NIH Policy Manual

3014-102 - Investigator Conflict of Interest and Government Royalties

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

Approving Official(s): DDIR

Release Date: 11/06/2020 ?
Partial Revision Date: 9/09/2024 ?
Technical Revision Date: 1/16/2026 ?

Transmittal Notice

1. **Explanation of Material Transmitted:** This policy describes how financial and non-financial conflicts of interest in human subjects research are managed to assure the protection of human subjects and the scientific integrity of the research; and describes how institutional conflicts of interest arising from government royalty rights are managed to assure the protection of human subjects and the scientific integrity of human subjects research at the NIH. Upon implementation, this policy fully supersedes the *SOP 21 Conflict of Interest Requirements for Researchers and Research Staff*. **Partial Revision Date 12/21/2022:** This policy is revised to indicate that there is only one Conflict of Interest (COI) Certification to be signed by any NIH investigator or statistician working on a Covered Research Protocol (CRP) who is not an NIH ethics filer. This policy is also revised to reflect process changes brought about by the implementation of the PROTECT electronic IRB system. **Partial Revision Date 09/09/2024:** This policy is revised to remind investigators to disclose to the IRB when they are listed as an inventor for any intellectual property that is being evaluated in the research study under review. Investigators are reminded to consult OHSRP for questions about whether the protocol is a Covered Research Protocol.
2. **Filing Instructions:**

- **Insert:** NIH Manual Chapter 3014-102, dated 11/06/2020, **Partial Revision Date:** 12/21/2022, **Partial Revision Date:** 09/09/2024
- **Implementation Date:** 3/1/2021

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. Describe how financial and non-financial conflicts of interest (COI) in human subjects research are managed to assure the protection of human subjects and the scientific integrity of the research.
2. Describe how institutional conflicts of interest arising from government royalty rights are managed to assure the protection of human subjects and the scientific integrity of human subjects research at the NIH.

B. Scope

1. This policy applies to individuals working at, or on behalf of, the NIH in relation to a Covered Research Protocol (CRP), who are:

    a. Engaged in human subjects research (investigators); or
    b. Involved in the statistical analysis of primary endpoint data obtained from human subjects research and whose role has the potential to bias the research results, even if they are not otherwise engaged in human subjects research.

2. This policy applies to the NIH Institutional Review Board (IRB) when it is the reviewing IRB.
3. This policy does not apply to NIH staff who only perform isolated tasks that are incidental to the research (for example, scheduling patient tests), and those individuals whose duties support research of many protocols through the performance of routine patient care tasks.
4. This policy does not cover the complete set of regulatory or federal policy requirements for government ethics. For more complete information review the NIH Ethics Program policy page or speak with your IC ethics official.

C. Policy

1. It is the Federal Government's policy to eliminate or minimize actual or perceived conflict of interest in the conduct of clinical research, through the implementation and enforcement of laws and regulations, applicable to all federal employees, intended to promote objectivity, maintain the public's trust and to avoid adverse impacts as a result of conflict of interests. These federal laws and regulations include: criminal statutes (18 U.S.C. §§ 201, 203, 205, and 207-209) and government-wide ethical conduct regulations (5 C.F.R. Parts 2634-2641). Additionally, the NIH implements and enforces the Supplemental Standards of Ethical Conduct for Employees of the Department of Health and Human Services (HHS) (5 C.F.R. Parts 5501-5502).

a. Employees of other federal agencies are subject to any agency-specific rules and are required as a matter of law and as a condition of employment to comply with the directives of their agency ethics program.

