7 IRB Review of Research: 7.1 Exempt Determinations	Effective Date: **2/12/2021** Revised: **2/12/2021**

Research involving human subjects may qualify as exempt from IRB review, providing the involvement of subjects is limited to certain categories defined by federal regulations. However, such projects must be conducted according to ethical principles established in the Belmont Report. An exempt determination by the IRB office or approval via **limited IRB review** is required prior to initiating the research.

1.0 Categories of research exempt from further IRB review:
Research activities involving human participants in which there is minimal or no risk and in which the IRB determines that the only involvement of human subjects will be in one or more of the following categories are eligible for exemption. The following restrictions apply:

- research involving prisoners is not eligible for exemption, except for research aimed at involving a broader subject population that only incidentally includes prisoners
- FDA-regulated research is not eligible for exemption, except under Category 6
- research with children:
    - is restricted in:
        - Exempt Category 2(i) and (ii) – may only be used for research involving children when the research is limited to educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. Research with children is not eligible under this category when it involves surveys, interviews, or observation of public behavior where the investigator will participate in the activities being observed.
    - Is NOT permitted in:
        - Exempt Category 2(iii) – use of educational tests, survey procedures, or observation of public behavior when the information obtained is recorded in such a manner that the identity of the human subjects can readily be ascertained.
        - Exempt Category 3 – benign behavioral interventions.

Note that investigators must file a protocol application with the IRB for a formal determination of exemption prior to initiating the research.

1.1 Category #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.

NOTE: Research involving normal educational practices in this category may include various methods and types of data (including identifiable data), such as:

- student course grades, test scores, assignments, journals
- videotapes, photos, or observation of classroom activity

- curriculum-related interviews or questionnaires with students, teachers, parents, administrators

Examples of educational research which may not qualify under this category include:

- Research conducted by department or program chairs who also hold responsibility for evaluation of faculty,
- Research involving the assignment of students to either a proven educational technique or a novel educational technique (i.e. experimental or quasi-experimental design).

When academic records will be used for research, the investigator is responsible for compliance with the Family Educational Rights and Privacy Act (FERPA). Refer to SOP *11.1 Use of Confidential Records* and the Office of Registration and Records for more information.

1.2 Category #2.

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

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

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a **limited IRB review** to make the determination required by §___.111(a)(7).

NOTE: *This category has limited applicability where children will be involved: research involving educational tests, or public observation where the investigator does not take part in the activities being observed. Surveys or interviews of children are not included in this category.*

1.3 Category #3.

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

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

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §___.111(a)(7).

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.

This category **may not** include children.

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**;

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

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use if regulated under 45 CFR parts 160- and 164, subparts A and E [HIPAA], for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

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

- By "secondary research," this exemption is referring to re-using identifiable information and identifiable biospecimens that are collected for some other 'primary" or "initial" activity. The information or biospecimens that are covered by this exemption would generally be found by the investigator in some type of records (in

the case of information) or some type of tissue repository (such as a hospital's department for storing clinical pathology specimens).

- In relation to Exemption 4(i), examples of identifiable information or identifiable biospecimens which are **publicly available**, include:
    - Use of archives in a public library,
    - Government or other institutional records where public access is provided on request,
    - From a commercial entity if the information is provided to members of the public on request of if the only requirement for obtaining the information is paying a user fee, registering or signing in as a visitor to an archive,
    - A commercial entity made identifiable biospecimens publicly available to anyone on request or for a fee.
- NDSU is NOT a HIPAA Covered Entity (CE); therefore, exemption 4(iii) may not be used unless the research will take place at a covered entity and that entity determines through their IRB procedures that the exemption applies or NDSU Formally enters into a Business Associate Agreement with the CE.
- It is important to recognize that this exemption does not cover any primary collections of either information or biospecimens. For example, if an investigator wants to collect information directly from research subjects by asking them to complete a questionnaire, that would not be covered by this exemption. If an investigator wants to collect biospecimens by having subjects swab their cheek, that would similarly not be covered by this exemption.

Refer to SOPs *11.2, Human Biological Specimens* and *11.3, Secondary Analysis of Existing* Data for more information.

<u>1.5 Category #5.</u>
Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

(i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal 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.

