

NDSU research may involve the collaboration or assistance of other research institutions, schools, hospitals, clinics, private businesses, or other entities in various ways. Each institution or entity involved in NDSU research shares responsibility for safeguarding the rights and welfare of research participants. Such projects may invoke additional or unique requirements for training, institutional assurances and agreements, and/or IRB review when the other entity is considered engaged in human subjects research.

1.0 Applicability:

Non-NDSU entities or institutions may play a variety of roles in NDSU human subjects research. These entities may or may not be considered engaged in human subjects research, may or may not have their own IRB, and may or may not hold approved federal assurances.

1.1 Cooperative research.

NDSU cooperative research projects are those projects that involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects.

1.1.1 Single IRB (sIRB) for Federally-Supported Cooperative Research - When NDSU is engaged in Federally-supported cooperative research, a single IRB (sIRB) of record will be utilized. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

1.1.2 The following research is not subject to the sIRB provision:

- Cooperative research not funded by one of the Common Rule agencies.
- Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe).
- Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.
- For research not subject to paragraph 1.1.1 of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangement for avoiding duplication of effort.

1.2 Multi-site research.

Multi-site research refers to research performed at more than one institution or entity, which may or may not include NDSU as one of the sites. When NDSU is engaged in multi-site research funded by the NIH in which each institution will engage in the same research protocol, a single IRB (sIRB) of record will be used for the review and oversight of that research.

1.3 Off-site research.

Off-site research refers to NDSU research performed at one or more geographic locations or facilities not owned or operated by NDSU.

1.4 Research involving other assistance from a non-NDSU entity.

Other entities may assist in an NDSU research project in ways that do not involve collaboration or acting as a **performance site**. This assistance may include: providing contact lists, recruiting or contacting participants, performing research procedures, analyzing data, or other related tasks.

2.0 Engagement in human subjects research.

Requirements for training, IRB review, or institutional assurances are determined by the extent of another entity's involvement in NDSU research. Based on federal guidance, NDSU has defined specific research activities and responsibilities to constitute 'engagement' on the part of an institution's **employees or agents**. Engaged institutions are considered '**collaborators**' for the purposes of this SOP. Training in human subjects protection is required for those individuals engaged in research.

2.1 Engaged in research.

An institution or entity is considered to be engaged in human subjects research when their employees or agents will perform any of the following:

2.1.1 Receive a direct award, grant or contract for human subjects research.

2.1.2 Direct or supervise the human subjects research project.

2.1.3 Intervene with participants for research purposes by performing invasive or noninvasive procedures, (*Exceptions – when an institution's activities are limited to those described in 2.2.1 – 2.2.4 below, the institution is not engaged*). Examples may include, but are not limited to:

- administering counseling or psychotherapy,
- drawing blood,
- obtaining buccal mucosa cells using a cotton swab,
- administering drugs or other treatment,
- utilizing physical sensors, or other measurement procedures.

2.1.4 Intervene with participants for research purposes by manipulating the environment. (*Exceptions – when an institution's activities are limited to those described in 2.2.1 – 2.2.4 below, the institution is not engaged*). Examples may include:

- controlling environmental light, sound, or temperature,
- presenting sensory stimuli,
- orchestrating environmental events or social interactions.

2.1.5 Interact with participants for research purposes. (*Exceptions – when an institution's activities are limited to those described in 2.2.1 – 2.2.4 below, the institution is not engaged*). Examples may include, but are not limited to:

- engaging in protocol dictated communication or interpersonal contact,

- asking someone to provide a specimen by voiding or spitting into a container,
- conducting research interviews,
- administering questionnaires.

2.1.5 Obtain informed consent of human subjects for non-exempt research. (*Exceptions – when an institution’s activities are limited to those described in 2.2.3 – 2.2.4 below, the institution is not engaged*).

