks to enrolls some prisoners (as defined in 45 CFR 46.303(c))
  - d. Minimal risk DHHS conducted or supported epidemiologic research, majority of study population are non-prisoners but PI seeks to enroll some prisoners (prisoners are not the focus of the study) and the sole purpose of the study is either: (1) to describe the prevalence or incidence of a disease by identifying all cases, or (2) to study potential risk factor associations for a disease



- e. Initial Subpart C review of study designed to be conducted in a prison or using prisoners (as defined in 45 CFR 46.303 (c)) – PI seeks to enroll already incarcerated subjects.

Under its authority at 45 CFR 46.115(b), OHRP requires the institution to also submit to OHRP a copy of the research proposal so OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2) and, if so, which one. Copies of the following materials should be enclosed for OHRP review when relevant:

- a. TAMUT IRB application
- b. Consent form(s)
- c. Master Protocol
- d. Copy of grant application
- e. Approval letter from the TAMUT IRB
- f. Approval from any other IRBs, if relevant to the project's oversight where prisoners will be studied
- g. FWA information, where applicable for external sites
- h. Minutes from the relevant TAMUT IRB meeting(s)

### 32.6 Modifications and Continuing Review

Minor modifications to research may be reviewed using either of the two expedited procedures described below, with selection of the appropriate expedited procedure to be based on the type of modification proposed.

- Modifications involving more than a minor change must be reviewed by the convened IRB and must use the same procedures for initial review, including the responsibility of the prisoner representative to review the modification and participate in the meeting (as described above).
- Continuing review must use the same procedures for initial review, including the responsibility of the prisoner representative to review the continuing review materials and participate in the meeting (as described above).
  - If no subjects have been enrolled, the research may receive continuing review using the expedited procedure under expedited category #8.

IRBs using the expedited procedure to review research involving prisoners may use either of the following two options:

For research involving direct interaction with prisoners:

- Research involving direct interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
  - The prisoner representative must concur with the determination that the research involves no greater than minimal risk.
  - The prisoner representative must review the research as a reviewer, designated by the chair, or as a consultant. The prisoner representative review may be as the sole reviewer or in addition to another reviewer, as appropriate.
  - Review of modifications and continuing review must use the same procedures for initial review outlined above, including requirements related to the prisoner representative.

For research that does not involve direct interaction with prisoners (e.g. existing data, record review):

- Research that does not involve direct interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
  - Review by a prisoner representative is not required.
  - The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair.
  - Review of modifications and continuing review must use the same procedures as initial review.

### 32.7 Subjects Who Become Incarcerated While Enrolled in a Research Study

If a subject becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C:

- When Subpart C applies:
  - Confirm that the subject meets the definition of a prisoner.
  - Terminate enrollment or review the research study under Subpart C if it is feasible for the subject to remain in the study.
  - Before terminating the enrollment of the incarcerated subject the IRB should consider the risks associated with terminating participation in the study.
  - If the subject cannot be terminated for health or safety reasons
    - Keep the subject enrolled in the study and review the research under Subpart C.
      - If some of the requirements of Subpart C cannot be met, but it is in the best interests of the subject to remain in the study, keep the subject enrolled and inform OHRP of the decision along with the justification.
    - Remove the subject from the study and keep the subject on the study intervention under an alternate mechanism such as compassionate use, off label use, etc.
- When Subpart C does not apply describe equivalent protections:
  - Confirm that the subject meets the definition of a prisoner.
  - Decide whether it is in the best interests of the subject to remain in the study or to terminate enrollment.
  - If it is in the best interests of the subject to remain in the study, keep the subject in the study and review the research at next meeting of the convened IRB.

Note: If a subject is incarcerated temporarily while enrolled in a study:

- If the temporary incarceration has no effect on the study, keep the subject enrolled.
- If the temporary incarceration has an effect on the study, handle according to the above guidance.

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SOP Title:	<b>Research Involving Children</b>		
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IRBs reviewing research involving children as subjects must consider the benefits, risks, and discomforts inherent in the proposed research and assess their justification in light of the expected benefits to the child-subject or to society as a whole. In calculating the degree of risk and benefit, the IRB should weigh the circumstances of the subjects under study, the magnitude of risks that may accrue from the research procedures, and the potential benefits the research may provide to the subjects or class of subjects. An IRB member or a consultant to the IRB with appropriate background and experience (in child development or pediatric medicine or other relevant topic) should be involved in the review of any protocol involving children.

Procedures that usually present no more than minimal risk to a healthy child include: urinalyses, obtaining small blood samples, EEGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests. The IRB must also consider the extent to which research procedures would be a burden regardless of whether the child is accustomed to the proposed procedures. The assessment of risk and burden should also be informed by an understanding of the anticipated physical health, emotional maturity and other internal and external factors of the proposed population of pediatric subjects.

### 33.1 Research in health care settings

With respect to pediatric research involving health care interventions or medical procedures, the assessment of the probability and magnitude of the risk may be different in sick children and may vary depending on the diseases or conditions the subjects may have. For example, obtaining blood samples from a hemophiliac child may present more than minimal risk to the child. On the other hand, IRBs might determine that children suffering from chronic illnesses who are accustomed to invasive procedures may not incur significant additional risk by involvement in research procedures related to their ongoing treatment, in contrast to children who have not had such experiences. Sick children should not be asked or expected to assume greater risks merely because they are already undergoing procedures or treatments.

In assessing the possible benefits of research intervention, the IRB should consider the variability in health statuses among potential subjects. For example, a potential subject might be a normal, healthy child, or a child who has been exposed to a disease or a toxin (e.g., meningococcus or lead) where it is known that a percentage of the children exposed will actually experience untoward consequences. A child may also be in an early state of disease, for example, an HIV-infected child, or may actually suffer from disease or other significant medical condition. Thus, the IRB must take into account the current health status of a child and the likelihood of progression to a worsened state without research intervention.

### 33.2 Research in school settings

With respect to non-health care related research involving children in an educational setting, studies should be carefully examined to determine both the level of risk and the potential benefit for the subjects. The risks involved in social science research are rarely physical; however, children may be susceptible to emotional and psychological risks as well as risks to their social standing. In addition to these considerations, the informed consent process for children within an educational setting is often quite

complex. As part of its review, the IRB would generally expect to see the researcher's plan to approach and obtain permission from the school district, the school site (e.g., principal or headmaster), and the classroom teacher (when applicable). In addition, provisions should be made for obtaining the permission of parent(s) of each participating child and the assent of the child subject, in accordance with the federal regulations. (See also 28).

The Protection of Pupil Rights Amendment (PPRA) provides parents with some rights over the review of third-party survey research and instructional materials developed by researchers when funded by the U. S. Department of Education. The PPRA applies when the subject matter includes: (1) political affiliation; (2) mental and psychological problems potentially embarrassing to the student and/or family; (3) sexual behavior and attitudes; (4) illegal, anti-social, self-incriminating and demeaning behavior; (5) critical appraisals of other individuals with whom respondents have close family relationships; (6) legally recognized privileged or analogous relationships, such as those with lawyers, physicians and ministers; or (7) income, other than that needed to determine eligibility for participation in a program or for receiving financial assistance under such a program.