2. All federal employees, including NIH institutional leaders, engaged in activities described in B.1. above, at or on behalf of the NIH, must comply with government-wide and applicable agency-specific ethics requirements and this policy.
3. Investigators and individuals who are not federal employees but who are engaged in activities described in B.1.above, at or on behalf of the NIH, must comply with the conflict of interest rules and policies of their employing entities, if any, and this policy.
4. The NIH requires that the potential for actual or apparent conflict of interest must be considered for all investigators and individuals engaged in activities described in B.1. above, in relation to a Covered Research Protocol.
5. When the NIH will receive income because a Covered Research Protocol involves a licensed or assigned invention, NIH requires that this expectation of payment be disclosed by the NIH Principal Investigator (PI) to the reviewing IRB along with the name(s) of any investigators (i.e., any NIH employee inventor identified as an investigator on the IRB protocol) who will, therefore, receive payment(s) pursuant to section 7 of the Federal Technology Transfer Act of 1986. 15 U.S.C. § 3710(a)(1)(A)(i).
6. When the NIH is the reviewing IRB for multi-site research, the relying institution will disclose the presence of any financial conflicts of interest to the NIH IRB and provide a summary of the management plan, if one has been provided, unless otherwise specified in the terms of the reliance agreement.
7. When the NIH IRB is the reviewing IRB, and the IRB is informed of a financial conflict of interest for an investigator of a relying institution, the NIH IRB will review the summary management plan (if one has been provided) and will determine if additional measures are needed to protect the rights, and welfare of subjects participating on the research, and consistent with the terms of the reliance agreement.
8. When the NIH is relying on an external IRB for the review of covered research protocol, it will provide local context information to the reviewing IRB assuring that all applicable legal and NIH policy requirements related to Conflicts of Interest have been satisfied.

D. Definitions

OHSRP has developed a comprehensive glossary of definitions that describe the terms listed below. The glossary can be found at the following link: NIH IRP HRPP Policy Glossary

Note: There may be more than one definition per term, so please review terms carefully to make sure they match the terms listed below. Qualified terms are indicated with a parenthetical qualification. When reviewing a definition, be sure that you are reviewing the appropriate definition that links to this policy. To further assist the reader, each term in the glossary cites the relevant policy number(s) indicating where the term is utilized.

1. Appearance of Conflict of Interest
2. Conflict of Interest
3. Covered Research Protocol

    a. Non-covered research protocol

4. Cooperative Research and Development Agreements (CRADAs)
5. Disqualifying Financial Interests for Federal Employees
6. Engaged in human subjects research
7. Federal Employee (For Conflicts of Interest only)
8. Guest Researcher
9. Individual or Institutional Investigator Agreement (IIA)
10. Principal Investigator
11. Reliance (Authorization) Agreement
12. Special Volunteer
13. Substantially Affected Organization (SAO)

E. Responsibilities and Requirements

1. **NIH Principal Investigator (PI) Responsibilities**

    a. Determine whether the protocol (and/or any sub-studies) meets the definition of a Covered Research Protocol (CRP). Questions about whether a protocol meets the definition of a CRP should be directed to OHSRP consistent with E.4.a. below.
    b. For all covered research protocols:

        I. Provide a copy of the *Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Clinical Research at the NIH* to all investigators and individuals (including NIH employees, non-NIH federal employees, and individuals who are not federal employees) who will be engaged in activities described in B.1 above.
        II. Ensure that assessment of actual and apparent conflicts of interest (COI), financial and non-financial, is completed for all investigators and individuals who will be engaged in activities described in B.1 above at the following timepoints: (1) at the time of initial and each continuing review; (2) upon request for a modification involving the addition of investigators; (3) if an on-going protocol becomes a Covered Research Protocol; and (4) if there are changes to an IND/IDE or for-profit entity (e.g., a Sponsor, Substantially Affected Organization (SAO) or Cooperative Research and Development Agreement (CRADA) partner who is receiving data or specimens for the purposes of product development).
        III. At each relevant timepoint described in E.1.b.II. above, the NIH PI must:

            i. Complete and collect a signed *Conflict of Interest (COI) Certification form* from each investigator or individual who is, or will be, engaged in activities described in B.1 above, who does not

file a public or confidential financial disclosure report as an NIH federal employee, and submit such forms to their Institute/Center (IC) Ethics Office, or NIH Ethics Office (NEO) as appropriate.

ii. Obtain clearance of the Covered Research Protocol from the PI's IC Ethics Office

iii. Ensure that evidence of DEC clearance is provided to the reviewing IRB at timepoints specified in E.1.b.II. above.

c. When an investigator engaged in the research is identified as an inventor on intellectual property that is being evaluated in the research, the NIH PI must disclose this to the Reviewing IRB in the electronic IRB system. (See the *Information sheet for PROTECT question on Investigator inventions* for more information.)

d. Ensure that human subjects research done under a covered research protocol is conducted in compliance with any management plan established by the Reviewing IRB.

