NIH Policy Manual

3014-405 - Research Involving American Indian/Alaska Native Persons, Their Data and Biological Materials

Issuing Office: OD/OIR/OHSRP **Phone:** (301) 402-3713

Approving Official(s): DDIR

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Transmittal Notice

1. Explanation of Material Transmitted: This policy describes the policy requirements that apply when the NIH Institutional Review Board (IRB) is reviewing, or when an NIH Investigator seeks to conduct, certain human subjects research in which American Indian/Alaska Native (AI/AN) persons are participants, and/or when samples/data from AI/AN persons are used in secondary research conducted by NIH Intramural Research Program (IRP) Investigators.
2. Filing Instructions:
    - Insert: NIH Manual Chapter 3014-405, dated 7/09/2025
3. PLEASE NOTE: For information on:
    - The current policies can also be found at: https://irbo.nih.gov/confluence/display/ohsrp/Policy.
    - Content of this chapter, contact the issuing office listed above.
    - NIH Policy Manual, contact the Division of Compliance Management, OMA, on (301) 496-4606, or enter this URL: https://oma.od.nih.gov/DMS/Pages/Manual-Chapters.aspx.

A. Purpose

1. To describe the additional policy protections and considerations that apply when conducting or reviewing certain human subjects research in which American Indian/Alaska Native (AI/AN) persons are participants in NIH Intramural Research Program (IRP) research, and/or when samples/data from AI/AN persons are used in secondary research conducted by IRP Investigators.
2. The intent of this policy is to assure that Tribal sovereignty is respected, and measures are taken in the design, implementation, and review of the research to promote community-based protections and to mitigate the potential for group harm, while also recognizing the autonomy of individuals who choose to enroll in research.

3. These measures are in addition to the protections afforded by the Common Rule (45 CFR 46), other applicable laws and NIH policies.

B. Scope

1. When conducting or reviewing research subject to this policy, this policy applies to:

    a. NIH Investigators, regardless of the affiliation of the reviewing Institutional Review Board (IRB) (e.g., NIH IRB or an external IRB).
    b. The NIH IRB.
    c. The NIH Office of Human Subjects Research Protections (OHSRP).
    d. The NIH Tribal Health Research Office (THRO).

2. This policy applies to exempt and non-exempt human subjects research (HSR) and to some research that might otherwise be considered "not human subjects research" (NHSR) when the research is: 1) likely to include AI/AN communities and/or persons self-identifying as AI/AN to the extent that such research will make inferences about defined AI/AN populations or communities, or 2) will use data and/or biospecimens in secondary research that are known to have been collected from AI/AN persons to the extent that such secondary research will make inferences about defined AI/AN populations or communities. Examples include, but are not limited to, the following:

    a. Any aspect of the research, including recruitment, that takes place entirely or in part within tribal jurisdiction.
    b. The research will intentionally recruit AI/AN persons as participants and/or AI/AN populations are the focus of the research.
    c. Secondary research using data and/or biospecimens known to have been collected from AI/AN persons that were originally collected for other purposes (e.g., collected for clinical care or under a different research protocol) and will make inferences about defined AI/AN populations or communities. This may include data and/or biospecimens that are not readily identifiable to the NIH investigator and that therefore might otherwise be considered not human subjects research.
    d. Secondary research using data and/or biospecimens that were originally collected within Tribal jurisdiction is subject to this policy, regardless of the aims of the secondary research. This may include data and/or biospecimens that are not readily identifiable to the NIH investigator and that therefore might otherwise be considered not human subjects research.

3. This does not include research that may incidentally include AI/AN persons as part of the research, if not intentionally recruited as participants based on being an AI/AN person, and the research will not make inferences about defined AI/AN communities or populations.
4. Nothing in this policy is intended to prevent AI/AN persons from being considered for enrollment in NIH Intramural research for which they are otherwise eligible.

