University of Maine
Policies and Procedures for the Protection of Human Subjects of Research
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I. Administrative Procedures for Human Subject Research

1. Introduction

Research with human subjects at the University of Maine shall be guided by three general ethical principles: respect for persons, beneficence, and justice. These principles and the rules that may be derived from them shall form the analytical framework for determining whether and how research with human subjects may be conducted. Researchers must respect and protect the rights and privacy and welfare of individuals recruited for and participating in research. More precisely, all human subject research must comply with the US Department of Health and Human Services (DHHS) "Common Rule" 45 CFR 46; 21 CFR 50; the *Belmont Report*; *The Nuremburg Code*; and the *Declaration of Helsinki*.

The University shall maintain and support an Institutional Review Board for the Protection of Human Subjects (IRB), whose function it is to determine whether and how research with human subjects may be conducted, and to educate the community with regard to the protection of human subjects.

No research with human subjects shall be conducted until the IRB has reviewed the research protocol. Before action is taken, proper consideration shall be given to the risks to the subjects, the anticipated benefits to the subjects and others, the importance of the knowledge that may reasonably be expected to result, and the informed consent process to be employed.

The University of Maine shall acknowledge and accept responsibility for protecting the rights and welfare of human subjects of research. University Policies and Procedures for the Protection of Human Subjects of Research apply to all activities which include research with human subjects and:

- are sponsored by the University; or
- are conducted by or under the direction of any faculty, staff member, or student of the University in connection with their institutional responsibilities; or
- are conducted by or under the direction of any faculty, staff member, or student of the University using any property or facility of the University; or
- involve the use of the University's nonpublic information.

The University of Maine shall encourage and promote constructive communication among research administrators, department chairs, deans and directors, research investigators, research staff, human subjects, and University officials as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.

The University of Maine shall comply with all federal, state, and local regulations pertaining to the protection of human subjects.

2. Definitions

Adverse Event, Serious: Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure.

Serious Adverse Events include those that:

- Are fatal or life threatening;
- Result in significant or persistent disability;
- Require or prolong hospitalization;
- Result in a congenital anomaly/birth defect; or
- Represent other significant hazards or potentially serious harm to research subjects or others, in the opinion of the investigators.

Unexpected Serious Adverse Events are those that have not been described in the:

- Package insert for a given drug or investigator's brochure (for FDA investigational agents);
- Approved protocol; or
- Informed consent document. [21 CFR 312.32(a)]

Adverse Research Event: Adverse research events include a wide spectrum of events. Adverse events include, but are not limited to:

- Physical or psychological harm or injuries;
- Threats to privacy or safety;
- Unusual attrition of human subjects;
- Breaches of confidentiality or emotional harms such as the emotional distress that could be triggered by questions about traumatic life events or a subject's complaints about the experimental procedures or the conduct of the investigators.

Certificate of Confidentiality: A discretionary document issued by the National Institutes of Health (NIH), which helps researchers protect the privacy of human research participants enrolled in biomedical, behavioral, clinical, and other forms of sensitive research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant. Further information is available at the NIH website on Certificates of Confidentiality.

Coercion: To bring about participation in research by force or threat, actual or perceived, or through any other imbalance of power.

Common Rule: The federal regulation that is the primary source of human subjects' protections. This is the common reference for 45 CFR 46, PROTECTION OF HUMAN SUBJECTS.

Generalizable Knowledge: Currently, US DHHS Office of Human Research Protection (OHRP) **does not** have a formal position on what does and does not constitute "generalizable knowledge" beyond the language of the Common Rule. The University of Maine adopts the following definition of generalizable knowledge:

Generalizable knowledge is information which has the potential to be expanded from the isolated circumstances in which it is acquired to any broader context.

Thus, a case study, designed to illuminate the course of a single individual's experience generally **will not** be considered to be developing or contributing to generalizable knowledge. A series of case studies, intended to lead to improvements in the management of a particular circumstance or condition, generally **will** be considered generalizable knowledge.

Human Subject: "A living individual(s) about whom an investigator (whether professional or student) conducting research [45 CFR 46.102(e)]:

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
(ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens."

