Institutional Review Board for Protection of Human Subjects
Policies and Procedures Manual for Faculty, Staff, and Student Researchers

Office of Research and Economic Development
University of Wyoming

Office of Research and Economic Development
Dept. 3355, 1000 University Avenue
Old Main Room 308
Laramie, Wyoming 82071
Phone: (307) 766-5320
Fax: (307) 766-2608
http://uwacadweb.uwyo.edu/research/institutional1.asp

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Section 1: Introduction

1.0 Purpose and Scope of Manual

The University of Wyoming (UW) Institutional Review Board (IRB) documents its written procedures according to Federal Protection of Human Subjects Regulations 45 C.F.R. 46.115(a)(6), 45 C.F.R. 46.103(b)(4), and 45 C.F.R. 46.103(b)(5). This manual contains current policies and procedures and will be regularly updated to reflect new standards, regulations, and UW policy. All research projects involving human participants conducted by faculty, staff, and students associated with UW must receive IRB approval prior to initiating the research. For more information about the United States Department of Health and Human Services (HHS) policy for the Protection of Human Subjects see 45 C.F.R. Part 46. For more information about basic ethical questions in the conduct of research consult The Belmont Report.

The procedures set forth in this manual are applicable to all faculty, staff, employees, and students at UW who propose to use humans as subjects in research, and are provided so that investigators may better understand the reasons for ethical review of research with human participants, the primary ethical principles that govern such research, and the statutory basis of these principles.

This document also contains information that should be sufficient to allow researchers to submit an acceptable research proposal for IRB review of a project involving human subjects. The description of information that must be submitted and a sample consent form may in Appendix A or can be accessed at http://uwacadweb.uwyo.edu/research/institutional1.asp.

1.1 Federal Wide Assurance

UW has made the following assertions in its Federal Wide Assurance (FWA) for the Protection of Human Subjects:

1. UW assures that all of its activities related to human subject research, *regardless of funding source*, will be guided by the ethical principles in The Belmont Report.

2. UW assures that all of its activities related to federally-conducted or federally-supported human subject research will comply with the Terms of Assurance for Protection of Human Subjects for Institutions within the United States.

3. UW elects to apply 45 C.F.R. 46 and all of its subparts (A, B, C, D) to all of its human subject research *regardless of support*.
    a. Subpart A—Basic HHS Policy for Protection of Human Research Subjects (The Common Rule)
    b. Subpart B—Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
    c. Subpart C—Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
    d. Subpart D—Additional Protections for Children Involved as Subjects in Research

1.2 Office for Human Research Protections

The Office for Human Research Protections (OHRP) implements a program of compliance oversight for HHS regulations for the protection of human subjects. OHRP protects those who volunteer to participate in research that is conducted or supported by agencies of HHS. To carry out its mission, OHRP has formal agreements with more than 10,000 federally funded universities, hospitals, and other medical and behavioral research institutions in the U.S. and abroad where they agree to abide by the human subject protection regulations found in 45 C.F.R. Part 46.

OHRP evaluates all written substantive allegations or indications of noncompliance with HHS regulations. The relevant institution is notified of the allegation and is asked to investigate the basis for the complaint. The institution then provides a written report of their investigation, along with relevant institutional IRB and research records, to OHRP which determines what, if any, regulatory action needs to be taken.

OHRP provides guidance to IRB members and staff as well as to scientists and research administrators on the complex ethical and regulatory issues relating to human subject protections in medical and behavioral research. The office conducts national educational workshops in partnership with other related federal agencies and organizations. OHRP also provides on-site technical assistance to institutions conducting HHS-sponsored research.

Additionally, OHRP provides quality improvement consultation and research ethics training to domestic and foreign institutions involved in international biomedical and behavioral research to help ensure that recognized ethical protections are afforded to persons participating in research conducted in countries outside the United States. OHRP prepares policies and guidance documents as well as interpretations thereof on human subject protections and disseminates this information to the research community. In addition, every institution engaged in human subjects research conducted or supported by HHS must obtain an assurance of compliance approved by OHRP.

Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852
Toll-Free Telephone within the U.S. (866) 447-4777
Telephone: (240) 453-6900
Fax: (240) 453-6909
e-mail: OHRP@hhs.gov
http://www.hhs.gov/ohrp/

1.3 Applicable State of Wyoming Laws

Wyoming's child protection laws contain a provision which requires the reporting of child abuse or neglect (W.S. § 14-3-205). The following information will provide guidelines on what actions or inactions constitute child abuse or neglect, who is required to report, and where the report must be made.

Child abuse and neglect are defined in the following manner:

1. **Physical abuse:** deliberate physical injuries or physical injuries resulting from indifference, negligence, or improper supervision. Also included are dangerous acts which could cause a serious risk to a child's physical or mental health such as severely shaking a child five years of age or younger, choking or gagging a child, electric shock or slapping, or using physical discipline on an infant.

2. **Sexual abuse:** any sexual exploitation of a child (molestation, masturbation, incest, oral-genital contact, sodomy, etc.).

3. **Nutritional deprivation:** underfeeding or failure to feed.

4. **Medical care neglect:** refusal or failure to obtain and maintain treatment services necessary for the child's continued health including failure to give prescribed medication or withholding medical treatment from a child with serious, acute disease or injury.

5. **Intentional drugging or poisoning.**

6. **Psychological or emotional abuse:** including psychological terrorism (e.g., locking a child in a dark cellar or threats of mutilation, etc.).

7. **Negligent treatment:** failure to provide adequate food, clothing, shelter, education, health care, or supervision.

Under Wyoming law, a child is defined as "any person under the age of eighteen (18)." Even abuse or neglect which alleged to have occurred in years past (and the victim is now beyond the age of 18), must be reported in order to make a determination of the present risk that the alleged perpetrator may have to other children.

Who must report

The law requires *any* person who knows or has reasonable cause to believe or suspect that a child has been abused or neglected, or who observes any child being subjected to conditions that would reasonably result in abuse or neglect, to report.

Privileged communications between doctor and patient and psychologist and patient are not exempt from the reporting requirements. Mandated professional reporters who fail to report suspected cases of abuse or neglect may be referred to the Attorney General or the relevant licensing board for appropriate action.

In addition, if a person reporting abuse or neglect is a member of the staff of a medical or other public or private institution, school, facility, or agency, he or she must notify the person in charge as soon as possible. The person in charge is responsible to make a report or cause it to be made.

Where to report

A report of suspected child abuse or neglect must be made immediately by telephone. In the Laramie area all cases of suspected abuse or neglect can be reported to the Laramie Field Office of the Department of Family Services at (307) 745-7324 (Monday-Friday between 8 a.m. and 5 p.m.). After 5 p.m. all calls to the Laramie Field Office will automatically be referred to the local police department or a recording will instruct the caller how to file a report. In other areas of the state, reports may be made to any local county field office or to any local law enforcement agency.

Professional reporters will be requested to confirm any telephone or oral reports in writing to the local field office.

1.4 Administration of Research Ethics at the University of Wyoming

The Office of Research and Economic Development is responsible for the functioning of the IRB.

If you have questions about the rules or procedures for ethical review or the applicability of the information in this manual to your proposal, contact:

Office of Research and Economic Development
Old Main 308
Phone: (307) 766-5320
Fax: (307) 766-2608
e-mail: amiller@uwyo.edu
http://uwacadweb.uwyo.edu/research/institutional1.asp

1.5 Designation of the Institutional Review Board

UW has one IRB responsible for conducting initial and continuing reviews and providing oversight for all research activities involving the use of human subjects performed on the campus or at any location under the purview of UW. The IRB will conduct initial and continuing reviews of research activities according to Section 6 and Section 7 of this manual. All review procedures will meet or exceed the requirements set forth in 45 C.F.R. 46.

1.6 The Institutional Review Board

The IRB is composed of eight regular voting members and two non-voting members. The IRB may use, as necessary, non-voting members and consultant reviewers' considerations and discussions. The Common Rule and UW's FWA require that the IRB have at least five regular voting members, including the Chair. At least one member on the IRB must have primarily scientific concerns, one must have primarily nonscientific concerns, and one must be unaffiliated with the University (community or lay member). UW's IRB maintains a roster of more than the minimum required number of members to ensure adequate and efficient review (see Appendix O).

The IRB membership reflects expertise in both science and non-science fields. The committee shall be composed of at least one representative from each academic unit interested and involved in research related to human subjects, the Vice President or Associate Vice President for Research and Economic Development, a medical representative, and at least one qualified non-university individual (see UW Regulation 1-2). Scientific members of the IRB generally will have had experience in research involving human subjects. Nonscientific members will have professional expertise in a non-scientific area, such as law, ethics, or human or patient rights. In addition to faculty members representing different disciplines, the IRB currently has two community members. The community members will be knowledgeable about the local community and willing to discuss issues and research from that perspective. They are chosen from Laramie and its vicinity. Neither they nor their immediate families may have an affiliation with UW. Candidates for these positions include but are not limited to, clergy, lawyers, teachers, state employees, medical personnel, and businesspersons.

At times, the IRB may not have the necessary expertise to judge the scientific soundness of a research protocol and may be unable to make a fair and accurate determination of the risk to benefit ratio. For these protocols, the IRB may call upon ad hoc consultants for assistance in review for scientific merit.

The Associate Vice President for Research and Economic Development and the IRB Chair annually review IRB membership. This review includes examination of attendance, specialty, expertise, education, affiliation and diversity. Thus, the membership and composition of the IRB is periodically reviewed and adjusted to meet regulatory and organizational requirements.

The Associate Vice President submits membership recommendations to the UW President annually, who formally appoints IRB members and the IRB Chair. The Associate Vice President considers the following factors in the selection process: experience, expertise, racial, cultural, and gender diversity, and community involvement. Thus, the IRB will be able to ascertain the acceptability of proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice (see 45 C.F.R. 46.107).

Section 2: The Institutional Review Board

2.0 General IRB Policies

The governing regulations for UW's IRB are 45 C.F.R Part 46 and the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule. UW's Federal Wide Assurance (# 00000186) with OHRP specifies that the institution will follow 45 C.F.R. 46 and all of its subparts (A, B, C, D) for all human subject research *regardless of source of support*.

2.1 Functions and Responsibilities of the IRB

1. Safeguarding the rights and welfare of subjects at risk in any research activity, whether financially supported or not, and irrespective of the source of any supporting funds, is primarily the responsibility of the institution. In order to provide for the adequate discharge of institutional responsibility, no research activity involving human subjects may be undertaken by any faculty, staff, employee, or student at UW unless our IRB has reviewed and approved the research prior to commencing the research activity.

2. The review will determine whether the subjects will be placed at risk and, if risk is involved, that:

    a. Risks to participants are minimized by using procedures which are consistent with sound research design and do not unnecessarily expose participants to risk.

    b. Risks to participants are minimized whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.

    c. Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result.

    d. Selection of participants is equitable.

    e. Informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with, and to the extent required by the regulations.

    f. Informed consent will be appropriately documented, in accordance with, and to the extent required by the regulations.

    g. When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of participants.

    h. When appropriate, there are adequate provisions to protect the privacy of participants.

i. When appropriate, there are adequate provisions to maintain the confidentiality of data.

j. When some or all of the participants 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 participants.

k. The conduct of the activity will be reviewed at intervals determined by the IRB, but not less than annually.

3. The determination of when a research subject is at risk is a matter of common sense and sound professional judgment and relates to the circumstances of the research activity in question.

   a. The IRB will carefully weigh the relative risks and benefits of the research procedures.

   b. Research activities designed to yield fruitful results for the benefit of individual subjects or society in general may incur risks to the subjects provided such risks are outweighed by the benefit to be derived from activities.

   c. The degree of risk involved in any activity should never exceed the humanitarian importance of the problems to be solved by that activity. Likewise, compensation to volunteers should never be such as to constitute an undue inducement to the subject.

   d. There is a wide range of medical, social and behavioral research projects and activities in which no immediate physical risk to the subject is involved (e.g., those utilizing personality inventories, interviews, questionnaires, or the use of observation, photographs, taped records, stored data, or existing tissues, body fluids, and other materials obtained from human subjects). However, some of these procedures may involve varying degrees of discomfort, harassment, or invasion of privacy.

4. Investigators from other institutions who wish to conduct research on the UW campus must similarly obtain UW IRB approval prior to the start of their research.

5. Any activity involving the use of radiation, lasers, biohazards, or otherwise prohibited or restricted material, device, or process must have approval from UW's Office of Environmental Health and Safety before the IRB can issue approval.

6. Compliance with this policy or the procedures set forth herein will in no way render inapplicable pertinent laws of the State of Wyoming, any local law which may bear upon the proposed activity, or UW Regulations.

2.2 Confidentiality of the Review Process

During the process of initial or continuing review of an activity, material provided to the IRB shall be considered privileged information and the IRB shall assure the confidentiality of the data contained therein.

2.3 Research Determinations

Determinations about whether an activity represents human subjects research are based on the definition of "research" and "human subjects" as defined by the federal regulations.

The regulatory definition of "research" is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. To generalize is to derive general conclusions from particulars. Generalizable knowledge is a goal of most basic research. Even research about the most narrowly defined topic, such as an individual case study or the study of an isolated community, may be intended to contribute to a body of knowledge (45 C.F.R. 46.102(d)).

A "human subject" is a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. "Intervention" includes both physical procedures by which data are gathered (for example, drawing blood) and manipulations of the subject or the subject's environment that are performed for research purposes. "Interaction" includes communication or interpersonal contact between the researcher and the subject (45 C.F.R. 46.102(f)).

Investigators seeking guidance regarding whether an activity is human subjects research should consult with the Office of Research and Economic Development. The Associate Vice President for Research and Economic Development, the IRB Chair, or a designee will determine whether the activity represents human subjects research.

2.4 Suspension & Termination Policy

Suspension means a temporary withdrawal of approval of some or all research, or a permanent withdrawal of approval of some research activities. A suspended protocol requires continuing review. Termination means a permanent withdrawal of approval of all research activities. A terminated protocol does not require continuing review. The IRB has the authority to suspend or terminate approval of a research protocol that has been determined to not be conducted according to UW's human subjects research policies and procedures, or in cases in which there has been unexpected serious harm to participants. See Section 7.3 for details on the IRB's monitoring program.

While the IRB Chair or the Associate Vice President for Research and Economic Development has the right to suspend a study that poses an immediate risk to participants, generally suspensions will be determined by a vote of the full IRB. Suspensions or terminations ordered by the IRB Chair or the Associate Vice President must be placed on the agenda of the next IRB

meeting for consideration of continuation or reversal of the suspension. Should a study be suspended or terminated so that interventions or interactions with current participants will stop or change, the IRB will communicate to the principal investigator (PI) that the PI must inform current participants that the study has been suspended or terminated along with the reasons for such suspension or termination. Before suspending or terminating research, the individual or the IRB ordering the suspension or termination will consider whether the action might adversely affect the rights or welfare of current participants. In such cases, the IRB will require explicit conditions for participant withdrawal. The IRB will consider whether follow-up of participants for safety reasons is necessary and if so, the IRB will require that the PI notify participants and require the PI to continue to report unanticipated problems. Such information must be formally submitted to the IRB for their review and approval.

The report of the IRB's suspension or termination of approval will be written by IRB staff for review and approval by the full IRB. The IRB Chair and the Associate Vice President will sign the written report. Information to be included in the written report include level of study risk, category of review, a summary of the events, previous non-compliance history for the PI, the co-PI and the faculty sponsor, how the event was reported to the IRB, steps (if any) that the PI has taken to rectify the situation, reasons for IRB suspension or termination, findings of the IRB, actions taken by the IRB, and future plans. This report will be distributed according to the reporting policy detailed below.

2.5 Reporting Policy

The IRB enacts the following reporting policy when one or more of the following occurs:

1. The IRB determines an unanticipated problem involves risks to participants or others;
2. The IRB makes a determination of serious or continuing non-compliance with the federal regulations, UW policies and procedures, or IRB determinations; or
3. The IRB, the IRB Chair, or the Associate Vice President for Research and Economic Development suspends or terminates a previously approved research protocol.

IRB staff will prepare a report. Reports will be reviewed and approved by the IRB Chair, who will also sign the report. Staff will ensure that the previous reporting steps are completed within 21 days.

The report is promptly delivered to the PI and copied to:

1. Vice President for Research and Economic Development
2. Associate Vice President for Research and Economic Development
3. Dean of PI's College or School
4. Chairman or department head of PI's department
5. IRB Chair
6. Project file
7. Faculty advisor (if applicable)

8. Any federal department that has oversight due to funding, conduct, or assurance, including but not limited to, OHRP, National Institutes of Health (NIH), Food and Drug Administration (FDA), Department of Education, etc.
9. The complainant (when necessary)

Unanticipated problems are appropriately reported to the IRB, and are reflected in the monthly IRB minutes.

2.6 Meetings

The IRB holds one regularly scheduled meeting per month during the academic year, at a time and place to be pre-determined and posted on the web site at http://uwacadweb.uwyo.edu/research/IRB%20meeting%20dates.asp. IRB staff will deliver all agenda items for review to IRB members at least 5 business days prior to each scheduled meeting date.

Full board research protocols (all protocols other than exempt or expedited) will be reviewed only at convened meetings of the IRB at which quorum has been established and includes at least one non-scientific member. To be approved, a protocol must receive a majority of votes of members present at the meeting. If quorum fails during a meeting, due to a lack of a majority of IRB members being present, an absence of a nonscientific member, or a conflicting interest (see Section 3.5), the IRB will not take further actions or votes until the quorum is restored.

Prior to each full board meeting, IRB staff or the IRB pre-reviewer will review the agenda of protocols (full board) and will assign a primary and a secondary reviewer knowledgeable about or experienced in working with the proposed research content area. IRB staff ensures that either the primary or secondary reviewer is either present at the meeting or available by teleconference during the convened meeting. Should such experience within the IRB membership not be available, relevant consultation will be obtained.

2.7 IRB Minutes

Minutes of each IRB are recorded in writing. Minutes are distributed monthly to all IRB members and a vote for approval of those minutes takes place at the next convened meeting.

Minutes include the following:

1. Attendance at the meeting for each action;

2. A list of all full board proposals with the respective information:

    a. Actions taken and decisions made by the IRB
        i. Approved
        ii. Approved with explicit conditions or modifications
        iii. Tabled
        iv. Disapproved

b. The number of members voting for, against, and abstaining, and the names of IRB members who were absent from the vote;

c. Basis for requiring modifications to the research proposal or consent documents or for disapproving the research proposals;

d. A summary of controversial issues and their resolution;

e. A summary of issues pertinent to the protocol;

f. Minutes will also document, by referencing the IRB protocol file, determinations required by the regulations along with project specific findings that justify each determination. These determinations include those for waiver or alteration of consent, waiver of consent documentation, research involving children, prisoners, pregnant women, fetuses, and neonates;

g. The minutes will also document, by referencing the IRB protocol file, justification for any deletion or substantive modification of information concerning risks or alternative procedures contained in the informed consent document, and for initial and continuing review, the approval period; and

h. The names of IRB members who absented themselves from the meeting due to conflict of interest.

3. A list of all actions that were taken administratively during the previous month including proposals approved under the expedited review procedure and proposals approved as exempt.

2.8 Approval Timeframes

Exempt, expedited, and full-board proposals are generally approved for a one year period but may be shorter. The expiration date is calculated from the date of review by the convened IRB, Chair or designated reviewer and the date the protocol was approved or approved with stipulations. Continuing review approval periods are one year from the date of formal re-approval, unless otherwise necessitated (see Section 7.3).

Proposals may be submitted for review at any time. Processing of **complete** applications for exempt status and expedited review is estimated to take 10-15 business days. Applications for full board review must be submitted three weeks in advance of the scheduled IRB meeting. Even if proposals are received by the proposal due date, they may be deferred to the next scheduled meeting due to application volume. All attempts are made to limit application deferrals. Proposals received after the due date will be deferred to the next scheduled meeting.

2.9 Expiration of Research

PIs desiring to continue research beyond the study approval period must submit a continuing review (see Section 7.0). PIs do not need to file continuing reviews for data analysis only, provided there is no risk of a breach of confidentiality to participants. Upon expiration, all research and research related activities must immediately cease, including enrollment, recruitment, interventions and interactions on current participants, and data analysis. When an investigator does not provide continuing review information to the IRB or the IRB has not approved a protocol by the expiration date, interventions and interactions on current participants may continue ONLY when the IRB finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants. If the PI does not request a continuation, the study is inactive.

2.10 Protocol Files

Protocol files are maintained in file cabinets in the Office of Research and Economic Development, which encompasses the IRB. Each file contains the following:

1. A copy of the complete research proposal (see IRB Proposal Guideline, Appendix A, and at http://uwacadweb.uwyo.edu/research/institutional1.asp).

2. Any correspondence with the IRB, both formal and informal (including all emails), related to the research protocol.

3. Completed designated reviewer checklists and determinations, justifications, and findings of the IRB. For initial and continuing review of expedited studies, reviewer checklists include the specific permissible category (see Appendix J). For initial review of exempt studies, the specific category of exemption is documented (see Appendix I).

4. Official notification of IRB action.

5. Any changes made to the original research proposal, as requested by the IRB.

6. Applications for continuing review and all correspondence and records related to that review (see Annual Review, Appendix B, and at http://uwacadweb.uwyo.edu/research/institutional1.asp).

7. Applications to amend a protocol and all correspondence and records related to that review.

8. Reports of unanticipated problems and related IRB review and action.

9. Any IRB action regarding non-compliance and related correspondence.

10. Reports of injuries to participants.

11. Statements of significant new findings provided to participants.

2.11 IRB Complaints, Feedback, Concerns, and Issues

All complaints, feedback, concerns, or related issues should be directed to the Associate Vice President for Research and Economic Development:

Office of Research and Economic Development
Dept. 3355, 1000 University Avenue
Old Main Room 308
Laramie, Wyoming 82071, (307) 766-5320.
Phone: (307) 766-5320
Fax: (307) 766-2608
Email: dyates4@uwyo.edu
http://uwacadweb.uwyo.edu/research/institutional1.asp

Any allegations of noncompliance will be directed to the Associate Vice President for Research and Economic Development and adjudicated accordingly. The Associate Vice President can direct the IRB to review the complaint or meet with the involved parties to reach a satisfactory resolution. Complaints will be formally documented with resolutions noted as formal actions in the protocol files. PIs may bring forward to the Associate Vice President concerns or recommendations regarding the human research protection program, including the IRB review process.

