Title: Cooperative Research, Reliance Agreements, and Single IRB (sIRB)
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Standard Operating Practice: 17

17.1 Executive Summary

This document addresses the IRB unit standard for multi-site or cooperative research with human subjects completed by NC State University researchers. In this document you will find the policy and standard operating procedures for the use of reliance agreements and how the NC State University IRB facilitates cooperative research.

17.2. Standard Operating Practice

NC State University researchers engaging in federally funded research with human subjects that spans multiple sites or that is determined to be cooperative research as defined by federal law 45 CFR 46.114 (opens in a new window) must have their research reviewed and approved by a single IRB before research with human subjects begins. Single IRB review and approval will be enacted for cooperative research and multi-site non-exempt studies through the use of reliance agreements. For unfunded or privately sponsored research, the NC State IRB will engage in reliance agreements as appropriate.

17.3. Operational Procedures

A reliance agreement is an agreement between institutions allowing the IRB of one institution to rely on the IRB of another institution for review of human subjects research by establishing the IRB of Record (which could be NC State University or another institution). The IRB of Record must hold a Federalwide Assurance (FWA) with the Office of Human Research Protections (OHRP) of the U.S. Department of Health and Human Services (HHS). The reliance agreement must be signed by the institutional official or designee at each institution. Based on the level of review or researcher affiliation, other types of agreements or acknowledgments may be required.

17.3.a. Types of Reliance Agreements

17.3.a.i. Institutional Authorization Agreement (IAA)

1. Institutional authorization agreements (IAA) are agreements between two institutions with a current FWA.

2. An IAA allows one institution with an FWA to rely on the IRB review of the other institution with an FWA.

3. IAAs can cover one project or multiple projects as described in the agreement itself.

4. IAAs are signed by the institutional official at each institution, or the institutional official's designee specifically empowered to sign such agreements.

5. IAAs are not issued for exempt level research, including FLEX exemptions. Please see section 17.3.a.iii on letters of acceptance of exemption determinations.

17.3.a.ii. Individual Investigator Agreement (IIA)

1. An individual investigator agreement (hereafter, IIA) is an agreement between NC State University and a researcher who is not affiliated with an IRB that has an FWA.

2. An IIA binds the unaffiliated researcher to NC State University's rules and regulations regarding research with human subjects.

3. An IIA is signed by NC State University's institutional official (or the institutional official's designee) and the individual unaffiliated researcher.

4. IIAs are required for all levels of IRB reviewed studies, including exemptions, when an individual not otherwise affiliated with an institution with an IRB wishes to assist an NC State University researcher with their research.

5. IIAs are not issued for individuals external to NC State University who wish to conduct their own research and have NC State University serve as the IRB of Record. NC State IRB can only serve as the IRB of Record when its agents (e.g., current faculty, staff, students) are engaged in the research within the defined scope of their University role.

17.3.a.iii. Letter of Acceptance of Exemption Determination

1. If another institution's IRB office has reviewed a study and given it an exemption determination, the NC State University IRB can accept this determination for NC State University investigators and not have to review the study independently. A letter of acceptance of an exemption determination is a letter that an IRB writes on behalf of their researcher that indicates that the IRB accepts the exemption determination of another IRB.

2. The NC State University IRB will provide NC State researchers with this letter if the NC State researcher provides documentation that the reviewing IRB is aware that the NC State researcher is involved in the reviewed project and that all procedures that the NC State researcher will complete have been reviewed and approved by another IRB involved in the cooperative or multi-site research.

3. It is expected that NC State University researchers proactively file with

the NC State IRB if they wish to serve on an exempt-level study that was/is reviewed and approved by another IRB.

4. It is expected that NC State University researchers proactively contact the other IRBs if they wish to conduct an exempt-level study that was/is reviewed and approved by the NC State IRB but involves research team members at other institutions with an IRB that has an FWA number.

17.3.b. Requesting a Reliance Agreement

17.3.b.i. Human Subjects Research Engagement

1. A researcher must be "engaged in human subjects research" as determined by the IRB overseeing the researcher for the IRB to consider entering into a reliance agreement.