Institutional Review Board (IRB): A research review committee whose primary purpose is to review all research involving human subjects and to provide oversight of human subjects' protections.

Interaction: A communication or interpersonal contact between investigator and subject for research purposes.

Intervention: Includes both physical procedures by which information or biospecimens are gathered (*e.g.*, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Key Research Personnel: Persons who have direct contact with subjects, contribute to the research in a substantive way, have contact with subjects' identifiable data or biological samples (*e.g.*, tissue, blood, urine, plasma, saliva), or use subjects' personal information.

Minimal Risk: "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 living or during the performance of routine physical or psychological examinations or tests." [45 CFR 46.102(j)]

Minor: An individual under the age of 18 years.

Minor Changes: Minor changes have no substantive effect upon an approved protocol or reduce the protocol risk already approved by the IRB. Examples of minor changes are:

- Changes in research personnel that do not alter the competence of the research team to conduct the research, or
- Minimal changes in compensation.

Principal Investigator (PI): Any University of Maine faculty, staff member, or student so designated in a protocol who is the primary person responsible for all aspects of the research project and assumes all responsibilities for the results.

Prisoner: Any individual, regardless of age, involuntarily confined or detained in a penal institution or a parolee detained in a treatment center as a condition of parole. 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. This definition also includes

data from non-publicly available databases and secondary sources. The University of Maine extends the term “prisoner” to include persons on pre-trial supervised release, on community supervision or on probation, or who is in any court-ordered deferred prosecution or diversion program.

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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (*e.g.,* a medical record).

Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Protected Population: (Also referred to as protected subject group). These groups of potential research subjects have specific regulatory compliance requirements and receive special protections under the Common Rule and/or other federal regulations. These groups include (but are not restricted to):

- Children/Minors (under the age of 18)
- Prisoners (includes non-publicly available secondary data)
- Pregnant women
- Fetuses and products of labor and delivery
- People with diminished capacity to give consent
- Mentally or physically challenged individuals

Protocol: Any type of research project that is submitted for IRB review (also known as a research project, proposal, submission, *etc*.).

Protocol Violation, Major: A major protocol violation occurs when there is a variance in a research study between the protocol that has been reviewed and approved by the IRB and the actual activities being performed. Major protocol violations include violations that:

- Cause or pose a significant risk of substantive harm to research participants;
- Damage the scientific integrity of the data collected;

- Show evidence of willful or knowing misconduct on the part of the investigator; or
- Demonstrate a serious or continued noncompliance with federal, state, or local research policy, laws, or regulations.

Protocol Violation, Minor: A minor protocol violation occurs when there is a variance in a research study between the protocol that has been reviewed and approved by the IRB and the actual activities being performed. Minor protocol violations include violations that:

- Have no substantive effect on the risks to research participants;
- Do not impact the value of the data collected (meaning the violation does not confound the scientific analysis of the results); and
- Do not result from willful or knowing misconduct on the part of the investigator(s).

Research: The University of Maine takes as its starting point the federal definition of research set forth in the Common Rule, [45 CFR 46.102(d)]:

> *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities). ***Please note that risk assessment plays no role in the determination of whether a proposed activity constitutes research. See also the definition of generalizable knowledge, above.***
>
> For purposes of this part, the following activities are deemed not to be research:

(1) Scholarly and journalistic activities (*e.g.,* oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor,

assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

Research Misconduct (42 CFR §93.103): means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

- Fabrication is making up data or results and recording or reporting them as if they were real.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- Research misconduct does not include honest error or differences of opinion.