Section 3: General Research Procedures

3.0 Extramural Research

The IRB requires all off campus research to have documented approval on file from the respective IRB of record for that site, if it exists. For example, extramural sites may include school districts, day care centers, nursing homes, private clinics, shelters, treatment facilities, churches, or businesses. In the event the extramural site does not have an IRB, the PI should request approval from the institutional entity or official with the necessary authority to approve research. The PI should determine and follow all host site's policies and procedures for human subjects research and should submit approval letters from these institutions or agencies. The letter should grant the PI permission to use the agency's facilities or resources and should indicate knowledge of the study. If these letters are not available at the time of IRB review, approval will be contingent upon their receipt.

3.1 Scientific Review

The IRB is responsible for evaluating the scientific or scholarly validity of the research (using its own expertise) so that the IRB can determine whether the research uses procedures consistent with sound research design, whether the research can answer its proposed question, whether the knowledge obtained will outweigh any risk, and whether the knowledge is generalizable. However, it is not the charge of the IRB to comment upon the value of the research proposal relative to other research proposals.

3.2 Confidentiality

Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without permission. Whenever researchers promise participants that their responses and data will be maintained in confidence, all research project members (investigators, directors, transcribers, students, staff, etc.) are required to prevent accidental and intentional breaches of confidentiality. In most cases, confidentiality can be assured by following fairly simple practices (e.g., substituting codes for identifiers, removing survey cover sheets that contain names and addresses, limiting access to identified data, and/or storing research records in locked cabinets). However, all measures used to assure confidentiality of data must be understood by all research staff before research is initiated and must be followed once research is initiated. Confidentiality procedures must be described in research proposals that come before the IRB. Researchers should recognize that the assurance of confidentiality includes keeping the identity of participants confidential.

Researchers proposing projects that will address sensitive, stigmatizing, or illegal subjects must explicitly outline the steps they will take to assure any information linking participants to the study is maintained in confidence. The requirement of signed consent forms is often waived in sensitive studies if the consent document is the only written record linking participants to the project and a breach of confidentiality presents the principal risk of harm anticipated in that research.

If the research proposal includes the use of a **focus group** (or some similar method), confidentiality cannot be guaranteed. The following language should be included in the informed consent form if focus groups are being utilized: "Although measures have been implemented by the researchers to ensure participant confidentiality, the researchers cannot guarantee what the other individuals in the focus group may do following the meeting."

If there is any chance that data or participants' identities might be sought by law enforcement agencies or subpoenaed by a court, a grant of confidentiality should be obtained. Under federal law (Public Health Act § 301(d)), researchers, prior to the initiation of the research project, may request grants of confidentiality to protect against forced data and participant identity disclosures. These grants provide protection for specific research projects where protection is judged necessary to achieve the research objectives.

If you believe your research project may require a grant of confidentiality, please contact the Office of Research and Economic Development.

For more information on Certificates of Confidentiality and their limitations, see: http://grants.nih.gov/grants/policy/coc/index.htm.

For Certificate of Confidentiality contacts at the NIH, see: http://grants.nih.gov/grants/policy/coc/contacts.htm.

For OHRP guidance on Certificates of Confidentiality, see: http://www.hhs.gov/ohrp/humansubjects/guidance/certconf.htm.

3.3 Privacy

Privacy is defined in terms of having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. When participants voluntarily permit investigators access to themselves, they exercise their right to privacy. Privacy is the right to authorize or decline access. It should not depend upon the participant's ability to exert control over another's access. An incapacitated adult or infant is unable to control access to their privacy, but still has a right to privacy. The informed consent process should disclose any risks to privacy and how investigators specifically plan to protect privacy. The IRB reviews proposals to ensure adequate privacy protections and prevent unnecessary invasions of privacy. Privacy is best protected by making sure the research is designed so that participants will be comfortable with the way investigators interact or intervene with them. Investigators must maintain the confidentiality of all private and identifiable information unless disclosure is mandated according to federal, state, or local law.

Investigators are required to follow the privacy protections outlined in the required Collaborative Institutional Training Initiative (CITI) Human Subjects Research course.

3.4 Protecting Participants' Health Information

Even in those circumstances where an exemption to the signed consent requirement applies, a signed authorization from the research participant, permitting the use and disclosure of his or her

Protected Health Information (PHI), will still be required, UNLESS specifically waived by the IRB (see Section 5.4).

3.5 Conflict of Interest

All investigators and IRB members are required to disclose any conflicts of interest according to the conflict of interest/conflict of commitment policy found in the University of Wyoming Employee Handbook (see http://uwadmnweb.uwyo.edu/hr/Employeehandbook91107.pdf).

Should an IRB member declare involvement in any way in a research protocol under review by the IRB, or state a conflict of interest with the research protocol, then the member is excluded from discussion and voting except to provide information requested by the IRB, must leave the meeting room for discussion and voting, and is not counted towards quorum.

3.6 Record Retention Requirements

The IRB collects, prepares, and maintains adequate documentation of the following types of IRB activities. All records will be accessible for inspection and copying by authorized representatives of OHRP, HHS, sponsors, university officials, and internal auditors at reasonable times and in a reasonable manner.

1. **Research Protocol Files:**

   Per 45 C.F.R. 46.115(a) and (b), pertinent information on all submitted research protocol files is kept in the Office of Research and Economic Development for three years after study closure (see Section 2.10 for details on information kept in the protocol files). At that time, they will be destroyed. Per 45 C.F.R. 46.115(a)(2), minutes of each IRB meeting are recorded in writing (see Section 2.7 for details of information recorded in minutes). Minutes are kept for at least seven years after the date of the IRB meeting in the Office of Research and Economic Development.

2. **Membership Files and IRB Roster:**

   The IRB roster includes the following information (see 45 CFR 46.103(b)(3), 46.115(a)(5)):

   a. Full Name
   b. Earned Degrees (e.g., PhD, PharmD, JD, etc.)
   c. Scientific status (scientific or non-scientific)
   d. Representative capacity
   e. Indications of experience (i.e., board certifications and licenses sufficient to describe each members' chief anticipated contributions to IRB deliberations)
   f. Relationship to the organization (employee or non-employee)
   g. Affiliation status
   h. Position on IRB (Chair; member; voting; non-voting; ex-officio)
   i. IRB training documentation

NOTE: Changes in committee membership will be reported to OHRP as required.

3. **Records required of and related to the PI of the study protocol:**

   The PI or project director shall maintain, in a designated location, all records relating to research which is conducted for at least three years after completion of the research. All records must be accessible for inspection and copying by authorized representatives at reasonable times and in a reasonable manner. Consent forms are to be available for inspection by authorized officials of UW administration, the IRB, HHS, regulatory agencies and/or sponsors as applicable to the research protocol in question.

   Should a PI or project director depart from UW prior to the completion of the research protocol, the PI is responsible for initiating mutually satisfactory arrangements with their department and the Office of Research and Economic Development as to the disposition of executed subject consents. Other than minutes, IRB records not related to a specific research activity (i.e., records that are not relevant to a specific protocol file) will be kept for three years and then destroyed.

3.7 Guidelines on Compensation for Research Subjects

The guidelines outlined below are meant to assist investigators in determining a reasonable amount of compensation that can be given to research participants and also place some boundaries on what is and is not "reasonable." The reasonableness of a particular sum of money or other form of payment should be based upon the time involved, the inconvenience to the subject, and reimbursement for expenses incurred while participating. The amount should not be so large as to constitute a form of undue influence or coercion. During the initial review of a research protocol, the IRB is required to review both the amount of compensation proposed and the method and timing of disbursement to assure that neither are coercive or present undue influence. The following are some additional guidelines:

1. Any compensation generally should not be contingent upon the subject completing the study, but should accrue as the study progresses.

2. Compensation given as a "bonus" or incentive for completing the study is acceptable to the IRB, providing that the amount is not coercive. The IRB is responsible for determining if the incentive amount is so large as to be coercive or represent undue influence.

3. The amount of compensation should be clearly set forth in the research proposal AND the informed consent document.

3.8 Guidelines for Research Advertisement Content

The IRB must review and approve all materials that will be used to recruit subjects to a specific research study. Generally, recruitment materials should be limited to information that a potential subject would need to determine if they are eligible and interested in participating. More specifically, the ads *should include information* such as:

1. Name and address of the research facility;
2. Focus of the research;
3. Purpose of the research with reference to the fact that the study is investigational;
4. Summary of criteria for eligibility to participate;
5. Time and other commitments that will be required of the subject;
6. Location of the study; and
7. The office to contact for further information.

THE ADS SHOULD NOT:

1. Contain explicit or implicit claims of safety, efficacy, equivalency, or superiority to approved procedures or treatments;
2. Emphasize the amount of reimbursement that subjects will receive. The ads *may* state that reimbursement for time, travel, etc. will be given;
3. Promise a favorable outcome or benefits;
4. Include exculpatory language;
5. Promise "free treatment" when the intent was only to say participants would not be charged for taking part in the investigation; or
6. Include a sign-up sheet.

Recruitment materials conforming to the above guidelines may be approved for any format, e.g., posted flyers, newspapers, internet advertisements, radio/television, emails, letters, etc. However, the IRB must review the final copy of printed advertisements. To avoid multiple requests for IRB review and approval, investigators should specify in their original request all recruitment materials that are anticipated.

3.9 Equitable Subject Recruitment

The IRB will only approve studies demonstrating equitable subject recruitment, taking into account the purposes of the research and the setting in which it will be conducted. The IRB evaluates all research applications to verify that investigators have demonstrated equitable selection and recruitment of all research subjects and have made every effort to ensure diversity of subject selection. In particular, the IRB evaluates any special problems that may occur with proposed research involving vulnerable populations, such as children, prisoners, pregnant women, cognitively-impaired individuals, and economically or educationally disadvantaged

persons. The IRB ensures that proposed sampling efforts do not favor some classes of participants solely due to ease of availability, compromised positions, or manipulability. IRB reviewers also require researchers to make every effort to include women and members of minority groups, if appropriate to the research purpose.

3.10 Best Practice Guidelines for Research Involving Exercise Training/Interventions and/or Exercise Stress Testing

1. The University of Wyoming Health History Screening Questionnaire (UWHHSQ; see Appendix H) will serve as the standard and required document to be utilized for pre-participation risk factor stratification prior to any research involving exercise training/intervention or exercise testing (submaximal or maximal), with or without aerobic/anaerobic fitness measurement in humans. Use of the UWHHSQ is required and intended to be a *guiding document* to facilitate comprehensive risk stratification and health appraisal in subjects prior to research participation, but should not replace expertise/experience of researchers, ***exercise professionals***, and clinicians in appraising and stratifying research participants on an individual (case by case) basis. The completed UWHHSQ will be reviewed by a qualified "***exercise professional***" for risk stratification.

2. It is *recommended* that all exercise-related research (testing and training/interventions) of moderate or high risk subjects include a collaborating medical director (defined as MD, DO, PA, NP, FNP with licensure in the State of Wyoming) who is knowledgeable of the testing protocols, measures, population demographics/characteristics, and qualifications of the research investigators and staff. If a collaborating medical director is utilized, a letter of support indicating his/her participation is required from the collaborating medical director.

3. *Exercise testing* is defined as a physical stimulus applied to a human research participant (subject) eliciting physiological changes *typical* of exercise, for example: increased heart rate and blood pressure, increased blood flow (circulation) to active regions, shunting of blood from inactive regions, accelerated respiration/ventilation which may or may not influence blood gas concentrations, and transient alteration in circulating biomarker, metabolite, or hormone concentrations typical of an exercise stimulus. *Exercise testing* may or may not include measurement of aerobic fitness (oxygen consumption; VO_2) by use of direct or indirect calorimetry or anaerobic fitness and may be at submaximal or maximal intensity levels.

4. A qualified physician (MD or DO) is defined as one who is board certified/licensed to practice within the state of Wyoming and who possesses knowledge, experience, and capability to supervise exercise tests on the appropriate age group. Inherent within this is the ability and competency to read/interpret electrocardiograms (rhythm strips or multi-lead ECG's) and monitor/assesses signs/symptoms and hemodynamic responses/changes before, during, and after exercise tests. This is commonly, but not always, indicated by privilege(s) to supervise exercise tests in clinical settings which might include but are not restricted to public/private clinics, hospitals, or rehabilitation facilities. Physicians must provide current documentation stating their experience/qualifications to supervise

exercise testing to the IRB (accompanying the IRB research application) and to the PI prior to initiation of the research. The documentation will be reviewed by the IRB to assess acceptable experience/qualifications to supervise exercise tests. The physician must be able to provide updates regarding qualifications as requested by the IRB or PI.

5. The qualified "***exercise professional***" is defined as an Advanced Cardiac Life Support (ACLS) certified exercise physiologist or health professional or an American College of Sports Medicine certified *Exercise Specialist*® who is also ACLS certified. Human research studies involving exercise may only be conducted under the supervision of a qualified "***exercise professional***". The ***exercise professional*** need not be the Principal Investigator (PI) but must be part of the research/investigative team (e.g. contracted, employee, consultant, hospital/rehabilitation employee for off-site research, clinician, etc.) participating in the exercise-related aspects of the research. Risk stratification and health appraisal are the responsibility of the ***exercise professional*** according to the criteria established within this document but often times may involve the expert judgment of a qualified physician or collaborating medical director. This process of risk stratification is intended to maximize research subject safety.

    a. ***Low risk stratification:*** Maximal or submaximal exercise testing may be administered or directly supervised by an ***exercise professional*** for low risk subjects determined by the UWHHSQ without medical (MD or DO) supervision;

    b. ***Moderate risk stratification:*** Submaximal exercise testing may be administered or directly supervised by an ***exercise professional*** for moderate risk subjects as determined by the UWHHSQ without direct medical (MD or DO) supervision. Written authorization from a subjects healthcare provider for participation in such submaximal exercise testing for moderate risk subjects is *recommended* unless deemed unnecessary by a collaborating medical director or participating qualified physician;

    c. ***Moderate risk stratification:*** Maximal exercise testing may be administered or directly supervised by an ***exercise professional*** for moderate risk subjects as determined by the UWHHSQ only with direct medical (MD or DO) supervision.* Exceptions, which must be approved by the UW IRB, might include situations in which a collaborating medical director authorizes participation in maximal exercise testing without direct medical (MD or DO) supervision after reviewing a specific subject's risk/safety ratio;

        * Consistent with the recently updated recommendation from the American College of Sports Medicine's, *Guidelines for Exercise Testing and Prescription*, Eighth edition (2009).

    d. ***High risk stratification:*** Maximal or submaximal exercise testing may be administered or directly supervised by an ***exercise professional*** for high risk subjects as determined by the UWHHSQ only with direct medical (MD or DO) supervision;

For situations in which research-related exercise testing may occur in clinical environments (e.g. hospital or clinic practice) where exercise testing practices are standard operating procedure and in which the clinical setting has existing procedures/protocols and emergency medical support personnel available for exercise testing, these supervision requirements may be reviewed, modified, and approved by the IRB on case-by-case situational basis.

6. ***Low risk stratification*** will be determined by the presence of all of the following:
    a. BP $\leq$ 120/80 mmHg
    b. LDL < 100 mg/dL
    c. HDL > 40 for male subjects and > 50 for female subjects
    d. Glucose $\leq$ 100 mg/dL

7. HDL greater than 60 mg/dL in male or female subjects will not discount another negative risk factor.

8. ***Moderate and High risk stratification*** are defined according to the most recent definitions provided by the American College of Sports Medicine's *Guidelines for Exercise Testing and Prescription*. Currently (6/15/2009), the most recent definitions are provided in the Eighth Edition (2009).

9. During risk stratification, ***exercise professionals***, staff, and collaborating healthcare practitioners must be attentive to the two hallmark differentiation points between the collective *low and moderate risk* stratifications compared to the *high risk* stratification. The two hallmark differentiation points include: a) low and moderate risk stratification is reserved for "Asymptomatic" subjects; and b) high risk stratification is for subjects with "known cardiovascular, pulmonary or metabolic disease or one or more signs and symptoms…". Along with comprehensive screening via the UWHHSQ, attention to these two points will help insure subject safety. If doubt about stratification level exists, safety should be the preeminent concern, the more conservative stratification should used, e.g. moderate versus low or high versus moderate, and guidance from a qualified healthcare provider (MD, DO, PA, NP, FNP) should be sought. Researchers conducting exercise training/interventions and/or exercise testing are required to be knowledgeable of the most recent edition (8^{th}) of the American College of Sports Medicine's *Guidelines for Exercise Testing and Prescription*.

10. Current ACLS certification is required for all ***exercise professionals*** conducting/supervising exercise testing or exercise training/interventions.

11. All investigative (research) staff are required to be certified in CPR (basic life support; BLS) with required recertification (typically every 1-2 years); each investigative unit will conduct mock emergency codes quarterly. CPR certifications are to be submitted with new IRB research applications and any request for continuation beyond the 1-year approval.

12. All exercise testing, with or without aerobic fitness (VO_2) measurement, will be monitored with at least a 3-lead electrocardiograph rhythm strip.

13. Emergency procedures will be posted in all areas where exercise testing and/or training will occur. Investigators/units will contact emergency personnel (fire department, EMS) and request a site visit prior to conducting any exercise testing/training research.

14. An automated emergency defibrillator (AED) will be immediately available and present during all exercise testing.

15. Individual [subject] research data collected will be available/provided to research participants upon their request unless doing so would compromise the integrity of the research study. Withholding individual data must be justified by the PI within the IRB research application and approved by the IRB. Communication of a subject's personal health information outside of the research team and university IRB or to a healthcare provider identified by the subject, may only occur following receipt of written and signed authorization from the subject indicating his/her desire to have the information sent to a specified healthcare provider. This authorization must be submitted to and retained by the PI. If necessary, a referral to a healthcare provider or the subject's personal healthcare provider for follow-up care may be made by the PI, qualified physician, or collaborating medical director if evidence warrants that such a referral is in the best interest of the subject.

16. The UW IRB will be provided with written emergency plans/procedures for each laboratory/unit.

17. Exercise training/interventions may be conducted in low, moderate, and high risk subjects. For high risk subjects participation in exercise training/interventions must be approved, prior to participation, by one of the following healthcare professionals: 1) the collaborating medical director qualified to assess subject risk/safety; 2) a qualified physician (see definition) able to assess subject risk/safety; or 3) a subject's personal healthcare provider (MD, DO, PA, NP, FNP) able to assess subject risk/safety. If a subject's personal healthcare provider approves participation in exercise training/interventions and the subject is high risk then written documentation/authorization must be obtained from the subject's healthcare provider and maintained in the possession of the research team.

18. Prior to participation in research involving exercise training/interventions by adults (18 years or older), it is *required* that subjects complete the Physical Activity Readiness Questionnaire (PAR-Q) with confirmation of **"NO"** on all seven items of the PAR-Q. A **"YES"** response to any of the seven item(s) *requires* approval for participation in exercise training/interventions according to #17 above.

19. The following risk statements relate to participating in exercise (training or testing at any level submaximal or maximal), and the research appropriate risk statements must be included in the IRB research application and communicated to subjects in the risk section

of the informed consent. The PI should include the risk statement(s) that are appropriate to the research being conducted. For example, studies including exercise testing but not exercise training should include the risk statement specific to exercise testing and studies including both exercise training and exercise testing should include the risk statements for both. Risk statement **(a)** is required in all applications and informed consents involving exercise.

a. Required statement: *"Participation in any physical activity or exercise has risk. These risks include but are not limited to, pain, fainting, dizziness, fatigue, nausea, shortness of breath, chest pain or angina, swelling, bruising, muscle/bone/joint soreness, joint damage, bone fracture, ligament/tendon/connective tissue damage, hospitalization, and death."*

b. Required statement for research involving exercise testing: "It is estimated that the risk of a cardiac event during exercise testing is approximately 6 events per 10,000 exercise tests."

c. Required statement for research involving exercise training/interventions: *"The risk of cardiac events is higher in adults than young adults (18-24 years). The risk of sudden cardiac death during vigorous physical activity is estimated at one death per year for every 18,000 people. The risk of cardiac event or death in sedentary individuals is higher than the risk in physically active individuals."*

d. *Suggested* statement for research involving young (traditionally college age) individuals involved in exercise training or testing: *"The risk of exercise-related death among high school and college athletes is one per 133,000 men and one per 769,000 women."*

20. Should an adverse event occur during any research involving exercise testing or training, the research study will be temporarily discontinued. The PI must notify the IRB of the adverse event within 48 hours of the event and will await review and feedback from the IRB before continuing (restarting) the research study.

Section 4: Training in the Protection of Human Subjects

4.0 NIH Policy on Required Training in Research Ethics

To increase the federal commitment to the protection of human research participants, several new initiatives to strengthen government oversight of research with human subjects were announced by HHS Secretary Shalala on May 30, 2000.

On October 1, 2000, the NIH required education on the protection of human research participants for all investigators submitting NIH applications for grants or proposals for contracts or receiving new or non-competing awards for research involving human subjects.

Before funds can be awarded by the NIH for competing applications or contract proposals involving human subjects, investigators must provide a description of education completed in the protection of human subjects for each individual identified as "key personnel" in the proposed research. Key personnel are defined as the PIs, co-PIs, and others, specified within each project, as having decision-making power over the investigation. The PI is that individual with signatory power on all documents related to the research project. This person has final authority over the project. The PI accepts responsibility for training all personnel associated with the study in compliance with human subjects regulations 45 C.F.R. Part 46. The PI may delegate responsibility, but must maintain oversight and retain ultimate responsibility for research conduct. The co-PI is that individual who co-signs on documents related to the project or who may be designated as a co-PI in grant-related documents. This person has decision-making power with regard to the conduct of the research. The co-PI reports to the PI who is ultimately responsible for the conduct of the research. Others with decision-making power may include such persons as project managers, directors, and trainers. These designations are not all-inclusive. Operationally, these individuals have some oversight responsibility for one or more portions of the project. Individuals in this category are determined uniquely for each project by the PI.

For further information on NIH policy, see Required Education in the Protection of Human Research Participants at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html and Frequently Asked Questions for the Requirement for Education on the Protection of Human Subjects at http://grants.nih.gov/grants/policy/hs_educ_faq.htm.