### 33.3 Categories of research involving children that may be approved by IRBs

- 33.3.1 Research not involving greater than minimal risk. [45 CFR 46.404; 21 CFR 50.51]
- 33.3.2 Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual subject. Research in this category is approvable provided: (a) the risk is justified by the anticipated benefit to the subject; and (b) the relationship of risk to benefit is at least as favorable as any available alternative approach. [45 CFR 46.405; 21 CFR 50.52]
- 33.3.3 Research involving greater than minimal risk with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. Research in this category is approvable provided: (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 settings; and (c) the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition. [45 CFR 46.406; 21 CFR 50.53]
- 33.3.4 Research that is not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Research that is not approvable under 45 CFR 46.404, 46.405, or 46.406 may be conducted or funded by DHHS provided that the IRB, and the Secretary, after consultation with a panel of experts, finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a significant problem affecting the health and welfare of children. The panel of experts must also find that the research will be conducted in accordance with sound ethical principles. [45 CFR 46.407; 21 CF 50.54]

In all cases, the IRB must determine that adequate provisions have been made for soliciting the assent of children and the permission of their parents or guardians. (See SOP 28.9)

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### 33.3.5 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.

### 33.3.6 Emancipation

According to Texas Law, emancipation alters the legal status of a minor, rendering the minor an adult for all intents and purposes. The effect of a final decree of emancipation is that the child has the same right to make contracts and conveyances, to sue and to be sued, and to transact business as if they were an adult.

#### 33.3.6.1 Additional circumstances that allow a child to be treated as an adult:

##### Certain Medical Conditions

A minor can give consent to a physician licensed to practice in Texas for medical treatment or care in limited circumstances. Specifically, a minor can consent when the services are for the "prevention, diagnosis and treatment of (i) venereal disease and other diseases reportable under Texas law (See Appendix I); (ii) pregnancy, (iii) abuse of controlled substances or alcohol, and (iv) emotional disturbance."

As the above exceptions show, a minor is generally able to give consent only when not allowing him/her to do so -- or requiring parental or guardian consent -- would cause worse

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harm than allowing treatment (i.e., through the spread of communicable disease or through endangerment of others because of the minor's condition). In such contexts, exceptions to the general rule requiring parental consent to non-emergency medical treatment have been created.

#### Marriage or Military Service

Apart from the formal emancipation process, there are two other methods by which a minor may alter his/her legal status. First, a minor who is legally married will be treated as an adult. Second, a minor who is serving in the armed forces of the United States will be treated as an adult.

#### 33.3.7 Age of majority

Under Texas state law, a child legally becomes an adult at the age of 18 and can then consent to participate in a research study. For research conducted in other states or countries, the investigator should determine the age of majority in those locales. One possible source of this information is a state's social services department. For further information on research involving children, refer to 45 CFR 46. (See Appendix B)

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SOP Title:	<b>Reporting to Institutional Officials and External Agencies: Unanticipated Problems, Terminations, Suspensions, and Non- Compliance</b>		
SOP Number:	34.0	Current Version Date:	9/30/14

TAMUT complies with all applicable local and State laws and federal regulations that pertain to reporting requirements. DHHS and FDA regulations require prompt reporting to the appropriate agency of any of the situations listed below:

- unanticipated problems involving risks to subjects or others (See SOP 19)
- serious or continuing noncompliance (See SOP 22)
- suspensions or terminations of previously approved research (See SOP 18.2)

TAMUT's Federalwide Assurance (FWA) with OHRP is restricted to research funded by the federal DHHS. However, the same process for conducting investigations and taking actions by the IRB will apply to all research regardless of funding source. TAMUT reserves the right to voluntarily report any event that is not associated with federal funding to OHRP. All reports will be sent to the Dean of ORSP, even if external reporting is not required.

34. 1. After completing an investigation, a report will be drafted promptly. It is the aim of ORSP to have a draft report sent to the appropriate agency within 30 days from the time the event is resolved to the satisfaction of the IRB. The report will be drafted by the IRB Chair and the Dean of ORSP. All correspondence with any federal agency will be sent on behalf and with knowledge of the Institutional Official. The draft report will be reviewed by the Office of University Counsel before submission to the appropriate federal agency. Following this internal review process, the report will be signed and sent by the IRB Chair.

34. 1. 1. The report should contain the following elements:

- Nature of the event
- Findings of the investigation
- Action plan to prevent future occurrence
- Actions taken by the IRB and/or the University and final resolution
- Reasons for the IRB's actions
- Plans for continued review, if warranted

34. 1. 2. When indicated, the report will be sent to the appropriate federal agency, which may include:

- OHRP, when research is covered by DHHS regulations
- FDA, when the research is FDA-regulated
- Other federal agencies, when the research is overseen by those agencies and they require reporting separate from OHRP
- Reports to funding agencies (e.g., NIH) will be sent under separate cover by the Institutional Official.

34. 1. 3. The report will be copied to the following individuals:

- President
- Dean of ORSP
- PI
- Vice president of Academic and Student Affairs
- Office of Compliance
- Office of University Counsel

In addition, copies may be sent, when appropriate, to:

- PI's Program Coordinator, Dean or Director
- Other interested parties, at the discretion of the Dean of ORSP

The Institutional Official is not responsible for reporting to federal agencies already aware of the event through other mechanisms, such as written reports by the investigator, sponsor or another organization.

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SOP Title:	<b>Broad Consent</b>		
SOP Number:	35.0	Current Version Date:	8/01/19

### 35.1 Broad Consent [§46.116(d)]

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) is permitted under the revised Common Rule. Broad consent is not currently recognized in FDA regulation or guidance.

### 35.2 General requirements for obtaining broad consent

When obtaining broad consent, the general requirements for informed consent described in section 26 apply except as noted. The following elements of broad consent [§46.116(d)] shall be provided to each subject or the subject's *legally authorized representative* (henceforth, LAR):

1. A description of any reasonably foreseeable risks or discomforts to the subject;
2. A description of any benefits to the subject or to others which may reasonably be expected from the research;
3. A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained;
4. 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;
5. For research involving biospecimens, a statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
6. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen);
7. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description *must include* sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;
8. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, *and* the types of institutions or researchers that might conduct research with the identifiable private information or identifiable

biospecimens;

9. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (period of time could be indefinite), *and* a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (period of time could be indefinite);
10. Unless the subject or LAR will be provided details about specific research studies, a statement that they **will not be informed** of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;
11. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and
12. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of research-related harm.

### 35.3 Applications seeking to undertake research and obtain broad consent

In their submission to the IRB, investigators seeking broad consent must include the following in their applications:

1. information regarding the circumstances under which broad consent will be obtained
2. the proposal for tracking of responses,
3. the proposed consent form(s) (or oral script if a waiver of documentation of consent is sought), and
4. any other consent materials (e.g., information sheet, audiovisual materials, etc.).

The TAMUT IRB will review the information provided to ensure that all requirements are satisfied. The outcome of the IRB's review will be communicated to the investigator in writing following the procedures outlined in the SOP manual.

### 35.4 Applications seeking to undertake research using identifiable information or biospecimens for which broad consent was obtained

When investigators propose research involving the use of identifiable private information and/or identifiable biospecimens research for which broad consent was obtained, the investigators must include the following in their IRB applications:

1. documentation of the IRB approval for the storage and maintenance of the information or specimens, and
2. a copy of the consent form and/or other materials relevant to the

receipt of broad consent.