Sensitive Information: According to the NIH Certificate of Confidentiality Kiosk, sensitive information is that which, if disclosed, may reasonably pose a risk to the subject's psychological, social, medical, legal, or economic well-being or quality of life. Categories of sensitive information include (but are not limited to):

- Sexual attitudes, preferences, or practices
- Use of alcohol, drugs, or other addictive products
- Information pertaining to illegal conduct
- Information that if released might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination
- Health and medical information contained in a medical record, chart, or insurance file (this category may also require a HIPAA review)

- Information pertaining to an individual's psychological well-being or mental health (this category may also require a HIPAA review)
- Genetic information or tissue samples (this category may also require a HIPAA review)

Signatory/Institutional Official: The signatory/institutional official (IO) is the highest institutional official who has the legal authority to represent the University of Maine's Assurance filed with the OHRP, and is responsible for the provisions of this policy. At the University of Maine, the signatory/institutional official is the Vice President for Research.

Specimen: Specimen is used to refer to biological specimens (*e.g.*, blood or tissue samples), as well as to other types of data "specimens" that could be stored for use in future research (*e.g.*, audio tapes, video tapes).

Substantive Changes Affecting Risk: Substantive changes are changes that may increase the research population's risk or are of questionable risk. Examples of substantive changes that are considered to increase the risk to the study/individual include, but are not limited to:

- Increasing the length of time a study participant is exposed to experimental aspects of the study.
- Changing the originally targeted population to include a more at-risk population (*e.g.,* previous exclusion for those with renal failure are now allowed to enroll, or adding children or pregnant women to the study).
- Adding an element that may breach the confidentiality of the subject such as tissue banking or genetic testing.

Undue Influence: Inappropriate compensation or any other form of compulsion offered to an individual that may unfairly compel that individual to participate as a human research subject.

Unanticipated Problem: Any event that is not expected given the nature of the research procedures and the subject population being studied, and places subjects or others at greater risk or harm/discomfort related to the research than was previously known or recognized. An event which was previously unforeseeable based on the information provided to the IRB.

Written or in writing: refers to writing on a tangible medium (*e.g.,* paper) or in an electronic format.

3. Student Class Projects

1. Class projects that involve systematic collection of data and for which the design or objective is to develop or contribute to generalizable knowledge are considered research and require IRB review.

2. Class projects that are designed: a) solely with the objective of providing students with training about and experience with research methods, **and** b) where data will not be used outside of the classroom context, **and** c) where data will be destroyed upon completion of the project, are not considered research and do not require IRB review. **However**, if the instructor allows a student to design a class project that involves protected populations or sensitive information, IRB review and approval are required. (SeeGuidelines for Class Projects for additional information.)

4. Collaborative Research Projects

1. If research involves multiple sites, there may be a requirement to rely on one IRB. In those cases, we may need to enter into a reliance agreement that indicates the IRB of record and which institutions will rely on the IRB of record. The Office of Research Compliance (ORC) will assist with the agreement.

2. Non-exempt multi-site research studies funded by NIH are required to use a single IRB (sIRB). For more information, see NIH NOT-OD-16-094.

5. IRB Review Process

5.1 Exempt - The Common Rule outlines certain types of research that are exempt from Institutional Review Board (IRB) oversight: 45 CFR 46.104(d); 21 CFR 50 and 56 [US Food and Drug Administration (FDA research)]. Only the IRB can determine if a proposed project qualifies as exempt from further review. Principal Investigators (PI) whose research is judged exempt from further review are not required to have any further interaction with the IRB unless adverse events occur, or there is a substantial change to the protocol.

5.1.2 Exempt Categories:

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

instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

   (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

   (ii) Any disclosure of the human subjects' responses outside the research would not 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) 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 to make the determination required by 46.111(a)(7).

3.

   (i) Research involving 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 if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

      A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

      B) Any disclosure of the human subjects' responses outside the research would not 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

C) 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 to make the determination required by 45.111(a)(7).

(ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that they will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms

are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 *et seq.*

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

(i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

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.

5.2 Expedited Review:

At UMaine, the expedited 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).

The IRB shall keep all members advised of research proposals that have been approved under the expedited review procedure by including a list of those proposals on the monthly agenda and subsequent minutes.

The department or agency heads[1] may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.

A. Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
B. The categories in this list apply regardless of the age of subjects, except as noted.
C. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate

[1] "Department or Agency heads" refers specifically to the heads of various federal departments or agencies, and not state government officials or campus department heads.

protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

D. The expedited review procedure may not be used for classified research involving human subjects.
E. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.
F. Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

5.2.1 Expedited Review Research Categories

1. Clinical studies of drugs and medical devices only when condition 1) or 2) is met.

    a) Research on drugs for which an investigational new drug application (21 CFR part 312) is not required. (Note: research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

    b) Research on medical devices for which (i) an investigational device exemption application (21 CFR part 812) is not required; or (ii) the medical device is cleared/approved for marketing, and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

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

    b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of

50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means.

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

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.
   Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. [45 CFR 46.101(b)(4)]. This listing refers only to research that is not exempt.)

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

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

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

    a) where(i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

    b) where no subjects have been enrolled and no additional risks have been identified; or

    c) where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where research categories 3.b. through 3.h. 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.

The IRB may use the expedited review procedure to review either or both of the following:

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

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

5.3 Full Board Review:

ORC staff along with the IRB Chair will perform a pre-review of the application. If the application requires revisions before Full Board, it is returned to the researcher for edits. Only complete applications will be sent to the Board for review. The Chair or Vice Chair will summarize the application for the Board before the discussion. All members attending a convened meeting will review the materials in sufficient depth to vote on the application at the meeting. The researcher on the application will be invited to attend the meeting to answer questions about the research. The researcher will not be present during the discussion or vote of the Board.

5.4 Lapse in Approval:

The regulations do not permit a grace period or approval extension after approval expiration for studies that require continuing review. Research that continues after the approval period has expired is research conducted without IRB approval. If the continuing review does not occur within the timeframe set by the IRB, all research activities must stop, including recruitment, enrollment, consent, interventions, interactions, and data collection, unless the IRB finds that it is in the best interests of individual participants to continue participating in the research interventions or interactions. Therefore, investigators must allow sufficient time for IRB review before the expiration date.

If approval has expired, IRB review and re-approval must occur prior to re-initiation of the research. If approval has lapsed more than 30 days and the PI has not provided the required continuing review information, the PI must submit a new application to the IRB for review and approval. If the study approval has lapsed 30 days or less and the PI provides the required continuing review information, the existing protocol may be reviewed for consideration of continued IRB approval.

If the PI received requested changes from the IRB at the time of the continuing review and the approval expires before the PI responds to the changes, the PI may not enroll

any new participants after the approval expiration date. Once the PI responds, the existing protocol will be reviewed for continuation. If the PI does not respond for an extended period, the IRB may vote to administratively close the study.

6. Responsibilities of the Principal Investigator

The individual faculty, staff member, or student of the University who conducts or directs research with human subjects exercises the following responsibilities:

1. The Principal Investigator shall submit an application for Approval of Research with Human Subjects to the Board. The application includes all criteria for submission.

2. The Principal Investigator and personnel named in the application or who will have access to data, shall complete the required research ethics training.

3. The Principal Investigator shall begin the research project ONLY after receiving written approval from the IRB.

4. The Principal Investigator shall make no alterations to the approved protocol without the prior approval of such alterations by the IRB.

5. The Principal Investigator shall report at once to the IRB any unanticipated harm to human subjects.

6. The Principal Investigator shall submit a status report to the IRB on the conduct of the research and shall seek approval for continuation of the research at least annually, and more frequently if the IRB so requires for expedited and full board reviews.

7. The Principal Investigator shall cooperate fully with the Protection of Human Subjects Review Board in monitoring the progress of the research.

8. The Principal Investigator shall promptly notify the Office of Research Compliance if a study should be closed. If the investigator is leaving the institution, ORC should be notified at least 30 days before the departure date.

7. IRB Membership

The IRB is responsible not only for reviewing, regulating, and monitoring human subject research, but also for educating the University community in the protection of human subjects.

1. The IRB shall have no fewer than five voting 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.

2. 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, *e.g.*, 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 US DHHS's OHRP.

3. The 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. 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. At least one member's area of expertise shall include children. At least one member shall be a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity.

4. Member Conflict of Interest: The IRB may NOT have a member participate in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB. The member must recuse themselves from the discussion and vote on the project. The member must leave the meeting during the discussion and vote; recusals must be documented in the meeting minutes.