4.1 UW's Policy for Required Training in Human Subjects Ethics

All human subjects research conducted by UW faculty, researchers, students, and faculty advisors, including researchers from other institutions who wish to conduct research at UW, are required to complete the Collaborative Institutional Training Initiative (CITI) Human Subjects Research course prior to submitting a proposal. Effective August 27, 2008, completion of this training is mandatory for all researchers and key personnel and must be completed every two years.

Faculty and staff must complete either the *Biomedical Research Investigators* learner group or the *Social & Behavioral Research Investigators* learner group. Students must complete the *Students conducting no more than minimal risk research* learner group. If student research involves more than minimal risk, the student must complete either the *Biomedical Research Investigators* learner group or the *Social & Behavioral Research Investigators* learner group.

Even though not required, we recommend that students complete either the *Biomedical Research Investigators* learner group or the *Social & Behavioral Research Investigators* learner group even if research is no more than minimal risk.

If you have any questions about the educational training requirements and procedures, please contact the Office of Research and Economic Development at (307) 766-5320.

4.2 Alternative Sources of Information on Human Subjects Ethics

For more information about the violations of human subject protections, the foundations for the mandate of consent, and the ethical treatment of human subjects, see: The Nuremberg Code (Appendix M), The Helsinki Declaration (Appendix N), The Belmont Report (Appendix L), 45 C.F.R. 46, and this manual.

Codes of research ethics have been developed, in part to address the historical disregard for human safety and dignity. The Nuremberg Code of 1947 was the first international code of research ethics. Another early code was the Helsinki Declaration, adopted by the World Medical Assembly at its meeting in Helsinki, Finland in 1964. The first ethical code covering social and behavioral research was a set of 10 ethical principles adopted by the American Psychological Association in 1972. The American Psychological Association's principles were the first to recognize the principle of confidentiality. Most professional organizations have ethical codes, and most require authors of manuscripts submitted to the journals of these organizations to state that they have followed these ethical principles in their research. The IRB encourages investigators to abide by their respective professional codes of conduct.

The U. S. Department of Health, Education, and Welfare issued ethical guidelines in 1971 that were codified into Federal Regulations in 1974. The primary incentive for current government ethical regulation, however, began with the establishment of a National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research under the guidance of the Department of Health, Education, and Welfare in 1974. The Commission was charged with identifying the basic ethical principles that should underlie research with human subjects. The report of the Commission, called The Belmont Report (Appendix L), was published in 1978. The Belmont Report identified three basic ethical principles:

1. **Respect for persons (autonomy):** This principle acknowledges the dignity and freedom of every person. It requires obtaining informed consent from all potential research subjects or their legally authorized representatives.

2. **Beneficence:** This principle requires that researchers maximize benefits and minimize harms or risks associated with research. Research-related risks must be reasonable in light of expected benefits.

3. **Justice:** This principle requires the equitable selection, recruitment, and fair treatment of research subjects.

These three principles were the underpinnings of both an early (1980) version of a common federal policy for the protection of human research subjects and the current version of that policy. Sixteen federal departments and agencies, including the Department of Health and Human Services, the National Science Foundation, the Department of Education, and the Central Intelligence Agency adopted the regulations. This federal policy, sometimes called the Common Rule, is codified as the Common Federal Policy for the Protection of Human Subjects and was published in the Federal Register in 1991. It is referred to as 45 C.F.R. Part 46. The regulations further require that each institution at which federally funded research is conducted adhere to the principles of The Belmont Report and set forth in writing its ethical principles, policies, and procedures. UW's agreement to abide by The Belmont Report and 45 C.F.R. Part 46 is approved by the federal agency that oversees ethical issues in human research. Because UW has an FWA, UW has determined that all research projects involving human subjects, *regardless of funding status*, abide by the same ethical and regulatory standards.

Section 5: Informed Consent of Research Participants

5.0 Informed Consent

Except as described in Section 5.5 and Section 5.6, investigators may not enroll human subjects in research unless they have obtained the legally effective, written, informed consent of the subject or the subject's legally authorized representative, prior to enrollment of the subject in the research. Investigators are responsible for ensuring that the subjects, or their representatives, are given sufficient opportunity to consider whether or not to participate and must seek to avoid coercion or undue influence. The IRB is responsible for evaluating the informed consent process.

The IRB may request to observe the informed consent process to ensure adequate consent when the research involves particularly vulnerable populations. The PI may not involve a human being as a participant in research unless the investigator has obtained the legally effective informed consent of the participant or the participant's legally authorized representative. Information given to potential subjects or their representatives must be in a language that is understandable to the subject or representative. No process of obtaining consent may include exculpatory language through which subjects waive any of their legal rights or releases or appear to release the investigator, sponsor, or institution or its agents from liability for negligence. The consent process must provide sufficient opportunity to consider whether to participate.

Occasionally, the institutional setting in which the consent is sought will pose the possibility of coercion or undue influence. Conducting research at institutions that provide services to subjects may be perceived as implying that continued service is dependent upon participation in the research. Students in the educational setting may be concerned that refusal to participate will affect their grades. These institutional pressures should be addressed in the research design. The protocol must adequately preserve the right to refuse participation.

There are many other examples of possible sources of undue influence on subjects. It may not be possible to remove all sources of undue influence, but the principal investigator must examine each project to assure the elimination of coercion and minimization of undue influences. The requirement to obtain informed consent should be seen as not only a legal obligation, but also as an ethical obligation. The research design must adequately address how informed consent will be obtained and what information will be given to prospective subjects. The IRB looks at the issues of coercion and undue influence in each proposal and insists on protocols where the circumstances of the consent process minimize the possibility of coercion and undue influence to participate.

For research studies involving non-English speaking participants, the IRB requires the submission of the translated consent as an explicit condition for approval.

5.1 Elements of Informed Consent and Assent Forms

Current informed consent documents may be found in Appendix A, Sample Consent Form, and at http://uwacadweb.uwyo.edu/research/institutional1.asp. The sample consent form contains all

the required consent elements. **The following are the basic required elements (**45 C.F.R. 46.116**):**

1. 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, 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 persons that 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 (see Appendix Q for definition), 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 about research subjects' rights using the following language: "If you have questions about your rights as a research subject, please contact the University of Wyoming IRB Administrator at 307-766-5320."

8. An explanation of whom to contact for answers to pertinent questions about the research; **and**

9. 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.

Whenever appropriate, one or more of the following elements of information shall also be provided to each subject:

1. If the risks of any research procedure are not well known, for example because of limited experience in humans, a statement that the particular treatment or procedure may involve risks to the participant which are currently unforeseeable.

2. If the research includes women of child bearing potential or pregnant women, and the effects of any research procedures on embryos and fetuses is not well known, a statement that the particular treatment or procedure may involve risks to the embryo or fetus, if the participant is or may become pregnant, which are currently unforeseeable.

3. If there are anticipated circumstances under which the participant's participation will be terminated by the investigator without regard to the participant's consent, a list of anticipated circumstances under which participation may be terminated by the investigator without the participant's consent.

4. If there are costs to the participant that may result from participation in the research, a list of additional costs associated with study participation.

5. If there are adverse consequences (e.g., physical, social, economic, legal, and/or psychological) of a participant's decision to withdraw from the research, a list of consequences of a participant's decision to withdraw from the research and procedures for an orderly termination of participation.

6. If significant new findings during the course of the research that may relate to the participant's willingness to continue participation are possible, a statement will be provided to the participant stating such.

7. If the approximate number of participants involved in the study might be relevant to a decision to take part in the research, an approximate number of participants involved in the study.

Informed consent forms should be written in plain language at a reading level appropriate for the age or maturity-level of the participants. The informed consent form should be written in second person for clarity and readability (i.e., there is minimal risk to you; you will be required to perform a certain procedure; etc.).

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. 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.

See Section 8.3 for consent and assent requirements for research involving children.

5.2 Additional Consent Information for Different Types of Studies

1. **Studies involving blood samples:** The consent form should contain a statement such as, "Blood samples will be obtained by venipuncture. This method involves inserting a needle into a vein in the arm and withdrawing a sample of blood. It is routinely used to obtain blood for physical examinations. Venipuncture is accompanied by minor discomfort at the site of the needle entry and may result in slight bruising and a feeling of faintness. In this study a trained technician will obtain a 30 ml (about 2 tablespoonfuls) sample of your blood that will be analyzed for…"

2. **Studies involving blood, tissue, or body fluid for possible genetic research:** If the research involves the use of a subject's blood, tissue, or body fluid for current or future genetic research, the researcher should modify the consent form to explain subjects' rights, including:
    a. The fact that the specimens will be maintained without identifiers;
    b. The risk level to the subject if they agree to participate;
    c. Where the specimens will be stored;
    d. Who owns the specimens; and
    e. How the specimens will be used in the future.

3. **Studies that involve physical risk**: The university does not have a plan to provide facilities or insurance to cover research-related injuries. UW student participants will be afforded access to the designated services available to all students through UW's Student Health Services. Other research participants are not covered. If the study involves physical risk, assess the risk and add a statement such as, "The University of Wyoming, the principle investigator, and the research team are not liable for any injury participants might sustain while participating in this study and are not able to offer financial compensation or absorb the costs of medical treatment should the participant sustain such an injury." If emergency treatment for research related injuries is arranged by (for example) having a medical doctor available for emergency treatment, that should be stated, but a disclaimer for extended care should be put into the consent form, such as "You will be charged for continuing medical care and hospitalization for research-related injuries. The university has no plan to provide financial compensation."

4. **Studies that involve a risk to a fetus:** The female participant must be informed of the risk and the methods to be used (such as a pregnancy test) to minimize the risk.

5. **Studies that involve drugs:** The participants must be given a statement of known side effects, warned about possible drug interactions (including interactions with alcohol), and warned about activities that may be dangerous (such as driving with a drug that has a sedative effect).

6. **Studies that involve psychological risk:** The principles that apply to studies that involve psychological risk or mental stress are similar to those that involve physical risk. Participants should be informed of the risk and told that the university has no plan to provide treatment. They should be given the names and telephone numbers of agencies that may alleviate their mental concerns, such as a crisis hot line, the UW Psychology Clinic, the UW Counseling Center, and the UW Educational Psychology Clinic. If the PI or the faculty sponsor of a student investigator is qualified to treat mental health problems, that person may be listed as a resource.

7. **Studies that involve sensitive topics:** Participants should be told that some of the questions are of a personal or sensitive nature and should be given examples of the topics or questions. If questionnaires or interviews may generate reports of child physical or sexual abuse, the participant must be informed that the researcher is legally required to report this information to the Department of Family Services. The following language is

recommended: "If the researcher, or anyone involved in the research, knows or has reasonable cause to believe or suspect that a child has been abused or neglected or who observes any child being subjected to conditions that would reasonably result in abuse or neglect, he or she is required to report to the Department of Family Services." If the questionnaire or interview may generate reports that the participant plans to harm him or herself or others, the participant must be told that the investigator is ethically required to report that information to the local police department. Information about the legal obligations to report abuse and threats of harm to oneself or others may be omitted if the responses are anonymous.

8. **Studies that involve deception:** Deception should be employed *only* when there are no viable alternative procedures. Where deception is a necessary part of an experiment, the IRB will generally require that a preliminary consent be obtained, in which the investigator informs the subject of the research. After the experiment, the subject should be informed of the deception and its purpose through a debriefing process explicitly outlined in the research proposal. The IRB recognizes that there are rare instances in which no consent can be obtained or debriefing done. Deception requires that a PI get formal approval of a waiver of informed consent.

9. **Studies that involve audio or video recordings:** The following information must be included in the proposal and the informed consent:

    a. Who will have access to the audiotapes, where the tapes will be stored, when the tapes will be destroyed (or that they will be kept indefinitely and why), and whether the tapes will be used in other studies or for future research.

    b. If the recordings will be kept indefinitely, the consent should state that subjects have the right to review and delete recordings that will be kept indefinitely or shared outside of the research team.

    c. Include a check-box or signature line for consent to be audio or video recorded (this requirement will be assessed on a case-by-case basis based on the nature of the research proposal).

    d. If the researcher wishes to present the recordings at a convention or to use them for other educational purposes, he or she should get special permission to do so by adding, after the signature lines on the consent form, the following statement, "We may wish to present some of the tapes from this study at scientific conventions or as demonstrations in classrooms. Please sign below if you are willing to allow us to do so with the tape of your performance." Additionally, a second signature line should be added with the preface, "I hereby give permission for the video (audio) tape made for this research study to be also used for educational purposes." This procedure makes it possible for a participant to agree to being taped for research purposes and to maintain the confidentiality of the information on that tape.

10. **Studies that involve monetary or other compensation:** The amount and type of the stipends or other compensations and the requirements to earn them must be clearly specified. If the study extends over a period of time, it is acceptable to reward a participant with a bonus if he or she completes all the interim components of the study.

11. **Studies that involve exercise training/interventions and/or exercise stress testing (see Section 3.10 for research proposals involving exercise):** The following risk statements relate to participating in exercise (training or testing at any level submaximal or maximal), and the research appropriate risk statements must be included in the IRB research application and communicated to subjects in the risk section of the informed consent. The PI should include the risk statement(s) that are appropriate to the research being conducted. For example, studies including exercise testing but not exercise training should include the risk statement specific to exercise testing and studies including both exercise training and exercise testing should include the risk statements for both. Risk statement **(a)** is required in all applications and informed consents involving exercise.

    a. Required statement: *"Participation in any physical activity or exercise has risk. These risks include but are not limited to, pain, fainting, dizziness, fatigue, nausea, shortness of breath, chest pain or angina, swelling, bruising, muscle/bone/joint soreness, joint damage, bone fracture, ligament/tendon/connective tissue damage, hospitalization, and death."*

    b. Required statement for research involving exercise testing: "It is estimated that the risk of a cardiac event during exercise testing is approximately 6 events per 10,000 exercise tests."

    c. Required statement for research involving exercise training/interventions: *"The risk of cardiac events is higher in adults than young adults (18-24 years). The risk of sudden cardiac death during vigorous physical activity is estimated at one death per year for every 18,000 people. The risk of cardiac event or death in sedentary individuals is higher than the risk in physically active individuals."*

    d. *Suggested* statement for research involving young (traditionally college age) individuals involved in exercise training or testing: *"The risk of exercise-related death among high school and college athletes is one per 133,000 men and one per 769,000 women."*

12. **Cover Letters**: Cover letters, rather than consent forms, may be used for some categories of exempt minimal-risk research with adults such as survey or questionnaire research on non-sensitive topics. The cover letter should state the purpose of the survey, the expected number of respondents, a description of the topic of the survey, the content of the questions on the survey, a description of any reasonably foreseeable risks, a statement about confidentiality or anonymity, and a statement about how the participant may obtain additional information about the study. The cover letter should also state that "Participation is voluntary, refusal to participate will involve no penalty or loss of

benefits to which you are otherwise entitled, and you may discontinue participation at any time." Also state that "completing and submitting this survey instrument indicates your implied consent."

5.3 Authorization to use Personal Health Information (PHI)

Authorization to use Personal Health Information (PHI) must be obtained from the individual through a form separate from the informed consent form described above (see Appendix E for a medical release form template). Per 45 C.F.R. 164.508, the authorization form must include the following:

1. A description of the information to be used or disclosed that identifies the information in a specific or meaningful fashion.

2. The name or other specific identification of the person(s), or class of persons, authorized to make the requested use or disclosure.

3. The name or other specific identification of the person(s), or class of persons, to whom the covered entity may make the requested use or disclosure.

4. A description of each purpose of the requested use or disclosure. The statement, "at the request of the individual" is a sufficient description of the purpose when an individual initiates the authorization and does not, or elects not to, provide a statement of the purpose.

5. An expiration date or an expiration event that relates to the individual or the purpose of the use or disclosure. A statement of the individual's right to revoke the authorization in writing and the exceptions to the right to revoke, together with a description of how the individual may revoke the authorization. The statement, "end of the research study," "none," or similar language is sufficient if the authorization is for a use or disclosure of protected health information for research, including for the creation and maintenance of a research database or research repository.

6. Signature of the individual and date. If the authorization is signed by a personal representative of the individual, a description of such representative's authority to act for the individual must also be provided.

The authorization must be written in plain language. If a covered entity seeks an authorization from an individual for a use or disclosure of PHI, the covered entity must provide the individual with a copy of the signed authorization.

In addition to the core elements, the authorization must contain statements adequate to place the individual on notice of the following (45 C.F.R. 164.508):

1. The individual's right to revoke the authorization in writing, and either: (A) the exceptions to the right to revoke and a description of how the individual may revoke the authorization; or (B) a reference to the covered entity's notice; and
2. The ability or inability to condition treatment, payment, enrollment or eligibility for benefits on the authorization, by stating either: (A) The covered entity may not condition treatment, payment, enrollment or eligibility for benefits on whether the individual signs the authorization; or (B) The consequences to the individual of a refusal to sign the authorization when the covered entity can condition treatment, enrollment in the health plan, or eligibility for benefits on failure to obtain such authorization; and

3. The potential for information disclosed pursuant to the authorization to be subject to re-disclosure by the recipient and no longer be protected by this subpart.

5.4 Waiver of Authorization for Use and Disclosure of PHI

If a researcher seeks a Waiver of HIPAA Authorization (45 C.F.R. 164.512(i)(2)(iii)) for research purposes, all of the following criteria must be articulated in the IRB proposal:

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

    a. An adequate plan to protect the identifiers from improper use and disclosure;

    b. 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

    c. 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 study, or for other research for which the use or disclosure of PHI would be permitted.

2. The research could not practicably be conducted without the waiver or alteration.

3. The research could not practicably be conducted without access to and use of the PHI.

If all of the criteria are satisfied, the IRB will return the "IRB Waiver of HIPAA Authorization" form to the researcher. The purpose of the form is to:

1. Assist the IRB in making and documenting the determinations required to grant or deny a waiver of HIPAA authorization for research purposes, based on federal law.

2. If waiver is granted, this completed form serves as written permission from the IRB to the researcher to access, use, or disclose PHI without subject authorization.

3. The researcher provides this form to the covered entity maintaining the PHI as documentation that the UW IRB has granted a waiver of HIPAA authorization.

On the form, the IRB will indicate the purpose of waiver of HIPAA authorization:

1. Waiver is granted only for prescreening records containing PHI. When prescreening is complete, researcher must obtain HIPAA Authorization from eligible subjects for any other access of PHI; and/or

2. Waiver is granted for complete access, use, and creation of records containing PHI, but only as described in the IRB approved application.

5.5 Waiver of Documentation of Informed Consent

The IRB can waive the requirement that the consent process include a signed consent form. Investigators desiring to not have a signed consent form must still provide participants with a consent document or verbal script disclosing all the required elements necessary for informed consent. In such cases, the IRB encourages investigators to use the consent templates and remove the signature section. According to 45 C.F.R. 46.117(c), an IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds:

1. The only record linking the subject and the research would be the consent document; and

2. The principle risk would be potential harm resulting from a breach of confidentiality.

Or,

1. The research presents no more than minimal risk of harm to subjects; and

2. The research involves procedures for which written consent is normally required outside of the research context (e.g., cultural barriers).

The regulatory language and reasons for requesting waiver of documentation of informed consent must be clearly outlined by the PI in the research proposal.

5.6 Waiver of Informed Consent

The IRB may waive the requirements for obtaining informed consent or approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent listed in Section 5.1, provided that **all** of the following four conditions are met:

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

2. The waiver or amendment will not adversely affect the rights and welfare of the subjects;

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

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

*It is important to note that the CITI training module, which is a required training for all human subject researchers at UW, states with regard to waiver of informed consent that "impracticable does not mean time consuming, expensive, or inconvenient. Researchers will have to provide acceptable evidence to their IRBs that securing consent is not feasible (capable of being done or carried out), regardless of cost and time."

The regulatory language and reasons for requesting waiver of informed consent must be clearly outlined by the PI in the research proposal.

Section 6: Initial IRB Review of a Research Proposal Involving Human Subjects

6.0 Requirements for Initial IRB Review

Any faculty member, staff, or student from UW who proposes to engage in any research activity involving the use of human subjects **must submit the following** to the Office of Research and Economic Development:

1. A research proposal describing the rationale for the study, research questions to be answered, methods, procedures, data analysis plan, and other required information (see Appendix A and http://uwacadweb.uwyo.edu/research/institutional1.asp for template of research proposal). The research proposal must follow the outline in the proposal outline template.

2. An informed consent form or justification for waiver of informed consent or waiver of documentation of consent (see Appendix A, Sample Consent Form);

3. Copies of questionnaires, surveys, or similar instruments, if applicable;

4. Training verification. All human subjects research conducted by UW faculty, researchers, and students, including researchers from other institutions who wish to conduct research at UW, are required to complete the Collaborative Institutional Training Initiative (CITI) Human Subjects Research course at http://www.citiprogram.org/default.asp. Faculty and staff must complete either the *Biomedical Research Investigators* learner group or the *Social & Behavioral Research Investigators* learner group. Students must complete the *Students conducting no more than minimal risk research* learner group. If student research involves more than minimal risk, the student must complete either the *Biomedical Research Investigators* learner group or the *Social & Behavioral Research Investigators* learner group. Even though not required, we recommend that students complete either the *Biomedical Research Investigators* learner group or the *Social & Behavioral Research Investigators* learner group even if research is no more than minimal risk.

5. The certificate of completion is automatically sent to the Office of Research and Economic Development upon completion.

6. Site letters, if applicable, for extramural research (see Section 3.0).

7. Additional approval documentation from other IRBs or ethical entities (especially if conducting international research).

8. Recruitment materials (flyers, posters, web-pages, email messages, letters, etc.).

9. If the PI is a graduate or undergraduate student, a *formal* letter or e-mail from the faculty advisor, thesis or dissertation committee chair indicating review and approval of the proposal for submission to the IRB and approval of project concept and design by the graduate committee. The faculty advisor is also required to complete the Collaborative Institutional Training Initiative (CITI) Human Subjects Research course at http://www.citiprogram.org/default.asp.

