2.6 Exempt Research

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements for determining if a research proposal is eligible for exemption under 45 CFR 46.104(d) and 21 CFR 56.104, with appropriate protections in place for research subjects.

2.0 Policy

It is the policy of the Organization that:

- 2.1. All proposed exempt research must be reviewed and approved by the Office of Regulatory Affairs (ORA) prior to initiation.
- 2.2. The ORA has the authority to refer to the full IRB for review and approval any exempt human subject research where such review and approval would meaningfully enhance protection of the rights and welfare of human subjects.
- 2.3. Exempt human subject research must be conducted in accordance with sound ethical standards and all applicable HRPP and institutional policies.

3.0 Categories of Exemption

- 3.1. The following research is exempt from 45 CFR 46:
  - 3.1.1. Category 1: Research which specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods (45 CFR 46.104(d)(1))
    - 3.1.1.1. Per HRPP Policy to be eligible for exemption under category 1
      - 3.1.1.1.1. Study procedures must not involve sensitive subjects (e.g., sex or substance abuse education)
      - 3.1.1.1.2. The research is not regulated by the US FDA.
      - 3.1.1.1.3. Provisions must be made to ensure the existence of a non-coercive environment for those students who choose not to participate
      - 3.1.1.1.4. The school or other institution must grant written approval for the research to be conducted
      - 3.1.1.1.5. Informed consent must be obtained from the prospective subject or their parent or guardian.
  - 3.1.2. Category 2: Research which only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met: (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; or (ii) any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or (iii) the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a

limited IRB review per HRPP policy 2.8 (Limited IRB Review) (45 CFR 46.104(d)(2))
    - 3.1.2.1. Research involving the observation of public behavior of minors is only eligible for exemption if the investigator does not participate in the activities being observed AND if criterion (i) or (ii) above are met.
    - 3.1.2.2. Research involving the use of survey or interview procedures involving minors is not eligible for exemption under this category.
    - 3.1.2.3. Research involving minors is not eligible for exemption under criterion (iii) above.
    - 3.1.2.4. Research regulated by the US FDA is not eligible for exemption under this category.
- 3.1.3. Category 3: Benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met: (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; or (ii) any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or (iii) the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review per HRPP policy 2.8 (Limited IRB Review) (45 CFR 46.104(d)(1)).
    - 3.1.3.1. Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.
    - 3.1.3.2. Consent of the subject is required, as per section 6.7 below.
    - 3.1.3.3. If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.
    - 3.1.3.4. Research involving minors is not eligible for exemption under category 3.
    - 3.1.3.5. The research is not regulated by the FDA.
- 3.1.4. Category 4: Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met: (i) The identifiable private information or identifiable biospecimens are publicly available; or (ii) information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; or (iii) the research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under the HIPAA Privacy Rule (45 CFR 164 subpart E) (45 CFR 46.104(d)(4)); or (iv) The research involves only information collection and analysis, that either involves research conducted by, or on behalf of, a federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 or Privacy Act of 1974, 5 U.S.C. 552a.
    - 3.1.4.1. It is expected that use of this exemption will include, where appropriate, individual's authorization for future, secondary research use of PHI, or waiver of authorization per HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).
    - 3.1.4.2. This exemption does not apply where the PHI originates at an entity subject to HIPAA but is disclosed to an investigator who is not subject to HIPAA.
- 3.1.5. Category 5: Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs (45 CFR 46.104(d)(5)).
    - 3.1.5.1. The research or demonstration project must be listed on a Federal Web site maintained by the department or agency, as per requirements of 45 CFR 46.104(d)(5)(i).
    - 3.1.5.2. The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act). State programs are not included in this exemption unless the Federal Government has contracted or otherwise entered into an agreement with the State to evaluate a program.
    - 3.1.5.3. There must be no statutory requirement that the project be reviewed by an