5. Use of Consultants: The IRB may invite consultants to provide scientific or scholarly expertise beyond or in addition to that available to the IRB; such individuals may not vote with the IRB. The IRB Chair, in consultation with

the Office of Research Compliance, is responsible for determining when a consultant is needed.

6. Members are appointed for one- to three-year terms and may be reappointed to additional terms.

7. All IRB members are formally confirmed by the President (or designee) of the University; any designation must be specific and in writing.

8. The Chair of the IRB should be a tenured faculty member with experience in conducting human subject research. Appointment is confirmed officially by the President or designee and is for two years; may be reappointed to additional terms. A Vice Chair may be appointed, if desired, using the same confirmation procedure.

8. IRB Functions and Operations

The IRB shall:

1. Follow written procedures in the same detail as described in 45 CFR 46.103(b)(4), and to the extent required by 45 CFR 46.103(b)(5).

2. Except when an expedited review procedure is used, 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.

9. IRB Review of Research

1. All research shall be reviewed by the IRB. The IRB shall make the final decision on whether research is exempt from further review or meets the requirements for an expedited review. The IRB shall review protocol applications and has the authority to approve, require modifications, or disapprove research activities with human subjects.

2. Ensures that legally effective informed consent of human research subjects will be obtained in a manner and method that meets the requirements of federal, state, and local rules and laws and in accordance with section K.

3. The IRB shall require documentation of informed consent or may waive documentation or alter some or all of the required elements of informed

consent. A waiver or alteration of informed consent should be documented in writing.

4. The IRB shall notify investigators and the Institutional Official 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.

5. The IRB shall monitor the research it has approved by any means it deems appropriate, including observation of the consent process and the research activities and appointment of a third party to undertake such observations.

6. The IRB shall conduct continuing review of approved research activities at intervals appropriate to the degree of risk, but not less than once per year, except as described in 7 below.

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

   i) Research eligible for expedited review in accordance with 46.110.
   ii) Research reviewed by the IRB in accordance with the limited IRB review described in 46.111
   iii) 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:

      (a) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
      (b) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

10. Criteria for IRB Approval of Research

The IRB approves research only when it has determined that all of the following requirements are satisfied:

1. Risks to subjects are minimized. Procedures used are consistent with sound research design and do not unnecessarily expose subjects to risk. Whenever appropriate, the research uses procedures already being

performed on the subjects for other purposes, such as diagnosis or treatment.

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to the subjects, and the importance of the knowledge that may reasonably be expected to result. The IRB considers only those risks and benefits that may result from the research. The IRB does not consider possible long-range effects of applying knowledge gained in the research as among those research risks that fall within the purview of its responsibility.

3. The selection of subjects is equitable, taking into account the purpose of the research and the setting in which the research will be conducted.

4. Informed consent is sought from each prospective subject or the subject's legally authorized representative. The IRB conforms to federal regulations of informed consent procedures and may impose additional requirements.

5. Informed consent is appropriately documented or appropriately waived, in accordance with, and to the extent required by, federal regulations. The IRB may also impose documentation requirements in addition to those required by federal regulations.

6. When appropriate, the research protocol 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.

8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, appropriate additional safeguards have been included in the protocol to protect the rights and welfare of these subjects.

11. Obtaining Informed Consent from Research Participants

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.

11.1 Basic Elements of Informed Consent

a. 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;

b. A description of any reasonably foreseeable risks or discomforts to the subject;

c. A description of any benefits to the subject or to others which may reasonably be expected from the research;

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

e. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

f. 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;

g. 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

h. 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.

i. Notice about whether participants' information or biospecimens collected as part of the current research might be stripped of identifiers and used for other research in the future. Consent forms must indicate either that information or biospecimens collected for the research might be stripped of identifiers and used in other research in the future, or that this will not occur. Note that this is only about future research use of information and biospecimens that will be stripped of identifiers.