The TAMUT IRB will review the information provided to ensure all requirements are satisfied. The outcome of the IRB's review will be communicated to the investigator in writing following the procedures outlined in the SOP manual.

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## Appendix A: The Belmont Report

<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>

**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.

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

*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.*

### Contents

#### Ethical Principles and Guidelines for Research Involving Human Subjects

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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<sup>1</sup> intended to assure that research involving human subjects would be carried out in an ethical manner.

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

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

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

## **Part A: Boundaries Between Practice & Research**

### **A. Boundaries Between Practice and Research**

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

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.<sup>2</sup> 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.<sup>3</sup>

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

## **Part B: Basic Ethical Principles**

### **B. Basic Ethical Principles**

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

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

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

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

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

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

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

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

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

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



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

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

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

## **Part C: Applications**

### **C. Applications**

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

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

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

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

selected, the person responsible for the research, etc.

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

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

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

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

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

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

**Voluntariness.** An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue

influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

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

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

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

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

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

The Systematic Assessment of Risks and Benefits-- It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less

subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

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

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

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

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

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

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently

compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

<sup>1</sup> 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.

<sup>2</sup> 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.

<sup>3</sup> 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 B: 45 CFR 46

## 45 CFR 46

### §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:<sup>1</sup>

(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 a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(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 or 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 Protection from Research Risks, National Institutes of Health, Department of Health and



Human Services (DHHS), and shall also publish them in the Federal Register or in such other manner as provided in Department or Agency procedures.<sup>1</sup>

<sup>1</sup> Institutions with DHHS-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, fetuses, pregnant women, or human in vitro fertilization, Subparts B and 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.

#### **§46.102 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, (e.g., 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 (e.g., 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 (e.g., 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 (e.g., 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.

(j) Certification means the official notification by the institution to the supporting Department or Agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

**§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 Protection from Research Risks, National Institutes Health, DHHS, and approved for Federal-wide use by that office. When the existence of an DHHS-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 Protection from Research Risks, National Institutes of Health, DHHS.

(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 record keeping 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 a DHHS-approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Protection from Research Risks, National Institutes of Health, DHHS.

(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 9999-0020.)

#### **§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 9999-0020.)

**§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 Protection from Research Risks, National Institutes of Health, DHHS, Bethesda, Maryland 20892.

(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 non-expedited 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.

**§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 (e.g., 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 disable 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 or 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 9999-0020.)

#### **§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 9999-0020.)

**§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 9999-0020.)

#### **§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 9999-0020.)

#### **§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**

#### **§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 Sec. 46.101(b)(1) through (6) are applicable to this subpart.

(c) The provisions of Sec. 46.101(c) through (i) are applicable to this subpart. Reference to State or local laws in this subpart and in Sec. 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 Sec. 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 Sec. 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 Sec. 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 Sec. 46.204 or Sec. 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 (e.g.: 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 Sec. 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 DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects**

#### **§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.

**§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 Secretary, 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:

(A) 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;

(B) 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;

(C) research on conditions particularly affecting prisoners as a class (e.g., 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

(D) 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 DHHS Protections for Children Involved as Subjects in Research**

##### **§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 no substantive, 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.

#### **§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.**

DHHS 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.**

DHHS 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.**

DHHS 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.**

DHHS 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 (e.g.: 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 (e.g., 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 inappropriate 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.

## Appendix C: 21 CFR 50

## 21 CFR 50

### Subpart A— General Provisions

#### Section 50.1 Scope.

(a) This part applies to all clinical investigations regulated by the Food and Drug Administration under sections 505(i) 507(d), and 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Additional specific obligations and commitments of, and standards of conduct for, persons who sponsor or monitor clinical investigations involving particular test articles may also be found in other parts (e.g., 21 CFR parts 312 and 812). Compliance with these parts is intended to protect the rights and safety of subjects involved in investigations filed with the Food and Drug Administration pursuant to sections 406, 409, 502, 503, 505, 506, 507, 510, 513-516, 518 520, 706, and 801 of the Federal Food, Drug and Cosmetic Act and sections 351 and 354-360F of the Public Health Service Act.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21, unless otherwise noted. [45 FR 36390, May 30, 1980; 46 FR 8979, Jan. 27, 1981]

#### Section 50.3 Definitions.

As used in this part:

(a) *Act* means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201-902, 52 Stat. 1040 et seq. as amended (21 U.S.C. 321-392)).  
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(b) *Application* for research or marketing permit includes:

- (1) A color additive petition, described in part 71.
- (2) A food additive petition, described in parts 171 and 571.
- (3) Data and information about a substance submitted as part of the procedures for establishing that the substance is generally recognized as safe for use that results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in §§ 170.30 and 570.30.
- (4) Data and information about a food additive submitted as part of the procedures for food additives permitted to be used on an interim basis pending additional study, described in § 180.1.
- (5) Data and information about a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials described in section 406 of the act.
- (6) An investigational new drug application, described in part 312 of this chapter.
- (7) A new drug application, described in part 314.
- (8) Data and information about the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in part 320.
- (9) Data and information about an over-the-counter drug for human use submitted as part of the procedures for classifying these drugs as generally recognized as safe and effective and not misbranded, described in part 330.

- (10) Data and information about a prescription drug for human use submitted as part of the procedures for classifying these drugs as generally recognized as safe and effective and not misbranded, described in this chapter.
- (11) Data and information about an antibiotic drug submitted as part of the procedures for issuing, amending or repealing regulations for these drugs, described in § 314.300 of this chapter.
- (12) An application for a biological product license, described in part 601.
- (13) Data and information about a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, described in part 601.
- (14) Data and information about an in vitro diagnostic product submitted as part of the procedures for establishing, amending, or repealing a standard for these products, described in part 809.
- (15) An Application for an Investigational Device Exemption, described in part 812.
- (16) Data and information about a medical device submitted as part of the procedures for classifying these devices, described in section 513.
- (17) Data and information about a medical device submitted as part of the procedures for establishing, amending, or repealing a standard for these devices, described in section 514.
- (18) An application for premarket approval of a medical device, described in section 515.
- (19) product development protocol for a medical device, described in section 515.
- (20) Data and information about an electronic product submitted as part of the procedures for establishing, amending or repealing a standard for these products, described in section 358 of the Public Health Service Act.
- (21) Data and information about an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in § 1010.4.
- (22) Data and information about an electronic product submitted as part of the procedures for granting amending, or extending an exemption from a radiation safety performance standard, as described in § 1010.5.

(c) *Clinical investigation* means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies.

(d) *Investigator* means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

(e) *Sponsor* means a person who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator) and the employees are considered to be investigators.

(f) *Sponsor-investigator* means an individual who both initiates and actually conducts, alone or with others a clinical investigation, i.e., under whose immediate direction the test article is administered

or dispensed to, or used involving, a subject. The term does not include any person other than an individual, for example, corporation or agency.

(g) *Human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article as a control. A subject may be either a healthy human or a patient.

(h) *Institution* means any public or private entity or Agency (including Federal, State, and other agencies). The word facility as used in section 520(g) of the act is deemed to be synonymous with the term institution for purposes of this part.

(i) *Institutional review board (IRB)* means any board, committee, or other group formally designated by an institution to review biomedical research involving humans as subjects, to approve the initiation of and conduct periodic review of such research. The term has the same meaning as the phrase institutional review committee as used in section 520(g) of the act.