6.1 Submission Schedule Requirements

The IRB has one regularly scheduled meeting per month during the academic year. See http://uwacadweb.uwyo.edu/research/IRB%20meeting%20dates.asp for the list of meeting dates and submission deadlines. Proposals may be submitted for review at any time. However, proposals which require review by the full board must be submitted to the Office of Research, Room 308, Old Main, or by email to amiller@uwyo.edu by the proposal due date **(three weeks prior to the scheduled meeting)**. Even if proposals are received by the proposal due date, they may be deferred to the next scheduled meeting due to application volume. All attempts are made to limit application deferrals. Proposals received after the due date will be deferred to the next scheduled meeting. Electronic submission of proposals as a single Word or PDF file via email is preferred. Supplementary application materials should be contained within the single document as individual appendices (clearly labeled). Following these recommendations will facilitate efficient electronic review and limits the number of applications deferred to later meetings. It is recommended that three months be allowed and planned for completion, review, and approval of projects involving human subjects.

6.2 Exempt Research Review Process

Federal regulations identify specific categories of research activities that are exempt from the federal regulations on the protection of human subjects in research. It is important to note that while a project may be exempt from the regulations, the ethical principles of conducting research with humans still apply:

1. All investigators and co-investigators are trained in the ethical principles, relevant federal regulations, and institutional policies governing human subject research;

2. Human subjects will voluntarily consent to participate in the research when appropriate and will provide subjects with pertinent information (e.g., risks and benefits, contact information for investigators and the IRB, etc.);

3. Human subjects will be selected equitably, so that the risks and benefits of the research are justly distributed;

4. The IRB will be immediately informed of any unanticipated problems that would increase the risk to the human subjects and cause the category of review to be upgraded to expedited or full board review;

5. The IRB will be immediately informed of any complaints from participants regarding their risks and benefits; and

6. Confidentiality and privacy of the subjects and the research data will be maintained appropriately to ensure minimal risk to subjects.

The investigator may not make the determination of exempt status. To request exempt status, investigators should submit a research proposal to the Office of Research and Economic Development. Processing of **complete** applications for exempt status is estimated to take 10-15 working days, though IRB staff and the designated pre-reviewer will work to process as rapidly as possible. Processing time may increase if the application is incomplete, or the pre-reviewer or staff must seek additional information to complete the determination.

An exempt determination requires that the research activity meets the criteria for exempt status under the federal regulations. The pre-reviewer will review the complete proposal using the exempt reviewer sheet (see Appendix I) and make the determination, consulting with the chair of the IRB, or other members of the IRB, as appropriate. The IRB staff will then issue a letter of exempt designation to the investigator.

All administratively approved protocol titles and the respective PIs will be reported in the appropriate agenda and minutes to the IRB at the next meeting.

6.3 Criteria for Exempt Status

The investigator may not make the determination of exempt status. To request exempt status, investigators should submit a research proposal to the Office of Research and Economic Development.

Categories exempt from IRB review include the following:

Category 1: Research conducted in established or commonly accepted educational settings, involving normal educational practices.

Category 2: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior.

NOTE: If the research involves any of the following, then this exemption does **NOT** apply:

1. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation; or

2. Research involves children and the collection or surveys, interviews, or observations of public behavior if the investigator participates in the activities being observed.

Category 3: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under Category 2, if:

1. The human subjects are elected or appointed public officials or candidates for public office; or
2. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Category 4: Research involving the collection or study of EXISTING data, documents, records, pathological specimens, or diagnostic specimens, if:

1. The sources are publicly available; or
2. Information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to subjects and involves the following:
    a. All of the data exists prior to the start of the research; and
    b. No identifiable information will be collected and no links to personal information will exist.

Category 5: Research and demonstration projects which are designed to study, evaluate, or otherwise examine public benefit or service programs, if:

1. The projects are conducted by or subject to the approval of federal department or agency heads;
2. There is no statutory requirements for IRB review;
3. The research does not involve significant physical invasions or intrusions upon the privacy of subjects; and
4. The exemption is invoked with authorization or concurrence by the funding agency.

NOTE: ALL of these criteria must be met for this exemption to apply.

Category 6: Taste and food quality evaluation and consumer acceptance studies, if:

1. Wholesome foods without additives are consumed; or
2. 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.

The exempt criteria are applied to all research *regardless of funding or funding source*.

To be classified as exempt, the research:

1. Must involve only procedures or be a type of study listed in one or more of the exempt categories listed above;
2. Cannot involve children being surveyed, interviewed or interactively publicly observed;
3. Cannot involve prisoners as research subjects;
4. Cannot be greater than minimal risk; and
5. Cannot be FDA-regulated, except for category 6.

Under federal regulations, 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 (45 C.F.R. 46.102(i)).

6.4 Research Populations for Which the Exempt Determinations May Not be Used

Children. Research involving children **cannot** be classified as exempt if the research involves:

1. Survey procedures;

2. Interview procedures; or

3. Observations of public behavior when the investigator participates in the activities being observed.

Prisoners. The federal regulations on exemptions listed above do not apply to research involving prisoners. Research involving prisoners as subjects is **never** exempt from the regulations.

6.5 Criteria for Expedited Review

The investigator may not make the determination of expedited review. Investigators should submit a research proposal to the Office of Research and Economic Development. Processing of **complete** applications for expedited review is estimated to take 10-15 working days, though IRB staff and the designated pre-reviewer will work to process as rapidly as possible. Processing time may increase if the application is incomplete, or the pre-reviewer or staff must seek additional information to complete the determination.

Applicability for initial review:

1. Research activities that:

    a. Present no more than minimal risk to human subjects; and

    b. Involve only procedures listed in one or more of the expedited review categories (listed below) may be reviewed by the IRB through the expedited review procedure authorized by 45 C.F.R. 46.110.

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.

2. The categories in this list apply regardless of the age of subjects.

3. 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 would be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented, so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

4. Researchers are reminded that the standard requirements for informed consent (or its waiver, amendment, or exception) apply, regardless of the type of review (expedited or full board) utilized by the IRB.

Per federal regulations, the categories that fall under expedited review may include the following (for both initial and continuing review). **However, to ensure adequate protection of UW employees and human subjects, *most* of the research proposals that fall under the following categories will go to the full board for review:**

Category 1: Clinical studies of drugs and medical devices if:

1. Research on drugs for which an investigational new drug application (21 C.F.R. 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); or

2. Research on medical devices for which (i) an investigational device exemption application (21 C.F.R. 812) is not required; or (ii) the medical device is cleared or 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:

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

2. 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.

Category 3: Prospective collection of biological specimens for research purposes by noninvasive means. Examples include:

1. Hair and nail clippings in a non-disfiguring manner;

2. Deciduous teeth at time of exfoliation, or if routine patient care indicates a need for extraction;

3. Permanent teeth, if routine patient care indicates a need for extraction;

4. Excreta and external secretions (including sweat);

5. 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;

6. Placenta removed at delivery;

7. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

8. Supra- and sub-gingival 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;

9. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;

10. 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 include:

1. 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;

2. Weighing or testing sensory acuity;

3. Magnetic resonance imaging;

4. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; or

5. 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 under 45 C.F.R. 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 under 45 C.F.R. 46.101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.

Expedited review process guidelines:

1. The reviewer may approve the protocol or request modifications in order to secure approval.

2. When requesting modifications, if the reviewer and investigator cannot agree on the proposed modifications, the protocol is sent to a convened IRB for review.

3. If a reviewer believes the protocol should be disapproved, the protocol is sent to the convened IRB for review.

4. In conducting initial or continuing review, the reviewer must determine that all applicability criteria are met and that all research activities fall into one or more categories of research allowing review by the expedited procedure.

5. In conducting review of modifications to a previously approved protocol, the reviewer must make sure that the modification is a minor change as defined by policies and procedures.

6. In order to grant approval the reviewer must determine that the protocol meets all regulatory requirements for approval.

7. When granting initial or continuing approval the reviewer must document the category allowing review by the expedited procedure (see Appendix J).

8. When granting initial review, the reviewer must document any determinations required by the regulations for waiver or alteration of consent, waiver of consent documentation, research involving prisoners, pregnant women, fetuses, neonates or children, and must document protocol specific findings that justify those determinations.

Applicability for Continuing Review

There are two categories of continuing review that can qualify for expedited review:

1. Research eligible for initial review by an expedited procedure; or

2. Research previously approved by the convened IRB as follows where:

    a. The protocol is permanently closed to the enrollment of new participants, all participants have completed all research-related interventions, and the protocol remains active only for long-term follow-up of participants;

    b. Where no participants have been enrolled and no additional risks have been identified; or

    c. Where the remaining research activities are limited to data analysis.

In addition, each of the above items must meet the following criteria:

1. The research presents no more than minimal risk to subjects; and

2. 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.

Applicability for Review of Modifications to Previously Approved Research

A modification to previously approved research falls under expedited review if:

1. The modification to the protocol or consent forms is minor (a modification that does not increase the risk or decrease the potential benefit to participants);

2. The modification does not involve the addition of procedures involving more than minimal risk to participants; and

3. All added procedures fall into categories 1-7 of research that can be reviewed by the expedited procedure.

6.6 Full Board Review Process

All submissions for initial review, continuing review, or review of modifications to previously approved research determined by the pre-reviewer to not be eligible for exemption or review by expedited procedures must be reviewed and approved at a fully convened IRB meeting. The IRB adheres to the process outlined below to facilitate the thorough review of each protocol according to 45 C.F.R. Part 46.

IRB staff provides a complete set of documents provided by the investigator to IRB members, each of whom is asked to review the protocols and supporting documentation in detail. Additionally, the pre-reviewer specifically assigns each new protocol to two IRB members for primary and secondary review. The pre-reviewer makes every effort to identify reviewers based upon expertise, relevance, interest, and possible conflict of interests.

The IRB meets monthly during the academic year to review and discuss each protocol. The protocols undergoing initial review are presented and discussed individually by the IRB, as well as those protocols undergoing continuing review. The primary and/or secondary reviewer presents each new study to the board, raising any additional points for discussion. Investigators and **faculty advisors** (if the investigator is a student) are strongly encouraged to attend the meeting to clarify any questions or concerns. After discussion, the Board may vote to (1) approve; (2) disapprove; (3) table; or (4) approve with explicit conditions.

A study may be tabled because the IRB did not have sufficient time, expertise, or appropriate personnel present (i.e., absence of prisoner advocate for a study involving prisoners) to vote on the study, or because the IRB needed substantive clarification or modifications regarding the protocol or informed consent documents.

A study may be approved with explicit conditions when the convened IRB is able to stipulate specific revisions that require simple concurrence by the investigator. If the IRB approves a study with explicit conditions, then the IRB member or another member designated by the IRB Chair may approve the revised research protocol under an expedited review procedure to determine whether the investigator has incorporated the specified explicit conditions into his or her project.

The potential IRB actions are:

1. **Approved:** Accepted and endorsed as written with no conditions.

2. **Approved with explicit conditions or modifications:** Accepted and endorsed with explicit minor changes or simple concurrence of the principal investigator. All explicit conditions requested of the investigator must be completed and documented prior to beginning the research. For these conditions, the IRB Chair or designated reviewer can, upon reviewing the PI's response(s) to stipulations, approve the research on behalf of the IRB. If the proposal has received approval with explicit conditions, a copy of the

corrections must be submitted to the Office of Research and Economic Development with any changes underlined or in bold.

3. **Tabled:** Generally, a research proposal is tabled if the protocol, consent form, or other materials have deficiencies that prevent accurate determination of risks and benefits. A research proposal is also tabled if the IRB requires significant clarifications, modifications or conditions that, when met or addressed, require full IRB review and approval of the PI's responses and revisions (the Office of Research and Economic Development will send an email to the PI with the requested revisions). If the study was tabled, revisions need to be submitted to the Office of Research and Economic Development with any changes highlighted in yellow, underlined, and in bold and will be reviewed at the next convened IRB meeting.

4. **Disapproved:** A research proposal is disapproved if the protocol describes a research activity that is deemed to have risks which outweigh potential benefits or the protocol is significantly deficient in several major areas.

Following the presentation and discussion of protocols receiving either initial or continuing review, a listing of protocols reviewed and administratively approved for continuation, a listing of protocol modifications, a listing of unanticipated problems reported (off-site and at UW), a listing of those protocols approved through expedited review procedures and other information relating to ongoing research activities are reported to the IRB.

6.7 Non-Compliance with IRB Policies, Procedures, or Decisions

Human subjects research that deviates from the policies, procedures, stipulations, decisions, state, or federal law is non-compliant and subject to further inquiry by the IRB and the Office of Research and Economic Development. All reports and complaints of noncompliance should be directed to the Office of Research and Economic Development (via email, phone, mail, or in person). The Office of Research and Economic Development will immediately investigate all allegations of non-compliance. If necessary, IRB staff will send the investigators in question a notice requesting the immediate suspension of all specified research activities while the issue of non-compliance is reviewed, consistent with the federal regulations (45 C.F.R. 46.113). This initial notice will also include a statement detailing the rationale for the IRB's action.

The three categories of non-compliance are general, serious, and continuing. Other definitions include an allegation of non-compliance and a finding of non-compliance:

1. **Non-compliance**: Any deviation from UW IRB policies and procedures, federal regulations, or state law. Failure to follow requirements and determinations of the IRB is also considered non-compliance.

2. **Serious non-compliance**: All non-compliance substantially affecting participants' rights and/or welfare, or impacting upon the risks or benefits.

3. **Continuing non-compliance:** A pattern of non-compliance that indicates an inability or unwillingness to comply with the regulations or the requirements of the IRB.

4. **Allegation of non-compliance:** An unproven assertion of non-compliance.

5. **Finding of non-compliance:** Non-compliance that is true in fact. A finding of non-compliance may exist because there is clear evidence, an admission, or an investigation into an allegation that has determined the allegation to be true.

All allegations of non-compliance will be brought to the attention of the Associate Vice President for Research and Economic Development. If the general non-compliance is clearly neither serious nor continuing, and there is a corrective action plan that can be readily implemented to prevent recurrence, then the matter may be placed in the protocol file and no further action is needed (for example, failure to sign the application or lost consent forms). Otherwise, the Associate Vice President will refer allegations and findings of non-compliance to undergo an evaluation by the IRB.

The IRB will review the nature of the non-compliance at a convened meeting. When allegations are found not to have a basis in fact, the investigation is closed. For findings of non-compliance, the IRB considers the following recommendations:

1. Modifying the research protocol;

2. Modifying the consent process;

3. Contacting past or current participants with additional information (for current participants whenever that information might affect their willingness to continue to take part in the research);

4. Re-consenting participants;

5. Modifying the approval period;

6. Suspension; or

7. Termination.

The IRB will also recommend whether the non-compliance was serious or continuing. Deliberations and determinations of the convened IRB will be fully documented in the minutes. All cases of non-compliance which the IRB determines to be serious or continuing noncompliance will be reported according to the Reporting Policy found in Section 2.5.

Section 7: Continuing a Research Project: Annual Review, Amendments, Monitoring of Existing Protocols, and Data and Safety Plans and Boards

7.0 The Annual Review Procedure

Any research activity (including exempt, expedited, and full board) involving the use of human subjects that has received initial review and approval by an IRB is subject to continuing review and approval. Time intervals for such reviews shall be made at the discretion of the IRB but shall occur no less than annually. Annual reviews should be submitted to the Office of Research and Economic Development using the Annual Review Form (see Appendix B and http://uwacadweb.uwyo.edu/research/institutional1.asp).

Investigators should submit an annual review when any of the following apply:

1. Research is ongoing;

2. The remaining research activities include human subjects data collection; **or**

3. The research remains active for long-term follow-up of participants despite the protocol being permanently closed to the enrollment of new participants and all participants have completed all research related interventions.

For projects in which any of the above apply, an annual review form must be submitted to the IRB. It is the principal investigator's and the faculty sponsor's responsibility to turn in this form by the end of **11 months** of the project's start date in order for review to take place for continued data collecting. The form includes the following information:

1. The number of subjects accrued, including the number of subjects enrolled to date by ethnicity and race (if applicable);

2. A summary of any unanticipated problems and available information regarding adverse events;

3. A summary of any withdrawal of subjects from the research since the last IRB review (how many and why);

4. A summary of any complaints about the research since the last IRB review;

5. A summary of any recent literature that may be relevant to the research and any amendments or modifications to the research since the last IRB review;

6. Any relevant multi-center trial reports (if applicable);

7. Any other relevant information, especially information about risks associated with the research;

8. A copy of the current informed consent document and any newly proposed consent document; **and**

9. If necessary, a copy of the approved proposal (with any changes highlighted in yellow, underlined, and in bold).

The PI must submit renewal letters from cooperating IRBs as relevant (e.g., site still operational). If the site(s) in question did not have an IRB of record and thus submitted an official letter granting permission for the investigator to conduct the research, then a second letter is not required.

Annual reviews ensure that current informed consent documents are accurate and complete. Reviewers will compare the annual review materials with the prior years' submission materials to verify accuracy and precision.

The IRB may vote to (1) approve; (2) approve with explicit conditions; (3) table; or (4) disapprove the annual review.

Annual reviews for **expedited studies** are reviewed by the pre-reviewer, IRB chair, or IRB designee. No research protocol may continue until final approval for continuation is granted.

Full board annual reviews are subject to agenda deadlines and will be reviewed accordingly. Annual review approval periods are one year from the day of formal re-approval, unless otherwise necessitated (see Section 7.3). Annual reviews submitted prior to their expiration date but not formally reviewed and approved by the expiration date are expired and all research and research related activity must cease until formal IRB re-approval. OHRP provides PIs a 30-day grace period after the expiration date to submit an annual review. However, during this time all research and research related activities must cease.

If the findings of such investigations during the annual review process warrant corrective action, the IRB may suspend or terminate a research project to ensure the quality of research. Annual review materials are stored in the IRB protocol files.

Annual review may stop only when:

1. The research is permanently closed to the enrollment of new participants;

2. All participants have completed all research-related interventions; **and**

3. Collection of private identifiable information has been completed.

7.1 Amendments to Protocols

All amendments, modifications, or changes to protocols (exempt, expedited, and full board) or consent forms must be submitted to the Office of Research and Economic Development using the Protocol Update Form (see Appendix C). The Protocol Update Form will be reviewed and

approved, as appropriate, by the IRB under the same procedure as for initial review, prior to making any changes in study procedures. Requests must describe what modifications are desired, why the changes are required, and if the changes pose any additional risks to the subjects. PIs are required to submit complete and updated research materials and indicate all changes highlighted in yellow, underlined, and in bold.

Minor changes to the protocol or consent forms may be administratively approved according to 45 C.F.R. 46.110(b)(2). The IRB uses the expedited review procedure to review minor changes in previously approved research. Minor changes are defined as changes that involve minimal risk procedures and/or do not increase the risk or decrease the potential benefit to subjects and may include expedited review categories 1-7 (45 C.F.R. 46.110(a)). Typical minor changes include changes in key personnel, non-significant changes in sample size, an addition of a questionnaire that does not include sensitive or controversial questions, a change in the compensation schedule, or an addition of a site. Minor amendments submitted to the Office of Research and Economic Development will be forwarded to the pre-reviewer, IRB Chair, or designee for review and approval. At the reviewer's discretion, the amendment/update may be reviewed by the full convened IRB.

Changes considered to be more than minor must be reviewed at a convened IRB meeting. When amendments, modifications, or changes are reviewed by the convened IRB, all IRB members will be provided with a copy of all documents submitted by the investigator.

7.2 Identification and Reporting of Unanticipated Problems

The IRB requires PIs to promptly report a summary of each unanticipated problem to the IRB through the Office of Research and Economic Development using the Unanticipated Problem Report Form (see Appendix D and http://uwacadweb.uwyo.edu/research/institutional1.asp).

UW defines an "unanticipated problem involving risks to participants or others" as an event that (1) was unforeseen; (2) was more likely than not related to the research; and (3) either caused harm to participants or others, or placed them at increased risk of harm.

An unanticipated problem may include, but is not limited to, any of the following:

1. An unforeseen harmful or unfavorable occurrence to participants or others that relates to the research protocol (injuries, side effects, deaths);

2. An unforeseen development that potentially increases the likelihood of harm to participants or others in the future;

3. A problem involving data collection, data storage, privacy, or confidentiality;

4. A participant complaint about IRB approved research procedures;

5. New information about a research study (e.g., a publication in the literature, interim findings, safety information released by the sponsor or regulatory agency, or safety monitoring report) that indicates a possible increase in the risks of the research;

6. Changes in approved research initiated without IRB review and approval to eliminate apparent immediate hazards to the participant; or

7. Incarceration of a subject.

The process for reporting an <u>unanticipated</u> problem is as follows:

1. Reporting responsibilities of PI:

    a. Within 48 hours of knowledge of the unanticipated problem, the PI is asked to submit an Unanticipated Problem Report Form to the Office of Research and Economic Development.

    b. <u>Expected</u> adverse events (adverse events described in the risks section of the consent form) only have to be reported in the annual review application (not as an unanticipated problem).

2. Reviewing and reporting responsibilities of the IRB:

    a. Unanticipated problems not meeting the definition above involving risks to participants or others: The Associate Vice President for Research and Economic Development and the IRB Chair will confer to determine if the reported unanticipated problem is an event that (1) was unforeseen; (2) was more likely than not related to the research; and (3) caused harm to participants or other, or placed them at an increased risk of harm. For those unanticipated problems failing to meet the criteria, the Associate Vice President will work with the PI towards a satisfactory and reasonable resolution for all parties. If the event is determined to be an unanticipated problem, it will be referred to the full IRB for review.

    b. Unanticipated problems found to meet the definition above are placed on the agenda for the next IRB review.
        i. If after reviewing the information the IRB determines that the event was not an unanticipated problem, the issue will be returned to the Office of Research and Economic Development to be handled administratively.
        ii. If the IRB determines that the event was an unanticipated problem, the IRB votes to take one of the following actions:
            1. Accept the actions taken by the PI to report and resolve the incident;
            2. Notify current participants when information about the unanticipated problem might affect their willingness to continue to take part in the research;
            3. Alter the continuing review schedule;
            4. Approve with explicit changes;
            5. Suspend some or all research activities;

6. Approve the study for a shorter period of time (e.g., 6 months versus 12 months); or
7. Terminate the study for cause.

c. Deliberations and determinations of the IRB will be fully documented in the minutes.

Additional reporting requirements for unanticipated problems:

1. If a sponsor funds or supports the study, then the **PI is responsible for notifying the sponsor.**

2. Similarly, if the study is a multi-site project, and the unanticipated problem occurs at a site other than the university, then **the sponsor and the PI** are required to inform investigators of unanticipated problems or reactions that occur at other sites.