2.1.6 Obtain private identifiable information or specimens from any source for research purposes. (*Exceptions – when an institution’s activities are limited to those described in 2.2.1, 2.2.6, and 2.2.8 below, the institution is not engaged*). Examples may include, but are not limited to:

- observing or recording private behavior,
- using, studying or analyzing private identifiable information or specimens provided by another institution,
- using, studying or analyzing private identifiable information or specimens already in the possession of the investigator(s).

1.1.7 Utilize private information or human specimens (including de-identified materials) from any source for research subject to FDA regulations. This would include clinical investigations performed to assess the efficacy and/or safety of an FDA-regulated article (drug, biologic, medical device or other article regulated by the FDA). Refer to *11.5 FDA-Regulated Research* for more information.

2.2 Not engaged in research.

When the involvement of an institution’s employees or agents is *limited* to one or more of the following activities, the institution is considered NOT engaged in human subjects research:

2.2.1 Perform commercial or other services for investigators provided that:

- services do not merit professional recognition or publication privileges,
- services are typically performed for non-research purposes, and
- employees or agents do not administer any research intervention being evaluated under the protocol.

Some examples of services may include: interview transcription performed by a transcription company, blood draw or analysis performed by a hospital lab, data collection or analysis performed by a survey firm.

2.2.2 Permit use of facilities to allow another institution’s investigators to intervene or interact with subjects.

2.2.3 Assist with recruitment by informing or providing prospective subjects with information about research (may include a consent document or other IRB-approved materials) or contact information for investigators, provided they do not obtain consent or act as a representative for the research.

2.2.4 Seek or obtain prospective subjects permission for investigators to contact them directly.

2.2.5 Release lists of names/contact information, private information or biological specimens to another institution. (*IRB approval is required when releasing data or specimens originating from a research project.*)

2.2.6 Access or utilize identifiable private information only while visiting an institution engaged in the research (provided that their IRB has approved the study).

2.2.7 Author a paper, journal article, or presentation describing a human subjects research study.

2.2.8 Obtain de-identified or coded private information or human biological specimens from another institution involved in the research that retains a link to individually identifying information, and

- the NDSU investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
 - the NDSU investigator(s) and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances,
 - the releasing institution has IRB-approved written policies and operating procedures applicable to the research project that prohibit the release of the key to the NDSU investigator(s) under any circumstances, or
 - there are other legal requirements prohibiting the release of the key to the NDSU investigators.

The IRB has final authority to determine whether the use of private information or human biological specimens from living individuals constitutes engagement in human subjects research.

For questions regarding an entity's engagement in research, consult the IRB office.

3.0 Institutional assurances.

An institution must hold a FederalWide Assurance (FWA) and certify IRB review and approval when engaged in federally-supported, non-exempt human subjects research.

3.1 FederalWide Assurance.

Each institution engaged in non-exempt human subjects research funded through US Dept. of Health and Human Services (HHS) must hold an approved FederalWide Assurance (FWA) from the Office of Human Research Protections (OHRP). The FWA constitutes a commitment by an institution to comply with Federal Regulations (45 CFR 46) to protect the rights, safety and welfare of human research participants.

3.1.1 NDSU requirement.

NDSU holds an approved FWA from OHRP (# FWA00002439). Federal grant application forms often request information on an institution's FWA. The current expiration date and terms of NDSU's FWA are on the IRB website.

3.1.2 Collaborator requirement.

A collaborating institution engaged in non-exempt human subjects research funded by HHS or another **Common Rule** agency is also required to hold an approved FWA and certify IRB review and approval. The institution has two available options to fulfill the FWA requirement.

3.1.2.1 Hold or apply for own FWA. A collaborating research institution may already hold an approved FWA. Other collaborating institutions such as schools, clinics, private businesses or other entities that do not routinely conduct human subjects research would be unlikely to possess or otherwise require an FWA. These collaborators may choose to apply to OHRP for their own FWA; contact HRPP staff for more information.