(j) *Test article* means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

(k) *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.

(l) *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.

(m) *Family member* means any one of the following legally competent persons: Spouse; parents; children (including adopted children); brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship. [45 FR 36390, May 30, 1980, as amended at 46 FR 8950 Jan. 27, 1981; 54 FR 9038, Mar. 3, 1989; 56 FR 28028, June 18, 1991; 61 FR 51497, Oct. 2, 1996; 62 FR 39440, July 23, 1997]

## **Subpart B - Informed Consent of Human Subjects**

### **Sec. 50.20 General requirements for informed consent.**

Except as provided in Secs. 50.23 and 50.24, no investigator may involve a human being as a subject in research covered by these regulations 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. [46 FR 8951, Jan. 27, 1981, as amended at 64 FR 10942, Mar. 8, 1999]

### **Sec. 50.23 Exception from general requirements.**

(a) The obtaining of informed consent shall be deemed feasible unless, before use of the test article (except as provided in paragraph (b) of this section), both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

- (1) The human subject is confronted by a life-threatening situation necessitating the use of the test article.
- (2) Informed consent cannot be obtained from the subject because of an inability to



communicate with, or obtain legally effective consent from, the subject. (3) Time is not sufficient to obtain consent from the subject's legal representative. (4) There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

(b) If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

(c) The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRB within 5 working days after the use of the test article.

(d) (1) Under 10 U.S.C. 1107(f) the President may waive the prior consent requirement for the administration of an investigational new drug to a member of the armed forces in connection with the member's participation in a particular military operation. The statute specifies that only the President may waive informed consent in this connection and the President may grant such a waiver only if the President determines in writing that obtaining consent: Is not feasible; is contrary to the best interests of the military member; or is not in the interests of national security. The statute further provides that in making a determination to waive prior informed consent on the ground that it is not feasible or the ground that it is contrary to the best interests of the military members involved, the President shall apply the standards and criteria that are set forth in the relevant FDA regulations for a waiver of the prior informed consent requirements of section 505(i)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)(4)). Before such a determination may be made that obtaining informed consent from military personnel prior to the use of an investigational drug (including an antibiotic or biological product) in a specific protocol under an investigational new drug application (IND) sponsored by the Department of Defense (DOD) and limited to specific military personnel involved in a particular military operation is not feasible or is contrary to the best interests of the military members involved the Secretary of Defense must first request such a determination from the President, and certify and document to the President that the following standards and criteria contained in paragraphs (d)(1) through (d)(4) of this section have been met. (i) The extent and strength of evidence of the safety and effectiveness of the investigational new drug in relation to the medical risk that could be encountered during the military operation supports the drug's administration under an IND. (ii) The military operation presents a substantial risk that military personnel may be subject to a chemical, biological, nuclear, or other exposure likely to produce death or serious or life-threatening injury or illness. (iii) There is no available satisfactory alternative therapeutic or preventive treatment in relation to the intended use of the investigational new drug. (iv) Conditioning use of the investigational new drug on the voluntary participation of each member could significantly risk the safety and health of any individual member who would decline its use, the safety of other military personnel, and the accomplishment of the military mission. (v) A duly constituted institutional review board (IRB) established and operated in accordance with the requirements of paragraphs (d)(2) and (d)(3) of this section, responsible for review of the study, has reviewed and approved the investigational new drug protocol and the administration of the investigational new drug without informed consent. DOD's request is to include the documentation required by Sec. 56.115(a)(2) of this chapter. (vi)

DOD has explained:

(A) The context in which the investigational drug will be administered, for example, the setting or whether it will be self-administered or it will be administered by a health professional;

(B) The nature of the disease or condition for which the preventive or therapeutic treatment is intended; and

(C) To the extent there are existing data or information available, information on conditions that could alter the effects of the investigational drug. (vii) DOD's recordkeeping system is capable of tracking and will be used to track the proposed treatment from supplier to the individual recipient. (viii) Each member involved in the military operation will be given, prior to the administration of the investigational new drug, a specific written information sheet (including information required by 10 U.S.C. 1107(d)) concerning the investigational new drug, the risks and benefits of its use, potential side effects, and other pertinent information about the appropriate use of the product. (ix) Medical records of members involved in the military operation will accurately document the receipt by members of the notification required by paragraph (d)(1)(viii) of this section. (x) Medical records of members involved in the military operation will accurately document the receipt by members of any investigational new drugs in accordance with FDA regulations including part 312 of this chapter. (xi) DOD will provide adequate follow-up to assess whether there are beneficial or adverse health consequences that result from the use of the investigational product. (xii) DOD is pursuing drug development, including a time line, and marketing approval with due diligence. (xiii) FDA has concluded that the investigational new drug protocol may proceed subject to a decision by the President on the informed consent waiver request. (xiv) DOD will provide training to the appropriate medical personnel and potential recipients on the specific investigational new drug to be administered prior to its use. (xv) DOD has stated and justified the time period for which the waiver is needed, not to exceed one year, unless separately renewed under these standards and criteria. (xvi) DOD shall have a continuing obligation to report to the FDA and to the President any changed circumstances relating to these standards and criteria (including the time period referred to in paragraph (d)(1)(xv) of this section) or that otherwise might affect the determination to use an investigational new drug without informed consent. (xvii) DOD is to provide public notice as soon as practicable and consistent with classification requirements through notice in the Federal Register describing each waiver of informed consent determination, a summary of the most updated scientific information on the products used, and other pertinent information. (xviii) Use of the investigational drug without informed consent otherwise conforms with applicable law.

(2) The duly constituted institutional review board, described in paragraph (d)(1)(v) of this section, must include at least 3 nonaffiliated members who shall not be employees or officers of the Federal Government (other than for purposes of membership on the IRB) and shall be required to obtain any necessary security clearances. This IRB shall review the proposed IND protocol at a convened meeting at which a majority of the members are present including at least one member whose primary concerns are in nonscientific areas and, if feasible, including a majority of the nonaffiliated members. The information required by Sec. 56.115(a)(2) of this chapter is to be provided to the Secretary of Defense for further review.

(3) The duly constituted institutional review board, described in paragraph (d)(1)(v) of this section, must review and approve: (i) The required information sheet; (ii) The adequacy of the plan to disseminate information, including distribution of the information sheet to potential recipients, on the investigational product (e.g., in forms other than written); (iii) The adequacy of the information and plans for its dissemination to health care providers, including potential side effects, contraindications, potential interactions, and other pertinent considerations; and (iv) An informed consent form as required by part 50 of this chapter, in those circumstances in which DOD determines that informed consent may be obtained from some or all personnel involved.

(4) DOD is to submit to FDA summaries of institutional review board meetings at which the proposed protocol has been reviewed.

(5) Nothing in these criteria or standards is intended to preempt or limit FDA's and DOD's authority or obligations under applicable statutes and regulations. [46 FR 8951, Jan. 27, 1981, as amended at 55 FR 52817, Dec. 21, 1990; 64 FR 399, Jan. 5, 1999; 64 FR 54188, Oct. 5, 1999]

**Sec. 50.24 Exception from informed consent requirements for emergency research.**

(a) The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

(1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

(2) Obtaining informed consent is not feasible because: (i) The subjects will not be able to give their informed consent as a result of their medical condition; (ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and (iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

(3) Participation in the research holds out the prospect of direct benefit to the subjects because: (i) Subjects are facing a life-threatening situation that necessitates intervention; (ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and (iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

(4) The clinical investigation could not practicably be carried out without the waiver.