7.3 Monitoring Program for Existing Protocols

{THIS SECTION IS BEING DEVELOPED}

7.4 Data and Safety Monitoring Plan and Data and Safety Monitoring Board

{THIS SECTION IS BEING DEVELOPED}

Section 8: Procedures for Research with Vulnerable Populations

8.0 Inclusion of Pregnant Women, Human Fetuses, and Neonates in Research

The IRB shall follow special procedures with respect to vulnerable populations. The procedures provide additional safeguards in research activities involving pregnant women, human fetuses, and neonates. This section is intended to follow the guidelines set forth in Subpart B of 45 C.F.R. 46. Investigators should include in the research proposal the rationale and details for the inclusion of pregnant women, fetuses, or neonates in research activities. Researchers should ensure that the informed consent process adequately addresses the risk to the fetus or neonate and pregnant women.

The IRB approves only those studies the IRB has determined to fulfill all necessary regulatory requirements. When reviewing research, the IRB ensures that there is adequate scientific and scholarly expertise to review the research. The UW IRB reserves the right to request expert consultation as necessary for adequate review.

Definitions (45 C.F.R. 46.202)

1. **Pregnancy:** Encompasses the period of time from implantation until delivery. Delivery means complete separation of the fetus from the woman by expulsion, or extraction, or any other means. A woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy, such as missed menses, until the results of pregnancy testing are negative or until delivery.

2. **Fetus:** The product of conception from implantation until delivery.

3. **Neonate:** A newborn.

Pregnant women or fetuses may be involved in research if all of the following conditions are met (45 CF.R. 46.204):

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;

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 which 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 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, the woman's consent is obtained;

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, 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 under (4) or (5) above is 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 Subpart D of 45 C.F.R. 46 for studies involving children;

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

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;

10. Individuals engaged in the research will have no part in determining the viability of a neonate; and

11. A data and safety monitoring plan has been established to monitor participants (see Section 7.4).

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met (45 C.F.R. 46.205(a)):

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 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; and

4. If the neonate is of uncertain viability (45 C.F.R. 46.205(b)), until it has been ascertained whether or not a neonate is viable, the following additional conditions are met:
    a. The IRB determines that 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 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

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 Subpart A of 45 C.F.R. 46, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest. **OR**

5. If the neonate is nonviable after delivery (45 C.F.R. 46.205(c)), all of the following additional 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; and

   e. The legally effective informed consent of both parents of the neonate is obtained, except that the waiver and alteration provisions of Subpart A of 45 C.F.R. 46 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, 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 requirement of this paragraph.

According to 45 CF.R. 46.207(b), 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 will be sent to the Secretary of HHS for review. The Secretary will determine the approvability of the research based on the conditions stated in 45 C.F.R. 46.207(b).

8.1 Inclusion of Prisoners in Research

Special procedures are in place in the federal regulations that provide additional safeguards for the protection of prisoners involved in research activities. Investigators using prisoners as participants should provide specific detail and rationale in the research proposal. Since prisoners may be influenced by their incarceration to participate in research, and, in order to assure that their decision to participate is not coerced, the IRB will adhere to Subpart C of 45 C.F.R. 46.

In the review of research involving prisoners, the IRB will apply the prisoner specific definition of minimal risk under 45 C.F.R. 46.303(d): "Minimal risk is the probability and magnitude of

physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons."

In the review of research involving prisoners, the IRB will follow the requirements for IRB membership outlined in 45 C.F.R. 46.107. If at some point while participating in a research project a participant becomes incarcerated, it is the responsibility of the PI to notify the Office of Research and Economic Development. The protocol will then be re-reviewed according to Subpart C of 45 C.F.R. 46 or the participant-prisoner will be withdrawn from research.

The IRB will review the proposed research to ensure one of the following four categories is applicable (45 C.F.R. 46.306):

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 of HHS 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; 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 of HHS 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.

The IRB will then proceed to confirm that the following items are applicable (45 C.F.R. 46.305(a)):

1. 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;

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

3. 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;

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

5. 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;

6. Where the IRB finds there may be a need for follow-up examinations or care of participants after the end of their participation, adequate provisions have been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact; and

7. A data and safety monitoring plan has been established to monitor participants (see Section 7.4).

8.2 Inclusion of Children in Research

Special procedures are in place in the federal regulations that provide additional safeguards for the protection of children involved in research activities. The IRB will adhere to Subpart D of 45 C.F.R. Part 46. The exemptions listed in 45 CF.R. 46.101(b)(1) through b(6) are applicable for research involving children except for 45 C.F.R. 46.101(b)(2) for research involving survey procedures, interview procedures, or interventions with children.

Studies involving children require parental, guardian, or legally authorized representative consent and participant assent. If any person other than the biological or adoptive parent claims to be the child's guardian (grandparents, foster parents, etc.), the PI must contact the Office of Research and Economic Development and IRB legal counsel will be consulted to determine whether the individual has the legal authority to make health care decisions on behalf of the child and therefore is the guardian as defined in the federal regulations. The IRB formally documents findings in the appropriate minutes.

Definitions (45 C.F.R. 46.402):

1. **Children:** Persons who have not attained the legal age for consent to treatments or procedures involved in research or clinical investigations, under the applicable law of the jurisdiction in which the research or clinical investigations will occur. In Wyoming, a

child can petition to be "emancipated" under W.S. § 14-1-202, but must do so by filing a written application and meeting the statutory requirements. Only if a child were "emancipated" as described above would the state of Wyoming consider the child an "adult."

2. **Assent:** The child's affirmative agreement to participate in research or clinical investigation. Mere failure to object may not, absent affirmative agreement, be construed as assent.

3. **Permission:** The agreement of parent(s) or guardian to the participation of the child in the research or clinical investigation.

4. **Parent:** The child's biological or adoptive parent.

5. **Guardian:** Pursuant to Wyoming's Probate Code, W.S. § 2-1-103(xviii), a "guardian" means the person appointed by the court to have custody of the person of the ward under the provisions of this code.

For studies involving children, the IRB may approve only the categories of research listed below provided all applicable criteria are met:

1. **Research not involving greater than minimal risk (**45 C.F.R. 46.404). If the IRB finds that no greater than minimal risk to children is presented, approval may be given only if adequate provisions are made for soliciting the assent of the children and the permission of at least one parent or guardian. Minimal risk means that the probability and magnitude of the 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 exams or tests.

2. **Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (**45 C.F.R. 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, **approval may be given 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;

    c. Adequate provisions are made for soliciting the assent of the children and permission of at least one parent or guardian; and

    d. A data safety monitoring plan has been established to monitor participants (see Section 7.4).

3. **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 (**45 C.F.R. 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 which is not likely to contribute to the well-being of the subject, **approval may be given only if 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 subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition;

    d. Adequate provisions are made for soliciting assent of the child and permission of both parents or guardians; and

    e. A data and safety monitoring plan has been established to monitor participants (see Section 7.4).

4. **Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (**45 C.F.R. 46.407**),** if the IRB does not believe the research meets the requirement of 46.404**,** 46.405, or 46.406, **approval may be given 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;

    b. The Secretary of HHS, after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment has determined either (1) that the research in fact satisfies the conditions of 404**,** 405, or 406; or (2) 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 the research will be conducted in accordance with sound ethical principles and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians; and

    c. A data and safety monitoring plan has been established to monitor participants (see Section 7.4).

8.3 Requirements for Consent and Assent Involving Children

In accordance with 45 C.F.R. 46.408(a), the IRB must determine that adequate provisions have been made for soliciting the assent of children, when in the judgment of the IRB the children are capable of providing assent. The IRB recommends that assent be sought for children ages five and older, but may be appropriate for younger children depending on their aptitude.

The IRB may determine that assent is not a necessary condition for proceeding with the research if:

1. The aptitude of some or all of the children is so limited that they cannot reasonably be assented (determinations of capacity to assent will be assessed by age, maturity, and psychological state, and may be made for one, some, or all children in the research as the IRB deems appropriate);

2. The intervention or procedure involved 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 research; or

3. The research meets the required criteria for waiver of consent stated in 45 C.F.R. 46.116(d) (see Section 5.6).

When assent is required, it must be documented. Assent can be oral or written depending on the age and aptitude of the child.

In addition to the children's assent, the PI is required to solicit consent of each child's parents or adoptive parents. If there is any other person who claims to be the child's guardian (grandparents, foster parents, etc.), the PI must contact the Office of Research and Economic Development and IRB legal counsel will be consulted to determine whether the individual has the legal authority to make health care decisions on behalf of the child and therefore is the guardian as defined in federal regulations.

Parents must be consented following criteria in 45 C.F.R. 46.116(a) (see Section 5.1) and any additional elements the IRB deems necessary. One parent's signature is sufficient for research that is minimal risk or greater than minimal risk with the prospect of direct benefit to the participant (see 45 C.F.R. 46.404 and 46.405).

For research conducted under 45 C.F.R. 46.406 and 45 C.F.R. 46.407, consent is required from both parents unless:

1. One parent is deceased, unknown, incompetent, or not reasonably available; or

2. When only one parent has legal responsibility for the care and custody of the child

Parental consent must be documented according to 45 C.F.R. 46.117.

Waiver of Parental Informed Consent

The OHRP has addressed whether parental permission can be "passive" on its website (see http://www.hhs.gov/ohrp/faq.html):

> Terms such as "passive" or "implied" consent are not referenced in the HHS regulations. However, OHRP is aware that these terms are sometimes used by investigators or IRBs to describe a process in which consent or parental permission requirements have been altered or waived, or for which the requirement to document consent or parental permission has been waived.
>
> The term "passive consent" is sometimes used in research with children to describe situations in which the investigator can assume that a parent is permitting a child to participate. For example, researchers collecting survey and behavioral data from children at school provide parents with information regarding the study by mail and ask the parent(s) to return a form if they do not want their child to participate. Sometimes this practice is referred to as an opt out procedure, which is not consistent with the regulatory requirement for seeking and obtaining parental permission.

Even though passive consent is not contemplated by the regulations, the IRB may waive the requirement to obtain parental permission. There are essentially two ways in which the IRB may waive this requirement when the research involves children:

1. Under 45 C.F.R. 46.408(c), the IRB may waive informed consent if the IRB finds and documents all of the following factors:

    a. The 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);

    b. An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted; and

    c. The waiver is not inconsistent with federal, state, or local law.

2. Under 45 C.F.R. 46.116(d), the IRB may waive informed consent if the IRB finds and documents all of the following factors (see Section 5.6):

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

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

    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.

It is important to note that the CITI training module, which is a required training for all human subject researchers at UW, states with regard to waiver of informed consent that "impracticable does not mean time consuming, expensive, or inconvenient. Researchers will have to provide acceptable evidence to their IRBs that securing consent is not feasible (capable of being done or carried out), regardless of cost and time."

8.4 Inclusion of Adults Who Lack Decision-Making Capacity in Research

Special procedures for IRB review and approval apply to research activities involving potential research subjects who, for a wide variety of reasons, are incapacitated to the extent that their decision-making capabilities are diminished or absent. Impaired capacity is not limited to individuals with neurologic, psychiatric, or substance abuse problems. Conversely, individuals with these problems should not be presumed to be cognitively impaired.

Generally, cognitively impaired potential or actual research subjects may not understand the difference between research and treatment or the dual role of the researcher. Therefore, when appropriate, it is essential that the consent/assent process clearly indicate the differences between individualized treatment (e.g., special education in classroom settings) and research.

PIs should also consider implementing DSMP to review the consent/assent process (see Section 7.4). PIs may want to consider using an independent expert to assess the participant's capacity to consent or assent. PIs need to specify in the research proposal consent, assent, and legally authorized representative procedures.

Participants unable to consent must have consent of their legally authorized representative. The IRB will evaluate whether participants unable to consent should be required to assent to participation. The IRB will only approve research involving adults that cannot consent provided the following criteria are met:

1. The research question cannot be answered by using adults able to consent;

2. The research is of minimal risk or more than minimal risk with the prospect of direct benefit to each individual participant;

3. The assent of the adult will be a requirement for participation unless the adult is incapable of providing assent; and

4. When assent is obtained, the PI will document the assent by noting on the consent or assent form that the participant assented to participate in research.

8.6 Student Research with Human Subjects

Student research involving human subjects falls into one of two categories: (1) research practica, or (2) directed or independent research projects.

Research Practica
Research practica are class projects or assignments designed to provide students an opportunity to practice various research methodology such as performing interviews, conducting surveys, observing subjects, holding focus groups, or analyzing data. Research practica are intended to provide students in the class with a learning experience about research. They are not intended to create new knowledge about the participants, to result in information that is generalizable, or to lead to scholarly publication.

Research practica do not require IRB review unless, due to the vulnerability of subjects or the potential risk to subjects, the project falls into one of the following categories:

1. Studies in which minors, pregnant women, prisoners, or cognitively impaired persons will be interviewed;

2. Studies in which students will be asking about illegal activities, such as underage drinking or illegal drug use, which place the data at risk of subpoena;

3. Studies in which subjects are at risk if confidentiality is breached, such as one that asks about socially stigmatized behaviors and attitudes; or

4. Studies that place subjects at risk due to emotionally charged subject matter.

If a class assignment moves from the category of "non-research" into the category of "regulated research" because faculty or students decide to use the data for further research and publication, approval by the IRB will be required prior to taking this next step.

Research Projects, Directed or Independent
Any research conducted by undergraduate students, graduate students, or faculty that does not fall under the definition of a research practicum, is considered a research project. A research project that uses human subjects and is intended to contribute to generalizable knowledge must be reviewed and approved by the IRB. This research includes, but is not limited to, independent undergraduate research projects and honors theses, masters' theses, and doctoral dissertations. A research project may be exempt from IRB review, but it must meet explicit criteria and the IRB must approve the exemption.

Responsibility of Faculty
If research practica involving human subjects will be taking place in the classroom, the faculty member must fill out and submit a one page informational sheet to the Office of Research and Economic Development (see Appendix G). Faculty have a responsibility to ensure that research pratica are conducted according to the ethical standards of the relevant discipline. Faculty also have a responsibility to determine when an undergraduate or graduate student project does not meet the definition of a practicum and must be reviewed by the IRB.

When student research activities are not practica, faculty have a responsibility to assist students in preparing and submitting an IRB proposal and to ensure that students complete the required human subjects research training module at https://www.citiprogram.org/. IRB approval will not

be granted without documentation of the required training. Although members of the IRB and staff strive for timely IRB approval, the process can be lengthy, and it is recommended that faculty and students look at the IRB proposal deadline and meeting schedule available at http://uwacadweb.uwyo.edu/research/IRB%20meeting%20dates.asp.

All student led research, regardless of whether it is a thesis, dissertation, or independent project, must be accompanied by a letter from a faculty sponsor stating that he or she has read and reviewed the research plan and will provide oversight of the project. The faculty sponsor will be the individual responsible to the IRB, should any adverse events occur.

APPENDIX A

Information and Guidelines for Proposal Approval or Exemption

The investigator may **not** make the determination of the appropriate level of review (exempt, expedited, or full board review). Investigators should submit a research proposal to the Office of Research and Economic Development, Room 308 Old Main, or by email to amiller@uwyo.edu, for any type of research/project that involves human subjects. The Institutional Review Board (IRB) will make the determination of the appropriate level of review.

Research which involves the participation of **human subjects** requires approval or exemption from the Institutional Review Board (IRB) prior to the initiation of the project. The Code of Federal Regulations defines **research** as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." The regulations define **human subject** as "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." These regulations extend to the use of human organs, tissues, and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects.

New policy regarding training: All persons affiliated with the university who conduct human subject projects/research requiring IRB review/approval are required to complete the human subjects research training module at https://www.citiprogram.org/. It is recommended that the CITI human subject training is completed *prior* to submission of the IRB application and supporting materials. Certificate of completion should accompany the proposal. IRB approval will not be granted without documentation of the required training.

Proposals for research projects which will involve human subjects should be submitted to the IRB in care of (email submission is strongly encouraged):

Institutional Review Board
Room 308, Old Main
1000 East University Avenue, Department 3355
Laramie, WY 82071

Phone: 307-766-5320
Fax: 307-766-2608
email: amiller@uwyo.edu

Proposals may be submitted for review at any time. Processing of **complete** applications for exempt or expedited review is estimated to take ten working days, but may be longer due to application volume. Processing time may increase if the application is incomplete, or the pre-reviewer or staff must seek additional information to complete the determination. Proposals which require review by the full board must be submitted to the Office of Research and Economic Development by the proposal due date **(three weeks prior to the scheduled meeting)**. Board meeting schedules are posted on the IRB web site at http://www.uwyo.edu/Research/IRB%20meeting%20dates.asp. Even if proposals are received by the proposal due date, they may be deferred to the next scheduled meeting due to application volume. All attempts are made to limit application deferrals. Proposals received after the due

date will be deferred to the next scheduled meeting. It is recommended that three months be allowed and planned for completion, review, and approval of projects involving human subjects.

Proposals may be submitted in any format: in hard copy typed on letter size white paper, or electronic format e-mailed to amiller@uwyo.edu. **Electronic submission via email is encouraged**. Electronic submission of proposals as a single Word or PDF file via email is preferred. Supplementary application materials should be contained within the single document as individual appendices (clearly labeled). Following these recommendations will facilitate efficient electronic review and will limit the number of applications deferred to later meetings.

PROPOSALS MUST BE WRITTEN IN TERMS WHICH CAN BE CLEARLY UNDERSTOOD BY REVIEWERS. The IRB is comprised of community professionals and university scientists. Reviewers, however, may not be specialists, or even familiar, with the area of study described in the proposal. Proposals must include the following information:

1) Name, title, department, address, phone number, fax number and e-mail address of principal investigator, co-investigators, and faculty supervisor (for students).

2) **Title of research project.**

3) Anticipated project duration.

4) Purpose of research project, including the significance of the study and a two-paragraph literature review

5) Description of human subject participation:

- age-range and gender of preferred subjects
- how subjects will be selected and solicited for participation (how subjects will be recruited)
- the number of subjects expected to be involved
- incentive, if any, for subject participation
- description of special classes of subjects, such as human fetus, in utero and ex utero, fetal material and placenta; pregnant women; children and minors; cognitively impaired persons; prisoners or incarcerated juveniles; traumatized or terminally ill patients; elderly/aged persons; minorities; students or employees; and international subjects
- criteria for potential subjects to be included or excluded from the subject pool

6) Procedure: <u>detailed</u> explanation of the research procedures including:

- description of subjects' participation and what subjects will be expected to do and how long it will take
- if applicable, description of what non-participants will do while other subjects participate in the research procedures (for example, in a classroom where some children may not have parental consent to participate or choose not to participate)

- details of what subjects will be told about the research project
- description of deception, if any, and procedures to debrief subjects
- reasonable estimate of time involved including frequency and duration
- where research will take place
- method of data collection (survey, instruments, interview questions, etc.)
- when and how subjects may terminate participation, and/or under what circumstances procedures may be stopped
- description of biological samples to be taken, if any, procedures to obtain samples, and qualification of person(s) obtaining samples
- description of equipment, if any, to be used on or by subjects
- for research projects where data is collected in a classroom setting, be specific about what data will be collected for research analysis outside of the classroom (actual coursework samples, test scores, observation notes, etc.) and describe how it will be used; clarify whether the entire class will take the curriculum being studied, or if only a part of the class will use the curriculum being studied and part will continue the old/current curriculum as a control

7) Description of the extent to which subjects will be identified, directly or indirectly through codes or identifiers, including:

- whether or not subjects will be identified, either by name, appearance, or nature of data (demographic data including age, gender, ethnicity, affiliations, etc.)
- procedure to protect privacy and confidentiality
- how and where collected data will be stored and for how long
- who will have access to the data and under what circumstances
- any other aspects regarding confidentiality

8) Description of benefits of the research in general and benefits to the subjects, if any:

- indirect benefits (to class of participants represented, general body of knowledge, or society-at-large)
- direct benefits to subjects (including monetary compensation or other tangible incentive to participate) or state that there are no direct benefits to the subjects

9) Detailed description of any reasonably foreseeable risks or discomforts to the subjects as a result of each procedure, including discomfort or embarrassment with survey or interview questions, exposure to minor pain, discomfort, injury from invasive medical procedures, or harm from possible side effects of drugs. All projects are deemed to involve some level of risk to human subjects, however obvious or obscure. Proposals that state there is no risk must qualify exactly why there is no risk. Generally, there is always some risk, even if minimal. Proposals must state:

- that minimal risk is involved when the proposed research is viewed as involving little or no risk to human subjects. Risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or

during the performance of routine physical or psychological examinations or tests. Even when risk is minimal, investigators must still state **what** the minimal is and **why** it is minimal.

- whether the research may involve greater than minimal risk, and what protection and/or treatment will be provided to subjects in the event of a research-related injury, including who will pay for necessary treatment and the availability of other financial compensation. When the research involves greater than minimal risk, a data safety and monitoring plan must be included.
- the likelihood, severity, duration, and effects of each potential risk. Common risks may include physical injury or harm; psychological trauma, stress or harm; social (invasion of privacy or breach of confidentiality) and/or related economic harm; legal risks (such as state or local law requirement to report child abuse or neglect).
- description of methods to minimize risks, including how and by whom treatment may be offered (including counseling for psychological distress), and qualifications of persons performing procedures or collecting data.
- description of treatment available, referrals for treatment and/or counseling, including estimate of costs involved and who will be responsible for those costs.

10) Description of procedure to obtain informed consent or other information to be provided to participant, including

- how and by whom subjects will be approached to obtain consent
- how information will be relayed to subject (read to, allowed to read, audiotaped, videotaped). If information will be audio or video recorded, the following information must be included in the proposal and the informed consent form: (1) who will have access to the audiotapes, where the tapes will be stored, when the tapes will be destroyed (or that they will be kept indefinitely and why), and whether the tapes will be used in other studies or for future research; (2) if the recordings will be kept indefinitely, the consent should state that subjects have the right to review and delete recordings that will be kept indefinitely or shared outside of the research team; and (3) a check-box or signature line for consent to be audio or video recorded (separate from the signature line for consent to participate).
- description of feedback, debriefing, or counseling referral to be provided
- procedure to obtain assent of children of an age and mental capacity deemed capable of providing such. Assent must be obtained in a separate document and/or in a separate location from the parent(s). Assent can be oral or written depending on age and maturity of the child.
- for curriculum-based action studies conducted in classroom settings, student subjects may have to complete all the class assignments for the curriculum as part of their normal course work for a grade, but students (and their parents) are free to give or withhold their permission for the investigator to use that work outside of the classroom for research.