Institutional Review Board (IRB).
    - 3.1.5.4. The research is not regulated by the US FDA.
  - 3.1.6. Category 6: Taste and food quality evaluation and consumer acceptance studies, i) if wholesome foods without additives are consumed, or ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or 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. (45 CFR 46.104(d)(6))
  - 3.1.7. Categories 7 and 8: Storage, maintenance and secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use; and Research involving the use of identifiable private information or identifiable biospecimens for secondary research use (45 CFR 46.104(d)(7 and 8).
    - 3.1.7.1. UNMC does not currently allow investigators within the Organization to use broad consent for storage, maintenance or secondary use of identifiable private information or identifiable biospecimens.
    - 3.1.7.2. Identifiable private information or identifiable biospecimens obtained under broad consent by investigators outside the Organization may be transferred to, and used by an investigator within the organization, provided appropriate Material Transfer Agreements and/or Data Use Agreements are in place, and the ORA has determined that:
      - 3.1.7.2.1. The Broad Consent form obtained by the outside investigator included all the required elements of broad consent per 45 CFR 46.116(d); and
      - 3.1.7.2.2. The research to be conducted within the Organization is within the scope of the general description of the types of research that might be conducted (per 45 CFR 46.116(d)(2)); that is, the broad consent form included sufficient information such that a reasonable person would expect that the broad consent would permit the types of research to be conducted within the Organization.
- 3.2. FDA Category (c): Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days (21 CFR 50.104(c))
  - 3.2.1. This exemption applies only to the first use of the test article within the Organization. Any subsequent use of the test article at the Organization is subject to IRB review per HRPP policy 6.4 (Emergency Use of a Test Article).
- 3.3. FDA Category (d): Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use 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. (21 CFR 50.104(d))

4.0 Limitations on Categories of Exemption

- 4.1. Research involving children where research involves survey or interview procedures or observation of public behavior that qualify under category 2 are not exempt if the investigator(s) will participate in the activities being observed (45 CFR 46.104(b)(3)).
  - 4.1.1. Research involving children may be exempt under category 2 only if the research activities are those involving educational tests or observation of public behavior where the investigators do not participate in the activity being observed. The use of survey or interview procedures is eliminated from this exemption, and so is research involving the observation of public behavior if the investigators participate in the activity being observed. To be exempt, these activities must also meet the condition that the data are recorded without individual identifiers, or the condition that disclosure of the recorded responses would not place the subjects at risk of criminal or civil liability or be damaging to their financial standing, employability, or reputation.
  - 4.1.2. Research involving children is not exempt under category 3 (benign behavioral interventions).
- 4.2. Research involving prisoners is not exempt, except for research aimed at involving a broader subject population that only incidentally includes prisoners (45 CFR 46.104(b)(2)).
- 4.3. Research involving vulnerable populations, sensitive topics (including but not limited to personal aspects of the subject's behavior, life experiences or attitudes), deception, or greater than minimal risk to subjects, even when allowable under sections 3.0 or 4.0 above, may be deemed not exempt, on a case by case basis. This decision is made by the IRB Administrator in consultation with the IRB Executive Chair or IO.
- 4.4. Any human subjects research where review by the full IRB would meaningfully enhance protection of the rights and welfare of human subjects may be deemed not exempt. This decision is made by the IRB Administrator in consultation with the IRB Executive Chair or IO review.

5.0 Procedures

- 5.1. Protocols which may be eligible for exemption are submitted to ORA using the following applications:
  - 5.1.1. Exempt Application will be used for the following:
    - 5.1.1.1. Categories 1-3, 5-6, and FDA category (d)
    - 5.1.1.2. Category 4 research which involves only identifiable private information not obtained from medical records.
  - 5.1.2. Human Biological Materials Research Application will be used for the following:
    - 5.1.2.1. Category 4 research which involves identifiable biospecimens, with or without associated medical records.
  - 5.1.3. Medical Records Research Application will be used for the following:
    - 5.1.3.1. Category 4 research which involves only identifiable private information from medical records.

