Guidance for Revision of Exempt Categories for Research in 45 CFR 46

On January 21, 2019, a number of revisions to 45 CFR 46 became effective. These regulations define policies for the review and approval of research involving human subjects by Institutional Review Boards (IRBs) and requirements for investigators operating under an IRB approval. These regulations have always included "Exempt Categories," providing specific categories of minimal risk research which require a less intensive review by the IRB and an abbreviated set of regulatory requirements. In the revised regulations, these Exempt Categories have been significantly revised. Lindenwood University has adapted these revisions as described in the following.

The spirit of the Exempt Categories remains the same. These categories allow for a more simplified application and review process by the IRB on account of the minimal risk involved with research falling into these categories. In addition, each Exempt Category involves strict prescriptions regarding the scope and nature of data collection which ensure the protection of human subjects. The basic policies regarding Exempt research at Lindenwood University remain the same:

- Investigators may only conduct Exempt Research after completing required IRB training.
- The LU IRB makes all determinations regarding Exempt Research.
- Participants must receive an IRB approved Exempt Information Sheet prior to participating in the research. The LU IRB has several templates available for different types of Exempt research.
- Investigators must handle all research data in compliance with policies regarding collection and use of human subjects data.

The following provides the new regulatory text for each Exempt Category and a brief description of how the LU IRB is handling all new features of the Exempt Categories. A key general revision applying to all Exempt Categories entails the applicability of Subpart B, C, and D within Exempt Review. These Subparts describe additional protections for pregnant women, human fetuses and neonates, prisoners, and children respectively:

- Pregnant women, human fetuses, and neonates may be enrolled in Exempt Research if the conditions of the Exemption are met.
- Prisoners may not be enrolled in Exempt Research "except for research aimed at involving a broader subject population that only incidentally includes prisoners."
- Children may be enrolled in Exempt Research falling under the following Exempt Categories if the conditions of the Exemption are met: Categories 1, 4, 5, 6, 7, 8. Children may only be enrolled under Category 2 "involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed." If a Limited IRB Review is required for the approval of Category 2, children may not be enrolled.

1. Exempt Category 1:

1.1. "Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods."

1.2. Exempt Category 1 makes a significant addition in stating that "normal educational practices" are those that are not likely to negatively impact any student's capacity or opportunity to learn. If the risk of randomizing students to novel teaching strategies is not well known, then the research would not be approvable under this Exemption as the IRB would not be able to affirm that any negative impact of the intervention has been mitigated. In addition, research that may place the teacher, educator, or administrator at harm, such as producing data which may negatively affect their employment status, may not be approved under this Exemption.

2. Exempt Category 2:

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

2.1.1. (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;

2.1.2. (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

2.1.3. (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."

2.2. Exempt Category 2 has been changed to include only "interactions," referring to verbal or written mechanisms designed to collect data from or about participants. Under this new Exempt Category, sensitive data may be collected if a Limited IRB Review is conducted to ensure that these sensitive data are not identifiable.

2.3. To ensure compliance with these new features of Exempt Category 2, Limited IRB Review will be completed by a designated IRB member during the traditional Exempt review process when the study may be collecting sensitive data. During this Limited IRB Review, the reviewer will consider the following and potentially pose contingencies ensuring that subjects remain protected in these circumstances:

2.3.1. The potential identifiability of the data
2.3.2. The necessity of sensitive data for meeting the outcomes of the research
2.3.3. Measures to reduce any risk associated with collection of sensitive data
2.3.4. Plans for compliance with LU policy regarding collection and use of sensitive research data

3. Exempt Category 3

3.1. "Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

3.1.1. (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;
3.1.2. (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
3.1.3. (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.
3.1.4. For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else. 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."

3.2. Exempt Category 3 is an entirely new Exempt Category. Exempt Category 2 applies to interactions required to collect data. Exempt Category 3 provides for interventions required to collect data. These interventions, however, must be "benign" in terms of potential risk, consistent with the terms described in this Exempt Category.
3.3. To ensure compliance with these new features of Exempt Category 3, Limited IRB Review will be completed by a designated IRB member during the traditional Exempt review process when the study may be collecting sensitive data. During this Limited IRB Review, the reviewer will consider the following and potentially pose contingencies ensuring that subjects remain protected in these circumstances:

3.3.1. The potential identifiability of the data
3.3.2. The necessity of sensitive data for meeting the outcomes of the research
3.3.3. Measures to reduce any risk associated with collection of sensitive data
3.3.4. Plans for compliance with LU policy regarding collection and use of sensitive research data

4. Exempt Category 4

4.1. "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:

4.1.1. (i) The identifiable private information or identifiable biospecimens are publicly available;
4.1.2. (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;
4.1.3. (iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or (iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for 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 applicable federal privacy standards found in the E-Government Act, Privacy Act and the Paperwork Reduction Act."

4.2. The scope of data collection approvable under Exempt Category 4 has been significantly expanded. In the prior Exempt Category 4, all data were retrospective and had to exist "on the shelf" prior to the point of collection by the researcher. The prior Exempt Category 4 was also limited to data and this new category includes "specimens." In this new category, both retrospective and prospective data and specimens may be collected without consent in cases where the research meets the conditions of the Exemption. Identifiable information related to data or biospecimens may be retained under this Exemption if additional HIPAA protections are applicable.

5. Exempt Category 5

5.1. "Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or

alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended. Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects."

5.2. The scope of Exempt Category 5 has been expanded to include demonstration projects funded by a federal agency. Studies meeting these criteria will be publicly posted on a federal website.

6. Exempt Category 6

6.1. "Taste and food quality evaluation and consumer acceptance studies: if wholesome foods without additives are consumed, or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture."

6.2. Exempt Category 6 has not been revised. It remains the only Exemption under which FDA regulated research may be conducted.

7. Exempt Category 7

7.1. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §__.111(a)(8).

7.2. This is a new Exempt Category. Lindenwood University will not implement the use of Exempt Category 7, as this Exempt Category was designed for institutions practicing large-scale biobanking. In addition, this Exempt Category requires the development of considerable infrastructure required to perform, document, and track broad consent. The collection of data and specimens will continue to be reviewed under Exempt Category 2 and 4, Expedited Category 2, 3, 4, 5, 7, and Full Board Review as applicable.

8. Exempt Category 8

8.1. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met: (i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §__.116(a)(1) through (4), (a)(6), and (d); (ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §__.117; (iii) An IRB conducts a limited IRB review and makes the determination required by §__.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and 479 (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from any legal requirements to return individual research results.

8.2. This is a new Exempt Category. Lindenwood University will not implement the use of Exempt Category 8, as this Exempt Category was designed for institutions practicing large-scale biobanking. In addition, this Exempt Category requires the development of considerable infrastructure required to perform, document, and track broad consent. The collection of data and specimens will continue to be reviewed under Exempt Category 2 and 4, Expedited Category 2, 3, 4, 5, 7, and Full Board Review as applicable.