Informed consent is a process, not just a form. Information about the research must be presented IN CLEAR, UNDERSTANDABLE LANGUAGE to enable persons to voluntarily decide whether or not to participate as a research subject. The procedures should be designed to educate the subject population in terms that they can understand. To be effective, informed consent forms must be written in "lay" language at an appropriate reading level to be understandable to the people being asked to participate or provide consent for a minor to participate. **The average individual only reads at an 8th grade level.** Informed consent forms should be written to the participant, for example, "You will be asked to fill out a survey." Requests for parental consent should be written to the parent referring to their child, for example, "I will ask your child to read aloud to the group," "Your child will be asked to complete a 3-page questionnaire."

Requests for participant assent (for subjects under 18 years of age) should be separate from the parental consent form and written at an age appropriate reading level. Assent can be obtained orally (but must be documented) depending on the age and maturity of the child.

Checklist for consent/information form (all of these items MUST be in the consent form):

- A statement that the study involves research, an explanation of the purpose of the research and the **expected duration** of the subject's participation, a description of the **procedures** to be followed, and identification of any **procedures which are experimental**.
- A detailed and specific description **of any potential risks or discomforts** to the subject. The consent form should state why minimal risk is involved when the proposed research is viewed as involving little or no foreseeable risk to human subjects.
- A **description of any benefits** to the subject or to others which may reasonably be expected from the research. Include indirect benefits such as contribution to the general body of knowledge to benefit the class of participants represented or society-at-large, and direct benefits to subjects including any monetary compensation or tangible incentive (or state that there are no direct benefits to the subjects).
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- A statement describing how and to what extent confidentiality of records identifying the subject will be maintained, including who will have access to the data, for what purposes, how the data will be stored, and for how long.
- For research involving more than minimal risk, an explanation as to whether any compensation will be provided and an explanation as to what medical treatments will be provided if injury occurs and, if so, what they consist of, who will be responsible for medical expenses, and where further information may be obtained.
- Information about who to contact for answers to questions about the research, including a UW department, principal investigator's name, faculty advisor name if an undergraduate or graduate student is the investigator, and phone number.

Also include contact information for questions about rights as a research subject (University of Wyoming IRB Administrator 307-766-5320).

- 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.

To obtain effective informed consent, the statement regarding voluntary participation must be understood by the person (subject) giving their consent, whether for themselves, or on behalf of their child. To insure that the voluntary nature of a subject's participation is fully understood, the voluntary statement must be written in age/education appropriate language. **THE FREEDOM OF CONSENT STATEMENT APPLIES TO ALL TYPES OF PROJECTS AND MUST APPEAR ON THE CONSENT FORM or OTHER INFORMATION THAT WILL BE GIVEN TO THE PARTICIPANTS.** For research involving children, it should be clear that the child subject will be free to refuse to participate and may withdraw participation at any time during the study, even if parental consent has been obtained. Remember that for curriculum-based action studies conducted in classroom settings, note that student subjects may have to complete all the class assignments for the curriculum as part of their normal course work for a grade, but students (and their parents) are free to give or withhold their permission for the investigator to use that work outside of the classroom for research.

- Description of how a subject may withdraw their participation.
- If appropriate, a statement that the particular treatment or procedure may involve risks which are currently unforeseeable.
- If appropriate, anticipated circumstances under which a subject's participation may be terminated by the investigator.
- If appropriate, any additional costs to the subject that may result from participation in the research.
- If appropriate, the consequences of a subject's decision to withdraw.
- Space for the **printed name** and **signature** of subject. Depending on the age and ability of subjects under 18 years of age, the IRB requires that the assent of the minor subject be on a separate form in addition to the consent of the parent or guardian.

The actual consent or assent form which will be provided to human subjects must be approved by the IRB and research subjects should receive a copy of the form at the time it is signed.

11) **Attach copies of survey instruments, interview questions, tests, and other pertinent documentation that will be used to conduct the research.** The name and phone number of an appropriate person to contact for more information about the study must appear on information letters or survey instruments for projects where a consent form is not required. Attach copies of flyers or other means to be used to advertise to solicit/recruit subjects. All recruitment and advertising

materials must be submitted to and approved by the IRB.

12) **If the principal investigator is a graduate or undergraduate student**, submit a letter from the faculty advisor, thesis or dissertation committee chair indicating review and approval of the proposal for submission to the IRB. The IRB will not approve a proposal without the proper letter(s) of support.

13) **If subjects will be solicited through an institution such as a school or hospital, or if the research will be conducted at such an institution, provide a letter of agreement/approval to do so from an authorized representative of that institution.** Letters of agreement/approval from the individuals at the institution that will work directly with the researcher either by allowing access to the subjects (i.e. teacher allowing access to classroom) or actively participating by collecting consent forms, distributing surveys, or collecting data are also desirable. The IRB will not approve a proposal without the proper letter(s) of support.

Questions regarding the submission of research proposals involving human subjects may be directed to Linda Osterman, Research Coordinator (766-5320; osterman@uwyo.edu), Tara Nelson, Legal Counsel (766-4121; trnelson@uwyo.edu), or Dorothy Yates, Associate Vice President of Research and Economic Development (766-5320; dyates4@uwyo.edu).

CONSENT FORM OUTLINE

I. General purpose of the study:

Why are you conducting this study? What do you hope to gain from this study? Why should subjects participate?

II. Procedure:

How and where will the study be conducted? **Who** will be conducting the study? **What** will the subject be expected to do? **How much** of the subject's **time** is needed?

III. Disclosure of risks

State why risks involved in participation are minimal, or if the project involves more than minimal risk, **describe in detail all potential risks of the study, and procedures to minimize risks.**

IV. Description of benefits:

List any direct/indirect benefits to the subject, including compensation or incentive, if any.

V. Confidentiality:

What level of confidentiality will be afforded to subjects? **How will confidentiality be protected? Who will have access to the data, how will the data be protected, and how long will the data be kept?** Will the data be used for research purposes at any time other than the purpose(s) stated above? Please note that confidentiality cannot be guaranteed, but you can describe the methods you will use to protect confidentiality. Confidential and anonymous are not the same, please use the applicable terminology for your study.

VI. Freedom of consent:

Include a statement such as: "My participation (my child's participation) is voluntary and my (my child's) refusal to participate will not involve penalty or loss of benefits to which I am (my child is) otherwise entitled, and I (my child) may discontinue participation at any time without penalty or loss of benefits to which I am (my child is) otherwise entitled."

For studies involving classroom students: "I understand that my (my child's) refusal to participate or my (my child's) withdrawal at any point will not affect my (my child's) course grade or class standing."

This statement should be written in language appropriate for the age and level of education of the subjects.

Include procedures for subject, or parent/guardian on behalf of subject, to withdraw from study.

VII. Questions about the research:

Include name, address and phone number where principal investigator/faculty advisor can be reached during normal business hours. Also include the statement "If you have questions about your rights as a research subject, please contact the University of Wyoming IRB Administrator at 307-766-5320."

VIII. Consent/assent to participate:

_____
Printed name of participant

_____ _____
Participant signature Date

IX. Parental consent required for all subjects under 18 years of age.

Parental consent must include all the elements of a normal consent form and must be **SEPARATE** from the minor's assent (the minor and parent need to consider participation independently).

PARENTAL SIGNATURE EXAMPLE:

As parent or legal guardian, I hereby give my permission for (child's name) _____ to participate in the research described above.
(printed name of participant)

_____
Printed name of parent/legal guardian

_____ _____
Parent/legal guardian signature Date

APPENDIX B

ANNUAL REVIEW FORM

For projects in which data collection lasts longer than one year, an annual review form must be submitted to the IRB. It is the principal investigator's and the faculty sponsor's responsibility to turn in this form by the end of 11 months of the project's start date in order for review to take place for continued data collecting.

Annual review forms should be submitted to the Office of Research and Economic Development, Room 308, Old Main or via email to amiller@uwyo.edu. **Electronic submissions are encouraged.**

Title of research project:

Principal investigator:

Mailing address:

Telephone number:

Email:

Faculty advisor (if relevant):

Duration of project: Starting date Expected end date

I. Project status (check one, choices continued on next page)

☐ **Continuing** with **no changes** in procedures, risks, or number of planned/approved human subjects since the last IRB review (and as outlined in the approved protocol).

Research is expected to be done by:

☐ **Revised** with **minor** changes as indicated on this form. For substantial changes, a new protocol must be submitted, indicating the manner in which the project was revised, and returned with this form.

Please indicate **minor** changes below (such as those in procedures, risks, or number of subjects). Attach a revised protocol if necessary.

☐ Research has not started yet, but is expected to begin on:

II. For continuing activity, please answer the following:

1. Number of subjects studied to date:

   Number of subjects studied this year:

   If continuing, total number of subjects to be studied:

   Complete the following tables. If ethnicity and/or race are not collected as part of the research, only complete the number of subjects above.

Ethnic Category	**Sex/gender**		
	Females	Males	Total
Hispanic or Latino			
Not Hispanic or Latino			
Ethnic category: total of all subjects*			

Racial Categories	**Sex/gender**		
	Females	Males	Total
American Indian/Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
Racial categories: total of all subjects*			

*The "ethnic category" must equal the "racial category"

2. Have any unanticipated problems occurred?

   An unanticipated problem is defined as "any incident, experience, or outcome" that (1) is unexpected (in terms of nature, severity, or frequency); (2) is related or possibly related to participation in the research; and (3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. Expected adverse events (adverse events described in the risks section of the consent form) are not considered unanticipated problems.

   ☐ Yes ☐ No

   If there has been any unanticipated problem(s), please fill out and attach the Unanticipated Problem Report Form.

3. Have any expected adverse events occurred (adverse events described in the risks section of the consent form)?

   ☐Yes ☐ No

   If yes, how many and describe the event(s):

4. Has there been any withdrawal of subjects from the research since the last IRB review?
   ☐Yes ☐ No

   If yes, describe how many, when, and why:

5. Have there been any complaints about the research since the last IRB review?
   ☐Yes ☐ No

   If yes, describe the complaint(s) and any response(s):

6. Is there any recent literature that may justify or suggest that the existing research project or procedures should be modified, ceased, or the risks of participation are greater than described in the initial protocol?
   ☐Yes ☐ No

   If yes, describe any amendments or modifications made to the research (and attach a revised protocol with changes indicated):

7. Are there any relevant multi-center trial reports?
   ☐Yes ☐ No

   If yes, describe:

8. Is there any other relevant information, especially information about risks associated with the research, that has come to light since the last review?
   ☐Yes ☐ No

   If yes, describe:

9. Attach a copy of your **current consent form**.

APPENDIX C
Protocol Update Form

*An update form must be submitted to the IRB for approval of any changes to an approved protocol. This form is to be used for **minor** changes to an IRB protocol that occur **outside** of the annual review process. For substantial changes, a new protocol must be submitted, indicating the manner in which the project was revised, along with this form.*

Protocol update forms should be submitted to the Office of Research and Economic Development, Room 308, Old Main or via email to amiller@uwyo.edu. **Electronic submissions are encouraged.**
Title of research project:

Principal investigator:

Mailing address:

Telephone number:

Email:

Faculty advisor (if relevant):

Describe any changes to the protocol (attached a revised protocol and/or informed consent form, with changes indicated, if necessary):

I certify that the approved protocol and the approved method for obtaining informed consent has been and will continue to be followed, including the changes indicated above.

_____ _____
Principal investigator Date

_____ _____
Faculty sponsor/advisor (if necessary) Date

APPENDIX D

Unanticipated Problem Report Form

Refer to the Policies and Procedure Manual for definitions and reporting requirements.

Unanticipated problem report forms should be submitted to the Office of Research and Economic Development, Room 308, Old Main or via email to amiller@uwyo.edu. **Electronic submissions are encouraged.**

I. General Information

Title of research project:

Principal investigator:

Mailing address:

Telephone number:

Email:

Did the problem occur at a local site ☐ or an outside site ☐?

Date of the unanticipated problem:

Date the research team discovered the problem:

Does the study include a drug? ☐ Yes ☐ No
If yes, provide the name(s) of the drug(s):

Does the study include a medical device? ☐ Yes ☐ No
If yes, provide the name(s) of the medical device(s):

Date and description of latest study-related intervention (relevant to this event):

Did the problem result in injury to the participant? ☐ Yes ☐ No
If yes, please describe:

Did the problem result in the death of the participant? ☐ Yes ☐ No

---

II. Description of unanticipated problem (adverse event, incident, experience, or outcome)

List key words describing the problem (e.g., a breach of confidentiality):

Briefly describe the problem (identify/describe the medical nature of the unanticipated problem, including background, relevant medical history, major medical problems, concurrent medications, associated medical or surgical treatments, and dates of treatment. If it is a social/behavioral study include information such as nature of the unanticipated problem, description of the situation that led to the problem, individuals present, referral for medical/psychological care, etc.):

III. Determination of unanticipated problem

☐ Yes ☐ No The problem 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.

If yes, explain the basis for determining that the problem is unexpected:

☐ Yes ☐ No The problem is **related or possibly related** to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).

If yes, explain the basis for determining that the problem is related or possibly related:

☐ Yes ☐ No The problem **places participants or others at a greater risk of harm** (including physical, psychological, economic, or social harm) than was previously known or recognized.

If yes, explain the basis for determining that the problem placed participants or others at a greater risk of harm:

If you checked NO to any of the items in Section III above, the problem is not considered an "unanticipated problem" and you are not required to complete and submit this form to the IRB. However, you are required to report the problem in the summary to the IRB at the time of continuing review (annual review).

IV. Corrective actions

☐ Yes ☐ No **Should the protocol be revised?**
If yes, provide a description of the proposed protocol changes and attach a revised protocol (with changes indicated):

☐ Yes ☐ No **Should the research be suspended or terminated?**
If yes, describe procedures you will follow for the suspension or termination of the research:

☐ Yes ☐ No **Should enrolled participants be notified about this problem/event?**
If yes, attach a revised consent form or draft letter of notification with this report.

☐ Yes ☐ No **Should other corrective action be taken in response to the unanticipated problem?**
If yes, provide a description of the proposed corrective action:

V. Notification of entities

☐ Yes ☐ No ☐ N/A Sponsor has been notified (either federal or non-federal).

FOR IRB USE ONLY

UW IRB chair/designee review of problem report:

The problem:

☐ **Does not** represent an unanticipated problem involving risks to participants or others (review by expedited procedures)

☐ **Does** represent an unanticipated problem involving risks to participants or others (refer to convened IRB for review)

_____ _____
Signature of IRB chair/designee Date

Investigator's signature	**Date**

APPENDIX E

Authorization to Use or Disclose Protected Health Information for Research (Medical Release Form)

An additional informed consent document for research participation may also be required.

Title of research project:

Principal investigator:

Mailing address:

Telephone number:

Email:

If you decide to join this research project, University of Wyoming (UW) researchers may be **using** (collecting) or **sharing** (disclosing) information about you that is considered to be protected health information (private information) for their research.

Using (collecting) protected health information refers to researchers obtaining information not directly from you through your participation in this specific research project but obtaining your protected health information from a second party, e.g., your personal physician, pre-existing health records, etc.

Sharing of protected health information refers to researchers sharing/communicating your protected health information that they obtain because you are participating in this specific research project with a second party, e.g., your personal physician. Below you will be able to identify the second parties whom the researchers may collect and/or share your protected health information with.

Protected health information to be used or shared. Federal law requires that researchers get your permission (authorization) to use or share your protected health information. If you give permission, the researchers may use or share only with the people identified in this Authorization any protected health information related to this research from your medical records and from any test results obtained from this research. Information, used or shared, may include but is not limited to the following:

1. All information relating to tests, procedures, surveys, or interviews as outlined in the consent form;
2. Medical records and charts; and/or
3. Name, address, telephone number, date of birth, race, and government-issued identification number.

Purposes for using private information. If you give permission, the researchers may use your protected health information for the purposes of: .

Sharing of private information. If you give permission, the researchers may share your protected health information with the research sponsor, the UW Institutional Review Board, auditors and inspectors who check the research, and government agencies such as the Department of Health and Human Services (HHS). The researchers may also share your information with the following named persons/groups (including physical address): .

Using (collecting) private information. If you give permission, the researchers may collect your protected health information from the following named persons/group (including physical address): .

Expiration date or event. If you give permission, the researchers can use your protected health information until . (NOTE TO RESEARCHERS: If the information will be kept indefinitely, state that there is no expiration date.)

Confidentiality. Although the researchers may report their findings in scientific journals or meetings, they will not identify you in their reports. The researchers will try to keep your information confidential, but confidentiality is not guaranteed. Any person or organization receiving the information based on this authorization could re-release the information to others and federal law would no longer protect it.

Voluntary choice. The choice to give UW researchers permission to use (collect) or share your private health information for their research is voluntary. It is completely up to you. No one can force you to give permission. However, you must give permission for UW researchers to use or share your protected health information.

Revoking permission. If you give UW researchers permission to use or share your private information, you have a right to revoke your permission whenever you want. However, revoking your permission will not apply to information that the researchers have already used, relied on, or shared. You may revoke your permission at any time by writing to .

Giving permission. By signing this form, you give UW and UW's researchers led by permission to (check all that apply):

☐ Use (collect) my protected health information

☐ Share my protected health information

Subject name:

_____
Printed Name

_____ _____
Signature of subject Date
Or parent if subject is a child (age 17 or under)

OR

_____ _____
Signature of legal representative* Date

*If signed by a legal representative of the subject, provide a description of the relationship to the subject and the authority to act as legal representative:

_____.

UW may ask you to produce evidence of your relationship.

A signed copy of this form must be given to the subject or the legal representative at the time this signed form is provided to the researcher.

APPENDIX F

IRB Waiver of HIPAA Authorization

University of Wyoming
Office of Research and Economic Development
Dept. 3355, 1000 University Avenue
Old Main Room 308
Laramie, Wyoming 82071
Phone: (307) 766-5353, (307) 766-5320
Fax: (307) 766-2608
http://uwacadweb.uwyo.edu/research/institutional1.asp

Waiver of HIPAA Authorization
Purpose of this form: 1. Assist the University of Wyoming IRB in making and documenting the determinations required to grant or deny a Waiver of HIPAA Authorization for research purposes, based on federal law. 2. If waiver is granted, this completed form serves as written permission from the IRB to the researcher to access, use, or disclose Protected Health Information (PHI) without subject authorization. **3.** The researcher provides this form to the covered entity maintaining the PHI as documentation that the UW IRB has granted a Waiver of HIPAA Authorization**.**
Researcher name: Date of IRB approval:
IRB application title:
Review type: □ Full IRB Review □ Expedited Review
Does the IRB approve the request for a Waiver of HIPAA Authorization? □ Yes □ No
Purpose of Waiver of HIPAA Authorization (check all that apply): 1. Waiver is granted only for prescreening records containing PHI. When prescreening is complete, researcher must obtain HIPAA Authorization from eligible subjects for any other access of PHI. □ **2.** Waiver is granted for complete access, use, and creation of records containing PHI, but only as described in the IRB approved application. □
Signature of IRB Administrator:
Printed Name:

OHRP Regulatory Justification for Waiver (45 C.F.R. 164.512(i)(2)(iii))		
All of the following criteria must be satisfied to grant a Waiver of HIPAA Authorization:	YES	NO
(A) The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:	□	□
(1) An adequate plan to protect the identifiers from improper use and disclosure;		
(2) 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		
(3) 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 study, or for other research for which the use or disclosure of PHI would be permitted.		
(B) The research could not practicably be conducted without the waiver or alteration.		
(C) The research could not practicably be conducted without access to and use of the PHI.	□	□
	□	□

APPENDIX G

Classroom Research Practica Involving Human Subjects

This informational sheet must be filled out and submitted by the faculty member assigning the research practica in his or her classroom before the first day of class during the semester in which the student will be conducting the research practica.

The informational sheet for classroom research practica involving human subjects should be submitted to the IRB in care of:

Institutional Review Board
Room 308, Old Main
1000 East University Avenue, Department 3355
Laramie, WY 82071

Phone: 307-766-5320
Fax: 307-766-2608
email: amiller@uwyo.edu

Informational sheets may be submitted in any format: in hard copy typed on letter size white paper, or electronic format e-mailed to amiller@uwyo.edu. **Electronic submission via email is encouraged**.

Please complete the following five sections:

1) **Name, title, department, address, phone number, fax number, and e-mail address of faculty member assigning the research practica**

2) **Code, class number, title, semester, year, and brief description of course**
   - Example: AGEC 1000. Agricultural and Applied Economics Orientation. Spring 2009. Directs students through a series of short writing and research exercises designed to improve the academic skills of new or prospective agribusiness majors.

3) **Brief description and purpose of research practica**

4) **Description of human subject participation, including:**
   - age-range and gender of preferred subjects
   - how subjects will be selected and solicited for participation
   - the number of subjects expected to be involved
   - criteria for potential subjects to be included or excluded from the subject pool

5) **Description of procedure to protect privacy and confidentiality, including:**
   - whether data will presented in a public forum
   - whether or not subjects will be identified, either by name, appearance, or nature of data
   - how and where collected data will be stored and for how long
   - who will have access to the data and under what circumstances
   - any other aspects regarding confidentiality

APPENDIX H

The **University of Wyoming**
Health History Screening Questionnaire (UWHHSQ)
Please complete thoroughly and accurately.

Date _____/_____/_____

Name:_____ Ethnicity:_____

Address:_____City:_____State:_____Zip:_____

Date of Birth: _____/_____/_____ Age:_____ Phone #:_____

Email:_____@_____

Emergency contact information: Name:_____ Phone #:_____

Personal healthcare provider to contact in case of an emergency:

Name_____ Phone #:_____

City:_____

CARDIOVASCULAR HEALTH HISTORY

Have you ever been diagnosed with or had any of the following?