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

a. 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;

b. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

c. Any additional costs to the subject that may result from participation in the research;

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

e. 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; and

f. The approximate number of subjects involved in the study.

g. Notice to participants about possible commercial profit from the research, whether clinically relevant research results will be returned to the participants, and whether research activities will or might include whole genome sequencing.

11.2 Waiver of Informed Consent

The IRB may approve a consent procedure that 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:

a. 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**

b. The research could not practicably be carried out without the waiver or alteration.

In addition, the 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:

a. The research involves no more than minimal risk to the subjects; **and**

b. The waiver or alteration will not adversely affect the rights and welfare of the subjects; **and**

c. The research could not practicably be carried out without the waiver or alteration; **and**

d. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

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.

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.

11.3 Documentation of Informed Consent:

a. 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 unless a waiver of signed consent is approved.

b. A copy shall be given to the person signing the form.

c. The consent form may be either of the following:

1. A written consent document that embodies the elements of informed consent. 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, written consent document stating that the 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; and
   - 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.
   - 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.

11.4 Waiver of Documentation of Informed Consent:

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds that:

i. 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

ii. 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.

iii. The subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, and that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

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.

12. Assurance of Compliance

The University of Maine conducts federally funded non-exempt human subject research; as such, it has a legally binding agreement with US DHHS -- a Federal Wide Assurance. This Federal Wide Assurance is administered by US DHHS's OHRP and governs all human subject research receiving, or eligible to receive federal (US DHHS) funds. This agreement is guided by the ethical principles of the *Belmont Report* and requires, at a minimum, compliance with 45 CFR 46 (The Common Rule). The University of Maine's Federal Wide Assurance number is: FWA00000479.

13. Review by Institution

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

14. Suspension or Termination of IRB Approval of Research

The IRB has 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. When the IRB exercises this authority, it promptly communicates its action and the reasons for the

action in writing to the Principal Investigator, Institutional Official, or other appropriate campus official, and the extramural sponsor of the research, if any.

15. IRB Records

1. The IRB shall prepare and maintain adequate documentation of its activities, including the following:

    a. 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.

    b. Minutes of IRB meetings shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; votes on actions including the number of members voting for, against, and abstaining; basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. A copy of the IRB meeting minutes for each meeting will be made available to the Institutional Official.

    c. Records of continuing review activities.

    d. Copies of all correspondence between the IRB and the investigator.

    e. A list of all IRB members in the same detail as described in section F.

    f. Written procedures for the IRB in the same detail as described in §46.108(a)(3) and 4) .

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

    h. Determinations of conflict of interest.

2. The records required by this policy shall be retained for at least 3 years; and records relating to research that is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspections and copying by authorized representatives of US DHHS OHRP at reasonable times and in a reasonable manner.

16. Applications and Proposals Lacking Definite Plans for Involvement of Human Subjects

Certain types of research proposals may not have fully defined plans set forth in the application or proposal. Such proposals may include 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 the IRB before an application for award can be filed, nor before an award may be made. However, no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB.

17. 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 the IRB.

18. 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.

19. Early Termination of Research Support: Evaluation of Applications and Proposals

1. The IRB, senior administrator responsible for the IRB, or the UMaine System may terminate or suspend an approved project if an investigator has failed to comply with the terms of this policy.

2. The IRB, senior administrator responsible for the IRB, or the UMaine System 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 1. 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 their judgment 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).

20. Conditions

With respect to any research project or any class of research projects, the senior administrator responsible for the IRB or the UMaine System may impose additional conditions necessary for the protection of human subjects.

II. Research Involving Children

1. Applicability

1. The regulations in this section are applicable to **all** biomedical and behavioral research involving children conducted by any member of the University of Maine.

2. All research involving children as subjects must comply with any state or local laws limiting such research.

3. The requirements of this section are in addition to those imposed under the other sections of the University of Maine Policies and Procedures for the Protection of Human Subjects of Research.

4. Note that the exemptions described in section C. of Administrative Procedures for Human Subjects Research and at 45 CFR 46.101(b)(1) and (b)(3) through (b)(6) are applicable to this section. The exemption at §46.101(b)(2) regarding educational tests is also applicable to this section. 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 section, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

2. Definitions

As used in this section:

1. 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.

