Appalachian State University Research Protections and Institutional Review Board Standard Operating Procedures		
SOP #13	Cooperative Research and sIRB	Date Effective:
Approved by IRB Chair	R. Andrew Shanely	Date: 01/30/2025
Approved by RP Director	Shante' Mathes	Date: 02/18/2025

I. PURPOSE
This document details Appalachian State University's Institutional Review Board's (IRB) standard for multi-site or cooperative research involving participants.

II. AUTHORITY
In accordance with 45 CFR 46, the HHS Policy for the Protection of Human Research participants, compliance with pertinent federal and State laws or applicable regulations that provide additional protections for participants must be followed. Any institution located in the United States that is engaged in federally funded non-exempt cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States (45.CFR.46.114).

III. RESPONSIBILITY

1. Research personnel are responsible for complying with all federal, state, and local laws pertaining to research with participants for any location where those research activities take place. Research personnel are expected to work with the Appalachian State University IRB office to enact all necessary agreements pertaining to cooperative research. Regardless of funding or review level, no research with participants may occur until the Appalachian State University researcher has their own IRB approval for study activities or until a formal executed agreement is in place for the project.

2. Research protections (RP) staff are responsible for facilitating the review and approval of cooperative research or facilitating and executing formal agreements for cooperative research. This includes providing "site context" to the IRB of Record or requesting "site context" when acting as the IRB of Record. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of participants and for complying with this policy.

IV. DEFINITIONS

1. Cooperative Research
   Cooperative research projects are those projects that involve more than one institution.

2. Employees and Agents of Appalachian State University
   Employees and agents are individuals who act on behalf of the institution, or exercise institutional authority or responsibility, or perform institutionally designated activities. Employees and agents can include faculty, staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation.

3. Engagement in participants Research
   An IRB will make an "engaged in research with participants" determination when their employees or agents, acting on behalf of the institution, for purposes of a participants' research project recruit and consent participants; generate data about the participants through intervention or interaction with

participants; obtain identifiable private data about the participants; or receives federal funding for a research project regardless if the funding passes through Appalachian State University or remains with Appalachian State University.

4. Federalwide Assurance (FWA)
   An FWA is a declaration of compliance with federal regulations for the protection of participants in research. The federal Office for Human Research Protections (OHRP) approves FWAs for all participants research conducted or supported by the Department of Health and Human Services. Each institution engaged in participants research conducted or supported by the Department of Health and Human Services must have an approved FWA on file with OHRP. An IRB may not enter into any formal agreement with another ethics board unless that board has an FWA.

5. IRB of Record or NIH's Single IRB (sIRB)
   The IRB of Record is also called the "Reviewing IRB" or "Single IRB" and is responsible for the review and approval of a cooperative or multi-site participants research protocol. 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 sIRB will be expected to carry out the regulatory requirements as specified under the HHS regulations at 45.CFR.46.

6. Institutional Authorization Agreement
   An Institutional Authorization Agreement, also called a "Reliance Agreement" is a formal agreement between IRBs allowing the IRB of one institution to rely on the review and approval of a non-exempt participants research protocol by another IRB with an FWA. The agreement documents respective authorities, roles, responsibilities, and communication between an institution/organization providing the IRB review and a participating site relying on the IRB of record. The reliance agreement must be signed by the Institutional Official or designee at each institution. Reliance agreements are typically implemented for research with participants that is reviewed at the expedited or convened full board level. In rare cases, reliance agreements may be completed for exemption determinations.

7. Individual Investigator Agreement
   This agreement allows Appalachian State University's IRB to provide oversight for an unaffiliated researcher (a researcher not associated with an IRB with an FWA) because, through this agreement, the unaffiliated researcher agrees to the rules and regulations set forth by Appalachian State University and its IRB.

8. Institutional Official
   The Institutional Official (IO) is the individual who is legally authorized to act for the institution and, on behalf of the institution, obligates the institution to the Terms of the Assurance. The IO is responsible for ensuring that the Human Research Protection Program (HRPP) functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving participants. The IO represents the institution named in the Federalwide Assurance (FWA). The IO is a Chancellor appointed individual of sufficient rank who has the authority to ensure that all obligations of the HRPP are carried out effectively and efficiently.

9. Multi-Site Research
   A "multi-site project" is a subset of cooperative research involving participants where the same research procedures/protocols are conducted at two or more research sites under the control of a participating researcher at each site.

10. Participating Site or Relying IRB
    All sites participating in a multi-site study are expected to rely on one IRB's review and approval of a research protocol. The participating site relies on the IRB of record to carry out the functions that are required for institutional compliance with IRB review set forth in the HHS regulations at 45 CFR 46. Participating sites are responsible for meeting other regulatory obligations, such as

obtaining informed consent, overseeing the implementation of the approved protocol, and reporting unanticipated problems and study progress to the IRB of record. Participating sites must communicate relevant information necessary for the IRB of record to consider "local context" issues and state/local regulatory requirements during its deliberations. Participating sites are expected to rely on the IRB of record to satisfy the regulatory requirements relevant to the ethical review.