Heart Attack?	Yes	No
Heart Surgery?	Yes	No
Cerebrovascular accident (e.g. Stroke)?	Yes	No
Transient Ischemic Attack (TIA)?	Yes	No
Carotid Artery Disease?	Yes	No
Cardiac Catheterization?	Yes	No
Coronary Angioplasty?	Yes	No
Pacemaker/Implantable Cardiac Device?	Yes	No
Irregular Heart Rate/Heart Rhythm Disturbance?	Yes	No
Atrial Fibrillation?	Yes	No
Heart Valve Disease?	Yes	No
Heart Failure?	Yes	No

Heart Murmur? Yes No

Heart Transplantation? Yes No

Congenital Heart Disease? Yes No

Have you ever experienced any of the following symptoms:

Chest discomfort with exertion? Yes No

Unreasonable breathlessness? Yes No

Dizziness, fainting, or blackouts? Yes No

Syncope (loss of consciousness)? Yes No

Hypoxia (low oxygen levels)? Yes No

Do you currently take heart medications? Yes No

If yes, what?_____

Have you been diagnosed with diabetes (Type 1 or Type 2) or problems with blood sugar levels? Yes No

If yes, please note Type 1 or Type 2_____

If you circled yes to any of the above statements in this section, consult your physician or other appropriate health care provider before engaging in exercise. You may need to use a facility with a ***medically qualified staff.***

CARDIOVASCULAR RISK FACTORS

Are you a male over 45 years old? Yes No

Are you a female over 55 years old? Yes No

Have you had a hysterectomy? Yes No

Have you had both of your ovaries surgically removed? Yes No

Are you postmenopausal? Yes No

Do you currently smoke or have you quit within the last six months? Yes No

Is your blood pressure greater than 140/90 mm Hg? Yes No I Don't Know

If known, what is your blood pressure? _____/_____ mm Hg

Do you currently take blood pressure medications? Yes No

Do you currently take any medications for your heart? Yes No

Is your total blood cholesterol level greater than 200 mg/dl? Yes No I Don't Know

Do you know your cholesterol level? Yes No

If yes, Total Cholesterol _____

LDL _____

HDL _____

Triglycerides _____

Do you have a close blood relative who has suffered a heart attack or had any kind of heart surgery before the age of 55 (for father or brother) or age 65 (for mother or sister)? Yes No

Are you more than 20 pounds overweight? Yes No I Don't Know

Are you physically <u>inactive</u> (i.e., do you get less than 30 minutes of physical activity less than three times a week)? Yes No

Have you had a recent surgery (in the past 2 years)? Yes No

Have you had an exercise stress test, heart catheterization, or echocardiogram? Yes No

If yes, please explain_____

_____

To the best of your knowledge, is there any reason that might make it **unsafe** for you to participate in exercise? Yes No

If you circled yes to two or more of the statements in the above section you should consult your physician or other appropriate health care provider before engaging in exercise. You might benefit from using a facility with a ***professionally/medically qualified exercise*** *program and staff.*

To the best of my knowledge, the information I have provided above is an accurate assessment of my health and medical history.

_____	_____	_____
Name of Participant	**Participant's Signature**	**Date**
_____	_____	_____
Name of Administering Staff	**Signature of Staff Member**	**Date**

Please stop here. The remainder of this Health History Screening Questionnaire will be administered to you by one of our staff.

STAFF: Administer the remaining portion of the UWHHSQ.

GENERAL MEDICAL HISTORY

Height:_____ Weight:_____ BMI (calculated):_____

Circle One

Do you drink alcohol? Yes No

If yes, how many drinks per week?_____

Are you taking any prescription or over-the-counter medication? Yes No

If yes, what medication and what dosage?_____

_____

Do you take any vitamins, supplements, or herbal/homeopathic medications? Yes No

If yes, what type and what dosage?_____

_____

Has your body weight been stable over the past 6 months? Yes No

If no, please explain_____

Have you been on a recent diet or a prescribed diet? Yes No

If yes, please explain_____

Have you been diagnosed with asthma, exercise-induced asthma, reactive airway disease, chronic obstructive pulmonary disease (COPD), or any other respiratory disease?

Yes No

If yes, please describe:_____

_____

_____

Have you ever been diagnosed with cancer? Yes No

If yes, please describe when and what type:_____

_____

Have you ever undergone a lymphectomy? Yes No

If yes, please describe when and why?_____

_____

Do you have musculoskeletal problems that limit your physical activity such as walking? Yes No

Do you have concerns about your safety when you exercise or exert yourself? Yes No

Have you ever experienced burning or cramping sensations in your l legs when walking short distances? Yes No

Do you have any other health problems, illnesses, diseases, infections, surgeries, allergies, or hospitalizations? Yes No

If yes, please explain_____

_____

_____

FAMILY HISTORY

Please check all that apply

Family Member	High Blood Pressure	Diabetes Type I or II	Heart Diseases	Comments
Mother				If yes, was it before the age of 65? **Yes No**
Father				If yes, was it before the age of 65? **Yes No**
Sibling				Gender: Age:
Sibling				Gender: Age:
Paternal Grandmother				Age:
Paternal Grandfather				Age:
Maternal Grandmother				Age:
Maternal Grandfather				Age:

FOR FEMALES ONLY:

Are you pre-____, peri-____ or post-____ menopausal?

If premenopausal, are you using **any form** of contraception (birth control) or hormone therapy for any reason? Yes No

If yes, why and what type?_____

If you are premenopausal:

Are you pregnant?	Yes	No	I Don't Know
Could you be pregnant?	Yes	No	I Don't Know
Are you trying to become pregnant?	Yes	No	

If you are peri- or postmenopausal:

For how long?_____

When was your last menstrual period? _____

Have you had a hysterectomy w/ or w/out ovary removal? Yes No

Have you had an oophorectomy without removal of your uterus? Yes No

Are you currently taking any type of hormone replacement therapy or using any form of contraception (birth control)? Yes No

If yes, what type?_____How long?_____Dosage_____

_____	_____	_____
Name of Administering Staff	**Signature of Staff Member**	**Date**

APPENDIX I

IRB Checklist: Exempt

Principal Investigator: **Principal Investigator**

Reviewer: **Reviewer** Date Reviewed: **x/xx/xx**

Human Subject Research

☐ Is it research? Systematic investigation designed to develop or contribute to generalizable knowledge.

☐ Are human subjects involved? Living individual where investigator obtains either (1) data through intervention or interaction with the individual, or (2) identifiable private information.

☐ Is research exempt? (see below)

Review Determination

☐ Not human subject research

☐ Qualifies for exemption (see pages 2-3)

Comments

Exemption Categories:

Category 1: Research conducted in established or commonly accepted educational settings, involving normal educational practices.	☐
Category 2: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior. NOTE: If the research involves any of the following, then this exemption does **NOT** apply: ☐ Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; **and** any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation. ☐ Research involves children and the collection surveys, interviews, or observations of public behavior if the investigator participates in the activities being observed.	☐
Category 3: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under Category 2, if: ☐ The human subjects are elected or appointed public officials or candidates for public office; or ☐ Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.	☐
Category 4: Research involving the collection or study of EXISTING data, documents, records, pathological specimens, or diagnostic specimens, if: ☐ The sources are publicly available, or ☐ Information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to subjects: ☐ All of the data exists prior to the start of the research. ☐ No identifiable information be collected and no links to personal information will exist.	☐

Category 5: Research and demonstration projects which are designed to study, evaluate, or otherwise examine public benefit or service programs, if: The projects are conducted by or subject to the approval of Federal Department or Agency heads and, ☐ There is no statutory requirements for IRB review, and ☐ The research does not involve significant physical invasions or intrusions upon the privacy of subjects, and ☐ The exemption is invoked with authorization or concurrence by the funding agency. NOTE: ALL of these criteria must be met for this exemption to apply.	☐
Category 6: Taste and food quality evaluation and consumer acceptance studies, if: ☐ Wholesome foods without additives are consumed, or ☐ 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.	☐

APPENDIX J

IRB Checklist: Expedited Review

Principal Investigator: **Principal Investigator**

Reviewer: **Reviewer** Date Reviewed: **x/xx/xx**

Review Determination

☐ Approve expedited review (see pages 2-3)

☐ Approve expedited review with modifications (see comments below)

Requirements for approval (45 C.F.R. § 46.111)

☐ Risks to subjects are minimized

☐ Risks to subjects are reasonable in relation to anticipated benefits

☐ Selection of subjects is equitable

☐ Informed consent will be sought from each prospective subject

☐ Adequate provisions for monitoring the data collected to ensure the safety of subjects

☐ Adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data

Comments

Expedited Review Categories:

Category 1: Clinical studies of drugs and medical devices only when condition **(a)** or **(b)** is met. **(a)** Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.) **(b)** Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.	☐
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, 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; **(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.	☐

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 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.	☐
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 subjects 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.	☐
Category 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).	☐
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: The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, UNLESS reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

APPENDIX K

IRB Checklist: Full Board

Principal Investigator: **Principal Investigator**

Reviewer: **Reviewer** Date Reviewed: **x/xx/xx**

Review Determination

☐ Defer to Full Board

Requirements for approval (45 C.F.R. § 46.111)

☐ Risks to subjects are minimized

☐ Risks to subjects are reasonable in relation to anticipated benefits

☐ Selection of subjects is equitable

☐ Informed consent will be sought from each prospective subject

☐ Adequate provisions for monitoring the data collected to ensure the safety of subjects

☐ Adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data

Reviewers

Primary reviewer:

Secondary reviewer:

Comments

APPENDIX L

The Belmont Report

Office of the Secretary

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

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

April 18, 1979

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

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

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

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare.

Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.

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

Members of the Commission

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

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

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

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

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

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

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

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

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

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

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

**** Deceased.*

Ethical Principles & Guidelines for Research Involving Human Subjects

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

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

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

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

Part A: Boundaries Between Practice & Research

A. Boundaries Between Practice and Research

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

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

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

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the

activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

Part B: Basic Ethical Principles

B. Basic Ethical Principles

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

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

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

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

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

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons

would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

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

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

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

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

3. Justice. -- Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when

some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are **(1)** to each person an equal share, **(2)** to each person according to individual need, **(3)** to each person according to individual effort, **(4)** to each person according to societal contribution, and **(5)** to each person according to merit.

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

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

Part C: Applications

C. Applications

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Finally, assessment of the justifiability of research should reflect at least the following considerations: **(i)** Brutal or inhumane treatment of human subjects is never morally justified. **(ii)**

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

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

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

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

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

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

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

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

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

APPENDIX M

The Nuremburg Code

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonable to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

   The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Reprinted from *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182.*. Washington, D.C.: U.S. Government Printing Office, 1949.

APPENDIX N

The Declaration of Helsinki

Adopted by the 18th World Medical Assembly, Helsinki, Finland,June 1964, amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975, and the 35th World Medical Assembly, Venice, Italy, October 1983.

Introduction

It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfilment of this mission.
The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration,"and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient. "
The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the aetiology and pathogenesis of disease.
In current medical practice most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.
Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects. In the field of biomedical research a fundamental distinction must be recognised between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.
Special caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.
Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the law of their own countries.

I. Basic Principles

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment and guidance.
3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The

responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.

4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.
6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
7. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.
9. In any research on human beings, each potential subject mustbe adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw visor her consent to participation at any time. The physician should then obtain the subject's freely given informed consent, preferably inheriting.
10. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who isn't engaged in the investigation and who is completely independent of this official relationship.
11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.
12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present declaration are complied with.

II. Medical Research Combined with Professional Care (Clinical Research)

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope of saving life, re-establishing health or alleviating suffering.

2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
3. In any medical study, every patient- including those of a control group, if any- should be assured of the best proven diagnostic and therapeutic method.
4. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.
5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (1, 2).
6. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge,only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III. Non-Therapeutic Biomedical Research Involving Human Subjects (Non-Clinical Biomedical Research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.
2. The subjects should be volunteers- either healthy persons or patients for whom the experimental design is not related to the patient's illness.
3. The investigator or the investigating team should discontinue the research if in his/her or their judgment it may, if continued, be harmful to the individual.
4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

Cite as:

- World Medical Organization. Declaration of Helsinki. *British Medical Journal* (7 December) 1996;313(7070):1448-1449.

APPENDIX O

IRB Member List 2009-2010

Dr. Anne M. Bowen
Professor/Director, Nightingale Center for Nursing Research
Department of Psychology
127 Bio Sciences Building
Department 3415
307/766-4327 -6303
abowen@uwyo.edu

Dr. Becki Burman**
DDS
1275 North 15th Suite 101
Laramie, Wyoming 82072
307/745-9261
bbdds@bresnan.net

Dr. Ann Marie Hart
Associate Professor
School of Nursing
431 Health Sciences Building
Department 3065
307/766-6564 -6569
annmhart@uwyo.edu

Dr. Kenneth B. Heinlein
Associate Director for Research
Wyoming Institute for Disabilities
Health Sciences 147B
Department 4298
307/766-2766 -2761
Heinlein@uwyo.edu

Rhett Ivey**
255 North 30th Street
Laramie, WY 82072
307/742-2142x2673
307/742-2976
trhett@bresnan.net

Tara Nelson NV
Associate General Counsel
206 Old Main
Department 3434
307/766-4019 -4121
trnelson@uwyo.edu

Kenneth L. Robertson
MD, FACP
255 North 30th Street
Laramie, Wyoming 82072
307/760-1000
krobertsoninwyo@pol.net

Dr. Derek Smith*
Associate Professor
Division of Kinesiology and Health
115 Corbett Building
Department 3196
307/766-5271 -5285
smithdt@uwyo.edu

Dorothy Yates[NV]
Associate Vice President for Research
Office of Research
308 Old Main
Department 3355
307/766-5320
Dyates4@uwyo.edu

Dr. Suzanne Young
Professor
College of Education
Education Building 6
Department 3374
307/766-3145
syoung@uwyo.edu

Coordinators
Linda Osterman/ Alice Miller
UW Office of Research
308 Old Main
307/766-5320
osterman@uwyo.edu; amiller@uwyo.edu

All campus addresses:
1000 East University Avenue
Department #
Laramie, WY 82071

*chair
**non-affiliated
[nv] Non-voting member

APPENDIX P

Federalwide Assurance (FWA) for the Protection of Human Subjects

U. S. Department of Health and Human Services (HHS)
Office for Human Research Protections (OHRP)

A. TERMS OF THE FEDERALWIDE ASSURANCE (FWA) FOR INSTITUTIONS WITHIN THE UNITED STATES

1. Human Subjects Research Must be Guided by Ethical Principles

All of the Institution's human subjects research activities, regardless of whether the research is subject to federal regulations, will be guided by the ethical principles in: (a) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, or (b) other appropriate ethical standards recognized by federal departments and agencies that have adopted the Federal Policy for the Protection of Human Subjects, known as the Common Rule.

2. Applicability

These terms apply whenever the Institution becomes engaged in human subjects research conducted or supported* by any federal department or agency that has adopted the Common Rule, unless the research is otherwise exempt from the requirements of the Common Rule or a department or agency conducting or supporting the research determines that the research shall be conducted under a separate assurance. In general, the Institution becomes so engaged whenever (a) the Institution's employees or agents intervene or interact with human subjects for purposes of federally-conducted or –supported research; (b) the Institution's employees or agents obtain individually identifiable private information about human subjects for purposes of federally-conducted or –supported research; or (c) the Institution receives a direct federal award to conduct human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

[*Federally-supported is defined throughout the FWA and the Terms of Assurance as the U.S. Government providing any funding or other support.]

3. Compliance with the Federal Policy for the Protection of Human Subjects and Other Applicable Federal, State, Local, or Institutional Laws, Regulations, and Policies

When the Institution becomes engaged in federally-conducted or -supported human subjects research to which the FWA applies, the Institution and the institutional review boards (IRBs) designated under the Institution's Assurance will comply with the Federal Policy for the Protection of Human Subjects.

The reference in the Code of Federal Regulations is shown below for each department and agency which has adopted the Common Rule:

7 CFR part 1c	Department of Agriculture
10 CFR part 745	Department of Energy
14 CFR part1230	National Aeronautics and Space Administration
15 CFR part 27	Department of Commerce
16 CFR part 1028	Consumer Product Safety Commission
22 CFR part 225	Agency for International Development
24 CFR part 60	Department of Housing and Urban Development
28 CFR part 46	Department of Justice
32 CFR part 219	Department of Defense
34 CFR part 97	Department of Education
38 CFR part 16	Department of Veterans Affairs
40 CFR part 26	Environmental Protection Agency
45 CFR part 46	Department of Health and Human Services
45 CFR part 46 (by Executive Order 12333)	Central Intelligence Agency
45 CFR part 690	National Science Foundation
49 CFR part 11	Department of Transportation

For any federally-conducted or -supported human subjects research to which the FWA applies, the Institution also will comply with any additional human subjects regulations and policies of the department or agency which conducts or supports the research and any other applicable federal, state, local, or institutional laws**,** regulations, and policies. When the Institution is engaged in human subjects research conducted or supported by the Department of Health and Human Services (HHS), the Institution will comply with all subparts of the HHS regulations at Title 45 Code of Federal Regulations part 46 (45 CFR part 46, subparts A, B, C, and D).

Human subjects research conducted or supported by each federal department or agency listed above will be governed by the regulations as implemented by the respective department or agency. The head of the department or agency retains final judgment as to whether a particular activity conducted or supported by the respective department or agency is covered by the Common Rule. If the Institution needs guidance regarding implementation of the Common Rule and other applicable federal regulations, the Institution should contact appropriate officials at the

department or agency conducting or supporting the research. For federally-conducted or –supported research covered by the FWA, the department or agency that conducts or supports the research retains final authority for determining whether the Institution complies with the Terms of Assurance. If HHS receives an allegation or indication of noncompliance related to human subjects research that is covered by the FWA and is conducted or supported solely by a Common Rule department or agency other than HHS, HHS will refer the matter to the other department or agency for review and action as appropriate.

Please note that if the Institution voluntarily extends the Common Rule or the Common Rule and subparts B, C, and D of the HHS regulations at 45 CFR part 46 to all research regardless of support, OHRP will have the authority to ensure that the Institution complies with this commitment for all research to which the FWA applies that is not federally-conducted or –supported.

4. Written Procedures*

a) The Institution submitting the FWA has written procedures* for ensuring prompt reporting to the IRB, appropriate institutional officials, the head of any department or agency conducting or supporting the research (or designee), any applicable regulatory body, and OHRP of any:

1. unanticipated problems involving risks to subjects or others;
2. serious or continuing noncompliance with the federal regulations or the requirements or determinations of the IRB(s); and
3. suspension or termination of IRB approval.

Upon request, the Institution will provide a copy of these written procedures to OHRP and any department or agency conducting or supporting research covered by the FWA.

b) The Institution must ensure that the IRB(s) designated under the FWA has established written procedures* for:

4. conducting IRB initial and continuing review (not less than once per year) of research, and reporting IRB findings to the investigator and the Institution;
5. 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 the previous IRB review; and
6. 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 subjects.

Upon request, the Institution will provide a copy of these written procedures to OHRP and any department or agency conducting or supporting research covered by the FWA.

[*For HHS-conducted or -supported human subjects research, see OHRP guidance on written IRB procedures on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd702.htm.]

5. Scope of IRB(s)'s Responsibilities

All human subjects research to which the FWA applies, except for research exempted or waived in accordance with Sections 101(b) or 101(i) of the Common Rule, will be reviewed, prospectively approved, and subject to continuing review at least annually by the designated IRB(s). The IRB(s) will have authority to approve, require modifications in, or disapprove the covered human subjects research. For research approved by the IRB(s), further appropriate review and approval by any department or agency conducting or supporting the research or by officials of the institution holding the FWA may be required.

6. Informed Consent Requirements

Except for research exempted or waived in accordance with Sections 101(b) or 101(i) of the Common Rule, informed consent for research to which the FWA applies will be:

a) sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, Section 116 of the Common Rule; and

b) appropriately documented, in accordance with, and to the extent required by, Section 117 of the Common Rule.

7. Requirement for Assurances for Collaborating Institutions

When the Institution holding the FWA is either a) the primary awardee under a federal grant, contract, or cooperative agreement supporting research to which the FWA applies, or b) the coordinating center for federally-conducted or –supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating institutions engaged in such research operate under an appropriate OHRP-approved or other federally-approved assurance for the protection of human subjects.

An institution holding an FWA may collaborate with another institution that does not have an FWA. In such circumstances, a collaborating institution may operate under the FWA with the approval of the department or agency conducting or supporting the research and the institution holding the FWA.

For federally-conducted or –supported research covered by the FWA, the department or agency that conducts or supports the research retains final authority for determining which institutions are engaged in the research and need to hold an assurance for the protection of human subjects.

8. Written Agreements with Independent Investigators Who are not Otherwise Affiliated with the Institution

When the Institution holding the FWA is either a) the primary awardee under a federal grant, contract, or cooperative agreement supporting research to which the FWA applies, or b) the coordinating center for federally-conducted or –supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating independent investigators

engaged in such research operate under an appropriate OHRP-approved or other federally-approved assurance for the protection of human subjects.

The engagement in federally-conducted or –supported human subjects research activities to which the FWA applies by each independent investigator who is not otherwise an employee or agent of the Institution may be covered under the FWA only in accordance with a formal, written agreement of commitment to relevant human subject protection policies and IRB review. OHRP's sample Individual Investigator Agreement (see http://www.hhs.gov/ohrp/humansubjects/assurance/unaflsup.rtf) may be used or adapted for this purpose, or the Institution may develop its own commitment agreement in coordination with the department or agency conducting or supporting the research. Institutions must maintain commitment agreements on file and provide copies upon request to OHRP and any department or agency conducting or supporting the research.

For federally-conducted or –supported research covered by the FWA, the department or agency that conducts or supports the research retains final authority for determining which independent investigators are engaged in the research and need to be covered by a written commitment agreement with the institution holding the FWA.

9. Institutional Support for the IRB(s)

The Institution will ensure that each IRB designated under the FWA has meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

10. Compliance with the Terms of Assurance

The Institution accepts and will follow items 1-9 above and is responsible for ensuring that (a) the IRB(s) designated under the FWA agree to comply with these terms; and (b) the IRB(s) possess appropriate knowledge of the local research context for all research to which the FWA applies (please refer to the OHRP Guidance on IRB Knowledge of Local Research Context on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/local.htm).

Any designation under the FWA of the IRB of another institution or organization must be documented by a written agreement between the Institution holding the FWA and the IRB organization outlining their relationship and include a commitment that the designated IRB will adhere to the requirements of the FWA. OHRP's sample IRB Authorization Agreement may be used for such purpose, or the parties involved may develop their own agreement. This agreement should be kept on file at both institutions/organizations and made available upon request to OHRP and any department or agency conducting or supporting research covered by the FWA.