2. An IRB will make an "engaged in research with human subjects" determination when their employees or agents, acting on behalf of the institution, for purposes of a human subjects' research project obtain:

   a. data about the subjects through intervention or interaction with them;

   b. identifiable private data about the subjects of the research; or

   c. the informed consent of human subjects for research purposes

3. "Employees and agents" are individuals who

   a. act on behalf of the institution or

   b. exercise institutional authority or responsibility or

   c. perform institutionally designated activities.

4. "Employees and agents" can include staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation.

17.3.b.ii. Institutional Authorization Agreement (IAA)

1. An IAA can be submitted to the IRB office at the initial submission of the research protocol or during protocol review. The IAA can be reviewed concurrently with the review of the research project but will not be executed until the research study has been approved.

2. An IAA can also be submitted after the protocol has been approved via

a protocol amendment request.

3. For all IAAs, the IRB application and approved protocol must:

    a. clearly state that the study involves cooperative or multi-site research plans

    b. name and detail the role(s) of all collaborators involved in the project

4. Cooperative research cannot commence work until after the IRB protocol is approved and an IAA is signed by the institutional officials (or designees) from NC State University and the relying institution(s) with an FWA number.

5. IAAs will not be executed for exempt level research, including FLEX exempt research. In rare and special circumstances, this may be waived.

17.3.b.iii. Site or Local Context Review

1. Site context review is also known as local context review.

2. Site context review is done by the relying IRB(s) and provided to the reviewing IRB of Record.

3. The site context review furnishes the reviewing IRB with all of the necessary information about human subjects protections and compliance at individual sites which enables the IRB of Record to make a determination.

4. Review processes

    a. When NC State University is the Reviewing IRB

        i. All relying IRBs must provide the necessary information to the NC State University IRB office:

            1. applicable state and local laws that may apply to the research

            2. all relevant conflict of interest information that is pertinent to the research being reviewed, including disclosures and any real or perceived conflicts of interest related to the proposed research project (refer to the IRB's unit standard on conflicts of interests)

3. all ancillary reviews required for the study to take place, such as:
    a. institutional biosafety committee (IBC)
    b. radiation safety
    c. institutional animal care and use committee (IACUC)
    d. health insurance portability and accountability act (HIPAA)
    e. export control
    f. other applicable reviews not otherwise specified

4. proof of successful and current human subjects research training completion for all members of the research team
    a. training must be applicable to the proposed research

b. When NC State University is the Relying IRB

    i. NC State University IRB will provide the IRB of Record with the following information:

        1. applicable information relating to North Carolina's local and state laws that may apply to the research

        2. all relevant conflict of interest information that is pertinent to the research being reviewed, including disclosures and any real or perceived conflicts of interest related to the proposed research project

        3. all ancillary reviews required for the study to take place, such as:
            a. institutional biosafety committee (IBC)
            b. radiation safety
            c. institutional animal care and use committee (IACUC)
            d. export control

        4. proof of successful and current human subjects research training completion for all members of the research team

        5. any applicable NC State University regulations, policies, or unit standards that are required for the

study's commencement

6. all reasonable requests for information by the IRB of Record with the necessary information

17.3.b.iv. Individual Investigator Agreement

1. This is a formal agreement between NC State University and an individual investigator who is not affiliated with an IRB with an FWA number.

2. This agreement can be reviewed and approved concurrently with the review of the research protocol.

3. An individual investigator agreement, if not approved concurrently with the research protocol, can be approved after the protocol is approved by the IRB through an amendment process.

4. Requests for individual investigator agreements can be submitted to the IRB at the initial submission of the research protocol, during the review of the protocol, or after the protocol has been approved.

17.3.c. Record Retention and Communication Between IRBs

17.3.c.i. When NC State University is the Reviewing Institution (IRB of Record)

1. Records must be retained and maintained for a minimum of three years and a maximum amount of time as required by the study procedures and applicable retention rules.