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

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

4. Parent means a child's biological or adoptive parent.

5. Guardian means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

3. Special IRB Duties

In addition to other responsibilities assigned to the IRB in this section, the IRB shall review research covered by this section and approve only research that satisfies the conditions of all applicable parts of this section.

4. Research not Involving Greater than Minimal Risk (45 CFR 46.404)

Research in which the IRB finds no greater than minimal risk to children to be present may be approved 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 below.

5. Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Subject (45 CFR 46.405)

If 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, the proposed research may be approved only if the IRB finds that:

1. The risk is justified by the anticipated benefit to the subjects;

2. 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

3. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians as set forth in H. in this section. [§46.408]

6. Research Involving Greater than Minimal Risk and no Prospect of Direct Benefit to the Individual Subject, but likely to Yield Generalizable Knowledge about the Subject's Disorder or Condition (45 CFR 46.406)

If 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 that is not likely to contribute to the well-being of the subject, the proposed research may be approved only if the IRB finds that:

1. The risk represents a minor increase over minimal risk;

2. 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;

3. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and

4. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians as set forth in H. in this section. [§46.408]

7. Research not Otherwise Approvable that Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children (45 CFR 46.407)

If the IRB does not think the proposed research meets the requirements of the three immediately preceding conditions, research may only be approved if:

1. 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

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

    a. The research in fact satisfies the conditions of 45 CFR 46.404, 46.405, or 46.406, as applicable, or
    b. the following:

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

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

3) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408.

8. Requirements for Permission by Parents or Guardians and for Assent by Children (45 CFR 46.408)

1. In addition to the determinations required under other applicable sections of this section, 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.

2. In addition to the determinations required under other applicable parts of this section, 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 guardians. 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.

3. In addition to the provisions for waiver contained in §46.116 of subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in A. in this section and paragraph 2. above provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

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

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

9. Wards

1. Children who are wards of the state or any other agency, institution, or entity can be included in research approved \ §46.406 or §46.407 only if such research is:

    a. Related to their status as wards; or

    b. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

2. If the research is approved under paragraph 1. above, 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.

III. Research Involving Prisoners

1. Applicability

1. The regulations in this section are applicable to **all** biomedical and behavioral research involving prisoners conducted by any member of the University of Maine.

2. All research involving prisoners as subjects must comply with any state or local laws limiting such research.

3. The requirements of this section are in addition to those imposed under the other sections of the University of Maine Policies and Procedures for the Protection of Human Subjects of Research.

2. 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 section to provide additional safeguards for the protection of prisoners involved in activities to which this section is applicable.

3. Definitions

As used in this section:

1. 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 that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. The University of Maine extends the term “prisoner” to include persons on pre-trial supervised release, on community supervision or on probation, or who is in any court-ordered deferred prosecution or diversion program.

2. 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.

4. Composition of IRB where Prisoners are Involved

In addition to satisfying the requirements in section F. of the Administrative Procedures for Human Subject Research, the IRB shall also meet the following specific requirements:

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

2. At least one member of the IRB 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 IRB only one Board need satisfy this requirement.

A prisoner representative with appropriate background may include an attorney with experience in criminal defense or prisoners' rights, a member of a prisoners' rights advocacy organization, a chaplain or a counselor or other similar professional who deals, or has dealt with, prisoners.

5. Additional Duties of the IRB where Prisoners are involved

1. In addition to all other responsibilities prescribed for the IRB under this part, the IRB shall review research covered by this subpart and approve such research only if it finds that:

    a. The research under review represents one of the categories of research permissible under 306(a)(2);

    b. Any possible advantages accruing to the prisoner through their 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 their ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

    c. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

    d. 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;

e. The information is presented in language which is understandable to the subject population;

f. Adequate assurance exists that parole boards, community release supervisors, and/or probation officers will not take into account a prisoner's participation in the research in making decisions regarding parole, community supervision, or probation, and each prisoner is clearly informed in advance that participation in the research will have no effect on their parole, community supervision, or probation; and

g. 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.