(5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Sec.50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) of this section.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least: (i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn; (ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits; (iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results; (iv) Establishment of

an independent data monitoring committee to exercise oversight of the clinical investigation; and (v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

(b) The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

(c) The IRB determinations required by paragraph (a) of this section and the documentation required by paragraph (e) of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with Sec.56.115(b) of this chapter.

(d) Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under Secs. 312.30 or 812.35 of this chapter.

(e) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor. [61 FR 51528, Oct. 2, 1996]

### **Sec. 50.25 Elements of informed consent.**

(a) Basic elements of informed consent. 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 and that notes the possibility that the Food and Drug Administration may inspect the records.
- (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.
- (8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that 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.
- (6) The approximate number of subjects involved in the study.

(c) The informed consent requirements in these regulations are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed for informed consent to be legally effective.

(d) Nothing in these regulations 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.

**Sec. 50.27 Documentation of informed consent.**

(a) Except as provided in Sec. 56.109(c), informed consent shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. A copy shall be given to the person signing the form.

(b) Except as provided in Sec. 56.109(c), the consent form may be either of the following:

- (1) A written consent document that embodies the elements of informed consent required by Sec. 50.25. 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.

- (2) A short form written consent document stating that the elements of informed consent required by Sec. 50.25 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 the 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.

## Appendix D: 21 CFR 56

## 21 CFR 56

**Subpart A—General Provisions****§ 56.101 Scope.**

(a) This part contains the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinical investigations regulated by the Food and Drug Administration under sections 505(i) and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Compliance with this part is intended to protect the rights and welfare of human subjects involved in such investigations.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21, unless otherwise noted.

[46 FR 8975, Jan. 27, 1981, as amended at 64 FR 399, Jan. 5, 1999; 66 FR 20599, Apr. 24, 2001]

**§ 56.102 Definitions.**

As used in this part:

(a) *Act* means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201–902, 52 Stat. 1040 *et seq.*, as amended (21 U.S.C. 321–392)).

(b) *Application for research or marketing permit* includes:

- (1) A color additive petition, described in part 71.
- (2) Data and information regarding a substance submitted as part of the procedures for establishing that a substance is generally recognized as safe for a use which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in § 170.35.
- (3) A food additive petition, described in part 171.
- (4) Data and information regarding a food additive submitted as part of the procedures regarding food additives permitted to be used on an interim basis pending additional study, described in § 180.1.
- (5) Data and information regarding a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 406 of the act.
- (6) An investigational new drug application, described in part 312 of this chapter.
- (7) A new drug application, described in part 314.
- (8) Data and information regarding the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in part 320.
- (9) Data and information regarding an over-the-counter drug for human use submitted as part of the procedures for classifying such drugs as generally recognized as safe and effective and not misbranded, described in part 330.
- (10) An application for a biologics license, described in part 601 of this chapter.
- (11) Data and information regarding a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, as described in part 601 of this chapter.



(12) An *Application for an Investigational Device Exemption*, described in parts 812 and 813.

(13) Data and information regarding a medical device for human use submitted as part of the procedures for classifying such devices, described in part 860.

(14) Data and information regarding a medical device for human use submitted as part of the procedures for establishing, amending, or repealing a standard for such device, described in part 861.

(15) An application for premarket approval of a medical device for human use, described in section 515 of the act.

(16) product development protocol for a medical device for human use, described in section 515 of the act.

(17) Data and information regarding an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for such products, described in section 358 of the Public Health Service Act.

(18) Data and information regarding an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in § 1010.4.

(19) Data and information regarding an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in § 1010.5.

(20) Data and information regarding an electronic product submitted as part of the procedures for obtaining an exemption from notification of a radiation safety defect or failure of compliance with a radiation safety performance standard, described in subpart D of part 1003.

(21) Data and information about a clinical study of an infant formula when submitted as part of an infant formula notification under section 412(c) of the Federal Food, Drug, and Cosmetic Act.

(22) Data and information submitted in a petition for a nutrient content claim, described in § 101.69 of this chapter, and for a health claim, described in § 101.70 of this chapter.

(23) Data and information from investigations involving children submitted in a new dietary ingredient notification, described in § 190.6 of this chapter.

(c) *Clinical investigation* means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous for purposes of this part.

(d) *Emergency use* means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

(e) *Human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.

(f) *Institution* means any public or private entity or agency (including Federal, State, and other agencies). The term *facility* as used in section 520(g) of the act is deemed to be synonymous with the term *institution* for purposes of this part.

(g) *Institutional Review Board (IRB)* means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review

of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase *institutional review committee* as used in section 520(g) of the act.

(h) *Investigator* means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

(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.

(j) *Sponsor* means a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

(k) *Sponsor-investigator* means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, for example, it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.

(l) *Test article* means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354–360F of the Public Health Service Act.

(m) *IRB approval* means the determination of the IRB that the clinical investigation 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. [46 FR 8975, Jan. 27, 1981, as amended at 54 FR 9038, Mar. 3, 1989; 56 FR 28028, June 18, 1991; 64 FR 399, Jan. 5, 1999; 64 FR 56448, Oct. 20, 1999; 65 FR 52302, Aug. 29, 2000; 66 FR 20599, Apr. 24, 2001]

### **§ 56.103 Circumstances in which IRB review is required.**

(a) Except as provided in §§ 56.104 and 56.105, any clinical investigation which must meet the requirements for prior submission (as required in parts 312, 812, and 813) to the Food and Drug Administration shall not be initiated unless that investigation has been reviewed and approved by, and remains subject to continuing review by, an IRB meeting the requirements of this part.

(b) Except as provided in §§ 56.104 and 56.105, the Food and Drug Administration may decide not to consider in support of an application for a research or marketing permit any data or information that has been derived from a clinical investigation that has not been approved by, and that was not subject to initial and continuing review by, an IRB meeting the requirements of this part. The determination that a clinical investigation may not be considered in support of an application for a research or marketing permit does not, however, relieve the applicant for such a permit of any obligation under any other applicable regulations to submit the results of the investigation to the Food and Drug Administration.

(c) Compliance with these regulations will in no way render inapplicable pertinent Federal, State, or local laws or regulations. [46 FR 8975, Jan. 27, 1981; 46 FR 14340, Feb. 27, 1981]

### **§ 56.104 Exemptions from IRB requirement.**

The following categories of clinical investigations are exempt from the requirements of this part for IRB review:

- (a) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.
- (b) Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.
- (c) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.
- (d) Taste and food quality evaluations 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. [46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28028, June 18, 1991]

### **§ 56.105 Waiver of IRB requirement.**

On the application of a sponsor or sponsor-investigator, the Food and Drug Administration may waive any of the requirements contained in these regulations, including the requirements for IRB review, for specific research activities or for classes of research activities, otherwise covered by these regulations.