11. Site Context Review
    Site context review is also known as "local context" review for some IRBs. Site context review is completed by the relying IRB and provided to the reviewing IRB of Record. The site context review furnishes the reviewing IRB with all of the necessary information about participants protections and compliance at individual sites which enables the IRB of Record to make appropriate determinations. This includes, but is not limited to, providing the IRB of record with information about the institution's own researchers conflicts of interest, participants' Training, and any institutional required ancillary reviews or relevant state and local applicable laws or regulations.

12. Unaffiliated investigator
    Researchers engaged in human subject research and unaffiliated with any IRB, or are working out of the scope of their role associated with an IRB, are considered "unaffiliated investigators."

V. PROCEDURES

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

A. Requesting an Agreement

An Appalachian State University researcher must initiate the request for a cooperative agreement with the Appalachian State University IRB office by submitting an "Agreement Request Form" to the IRB Office. Once received, an IRB office staff member will facilitate the remainder of the cooperative agreement process.

An IRB of record is selected by the IRB's themselves. The IRB of Record is determined by roles of researchers, funding, sites involved, and where the brunt of the work and risk takes place.

1. Requesting an Institutional Authorization Agreement or Reliance Agreement
    a. When Appalachian State university is the IRB of Record, all relying IRBs must provide the necessary information to the Appalachian State University IRB office including:
        i. Applicable state and local laws that may apply to the research
        ii. Additional Informed Consent requirements
        iii. 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
        iv. Proof of participants training completion applicable to the proposed research
        v. Information about any ancillary reviews such as
            1. institutional biosafety committee (IBC)
            2. radiation safety
            3. institutional animal care and use committee (IACUC)
            4. health insurance portability and accountability act (HIPAA)
            5. export control

6. other applicable reviews not otherwise specified

b. When Appalachian State University is the Relying IRB or Participating Site, the Appalachian State University IRB will provide the IRB of Record with the following information:
   i. Applicable state and local laws that may apply to the research
   ii. Additional Informed Consent requirements
   iii. 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
   iv. Proof of participants training completion applicable to the proposed research
   v. Any reasonable requests for information by the IRB of Record
   vi. Information about any ancillary reviews such as
      1. institutional biosafety committee (IBC)
      2. radiation safety
      3. institutional animal care and use committee (IACUC)
      4. health insurance portability and accountability act (HIPAA)
      5. export control
      6. other applicable reviews not otherwise specified

c. The process for requesting a Reliance agreement may happen concurrently with IRB review and approval of a project. This is dependent on the policies of each IRB engaged in the project.

2. Requesting an Individual Investigator Agreement
   a. When an Appalachian State University researcher is interested in completing participants research with an unaffiliated investigator as a part of the research team, the unaffiliated investigator must sign a formal agreement with the Appalachian State University IRB to ensure they will adhere to the IRB approved protocol and all other laws, policies, and regulations required of agents of Appalachian State University.
   b. This request process can happen concurrently with the Appalachian State University IRB review of the participants research protocol.

3. Amending an Agreement is possible and can be completed through the same request process for all agreements.

<u>B. Oversight of participants Research Protocol</u>

1. IRB of Record
   a. The IRB of record is responsible for the review and approval of the participants research protocol. This review should include all necessary or provided “site context” information provided by the relying sites.
   b. Any amendments or approval renewals associated with the approved protocol, should be communicated to the relying IRB by the relying IRB’s researchers.
   c. The Appalachian State University IRB will promptly and directly communicate any reportable events such as unanticipated problems, adverse events, participant complaints or concerns, and issues of noncompliance.

2. Relying IRB
   a. The Relying IRB is responsible for communicating all necessary site related issues to the IRB of Record before initial IRB approval is granted.
   b. The Relying IRB is responsible for maintaining and safeguarding the rights and welfare of participants.
   c. The relying IRB’s researchers are responsible for communicating any amendments or approval renewals associated with the IRB of Record’s approved protocol.

d. The relying IRB will promptly and directly communicate any reportable events to the Appalachian State University IRB. These include unanticipated problems, adverse events, participant complaints or concerns, and issues of noncompliance.

3. Communication and Reporting:
    a. When Appalachian State University is the IRB of Record, communication expectations for issues such as reportable events, approval renewals, amendments, personnel updates, consent posting requirements, expectations for post-approval monitoring, and how participant complaints are to be addressed.
    b. When Appalachian State University is the Relying IRB: 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.

4. Record Retention: 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.

C. Exceptions to the Single IRB Review and Cooperative Research Requirements

1. Under 45.CFR.46.114, 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.

2. Under NIH's sIRB policy: The Single IRB policy does not apply to foreign sites, career development, institutional training, or fellowship awards. The policy allows for exceptions in the following instances: Sites for which federal, state, or tribal laws, regulations, or policies require local IRB review. 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. 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.

3. Many IRBs will not enter into a collaborative agreement for studies that receive an exemption determination.
    a. The Appalachian State University IRB will provide the Appalachian State University researcher with a "Letter of Acceptance of an Exemption Determination" if another IRB knows of the researcher's involvement in the project and has reviewed and approved all activities that The Appalachian State University researcher will complete.
    b. The Appalachian State University IRB will not enter into cooperative agreement for studies that receive an exemption determination.