NOTE: *Guidance from OHRP indicates that institutions should consult the HHS funding agency before invoking this exemption. In addition, it clarifies that:*

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

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 or additive at or below the level and for a use found to be safe by the Food and Drug Administration, or
- agricultural chemical or environmental contaminant at or below the level found to be safe, approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

1.7 Category #7.
Storage or maintenance for which broad consent is required: Research involving the use 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).

- Broad consent must be obtained from subjects. Waivers or alterations of broad consent are NOT permitted. Waivers of documentation of broad consent are unlikely.
- Robust systems to track consent and refusals and the ability to flag records or specimens for which consent has not been obtained is necessary under this exemption as if broad consent was refused, consent cannot later be waived. **Due to this requirement, until such a time when an institution-wide tracking mechanism for refusals is established, the IRB will refrain from utilizing this exemption.**
- *Limited IRB review* is required for all research under this exemption.

1.8 Category #8.
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

(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 abiding by any legal requirements to return individual research results.

- This exemption will frequently be paired with the exemption at §___.104(d)(7), which permits the storage and maintenance of identifiable private information and identifiable biospecimens for secondary research use. The exemption at §___.104(d)(8) would apply to a specific secondary research study.
- This exemption could also apply if the investigator obtains appropriate broad consent from the subject in addition to the consent to an original specific study, and then proceeds to use the information or biospecimen in a secondary study.
- Limited IRB review is required for all research under this exemption, and includes review of:
  - Privacy and confidentiality procedures
  - Ensuring secondary research is within the scope of the broad consent.
- **Due to the robust, institutional systems needed to ensure valid broad consent has been obtained in order to track or flag records or specimens for which broad consent was refused, the IRB will refrain from utilizing this exemption category.**

2.0 Ethical principles:

When NDSU employees or agents will be engaged in research involving human subjects, (including research that qualifies under an exemption category) the research is to be conducted in accordance with the Belmont ethical principles of respect for persons, beneficence and justice. Although such projects may involve little risk of harm, research participants are to be afforded basic rights and protections, which include:

- the right to choose for themselves, in an environment free of coercion or undue influence, whether or not to take part in research
- the right to information about the research purpose, procedures, confidentiality limits, and any risks that may be involved
- the right to decline participation, or withdraw from research at any time without penalty
- the right to respect for their privacy and the confidentiality of their information
- the right to receive contact information for questions about the research (investigator and co-investigator's contact information)
- the right to receive contact information to express concerns or report a problem about a research project (NDSU IRB office contact information)

The basic elements of informed consent are to be communicated to each prospective subject, unless adequate justification has been provided for a waiver of this requirement. This may be accomplished by informing participants with printed information (a consent form, cover letter, handout), oral information (via a script), or electronic information in an email or online posting. When the elements of informed consent are to be given orally, the investigator must develop a written script (oral script) of the oral presentation; participants' signature is not typically required for most projects eligible for exemption, although it may be appropriate for some projects. Documentation of informed consent is required under Exemption Categories 3, 7 and 8 (when utilizing broad consent) unless a waiver is approved.

3.0 Exempt Determinations:
Investigators submit a protocol application for an exempt determination or limited IRB review.

3.1 Application materials and submission process.
Protocol applications are submitted through the IRB Module in Novelution (erac.ndsu.edu). Applications may be started by the Principal or co-investigator. The PI is required to certify application materials prior to submission. Relevant supplemental materials (e.g. attachments, recruitment materials, information sheet or oral scripts for consent, and research questionnaires) are uploaded into relevant sections.

Allow a minimum of 5 business days for processing and review; additional time may be required when the protocol application lacks sufficient detail, contains conflicting information, or the project is not eligible under one of the exemption categories.

3.2 Pre-submission Requirements
All members of the research team must have current CITI training before IRB Processing can begin. Once the PI has submitted (or completed PI certification) members of the research are automatically notified if training requirements must be met. The relevant department chair/head is also notified that department approval is needed.

3.3 IRB determination.
Upon receipt of a complete protocol application, training documentation is verified and the application is reviewed by a qualified HRPP staff member. A qualified HRPP staff member, IRB chair or designee determines if the protocol:

a) qualifies for exemption under one of the Exemption categories,
b) qualifies for exemption, but requires limited IRB review,
c) does not qualify for exemption, will require review by expedited or full review procedures.