2. The IRB shall carry out such other duties as may be assigned by the Secretary of the US DHHS.

3. The institution shall certify to the Secretary, in such form and manner as the Secretary may require, that the duties of the IRB under this section have been fulfilled.

6. Permitted Research Involving Prisoners

1. Biomedical or behavioral research not conducted or supported by DHHS may involve prisoners as subjects only if all of the conditions outlined above for general human subject research, and the special conditions for research with prisoners, are met.

2. Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:

a. The institution responsible for the conduct of the research has certified to the Secretary that the IRB has approved the research under 45 CFR 46.305; and

b. In the judgment of the Secretary, the proposed research involves solely the following:

1) 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;

2) 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;

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

4) 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.

3. Except as provided in paragraph F.2. of this section, biomedical or behavioral research conducted or supported by US DHHS shall not involve prisoners as subjects.

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

This subpart applies to all research involving pregnant women, human fetuses, neonates, and neonates of uncertain viability or nonviability.

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

This policy does not alter any present or future state or local laws or regulations that may otherwise be applicable and which may provide additional protections for human subjects. This subpart is intended to include the laws of federally recognized American Indian and Alaska Native Tribal Governments.

This policy does not alter any present or future foreign laws or regulations that may otherwise be applicable and which may provide additional protections for human subjects.

1. Definitions

1. Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she tests positive on a pregnancy test or 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.

2. Fetus means the product of conception from implantation until delivery.

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

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

5. Neonate means a newborn.

6. Viable, as it pertains to a neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

7. Nonviable neonate means a neonate after delivery that, although living, is not viable.

2. Research Involving Pregnant Women or Fetuses

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

1. 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.

2. The risk to the fetus is caused solely by interventions or procedures that have the prospect of direct benefit for the woman or the fetus; or, if there is no 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.

3. Any risk is the least possible for achieving the objectives of the research.

4. If the research has 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, their consent is obtained in accord with the informed consent provisions.

5. If the research has the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father must be obtained in accord with the informed consent provisions, 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.

6. Each individual providing consent must be fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.

7. For children who are pregnant, assent and permission are obtained in accord with the informed consent provisions for children.

8. No inducements, monetary or otherwise, can be offered to terminate a pregnancy.

9. Individuals engaged in the research can have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.

10. Individuals engage in the research can have no part in determining the viability of a neonate.

3. Research Involving Neonates

1. A neonate, after delivery, that has been determined to be viable may be included in research by and in accord with the requirements described in sections Administrative Procedures for Human Subject Research and Additional Protections for Children Involved as Subjects in Research.

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

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

    b. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

    c. Individuals engaged in the research will have no part in determining the viability of a neonate.

    d. Requirements outlined in 3. and 4. below have been met as applicable.

3. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

    a. IRB determines that:

        1) The research has 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

        2) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means, and there will be no added risk to the neonate resulting from the research.

b. 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 the section on Administrative Procedures for Human Subject Research, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

4. After delivery, nonviable neonates may not be involved in research unless all of the following conditions are met:

   a. Vital functions of the neonate will not be artificially maintained.

   b. The research will not terminate the heartbeat or respiration of the neonate.

   c. There will be no added risk to the neonate resulting from the research.

   d. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.

   e. The legally effective informed consent of both parents of the neonate is obtained. 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, 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.

4. Research Involving After Delivery, the Placenta, Dead Fetus, or Fetal Material

1. Research involving after delivery, the placenta, dead fetus, macerated fetal material; or cells, tissues, or organs excised from a dead fetus, must be conducted in accord with applicable federal, state, or local laws and regulations regarding such activities.

2. If information associated with 1. 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 considered research subjects.

V. Other Topics

1. Mandatory Reporting

Maine law states that certain persons who suspect child or elder abuse or neglect report this to the appropriate State agencies.

In studies where conditions of abuse or neglect might be revealed, mandated reporters should let research participants and/or the parent/guardian of participants (if applicable) know that the researcher is a mandated reporter.