2. Communication expectations for issues such as reportable events, renewals, amendments, personnel updates, consent posting requirements, expectations for post-approval monitoring, and how participant complaints are to be addressed must be included within the IRB application as procedures to be approved.

17.3.c.ii. When NC State University is the Relying Institution (Relying IRB)

1. Records must be retained and maintained for a minimum of three years and a maximum amount of time as required by the study procedures.

2. Communication expectations for issues such as reportable events, renewals, amendments, personnel updates, consent posting requirements, expectations for post-approval monitoring, and how participant complaints are to be addressed will be included as the reviewing institution requires.

17.3.d. Single IRB Review and Approval

Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. 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.

17.3.d.i. Cooperative Research 46 CFR 46.114 (opens in a new window)

1. This applies to all research located in the United States that is engaged in research that involves more than one institution.

2. Exception: Cooperative research for which more than a single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or 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.

17.3.d.ii. National Institutes of Health (NIH) Multi-Site Studies (Word document)

1. The use of a single IRB (sIRB) is required by NIH for all domestic sites of NIH-funded studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported by grants, cooperative agreements contracts, or the NIH Intramural Research Program.

2. Plans for the use of an sIRB must be included in all grant applications and contract proposals that are submitted to NIH.

3. This does not apply to foreign sites, career development, institutional training, or fellowship awards. The policy allows for exceptions in the following instances:

    a. Sites for which federal, state, or tribal laws, regulations, or policies require local IRB review.

    b. Other exceptions to allow for local IRB review may be considered by NIH based on compelling justification. These other exceptions must be reviewed and approved by NIH.

    c. The NIH sIRB policy allows the consideration of requests for other exceptions not based on a legal, regulatory, or policy requirement if there is a compelling justification for the exception. These other exceptions must be reviewed and approved by NIH.

Appendix A

Definition of Terms

Central IRB

Central IRB is where an IRB of record that provides the ethical review for all sites participating in a multi-site study. Generally, “single IRB review” and “central IRB review” mean the same thing: a single IRB of Record overseeing all sites participating in a multi-site study.

Cooperative Research

Cooperative research involves more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. The institutional official (IO) is the individual who is legally authorized to act for each institution and, on behalf of the institution, obligates the institution to the terms of its Federalwide Assurance.

Federalwide Assurance (FWA)

A Federalwide Assurance (FWA) is the documentation of an institution’s commitment to comply with federal regulations and maintain policies and procedures for the protection of human participants. An institution must have an FWA in order to receive Department of Health & Human Services (DHHS) support for research involving human subjects. This is the principal mechanism for compliance oversight by the Office for Human Research Protections (opens in a new window).

Independent IRB

An independent IRB is a review board that is not owned or operated by the research organization for which it provides review services. It is not associated with an institution. An independent IRB is subject to the same federal and state regulatory requirements applicable to all IRBs. Some research institutions have contracted with independent IRBs to provide outside review. Some institutional IRBs delegate jurisdiction and accept the review of an independent IRB when their institution is participating in a multi-site study.

- **Independent federal IRB** is an independent IRB created by a federal agency to support multiple institutions, generally for specific types of research

- **Independent commercial IRB** is a for-profit independent IRB that provides services for academic and non-academic institutions and researchers for a fee. They are hired to review research.

IRB of Record

The IRB of Record assumes primary responsibility for the review and approval of a study. Any IRB overseeing human subject protections for a study is considered an IRB of Record.

Multi-Site Study
A multi-site study is one that uses the same protocol to conduct non-exempt human research at more than one site.

Participating Site
In a multi-site study, a participating site is a domestic entity that will rely on the sIRB to carry out the site's IRB review of human research for the study.

Relying IRB
An IRB designated via an agreement to cede review to an external IRB for a particular study.

sIRB
An sIRB (single institutional review board) is the selected IRB of record that conducts the ethical review for participating sites of a multi-site study.

Single IRB
Single IRB is a process by which an IRB of record, selected on a study-by-study basis, provides the ethical review for all sites participating in a multi-site study. A single IRB may be either an independent IRB or associated with an institution engaged in the multi-site study.