The project may not be initiated prior to receipt of an exempt determination or approval letter from the IRB.

IRB actions may include any of the following:

3.3.1 Revisions required.
The IRB may determine that additional information and/or revisions are needed in order to:

- verify eligibility for exemption,
- meet Belmont ethical principles,
- or to meet the review criteria for Limited IRB review.

A qualified HRPP staff member notifies the investigator in writing to request the missing information or revisions. Once the revisions and/or additional information are received, qualified HRPP staff and/or IRB member ensure that the standards or review criteria are met. The investigator is notified of the exempt certification or approval in writing. Protocols are deemed inactive if a response has not been received within 90 days. All communication is documented in the protocol file.

3.3.2 Project not eligible for exemption.
The IRB may determine that the proposed project is not eligible for one or more allowable categories of exemption. Qualified HRPP staff notify the investigator in writing, citing the reason for the ineligibility; and may request additional materials for review by the expedited method or full board. In some instances, the investigator may elect to submit a revised protocol, with changes in the research methods, subject population, and/or collection of identifiable information in order to qualify the project for exemption.

The IRB retains the final authority in determining project eligibility for exempt status. Refer to SOPs *7.3 Expedited Review* and *7.4 Full Board Review* for more information.

3.3.3 Project eligible for exemption/Limited review not required.
The IRB may determine that the project, as submitted, is eligible for exemption, and Belmont ethical principles will be met in the conduct of the research. Qualified HRPP staff notify the investigator in writing with a letter of exempt certification; the research may then be initiated. The letter will specify the applicable exempt category, and the date which the next status update will be due (typically three years from the date of the determination letter).

3.3.4 Project eligible for exemption/Limited review required.
Research for which limited IRB review is a condition of exemption include Categories 2(iii), 3(i)(C), 7, and 8. Limited IRB review must be conducted by an experienced IRB member which may include a qualified HRPP staff.

3.3.4.1 Limited IRB Review for Exemption 2(iii) and 3(i)(C) – The IRB must determine through expedited review procedures that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

3.3.4.2 Limited IRB Review for Exemption 7 – The IRB shall determine through expedited review procedures that:

(i) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of §___.116(a)(1)-(4), (a)(6), and (d);

(ii) Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with § ___.117; and

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

3.3.4.3 Limited IRB Review for Exemption 8 – The IRB shall determine through expedited review procedures that:

(i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable

biospecimens was obtained in accordance with §___.(a)(1) through (4), (a)(6), and (d); (See SOP 9.5 Broad Consent for more details)

(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) that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data and makes the determination that the research to be conducted is within the scope of the broad consent; and

(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 abiding by any legal requirements to return individual research results.

3.4 Continuing review.

Exempt protocols remain open for three years following the determination of exemption. If the project will continue, the Principal Investigator must file for continuing review. An email notice will be sent from the system notifying the PI and any co-investigators that the study is due for continuing review. Requests for continuing review require verification of currently approved procedures, and may include submission of an updated consent document, or other relevant information. Research conducted without current IRB approval or determination of exemption is considered noncompliant, and subject to procedures described in SOP *12.3 Complaints or Allegations of Noncompliance*.

3.5 Appeals process

The investigator may appeal the IRB determination if new information becomes available, or evidence is provided that the IRB has failed to follow their own procedures, or incorrectly applied federal regulations, state law, or NDSU policy for the protection of research participants. A written appeal, citing specific federal regulations, NDSU policy or procedures, may be made to the HRPP office or IRB Chair.

In consultation with HRPP staff, the IRB Chair or Chair's designee makes a determination, and may forward the appeal to the board for consideration at the next convened meeting. The board's determination is considered final, and communicated in writing to the investigator and other entities as applicable.

3.6 Notification of exempt determinations to IRB.

IRB members are provided with a report of actions taken outside of a convened meeting. This includes exempt determinations and new and continuing protocols reviewed by the expedited method. All members have an opportunity to review the list and ask questions about the actions performed outside of full board deliberations.

3.7 Other institutional approval.

Some projects may be subject to further review and approval or disapproval by officials of the institution. These officials may not approve the research, however, if it has not been approved by the IRB.