3.1.2.2 NDSU extension of FWA. In some cases, NDSU may extend its FWA to a collaborating entity that does not hold an FWA, and does not routinely conduct human subjects research. NDSU must be the primary awardee of federal funds, and the research must be directed or supervised by an NDSU investigator. This FWA extension is subject to the approval of the Institutional Official (IO) or designee. Each employee of the collaborating entity engaged in the research signs an Individual Investigator Agreement (IIA) agreeing to comply with NDSU's policy and procedures for subject protections.

If a collaborating entity is a primary awardee of HHS funds, or routinely engages in human subjects research, the entity must obtain their own FWA from OHRP.

3.2 Other assurances.

Other federal funding agencies (e.g., US Dept. of Navy or others) may require additional or alternative assurances for institutions engaged in human subjects research. Consult HRPP staff for information regarding specific agency requirements.

4.0 IRB review.

Multiple IRBs may have jurisdiction over NDSU research projects involving other institutions or entities. Cooperative IRB review arrangements may be possible to eliminate duplication of effort. These arrangements will dictate requirements for training, documentation, and institutional agreements.

4.1 Non-NDSU entity not engaged in research.

The NDSU IRB reviews projects involving assistance from an outside institution or entity not considered engaged in human subjects research. Describe the role of each entity in the IRB protocol, but do not list non-NDSU employees as co-investigators or research team members. Training in human subjects protection is only required for those individuals engaged in research.

The principal investigator is responsible for complying with any additional requirements of an outside entity prior to initiating human subjects research. Even when an entity is not considered engaged in research, their own policies may require specific reviews and/or approvals, which may include review by their own IRB. Provide documentation of the outside entity's permission or IRB approval when applicable.

4.2 NDSU IRB as IRB of record.

The NDSU IRB may agree to serve as the IRB of record for NDSU-directed cooperative research. This decision is made on a case-by-case basis, subject to approval the Institutional Official or designee. Additional criteria may include, but are not limited to the following conditions:

- research is directed or supervised by an NDSU faculty or staff member,
- NDSU is primary awardee,
- requirement for knowledge of local research context can be met.

4.2.1 Exempt research:

If the collaborator's home institution has an IRB, they must contact their institutional IRB to determine if the institution is willing to rely on NDSU, or if they will require their own review. Provide documentation of the collaborator's home institution's willingness to rely on the NDSU IRB.

The principal investigator is responsible for ensuring that non-NDSU collaborators receive human subjects training appropriate to their role in the project. Training certificates should be uploaded into the IRB Protocol in Novelution.

4.2.2 Non-exempt research:

Describe the collaborator's role in the IRB protocol submission. In addition, one of the following agreements will be utilized:

4.2.2.1 IRB Authorization Agreement (IAA) or Reliance Agreement. When a collaborating institution holds an approved FWA, an IAA may be utilized to document the collaborator's reliance on NDSU IRB for review and oversight of the research. The IAA is prepared by HRPP staff, and signed by signatory officials at each institution; a copy is retained with the protocol. List Non-NDSU collaborators within the Research Team and upload copies of human subjects training certificates.

4.2.2.2 Independent Investigator Agreement (IIA). When a collaborating institution does not hold an approved FWA, each engaged individual must sign an IIA. This document signifies their agreement to abide by the terms of NDSU's FWA, and conduct the research project in compliance with policies of the NDSU IRB. HRPP staff retain copies in the protocol. Investigators list all non-NDSU collaborators engaged in non-exempt research on the IRB protocol form, and upload copies of human subjects training certificates.

4.3 Collaborator or independent IRB as IRB of record.

NDSU may rely on the review of a collaborating institution's IRB, or independent IRB for review and oversight of research. The collaborating institution or independent IRB must hold an approved FWA, and agree to provide review and oversight for the the research. Other factors may be considered in this decision:

- membership expertise,
- knowledge of local research context,
- ability to provide appropriate oversight,
- policies of collaborating entity are at least equivalent to those of the NDSU IRB.

The decision to rely on another IRB is made on a case-by-case basis, subject to approval by the Institutional Official or designee.