## **Subpart B— Organization and Personnel**

### **§ 56.107 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, 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 the 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 or 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 those 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 the scientific area 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 complex issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB. [46 FR 8975, Jan 27, 1981, as amended at 56 FR 28028, June 18, 1991; 56 FR 29756, June 28, 1991]

### **Subpart C— IRB Functions and Operations**

#### **§ 56.108 IRB functions and operations.**

In order to fulfill the requirements of these regulations, each IRB shall:

(a) Follow written procedures:

- (1) For conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution;
- (2) for determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review;
- (3) for ensuring prompt reporting to the IRB of changes in research activity; and
- (4) for ensuring that 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 where necessary to eliminate apparent immediate hazards to the human subjects.
- (5) Follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of:
- (6) Any unanticipated problems involving risks to human subjects or others;
- (7) any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or
- (8) any suspension or termination of IRB approval.

(b) Except when an expedited review procedure is used (see § 56.110), 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 FR 8975, Jan. 27, 1981, as amended at 56 FR 28028, June 18, 1991; 67 FR 9585, Mar. 4, 2002]

#### **§ 56.109 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 these regulations.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with § 50.25. The IRB may require that information, in addition to that specifically mentioned in § 50.25, 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 in accordance with § 50.27 of this chapter, except as follows:

(1) The IRB may, for some or all subjects, waive the requirement that the subject, or the subject's legally authorized representative, sign a written consent form if it finds 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 the research context; or

(2) The IRB may, for some or all subjects, find that the requirements in § 50.24 of this chapter for an exception from informed consent for emergency research are met.

(d) In cases where the documentation requirement is waived under paragraph (c)(1) of this section, the IRB may require the investigator to provide subjects with a written statement regarding the research.

(e) 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. For investigations involving an exception to informed consent under § 50.24 of this chapter, an IRB shall promptly notify in writing the investigator and the sponsor of the research when an IRB determines that it cannot approve the research because it does not meet the criteria in the exception provided under § 50.24(a) of this chapter or because of other relevant ethical concerns. The written notification shall include a statement of the reasons for the IRB's determination.

(f) An IRB shall conduct continuing review of research covered by these regulations 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.

(g) An IRB shall provide in writing to the sponsor of research involving an exception to informed consent under § 50.24 of this chapter a copy of information that has been publicly disclosed under

§ 50.24(a)(7)(ii) and (a)(7)(iii) of this chapter. The IRB shall provide this information to the sponsor promptly so that the sponsor is aware that such disclosure has occurred. Upon receipt, the sponsor shall provide copies of the information disclosed to FDA.

(h) When some or all of the subjects in a study are children, an IRB must determine that the research study is in compliance with part 50, subpart D of this chapter, at the time of its initial review of the research. When some or all of the subjects in a study that is ongoing on April 30, 2001 are children, an IRB must conduct a review of the research to determine compliance with part 50, subpart D of this chapter, either at the time of continuing review or, at the discretion of the IRB, at an earlier date. [46 FR 8975, Jan. 27, 1981, as amended at 61 FR 51529, Oct. 2, 1996; 66 FR 20599, Apr. 24, 2001]

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

(a) The Food and Drug Administration has established, and published 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, through periodic republication in the FEDERAL REGISTER.

(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 1 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 IRB chairperson from among the 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 review procedure set forth in § 56.108(c).

(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 Food and Drug Administration may restrict, suspend, or terminate an institution's or IRB's use of the expedited review procedure when necessary to protect the rights or welfare of subjects. [46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28029, June 18, 1991]

#### **§ 56.111 Criteria for IRB approval of research.**

(a) In order to approve research covered by these regulations 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 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 that 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 (e.g., 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, handicapped, or 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

part 50.

(5) Informed consent will be appropriately documented, in accordance with and to the extent required by § 50.27.

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

(7) Where 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, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study to protect the rights and welfare of these subjects. (c) In order to approve research in which some or all of the subjects are children, an IRB must determine that all research is in compliance with part 50, subpart D of this chapter. [46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28029, June 18, 1991; 66 FR 20599, Apr. 24, 2001]

#### **§ 56.112 Review by institution.**

Research covered by these regulations 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.

#### **§ 56.113 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 Food and Drug Administration.

#### **§ 56.114 Cooperative research.**

In complying with these regulations, institutions involved in multi-institutional studies may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.

### **Subpart D— Records and Reports**

#### **§ 56.115 IRB records.**

(a) An institution, or where 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 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, a member of governing panel or board, stockholder, paid or unpaid consultant. (6) Written procedures for the IRB as required by § 56.108 (a) and (b).

(7) Statements of significant new findings provided to subjects, as required by § 50.25.

(b) The records required by this regulation shall be retained for at least 3 years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

(c) The Food and Drug Administration may refuse to consider a clinical investigation in support of an application for a research or marketing permit if the institution or the IRB that reviewed the investigation refuses to allow an inspection under this section. [46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28029, June 18, 1991; 67 FR 9585, Mar. 4, 2002]

## **Subpart E— Administrative Actions for Noncompliance**

### **§ 56.120 Lesser administrative actions.**

(a) If apparent noncompliance with these regulations in the operation of an IRB is observed by an FDA investigator during an inspection, the inspector will present an oral or written summary of observations to an appropriate representative of the IRB. The Food and Drug Administration may subsequently send a letter describing the noncompliance to the IRB and to the parent institution. The agency will require that the IRB or the parent institution respond to this letter within a time period specified by FDA and describe the corrective actions that will be taken by the IRB, the institution, or both to achieve compliance with these regulations.

(b) On the basis of the IRB's or the institution's response, FDA may schedule a re-inspection to confirm the adequacy of corrective actions. In addition, until the IRB or the parent institution takes appropriate corrective action, the agency may:

(1) Withhold approval of new studies subject to the requirements of this part that are conducted at the institution or reviewed by the IRB;

(2) Direct that no new subjects be added to ongoing studies subject to this part;

(3) Terminate ongoing studies subject to this part when doing so would not endanger the subjects; or

(4) When the apparent noncompliance creates a significant threat to the rights and welfare of human subjects, notify relevant State and Federal regulatory agencies and other parties with a direct interest in the agency's action of the deficiencies in the operation of the IRB.

(c) The parent institution is presumed to be responsible for the operation of an IRB, and the Food and Drug Administration will ordinarily direct any administrative action under this subpart against the institution. However, depending on the evidence of responsibility for deficiencies, determined during the investigation, the Food and Drug Administration may restrict its administrative actions to the IRB or to a component of the parent institution determined to be responsible for formal designation of the IRB.

### **§ 56.121 Disqualification of an IRB or an institution.**

(a) Whenever the IRB or the institution has failed to take adequate steps to correct the noncompliance stated in the letter sent by the agency under § 56.120(a), and the Commissioner of Food and Drugs determines that this noncompliance may justify the



disqualification of the IRB or of the parent institution, the Commissioner will institute proceedings in accordance with the requirements for a regulatory hearing set forth in part 16.

(b) The Commissioner may disqualify an IRB or the parent institution if the Commissioner determines that:

- (1) The IRB has refused or repeatedly failed to comply with any of the regulations set forth in this part, and
- (2) The noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

(c) If the Commissioner determines that disqualification is appropriate, the Commissioner will issue an order that explains the basis for the determination and that prescribes any actions to be taken with regard to ongoing clinical research conducted under the review of the IRB. The Food and Drug Administration will send notice of the disqualification to the IRB and the parent institution. Other parties with a direct interest, such as sponsors and clinical investigators, may also be sent a notice of the disqualification. In addition, the agency may elect to publish a notice of its action in the FEDERAL REGISTER.