  Note: The Organization does not utilize Exemption categories 7 and 8.
- 5.2. Protocols which appear to be eligible for exemption are reviewed by a designated IRB Administrator. This individual will have no direct involvement in the activity he or she is reviewing or any other conflict of interest that would compromise objectivity as per HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification & Management).
- 5.3. The IRB Administrator will:
  - 5.3.1. In consultation, as necessary, with the IRB Executive Chair/designee, make the final determination of exempt status.
  - 5.3.2. Determine whether criteria for approval described in section 6.0 are satisfied. If necessary, the IRB Administrator is authorized to require clarification or modification of the IRB Application to determine whether the criteria re satisfied.
  - 5.3.3. Complete the Exempt Research Checklist which includes the category under which the research qualifies for exemption.
  - 5.3.4. Communicate the determination with the PI (or his/her designee)
- 5.4. Projects determined not to be exempt may be referred for expedited review provided the project qualifies under the categories specified at 45 CFR 46.110 or 21 CFR 56.110 (per HRPP policy 2.3: Expedited Review of Research).
  Note: If the Exempt Application was used, the PI will be instructed to fill out the Biomedical Research OR Behavioral and Social Science Research in order to provide the IRB with the information needed to perform a thorough review to ensure that the IRB approval criteria at 45 CFR 46.111 have been satisfied.
- 5.5. If Behavioral and Social Science Research Application is submitted and subsequently determined to be exempt, the PI is notified accordingly.

6.0 Criteria for Approval of Exempt Research

- 6.1. The research must qualify for exemption under the categories specified above (section 4.0)
- 6.2. The research must represent no more than minimal risks to subjects.
- 6.3. Selection of subjects must be equitable.
- 6.4. If identifiable private information is recorded, there must be adequate provisions to maintain the confidentiality of the data.
- 6.5. There must be adequate provisions to maintain the privacy interest of subjects.
- 6.6. The rights and welfare of research subjects must be adequately protected.
- 6.7. If the investigator or his/her staff interacts with subjects, there must be a process of informed consent that will disclose at least (1) a statement that the activity involves research; (2) a statement that participation is voluntary; (3) a description of the procedures; (4) a description of risks if any; and (5) the name and contact information for the researcher.
  - 6.7.1. The ORA and/or the Executive Chair or his/her designee may determine whether this informed consent must be documented by a consent form signed by the subject or his/her LAR, parent or legal guardian.
- 6.8. For exempt research under categories 2 or 3 where the information is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects (as per 45 CFR 46.104(d)(2)(iii) or 45 CFR 46.104(d)(3)(i)(C)), the IRB must conduct a limited review as described in HRPP policy 2.8 (Limited IRB Review).
- 6.9. For exempt research under category 4 where the research involves only information collection and analysis involving the investigator's use of identifiable health information (as per 45 CFR 46.104(d)(4)(iii)), the ORA must determine that such use is regulated under the HIPAA Privacy Rule (45 CFR 164 subpart E).

7.0 Actions

- 7.1. Approval and full release; initiation of the research is authorized: Criteria in section 6.0 are satisfied. The investigator will be notified of the approval in writing and is authorized to start the study.
- 7.2. Conditional approval; final ORA approval and full release contingent upon IRB Administrator acceptance of specified modifications: Criteria in section 6.0 will be satisfied if specified modifications are made by the investigator. Once the modifications are made, and are accepted by the IRB Administrator, the investigator will be notified of the approval in writing and is authorized to start the study.
- 7.3. Referred for expedited review: The protocol is referred for expedited review in accordance with the requirements of 45 CFR 46.110; 21 CFR 56.110.
- 7.4. Referred for full board review: The protocol is referred for review by the full IRB in accordance with section 4.0 above.

8.0 Review by Other Organizational Committees

- 8.1. Before the IRB will grant final approval and release, the ORA must receive verification of approval or completion of review by the following committees/offices as applicable:
  - 8.1.1. Fred & Pamela Buffett Cancer Center Scientific Review Committee
  - 8.1.2. Conflict of Interest Committee
  - 8.1.3. Sponsored Programs Administration/executed contracts office

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