4.0 Post-approval procedures:

4.1 Protocol amendments.
Prior IRB approval is required for proposed changes to a protocol to ensure that the project remains eligible for exemption, and the conduct of the project will continue to follow Belmont ethical principles. These changes may include, but are not limited to changes in: subject population, recruitment procedures, informed consent process, research procedures, type of information collected, or research setting. If a proposed change would alter the eligibility for exempt status, the project will require review by either the expedited method, or by the full board at a convened meeting. Refer to SOP *7.5 Protocol Amendments* for more information.

4.2 Adverse events or Unanticipated problems.
An Adverse Event report is required to the IRB within 72 hours of discovering an adverse event or unanticipated problems involving risks to participants or others. A research-related injury, or loss of confidential research data are examples of unanticipated events that would place participants at risk. Refer to SOP *7.7 Unanticipated Problems and Serious Adverse Events* for more information.

4.3 Protocol Deviation Reports.
Accidental or unintentional changes to, or non-compliance with the research protocol must be reported to the IRB by adding a Protocol Deviation to the protocol within Novelution.

4.4 Quality assurance and research compliance:
Research determined to be exempt from further review may still be subject to random (not-for-cause) or directed (for-cause) audits to ensure compliance with federal regulations and institutional policies. Refer to *Section 12 Quality Assurance and Research Compliance* for more information.

DEFINITIONS:

Adverse Event: an event that occurs during the course of a research protocol that either causes physical or psychological harm, or increases the risk of physical or psychological harm, or results in a loss of privacy and/or confidentiality to a research participant or others (such as family members).

Anonymized (de-identified): identifiers were originally collected, but have been irreversibly removed from previously identified samples; individual can no longer be identified or linked with their information

Anonymous: no identifiable information exists; individual identity cannot be known or deduced, no possibility of linkage with additional information or future data collection

Benign Behavioral Intervention: 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.

Coded: 1) identifiable information has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and 2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens

Disclosure: would include both intended (i.e., publication) and unintended release of information (i.e., breach of confidential data)

Existing data (documents, records or specimens): data or information that was already in existence ('on-the-shelf') prior to, and was collected for purposes other than, the currently proposed research

Human Subject: (HHS) a living individual, about whom, an investigator (whether professional or student) conducting research obtains:

- Data through intervention or interaction with the individual, or
- Identifiable private information

Human Subject: (FDA) an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. This would include individuals whose private information is used to test the safety or efficacy of a diagnostic device, even if the information is not individually identifiable, and was obtained in a retrospective fashion.

Identifiable: the identity of the subject is or may be readily ascertained or associated with the information; data can be linked to specific individuals either directly or indirectly through coding systems. Would also include some demographic information, or other unique information or key details that would allow individual identification to be deduced (i.e., using internet search engines or other means).

Interaction: includes communication or interpersonal contact between the investigator and participant

Intervention: includes both physical procedures by which data are gathered and manipulations of the subject or their environment that are performed for research purposes

Investigator: anyone involved in conducting the research; i.e., study design or supervision, data collection, obtaining informed consent, performing research procedures, obtaining coded private information or specimens, analyzing data

Limited IRB review: Research eligible for exemption under Categories 2(iii), 3(i)(C), 7, or 8 require review of research procedures to determine the appropriate privacy and confidentiality procedures are in place, and/or that broad consent has been adequately obtained, and/or that the research is consistent with the scope of the broad consent. Limited IRB review must be conducted by an experienced IRB member through expedited review procedures.

Obtained: received or accessed

Private information: information that has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. *The IRB has the sole authority to determine whether or not a research project constitutes the involvement of human subjects.*

Test article: any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to the Federal Food, Drug and Cosmetic Act.

REFERENCES:

Exempt categories (§___.104)
FederalWide Assurance Terms
Human subject definition §___.102(e)(1)
Belmont Report
OHRP guidance: Public Benefit and Service Programs
Family Educational Rights and Privacy Act (FERPA), Registration and Records

RELATED HRPP SECTIONS:

2 Applicability
7.3 Expedited Review
7.4 Full Board Review
7.5 Protocol Amendments
7.7 Unanticipated Problems and Serious Adverse Events
11.1 Use of Confidential Records
11.2 Human Biological Specimens
11.3 Secondary Analysis of Existing Data
12 Quality Assurance and Research Compliance