C. Policy

1. The OHSRP has final authority to determine whether research falls within the scope of this policy.
2. NIH Investigators must consult with THRO for any research that is subject to this policy, prior to submission to the IRB. THRO will provide the NIH investigator with written recommendations. THRO recommendations must be provided by the NIH Investigator to the IRB at the time of protocol submission, along with documentation that the recommendations have been considered.
3. THRO will provide written recommendations to the NIH Investigator advising whether Tribal engagement is needed, and if so, which Tribal Authority should be engaged. A Tribal Authority, for the purposes of this policy, is a Tribal entity with the legal authority to act on behalf of the Tribe (e.g., Tribal government or Tribal Council).
4. If Tribal engagement is recommended by THRO, the NIH Investigator must consult with the Tribal Authority prior to submitting the research to the NIH IRB.

    a. If the Tribal Authority requests that the NIH Investigator engage with another Tribal entity such as a Tribal IRB or another IRB designated by the Tribe (collectively referred to as Tribal IRB) and/or Tribal Research Review Board (RRB, a committee that is not a duly constituted IRB that may review research on behalf of a Tribe), the NIH investigator must consult with such entity.

5. When Tribal Authority approval is required by the Tribe, the NIH Investigator must obtain written approval and provide it to the reviewing IRB prior to any research activities commencing related to that Tribe.
6. For research subject to this policy and for which the provisions of the Common Rule that allow for review by more than a single IRB have been met and the Tribal Authority requests review by a duly constituted Tribal IRB, then approval from that IRB must be obtained prior to the research commencing. (45 CFR 46.114(b)(2))
7. For research subject to this policy but for which the provisions of the Common Rule that allow for review by more than a single IRB have not been met, and the Tribal Authority requests review by a Tribal IRB, then the following will apply in order to provide the NIH IRB with local context when making its determinations:

    a. If the research is occurring within Tribal jurisdiction, the NIH Investigator must submit the study documents to the IRB as requested by the Tribal Authority and provide the Tribal IRB outcome to the NIH IRB prior to research commencing.
    b. If the research is not occurring within Tribal jurisdiction, the NIH Investigator must submit to the IRB as requested by the Tribal Authority and provide the outcome of that review to the NIH IRB.

8. The NIH IRB will not approve research that is subject to this policy if it has not already been approved by the Tribal Authority when required as described above, including, if applicable, a Tribal IRB that has regulatory oversight authority under the conditions described in C.6. above.

9. If a Tribal Authority or a Tribal IRB that has regulatory oversight authority rescinds or otherwise terminates its prior approval of the research or the underlying memorandum of understanding (MOU), the NIH investigator must promptly inform the NIH IRB. The NIH IRB may, at its discretion, exercise its authority to suspend or terminate IRB approval of the research, if appropriate. (See *Policy 3014-200 – IRB Scope and Authority*.)
10. When the NIH IRB is the IRB of record, the initial review of research that is subject to this policy, including minimal risk research, will be conducted by the convened board. The convened board in this scenario will be comprised of a majority of members who are American Indian/Alaska Native, when feasible.

    a. Modifications to previously approved research that are substantive in nature will be reviewed by the convened board, regardless of overall risk level of the research.

11. When conducting research within Tribal jurisdiction, NIH investigators must comply with federal law, regulation and policy. All Tribal law and other Tribal requirements (e.g., tribal codes, constitutions, ordinances, resolutions, and regulations) that will apply to the conduct of the research should be negotiated in advance and documented in a MOU or similar agreement and signed by, at minimum, the involved institutions. (See E.1.d. below.)

D. Definitions

1. Human Subjects (2018 Common Rule)
2. NIH Investigator
3. Research (2018 Common Rule)

E. Responsibilities

1. **NIH Principal Investigator Responsibilities**

    a. The NIH Principal Investigator (PI) is responsible for being aware of whether their research falls within the scope of this policy as delineated in Section B above, and for complying with the requirements of this policy.

        I. If the NIH PI is uncertain whether the research is subject to this policy, they must consult with OHSRP for a determination.

    b. When the research is taking place within Tribal jurisdiction, the NIH PI in conjunction with IC leadership, should establish an MOU with the Tribe that describes the roles and responsibilities of each of the parties.
    c. The NIH PI must consult with THRO prior to submission of the protocol to the reviewing IRB. The NIH PI is responsible for submitting the recommendations provided by THRO to the reviewing IRB at time of initial submission. Applicable recommendations related to the conduct of the research provided by THRO

should be considered for incorporation into the protocol. If a recommendation is not accepted, an explanation why must be provided to the IRB.