4.3.1 Exempt research.

Upload a copy of the collaborating IRB's complete protocol, supplemental materials and approval documentation into Novelution. Documentation of training is required for only the NDSU faculty, staff or students involved in the research. HRPP staff conduct an administrative review, and if acceptable, document reliance on the determination of the other IRB with a signed letter. If not acceptable, a joint review will be performed, as in 4.4 below.

4.3.2 Non-exempt research.

Upload a copy of the collaborating IRB's complete protocol, supplemental materials, and approval documentation into the IRB modules in Novelution. Documentation of training is required for only the NDSU faculty, staff or students involved in the research. The IRB Chair or other experienced board member determines whether or not NDSU may rely on the other IRB for review and oversight of the research. If acceptable, an IRB Authorization Agreement (IAA) is prepared by HRPP staff, and signed by signatory officials at each institution. A copy of the IAA is retained with the protocol.

4.4 Joint review.

When a cooperative review arrangement is not possible, each IRB may elect to review all, or only that portion of, the research in which their institution is engaged. This arrangement is subject to the approval of the IRB Chair, Institutional Official or designee, and may be made under any of the following circumstances:

- IRBs involved are unable to agree on a primary IRB designation,
- collaborator's IRB policies and procedures are not equivalent to those of NDSU IRB.

When NDSU IRB reviews only the NDSU portion of the research, the collaborator's employees or agents are not listed on the IRB protocol. Provide documentation of training for only the NDSU faculty, staff or students involved in the research.

5.0 Training for non-NDSU collaborators.

Requirements for training in human subjects protection and documentation of training vary dependent on the role of a non-NDSU collaborator, IRB review arrangements, and FWA jurisdiction.

5.1 Training not required.

Individuals performing activities that do not constitute engagement in human subjects research do not require training in human subjects protection.

5.2 Training required.

All research team members, including non-NDSU collaborators, engaged in human subjects research require training in human subjects protection. The principal investigator is responsible for ensuring completion of training appropriate for each individual's role in the research.

DEFINITIONS:

Performance site: physical location where research procedures are performed.

Employees or agents: individuals who: 1) act on behalf of the institution; 2) exercise institutional authority or responsibility; or 3) perform institutionally designated activities. Employees or agents can include staff, students, contractors, volunteers, etc., regardless of whether they receive compensation.

Collaborator: a non-NDSU entity, organization or institution whose employees/agents are involved with or assisting NDSU research by performing activities that constitute engagement in human subjects research.

Common Rule: Federal Policy for the Protection of Human Subjects describing ethical standards for the performance and review of research involving human participants. Federal agencies which have adopted the Common Rule include:

- Department of Health and Human Services,
- Department of Homeland Security,
- Department of Agriculture,
- Department of Energy,
- National Aeronautics and Space Administration,
- Department of Commerce,
- Social Security Administration,
- Agency for International Development (USAID),
- Housing and Urban Development,
- Department of Labor,
- Department of Defense,
- Department of Education,
- Department of Veterans Affairs,
- Environmental Protection Agency,
- National Science Foundation,
- Department of Transportation.

REFERENCES:

45 CFR 46.101 To what does this policy apply? and 21 CFR 50.1 Scope

45 CFR 46.102 and 21 CFR 50.3 Definitions

45 CFR 46.103 Assuring compliance with this policy

45 CFR 46.114 and 21 CFR 56.114 Cooperative research

OHRP Correspondence: Determining When Institutions are Engaged in Research

Terms of FederalWide Assurance

OHRP FAQs: FWA

OHRP Guidance on Engagement of Institutions in Human Subjects Research

OHRP Guidance on Extension of an FWA to Cover Collaborating Individual Investigators

RELATED HRPP STANDARD OPERATING PROCEDURES:

2.1 Human Subjects Research

2.2 NDSU Engagement in Human Subjects Research
5.3 Training and Education – Research investigators
11.1 Use of Confidential Records
11.2 Human Biological Specimens

RELATED FORMS:

Individual Investigator Agreement
IRB Authorization Agreement
NDSU Collaborative, Multi-site or Off-Site Research Worksheet