(d) The Food and Drug Administration will not approve an application for a research permit for a clinical investigation that is to be under the review of a disqualified IRB or that is to be conducted at a disqualified institution, and it may refuse to consider in support of a marketing permit the data from a clinical investigation that was reviewed by a disqualified IRB as conducted at a disqualified institution, unless the IRB or the parent institution is reinstated as provided in § 56.123.

**§ 56.122 Public disclosure of information regarding revocation.**

A determination that the Food and Drug Administration has disqualified an institution and the administrative record regarding that determination are disclosable to the public under part 20.

**§ 56.123 Reinstatement of an IRB or an institution.**

An IRB or an institution may be reinstated if the Commissioner determines, upon an evaluation of a written submission from the IRB or institution that explains the corrective action that the institution or IRB plans to take, that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in this part. Notification of reinstatement shall be provided to all persons notified under § 56.121(c).

**§ 56.124 Actions alternative or additional to disqualification.**

Disqualification of an IRB or of an institution is independent of, and neither in lieu of nor a precondition to, other proceedings or actions authorized by the act. The Food and Drug Administration may, at any time, through the Department of Justice institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of, or after, disqualification. The agency may also refer pertinent

matters to another Federal, State, or local government agency for any action that that agency determines to be appropriate.

## Appendix E: IRB Guidance for Student Research and Class Projects

## IRB GUIDANCE FOR STUDENT RESEARCH AND CLASS PROJECTS

Federal regulations and university policies require Institutional Review Board (IRB) approval for research with human subjects. This applies whether the research is conducted by faculty or students, by individuals or a group. *Failure to obtain proper approval in advance may jeopardize your data, prevent you from publishing the results, and place you and the university in violation of federal regulations.* At the same time, many class projects are conducted for educational purposes and not as research, and will not require IRB approval. This guidance will help you determine whether you need to get IRB approval before conducting a given activity. Please note that the IRB does not have the option of granting “retroactive” approval after research is done; you should err on the side of submitting or consulting with the IRB if there is any doubt.

### STUDENT RESEARCH

Student research activities include, but are not limited to, projects that result in master’s theses or doctoral dissertations. *IRB approval is generally required if the intent is to develop or expand generalizable knowledge AND human subjects are involved, either directly or through use of identifiable data about them* Student researchers have the same submission options as any investigator. They may submit as Principal Investigator (PI) with a faculty advisor as co-signator, which may be appropriate for new projects where the student has a leading role. Alternatively, it may be appropriate for the student researcher to be included on an existing project that already has IRB approval, if the student activity is (or will be, after modification) subsumed under that existing study. This latter option precludes the need for a separate IRB application from the student. Each research scenario has its own set of circumstances that will dictate handling. Below are some common scenarios, with likely processing requirements:

**RESEARCH** that involves **direct interaction** with individuals (e.g., in person, or via mail, email, web survey, or telephone), or **data from human subjects for which the researchers will have access to identifiers.**

*→ Human Subjects Research, therefore IRB approval required  
→ Submit an IRB application, either with student as PI or listed as study personnel on faculty application; or modify existing study if student project is directly related.*

*Student researcher, co-investigators (if a group) and faculty advisor are required to have human subjects protection training.*

**RESEARCH** that is limited to **secondary analysis** of data, records or specimens that are either **publicly available, de-identified or otherwise impossible to be linked to personal identities.**

*→ Not Human Subjects Research, but if you need documentation from the IRB, submit an IRB application*

*A data use agreement between the researcher and the data custodian may still be required to verify that the researcher will not have access to identifying codes. It is this “de-linking” of data from personal identifiers that allows the IRB to make this determination.*

*If the IRB determines that this project is not human subjects research, human subjects protection training is not required by IRB, but may be required by the faculty advisor.*

**RESEARCH-like activities using departmental subject pools** (e.g., Psychology, Business, Political Science, Journalism and Mass Communication) even when the activity is conducted for educational purposes as a class requirement.

*→ IRB approval required → submit an IRB application for each activity by an individual or small group*

*Student researcher, co-investigators (if a group) and faculty advisor should have human subjects protection training.*

## CLASS PROJECTS

Class projects are generally conducted for educational purposes and not as research. While some require submission of an **IRB application** or a **determination that IRB approval is not required**, many class projects require neither. Instructors and departments are encouraged to contact the relevant IRB for guidance about ways to handle topics such as privacy, confidentiality, informed consent, and professional ethics when class projects are part of the course syllabus. IRB chairs and staff can share expertise related to managing risks of deductive disclosure, coercion-free recruiting, informed consent, and special considerations for projects that include potentially vulnerable individuals. These issues may still remain even when IRB approval is not required, in which case instructors, advisors, departments and schools play an even greater role in providing the appropriate guidance and oversight. Common scenarios:

**CLASS PROJECTS** involving **secondary data analyses** that are assigned and conducted as educational exercises, using data that are either publicly available data, de-identified or otherwise impossible to be linked to personal identities.

→ **No IRB action required (neither approval nor determination of human research status)**

**CLASS PROJECTS** involving **secondary data analyses** that are assigned and conducted as educational exercises, and that use datasets that include private information and codes that link to identifiers, but the students do not have access to the identifiers.

→ **No IRB action required (neither approval nor determination of human research status)**

Class instructor and department are responsible for providing the necessary training in respecting the confidentiality of the data.

**CLASS PROJECTS or PRACTICA** that involve **direct interaction** (e.g., in person, via mail, email, web surveys, or telephone), but where the purpose is training, an educational exercise or professional development, and **not research**. The project or practicum is not “research” even if students ask people questions as part of learning how to conduct interviews or surveys, take histories, administer assessments, or perform “in-house” evaluations as requested by the practicum site.

→ **No IRB action required (neither approval nor determination of human research status)** → but may be requested if instructor or students are unsure, or if documentation is required by gatekeepers (e.g., schools, businesses) for access to participants.

*Class instructor and department are responsible for providing the necessary training in respecting the privacy of the individuals and the confidentiality of any resulting information, along with training in the relevant professional ethics.*

Exception:

If a student decides *after* the completion of a practicum activity to pursue additional activities with the same information for dissemination (e.g., master’s project, conference paper, article), then an IRB application describing research use of secondary data should be submitted for approval, as above.

Instructor provides information about the assignment for the students to distribute to people who participate in these class projects. List the instructor as the appropriate contact person should questions arise.

**CLASS PROJECTS or PRACTICA** that involve **direct interaction** or **secondary analyses of private identifiable data** and are undertaken as **both an educational experience and as research** (e.g., results of these activities will be presented publicly or otherwise disseminated, or the data will be stored and used by the students or others as research data).

→ **IRB approval required** → When there are several students in a class doing similar projects, a **single IRB application may be submitted by the course instructor as PI**, listing all students who will be involved. If projects vary greatly, then it may be preferable to submit individual IRB applications with the student(s) as PI.

Submission Tip:

Such projects may be very similar to one another. For example, each student may interview one or more persons for a group of oral histories, or conduct telephone surveys as part of a yearly poll, but all in the class follow the same general script or

The PI must have research ethics certification. Taking into account the sensitivity of the information to be collected, the instructor can require that students complete the CITI online

guidelines. If class projects follow different protocols, a table or chart can describe these more individualized activities, under the umbrella of a single IRB application.

course, or the instructor may provide comparable training, with the approval of the IRB.