11. Assurance Training

The OHRP Assurance Training Modules (see http://137.187.172.153/CBTs/Assurance/login.asp) describe the major responsibilities of the Institutional Signatory Official, the Human Protection Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person), and the IRB Chair(s) that must be fulfilled under the FWA. OHRP strongly recommends that the Institutional Signatory Official, the Human Protections Administrator, and the IRB Chair(s) personally complete the relevant OHRP Assurance Training Modules, or comparable training that includes the content of these modules, prior to submitting the FWA.

12. Educational Training

OHRP strongly recommends that the Institution and the designated IRB(s) establish educational training and oversight mechanisms (appropriate to the nature and volume of its research) to ensure that research investigators, IRB members and staff, and other appropriate personnel maintain continuing knowledge of, and comply with, the following: relevant ethical principles; relevant federal regulations; written IRB procedures; OHRP guidance; other applicable guidance, state and local laws; and institutional policies for the protection of human subjects. Furthermore, OHRP recommends that a) IRB members and staff complete relevant educational training before reviewing human subjects research; and b) research investigators complete appropriate institutional educational training before conducting human subjects research.

13. Renewal of Assurance

All information provided under the FWA must be renewed or updated at least every 36 months (3 years), even if no changes have occurred, in order to maintain an active FWA. Failure to update this information may result in restriction, suspension, or termination of the Institution's FWA for the protection of human subjects.

DOMESTIC INSTITUTIONS ACCEPTING THESE TERMS MAY PROCEED WITH THE ASSURANCE FILING PROCESS

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B. TERMS OF THE FEDERALWIDE ASSURANCE (FWA) FOR INTERNATIONAL (NON-U.S.) INSTITUTIONS

1. Human Subjects Research Must Be Guided by Ethical Principles

All of the Institution’s human subjects research activities, regardless of whether the research is subject to U.S. federal regulations, will be guided by one of the following statements of ethical principles: (a) The World Medical Association's Declaration of Helsinki (as adopted in 1996 or 2000); (b) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research; or (c) other appropriate international ethical standards recognized by U.S. federal departments and agencies that have adopted the U.S. Federal Policy for the Protection of Human Subjects, known as the Common Rule.

2. Applicability

These terms apply whenever the Institution becomes engaged in human subjects research conducted or supported* by any U.S. department or agency that has adopted the Common Rule, unless the research is otherwise exempt from the requirements of the Common Rule or a U.S. federal department or agency conducting or supporting the research determines that the research shall be conducted under a separate assurance. In general, the Institution becomes so engaged whenever (a) the Institution’s employees or agents intervene or interact with human subjects for purposes of U.S. federally-conducted or –supported research; (b) the Institution’s employees or agents obtain individually identifiable private information about human subjects for purposes of U.S. federally-conducted or –supported research; or (c) the Institution receives a direct award to

conduct U.S. federally-supported human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

If a U.S. federal department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided by the U.S. Federal Policy for the Protection of Human Subjects, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided above, consistent with the requirements of section 101(h) of the U.S. Federal Policy for the Protection of Human Subjects.

[*Federally-supported is defined throughout the Assurance document and the Terms of Assurance as the U.S. Government providing any funding or other support.]

3. Compliance with Laws, Regulations, Policies, and Guidelines

When the Institution becomes engaged in U.S. federally-conducted or –supported human subjects research to which the FWA applies, the Institution and institutional review boards (IRBs) or independent ethics committees (IECs) designated under the FWA at a minimum will comply with one or more of the following:

a) The U.S. Federal Policy for the Protection of Human Subjects (see section 3 of the Terms of the FWA for Institutions within the United States for a list of U.S. federal departments and agencies that have adopted the Common Rule);

b) The Common Rule and subparts B, C, and D of the U.S. Department of Health and Human Services (HHS) regulations at 45 CFR part 46;

c) The U.S. Food and Drug Administration (FDA) regulations at 21 CFR parts 50 and 56;

d) The May 1, 1996, International Conference on Harmonization E-6 Guidelines for Good Clinical Practice (ICH-GCP-E6), Sections 1 through 4;

e) The 2002 Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects;

f) The 1998 (with 2000, 2002, 2005 ameendments) Medical Research Council of Canada Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans;

g) The 2006 Indian Council of Medical Research Ethical Guidelines for Biomedical Research on Human Subjects; or

h) Other standard(s) for the protection of human subjects recognized by U.S. federal departments and agencies which have adopted the U.S. Federal Policy for the Protection of Human Subjects.

All U.S. federally-conducted or -supported human subjects research to which the FWA applies will also comply with any additional human subjects regulations and policies of the U.S. federal department or agency which conducts or supports the research and any other applicable U.S. federal, international, state, local, or institutional laws**,** regulations, and policies.

The head of the U.S. federal department or agency retains final judgment as to whether a particular activity conducted or supported by the respective department or agency is covered by the Common Rule. If the Institution needs guidance regarding implementation of the Common Rule and/or other applicable U.S. federal regulations, the Institution should contact appropriate officials at the U.S. federal department or agency conducting or supporting the research. For U.S. federally-conducted or –supported research covered by the FWA, the U.S. federal department or agency that conducts or supports the research retains final authority for determining whether the Institution complies with the Terms of Assurance. If HHS receives an allegation or indication of noncompliance related to human subjects research that is covered by the FWA and is conducted or supported solely by a Common Rule department or agency other than HHS, HHS will refer the matter to the other U.S. federal department or agency for review and action as appropriate.

4. IRB/IEC Written Procedures*

a) The Institution submitting the FWA has established written procedures* for ensuring prompt reporting to the IRB/IEC, appropriate institutional officials, the head of any U.S. federal department or agency conducting or supporting the research (or designee), any applicable regulatory body, and OHRP of any:

1. unanticipated problems involving risks to subjects or others;

2. serious or continuing noncompliance with the applicable U.S. federal regulations or the requirements or determinations of the IRB(s)/IEC(s); and

3. suspension or termination of IRB/IEC approval.

Upon request, the Institution will provide a copy of these written procedures to OHRP and any department or agency conducting or supporting research covered by the FWA.

b) The Institution must ensure that the IRB(s)/IEC(s) designated under the FWA has established written procedures* for:

4. conducting IRB/IEC initial and continuing review (not less than once per year), of research, and reporting IRB/IEC findings to the investigator and the Institution;
5. 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 the previous IRB/IEC review; and

6. ensuring prompt reporting to the IRB/IEC of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB/IEC approval has already been given, may not be initiated without IRB/IEC review and approval, except when necessary to eliminate apparent immediate hazards to the subjects.

Upon request, the Institution will provide a copy of these written procedures to OHRP and any department or agency conducting or supporting research covered by the FWA.

[*For HHS-conducted or -supported human subjects research, see OHRP guidance on written IRB procedures on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd107.htm.]

5. Scope of IRB(s)/IEC(s)'s Responsibilities

All U.S. federally-conducted or -supported research to which the FWA applies, except for research exempted or waived in accordance with sections 101(b) or 101(i) of the U.S. Common Rule, will be reviewed, prospectively approved, and subject to continuing review at least annually by the designated IRB(s)/IEC(s). The IRB(s)/IEC(s) shall have authority to approve, require modifications in, or disapprove the covered human subjects research. For research approved by the IRB(s)/IEC(s), further appropriate review and approval by any U.S. federal department or agency conducting or supporting the research or by officials of the institution holding the FWA may be required.

6. Informed Consent Requirements

Except for research exempted or waived in accordance with Sections 101(b) or 101(i) of the U.S. Common Rule, informed consent for research to which the FWA applies will be:

a) sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, Section 116 of the U.S. Common Rule; and

b) appropriately documented, in accordance with, and to the extent required by, Section 117 of the U.S. Common Rule.

7. Considerations for Special Class of Subjects

For HHS-conducted or supported human subjects research, the Institution will comply with the HHS regulations at 45 CFR part 46, subparts B, C, and D, prior to the involvement of pregnant women, fetuses, or neonates; prisoners; or children, respectively. For non-HHS U.S. federally-supported human subjects research, the Institution will comply with any human subject regulations and/or policies of the supporting U.S. federal department or agency for these classes of subjects.

8. Requirement for Assurances for Collaborating Institutions

When the Institution holding the FWA is either a) the primary awardee under a U.S. federal grant, contract, or cooperative agreement supporting research to which the FWA applies, or b) the coordinating center for U.S. federally-conducted or –supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating institutions engaged in such research operate under an appropriate OHRP-approved or other U.S. federally-approved assurance for the protection of human subjects.

An institution holding an FWA may collaborate with another institution that does not have an FWA. In such circumstances, a collaborating institution may operate under the FWA with the approval of the U.S. federal department or agency conducting or supporting the research and the institution holding the FWA.

For U.S. federally-conducted or –supported research covered by the FWA, the U.S. federal department or agency that conducts or supports the research retains final authority for determining which institutions are engaged in the research and need to hold an assurance for the protection of human subjects.

9. Written Agreements with Independent Investigators Who are not Otherwise Affiliated with the Institution

When the Institution holding the FWA is either a) the primary awardee under a U.S. federal grant, contract, or cooperative agreement supporting research to which the FWA applies, or b) the coordinating center for U.S. federally-conducted or –supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating independent investigators engaged in such research operate under an appropriate OHRP-approved or other U.S. federally-approved assurance for the protection of human subjects.

The engagement in U.S. federally-conducted or –supported human subjects research activities to which the FWA applies by each independent investigator who is not otherwise an employee or agent of the Institution may be covered under the FWA only in accordance with a formal, written agreement of commitment to relevant human subject protection policies and IRB/IEC review. OHRP's sample Individual Investigator Agreement (see http://www.hhs.gov/ohrp/humansubjects/assurance/unaflsup.rtf) may be used or adapted for this purpose, or the Institution may develop its own commitment agreement in coordination with the U.S. federal department or agency conducting or supporting the research. Institutions should maintain commitment agreements on file and provide copies upon request to OHRP or any U.S. federal department or agency conducting or supporting the research.

For U.S. federally-conducted or –supported research covered by the FWA, the U.S. federal department or agency that conducts or supports the research retains final authority for determining which independent investigators are engaged in the research and need to be covered by a written commitment agreement with the institution holding the FWA.

10. Institutional Support for the IRB(s)/IEC(s)

The Institution will ensure that each IRB(s)/IEC(s) designated under the FWA has meeting space and sufficient staff to support the IRB's/IEC's review and recordkeeping duties.

11. Compliance with the Terms of Assurance

The Institution accepts and will follow items 1-10 above and is responsible for ensuring that (a) the IRB(s)/IEC(s) designated under the FWA agree to comply with these terms, and (b) the IRB(s)/IEC(s) possess appropriate knowledge of the local research context for all research to which the FWA applies (please refer to the OHRP Guidance on IRB Knowledge of Local Research Context on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/local.htm).

Any designation under the FWA of the IRB/IEC or another institution or organization should be documented by a written agreement between the Institution holding the FWA and the IRB/IEC organization outlining their relationship and include a commitment that the designated IRB/IEC will adhere to the requirements of the FWA. OHRP's sample IRB Authorization Agreement may

be used for such purpose, or the parties involved may develop their own agreement. This agreement should be kept on file at both institutions/organizations and made available upon request to OHRP and any U.S. federal department or agency conducting or supporting research covered by the FWA.

12. Assurance Training

The OHRP Assurance Training Modules (see http://137.187.172.153/CBTs/Assurance/login.asp) describe the major responsibilities of the Institutional Signatory Official, the Human Protection Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person), and the IRB/IEC Chair(s) that must be fulfilled under the FWA. OHRP strongly recommends that the Institutional Signatory Official, the Human Protections Administrator, and the IRB/IEC Chair(s) personally complete the relevant OHRP Assurance Training Modules, or comparable training that includes the content of these Modules, prior to submitting the FWA.

13. Educational Training

OHRP strongly recommends that the Institution and the designated IRB(s)/IEC(s) establish educational training and oversight mechanisms (appropriate to the nature and volume of its research) to ensure that research investigators, IRB/IEC members and staff, and other appropriate personnel maintain continuing knowledge of, and comply with the following: relevant ethical principles; relevant U.S. regulations; written IRB/IEC procedures; OHRP guidance; other applicable guidance; national, state and local laws; and institutional policies for the protection of human subjects. Furthermore, OHRP recommends that a) IRB/IEC members and staff complete relevant educational training before reviewing human subjects research; and b) research investigators complete appropriate institutional educational training before conducting human subjects research.

14. Renewal of Assurance

All information provided under the FWA should be renewed or updated every 36 months (3 years), even if no changes have occurred, in order to maintain an active FWA. Failure to update this information may result in restriction, suspension, or termination of the Institution's FWA for the protection of human subjects.

INTERNATIONAL INSTITUTIONS ACCEPTING THESE TERMS MAY PROCEED WITH THE ASSURANCE FILING PROCESS

APPENDIX Q

Glossary of Terms

Abstain: when an IRB member does not vote upon a protocol under review.

Agent: a representative who acts on behalf of other persons or organizations.

Assent: the affirmative agreement by a child, or an adult who lacks full decision-making capacity to participate in a research or clinical investigation. Mere failure to object may not, absent affirmative agreement, be construed as assent. [45 CFR §46.402(b)]

Assurance: an agreement between an organization and a federal agency that stipulates that the organization will comply with the agency's regulatory requirements. [45 CFR §46.103]

Children: persons who have not attained the legal age for consent to treatments or procedures involved in research or clinical investigations, under the applicable law of the jurisdiction in which the research or clinical investigations will occur. In Wyoming, a child can petition to be "emancipated" under W.S. § 14-1-202, but must do so by filing a written application and meeting the statutory requirements. Only if a child were "emancipated" as described above would the state of Wyoming consider the child an “adult.”

Conflict of interest: a PI or co-PI is said to have a conflict of interest whenever that PI or IRB member, his or her spouse, or dependent child falls under any of the following conditions:

1. Is an investigator or sub-investigator on the protocol (IRB members only, not applicable to PIs);
2. If the IRB member, the member's spouse, or dependent children are involved in the conduct of research;
3. Has entered into a financial arrangement with the sponsor or agent of the sponsor, whereby the outcome of the study could influence the value of the economic interest;
4. Acts as an officer, director, or agent of the sponsor; or
5. Has identified him or herself for any other reason as having a conflicting interest.

Consent: the agreement of participant or the parent(s) of guardian(s) to the participation of their child or ward in the research/clinical investigation.

Continuing review: the periodic review of a research study by an IRB to evaluate whether the study continues to meet organizational and regulatory requirements. Federal regulations stipulate that continuing review should be conducted at intervals appropriate to the level of risk involved in the study, and not less than once per year. [45 CFR §46.109(e)]

Data and safety monitoring plan (DSMP): a process that reviews the integrity, safety and progress of a research protocol with the purpose of protecting participants during the course of study and makes decisions regarding continuance, modification, or stopping of the study for reasons of efficacy or safety. A DSMP may take a variety of forms, such as an investigator

reviewing his or her own data, a review by another faculty member not otherwise involved in the conduct of the research, a committee of investigators, an independent committee, or an independent data and safety monitoring board. The type of safety monitoring that is adequate depends on the specifics of the research.

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

Decision making capacity: the ability to understand the choices presented, to appreciate the implications of choosing one alternative rather than another, and to make, and communicate, a choice.

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

Emancipated minor: In Wyoming, a child can petition to be "emancipated" under W.S. § 14-1-202, but must do so by filing a written application and meeting the statutory requirements. Only if a child were "emancipated" as described above would the state of Wyoming consider the child an “adult.”

Engaged in research: an institution becomes “engaged” in human subjects research when its employees or agents (all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility) (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)]. Solicitation of consent by performance site staff would be considered engagement.

FDA: the Food and Drug Administration.

Federal Wide Assurance (FWA): a document that fulfills the requirements of 45 C.F.R. Part 46 and is approved by the Secretary of Health and Human services. The University of Wyoming has an approved FWA on file with DHHS. The University of Wyoming’s FWA number is #00000186.

Fetus: the product of conception from implantation until delivery.

Guardian: Pursuant to Wyoming’s Probate Code, W.S. § 2-1-103(xviii), a “guardian" means the person appointed by the court to have custody of the person of the ward under the provisions of this code.

HIPAA: is the Health Insurance and Portability and Accountability Act of 1996 (HIPAA) Pricay Rule that protects the privacy of a research participant's health information.

Human subject research: The regulatory definition of research is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. To generalize is to derive general conclusions from particulars.

Generalizable knowledge is a goal of most basic research. Even research about the most narrowly defined topic, such as an individual case study or the study of an isolated community, may be intended to contribute to a body of knowledge (45 C.F.R. 46.102(d)).

Human subject: A human subject is a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Intervention includes both physical procedures by which data are gathered (for example, drawing blood) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between the researcher and the subject. [45 C.F.R. 46.102(f)]

Informed consent: the agreement to participate in research that is made voluntarily by an individual with legal and mental competence and the requisite decision-making capacity, after disclosure of all material information about the research. Informed consent means the knowing consent of an individual or his or her legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. Information conveyed in the informed consent procedure must include all essential elements listed in Section 5 of this manual.

Institution: any public or private institution or agency (including federal, state, and local government agencies).

Institutional Review Board (IRB): an independent committee comprised of scientific, non-scientific, and non-affiliated members established according to the requirements of federal regulations. Any board, committee, or other group formally designated by an organization to review research involving humans as participants, to approve the initiation of and conduct periodic review of such research. [45 CFR §46.402(g)]

Investigator: an investigator is each faculty member, principal investigator, or other researcher responsible for the design, conduct, or reporting of the research or other educational activity proposed for funding. In some cases, undergraduate students, graduate students and postdoctoral fellows may be responsible for the design, conduct, or reporting of research such that the graduate student or postdoctoral fellow is considered to be an investigator.

Key personnel: the PIs, co-PIs, and others, specified within each project, as having decision-making power over the investigation.

Legally authorized representative: an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to that subject's participation in the procedures involved in the research. [45 CFR §46.402(c)]

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 the participant's daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR §46.102(i)] In research involving prisoners, minimal risk is also defined as 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)]

Minimal risk research: research in which the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life (of normal subjects) or during the performance of routine physical or psychological examinations or tests. Clinical investigations are usually more than minimal risk.

Monitoring: may refer to data monitoring or monitoring the conduct of research. Data monitoring means the systematic tracking of data from a research study with the intent to evaluate the harms and benefits that accrue to participants. Monitoring the conduct of research mean the systematic tracking of the implementation of a research study with the intent to maintain compliance with the protocol and regulations, and maintain the integrity of the data.

Neonate: a newborn.

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

Office for Human Research Protections (OHRP): an office that is responsible for regulatory oversight of human subject research.

Parent: a child's biological or adoptive parent.

Permission: the agreement of parent(s) or guardian to the participation of the child in the research or clinical investigation.

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

Principal investigator (PI): the individual with signatory power on all documents related to the research project. This person has final authority over the project, is accountable for the overall conduct of a particular research protocol, and is accountable for the overall conduct of a study. The PI accepts responsibility for training all personnel associated with the study in compliance with the human subjects regulations of 45 C.F.R. 46. "Co-principal investigator" is that individual who co-signs on documents related to the project or who may be designated as a co-principal investigator in grant-related documents. This person has decisionmaking power with regard to the conduct of the research. The co-principal investigator reports to the principal investigator who is ultimately responsible for the conduct of the research.
Others with decision-making power may include such persons as project managers, directors, and trainers. These designations are not all-inclusive. Operationally, these individuals have some oversight responsibility for one or more portions of the project. Individuals in this category are determined uniquely for each project by the principal investigator.

Protocol: a formal plan that includes, at minimum, the objectives, rationale, design, methods and other conditions for the conduct of a research study.

Quality Improvement (QI): Periodic examination of organizational activities, policies, procedures and performance to identify best practices and target areas in need of improvement; includes implementation of corrective actions or policy changes where needed.

Reporting Requirements: Wyoming's child protection laws contain a provision which requires the reporting of child abuse or neglect (W.S. § 14-3-205). The law requires any person who knows or has reasonable cause to believe or suspect that a child has been abused or neglected, or who observes any child being subjected to conditions that would reasonably result in abuse or neglect, to report.

Research: defined by HHS is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

Research staff: individuals who are delegated responsibility by the PI for specific research tasks.

Secretary: the Secretary of Health and Human Services and/or any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

Serious unanticipated problem: any event that results in death, a life-threatening situation, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity or a congenital anomaly/birth defect or requires medical intervention to prevent one of the outcomes listed above. Serious unanticipated problems require prompt reporting to the IRB.

Site: a site whose staff, facilities or private records of identifiable individuals are engaged in the conduct of research; or, a site that receives HHS funds. The performance site is the actual place where the research activity takes place (e.g., clinic or hospital). The performance site's location may be different from the location where the IRB review takes place.

Student: any individual who is enrolled at the University of Wyoming.

Unanticipated problem: the university defines an unanticipated problem as any of the following:

1. An actual unforeseen harmful or unfavorable occurrence to participants or others that relates to the research protocol (injuries, side effects, deaths);
2. An unforeseen development that potentially increases the likelihood of harm to participants or others in the future;
3. A problem involving data collection, data storage, privacy, or confidentiality;
4. A participant complaint about IRB approved research procedures
5. New information about a research study (e.g., a publication in the literature, interim findings, safety information released by the sponsor or regulatory agency, or safety monitoring report) that indicates a possible change in the risks of the research; or

6. Changes in approved research initiated without IRB review and approval to eliminate apparent immediate hazards to the participant.

Unanticipated problem involving risks to participants or others: an event that was (1) unforeseen, (2) related to the research procedures, and (3) either caused harm to participants or others, or placed them at increased risk of harm.

Unexpected unanticipated problem: any unanticipated problem that was unanticipated or not previously observed (e.g., not included in the consent form or investigator brochure). This includes adverse effects that occur more frequently or with greater severity than anticipated. Events that are unexpected and serious require prompt reporting to the IRB.

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.

Vulnerable participants: individuals who lack the capacity to provide informed consent or whose willingness to participate in research may be subject to undue influenced or coercion. Vulnerable subjects include, for example, children, prisoners, individuals with emotional or cognitive disorders/impairments, and economically or educationally disadvantaged persons. [45 CFR §56.107, §56.111(a)(3), §56.111(b)]