I. For previously approved research for which the NIH PI intends to modify the protocol such that the research will become subject to this policy, the NIH PI must comply with the requirements of this policy and consult with THRO prior to submission of the modification to the reviewing IRB for approval. Recommendations provided by THRO must be provided to the reviewing IRB at the time of the submission. If a recommendation is not accepted, an explanation why must be provided to the IRB.

d. As required by this policy, the NIH PI is responsible for consulting with applicable Tribal Authority(ies) as identified by THRO and obtaining any required Tribal Authority approvals.

I. The NIH PI is responsible for submitting documentation of any required Tribal Authority approval(s) in accordance with C.5. and C.6. above to the NIH IRB.
II. Research may not commence until any required Tribal Authority approvals have been obtained.

e. When the Tribal Authority requests review consistent with C.6. and C.7. above, the investigator must submit the required documentation to the IRB in accordance with policies and procedures.
f. When the reviewing IRB is an external IRB, the NIH PI must submit to the Office of IRB Operations (IRBO) for pre-review:

I. THRO recommendations per E.1.c. above.
II. All required approvals from Tribal Authorities, and when applicable, the Tribal IRB that has regulatory oversight authority, per E.1.d and E.1.e. above.

2. **Tribal Health Research Office (THRO) Responsibilities**

a. The NIH Tribal Health Research Office is responsible for providing consultation and guidance to NIH Investigators seeking to conduct research subject to this policy. THRO will:

I. Provide written recommendations to the NIH PI regarding Tribal oversight for the study,
II. Assist NIH Investigators to identify and connect with the appropriate Tribal Authorities to obtain any necessary approvals, and
III. Provide guidance, when requested, on aspects of study design that may require special considerations.

3. **NIH Institutional Review Board (IRB) and IRBO Responsibilities**

a. The IRBO is responsible for determining whether research falls within the scope of this policy.

    I. If there is uncertainty as to the applicability of this policy to a specific research proposal, the IRBO will consult with THRO when making the final determination.

b. When reviewing research subject to this policy, the NIH IRB is responsible for reviewing the THRO recommendations to ensure that any required Tribal approvals have been obtained.

    I. If the NIH IRB is uncertain whether all required Tribal approvals have been sought and obtained, it will seek guidance from the NIH THRO.

c. When the NIH IRB is the reviewing IRB, it is responsible for ensuring that final approval of research subject to this policy is not issued until the research has received any required approvals from Tribal Authorities and, when applicable, a Tribal IRB that has regulatory oversight authority. This includes initial reviews or modifications that result in previously approved research becoming subject to this policy.
d. When the NIH IRB is the reviewing IRB and the research does not meet the provisions of the Common Rule that allow for review by more than a single IRB, the NIH IRB is responsible for considering as local context information any reviews provided by a Tribal IRB or Tribal RRB when conducting its review of the research.
e. When an external IRB is the reviewing IRB, the IRBO is responsible for ensuring that administrative approval to submit to the reviewing IRB is not issued to the NIH Investigator for the NIH site, until any required approvals have been received from Tribal Authorities and, when applicable, the Tribal IRB that has regulatory oversight authority.
f. When the NIH IRB is the reviewing IRB, the IRBO is responsible for ensuring initial review and any subsequent modifications to the research that are substantive in nature, is conducted by a duly constituted IRB that, when feasible, is comprised of a majority of members who are AI/AN. The composition of this board will comply with the requirements of *Policy 3014-201 – IRB Membership and Composition*.

F. References

1. Federal Regulations:
   HHS: 45 CFR 46
2. NIH Policies:
   Policy 3014-001 – Introduction to NIH Human Research Protection Program
   Policy 3014-200 – IRB Scope and Authority
   Policy 3014-201 – IRB Membership and Composition