## Appendix F: ORSP Informed Consent Checklist

## ORSP Informed Consent Checklist

### Informed Consent Checklist - Basic and Additional Elements

A statement that the study involves research

An explanation of the purposes of the research

The expected duration of the subject's participation

A description of the procedures to be followed

Identification of any procedures which are experimental

A description of any reasonably foreseeable risks or discomforts to the subject

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

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

A statement describing the extent, if any, to which confidentiality of records identifying the subject 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

Research Qs  
Rights Qs

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

Injury Qs

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

### Additional elements, as appropriate

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

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

The approximate number of subjects involved in the study

### §46.117 Documentation of Informed Consent Checklist

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.

#### **WRITTEN**

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 should give either the subject or the representative adequate opportunity to read it before it is signed.

#### **DONE ORALLY**

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.

#### **WAIVER of req't for signed 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.

### **IRB Latitude to Approve a Consent Procedure that Alters or Waives some or all of the Elements of Consent**

**§ 46.116** - 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:

**C:** 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

**C:** 2. The research could not practicably be carried out without the waiver or alteration.

**D:** 1. The research involves no more than minimal risk to the subjects;

**D:** 2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;

**D:** 3. The research could not practicably be carried out without the waiver or alteration; and

**D:** 4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

### **Special Requirements - 45 CFR 46 Subpart D - Additional DHHS Protections for Children as Subjects in Research**

Assent/  
Waiver    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. 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.

Parents 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.

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.

## Appendix G: Confidentiality Statement

## Confidentiality Statement

[The following agreement should be signed by all members and guests attending IRB meetings and others serving as consultants to the IRB. Members may sign once and have their agreement kept on file.]

I acknowledge that confidential, proprietary and/or other sensitive information may be distributed or discussed at meetings of the Texas A&M University-Texarkana Institutional Review Board (IRB). Except to the extent disclosure may be required by law, I affirm that I will hold in strictest confidence all information I receive during the course and scope of my service to the IRB and/or attendance at IRB meetings.

If I am attending the meeting as a guest/observer, I further agree that I will not participate in or interrupt the meeting, and that any questions or comments I might have will be discussed with the Chair outside of the meeting.

Check one:  Guest (including observer or prospective member)

Member

Consultant

\_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Date)

\_\_\_\_\_  
(Printed name)

## Appendix H: Individual Identifiability of Data

## Individual Identifiability of Data

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Definition of data that is not individually identifiable: This is a table of direct and indirect identifiers that must be stripped from data in order for the data to be considered de-identified.

- \_\_\_ Names
- \_\_\_ Telephone numbers
- \_\_\_ Any elements of dates (other than year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death. For ages over 89: all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 and older
- \_\_\_ Any geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code and their equivalent geocodes, except for the initial three digits of a zip code
- \_\_\_ Fax numbers
- \_\_\_ Electronic mail addresses
- \_\_\_ Social security numbers
- \_\_\_ Medical record numbers
- \_\_\_ Health plan beneficiary numbers
- \_\_\_ Account numbers
- \_\_\_ Certificate/license numbers
- \_\_\_ Vehicle identifiers and serial numbers (VIN), including license plate numbers
- \_\_\_ Device identifiers and serial numbers (e.g., implanted medical device)
- \_\_\_ Web universal resource locators (URLs)
- \_\_\_ Internet protocol (IP) address numbers
- \_\_\_ Biometric identifiers, including finger and voice prints
- \_\_\_ Full face photographic images and any comparable images
- \_\_\_ Any other unique identifying number, code, or characteristic, other than dummy identifiers that are not derived from actual identifiers and for which the re-identification key is maintained by the health care provider and not disclosed to the researcher

## Appendix I: IRB Reviewer Checklists

## IRB Reviewer Checklist for Online Applications

IRB# \_\_\_\_\_ PI \_\_\_\_\_ Reviewer \_\_\_\_\_ Date \_\_\_\_\_

Section	Questions and relevant section IRB Application	Y/N/NA	Comments/Concerns
A.1	Are the rationale (background) and study purpose (hypothesis) adequately described?		
A.1	Are the objectives and outcome measures consistent with the rationale?		
A.1 Also see A.5	Will the study result in generalizable knowledge that benefits society?		
A.2	Are the study groups clearly described?		
A.2	Is the selection of subjects equitable?		
A.2	If vulnerable populations are involved, are adequate protections in place? <b>Specify</b>		
A.3	Are inclusion /exclusion criteria appropriate and do they minimize risk to subjects?		
A.4	Is the study design adequately justified? (e.g., randomization, placebo, phase, deception)		
A.4	Will procedures be performed at proper facilities by qualified personnel?		
A.4.A	Is there a valid IND or IDE from the FDA (when applicable)?		
A.4.A	Are experimental procedures distinguished from standard of care or treatment?		
A.5	Are the potential benefits to subjects and/or society adequately described?		
A.6	Are foreseeable risks clearly defined?		
A.6	Are risks to subjects reasonable when compared to anticipated benefits?		
A.6	Are risks minimized by using procedures consistent with sound research design, avoiding unnecessary exposures(s), and/or using procedures already performed for diagnosis or treatment?		
A.6	Level of risk constituted by the research?		<b>Minimal</b> <b>Greater than minimal</b>
A.6	If a medical device, what is the risk?		<b>Non-significant Risk</b> <b>Significant Risk</b>
A.7	Are data monitoring provisions adequate for subject safety?		
A.10	Are provisions to maintain confidentiality of collected data/specimens adequate?		
A.12	Are plans for post-study disposition of identifiable data/specimens adequate?		
B.1	Are recruitment practices fair and equitable?		
B.2	Is a limited waiver of HIPAA authorization to identify potential subjects justified?		



Section	Questions and relevant section IRB Application	Y/N/NA	Comments/Concerns
8.3	Is the study duration (and visit frequency) appropriate to achieve stated objectives?		
8.3	Are provisions to protect subject privacy adequate?		
8.3 Also see A.4	Are the time demands, number of visits, procedures, and interventions clearly outlined?		
8.4	Are inducements for participation reasonable and adequately described?		
8.4	Will incentives exceed \$200 per year so that SSN collection required?		
8.5	Are costs to be borne by subjects adequately described?		
0.1	Will consent/assent be obtained from all potential subjects or LARs? (check CF lines)		
0.2	Are criteria for waiving written documentation of consent satisfied?		
0.3	Are criteria for waiving consent (partially or entirely) satisfied?		
IR8 Coordinator to Assess	Are there Conflicts of Interest with this study, disclosed by PI or perceived by reviewer?		
See Consent Forms	Are the signature line(s) on the consent forms appropriate to the study?		
See Consent Forms	Is consent form complete, adequate to address questions, and consistent with application and DHHS-approved sample consent documents?		
See Attachments	Is IR8 application consistent with supporting documents (e.g., grants, sponsor protocol)?		

REVIEWER'S RECOMMENDATION?

Approval without conditions	
May be approved with minor stipulations	
Defer and return to full IRB	
Disapprove	
Frequency of Continuing Review (regulations require review at least every 12 months)	
Required findings for special populations (e.g., children, pregnant women, prisoners). Include study specific justification	

Additional comments:

## Appendix J: Decision Algorithm for Unanticipated Problems and Adverse Reporting