2. **All investigators and individuals engaged in activities described in section B.1 above**

a. Federal employees (of NIH or any other Executive Branch agency) must:

I. Complete new entrant and annual government ethics training as required by their employing agency.

II. Review the *Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Clinical Research at the NIH.*

III. Complete any public, confidential, or supplemental financial disclosure reports required by their employing agency.

IV. Individuals who are not employed by NIH must sign a COI Certification.

V. NIH employees who do not file financial disclosure reports must sign a COI Certification.

VI. Abide by all government-wide and applicable agency-specific government ethics laws and regulations as noted in C.1, above, including prohibitions on the acceptance of payments or other things of value from any payor other than the U.S. Government for work, including clinical and human subjects research, done as part of official duties. This includes prohinitions on conducting clinical and human subjects research (i.e., doing U.S. Government work), while holding a Disqualifying Financial Interest, in the absence of a waiver from the NIH Director from the COI requirements related to the research under review.

VII. When the NIH Investigator is an inventor who may recieve income because a Covered Research Protocol involves a licensed or assigned invention, disclose the licensed or assigned invention to the NIH PI.

b. Investigators and individuals who are not federal employees must:

I. Review the *Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Clinical Research at the NIH.*
II. Sign a COI Certification.
III. Abide by the Conflict of Interest Policy of their non-federal employer.

3. **Ethics Office Responsibilities**

a. Upon receipt of a request for clearance of a Covered Research Protocol, conduct and complete the assessment of actual and apparent conflicts of interest for all investigators and individuals who are, or will be, engaged in activities described in B.1 above, based upon review of existing government ethics records and financial disclosure reports of NIH employees, and review of any submitted COI Certification forms as described in E.2.a. and b., above.
b. In the event any federal employee is found to have an actual or apparent conflict of interest, work with the employee, the NIH PI, NIH ethics official(s), and as needed or appropriate, the NEO Director and/or the Office of the General Counsel, Ethics Division, to identify an appropriate remedy under applicable law. Remedies include:

I. Disqualification of the conflicted employee from participation in the research;
II. Divestiture of one or more conflicting financial interest(s), complete or partial (to below the regulatory de minimis level); and/or
III. The issuance of a waiver, with approval of the NIH Director, following consultation with the HHS Designated Agency Ethics Official and the Office of Government Ethics, to permit participation in all or a portion of the research project.

c. Upon completion of the COI review, indicate to the submitting PI and the NIH IRB that the clearance is complete.

4. **Office of Human Subject Research Protections (OHSRP) and NIH IRB Responsibilities**

a. OHSRP is responsible for addressing questions or disagreements regarding the identification of a protocol as a "Covered Research Protocol". OHSRP will consult with others as needed, to provide a final determination.
b. When the NIH IRB is the reviewing IRB it will ensure that for all Covered Research Protocols, proof of DEC clearance by the IC DEC has been provided prior to IRB approval (or in the case of an active study, continued approval).
c. When the NIH is relying on an external IRB for the review of a Covered Research Protocol, it will ensure that local context information is provided to the reviewing IRB assuring that NIH conflict of interest requirements have been met, consistent with C.8.above.

d. The OHSRP or the NIH IRB may request from the Office of Technology Transfer a determination as to whether any individual engaged in a research protocol is or may be expected to receive royalty payments or licensing fees related to the research protocol under review.
e. When the NIH IRB is the reviewing IRB, the OHSRP or NIH IRB may ask the NIH PI's DEC whether any NIH investigator has received a conflict of interest waiver from the NIH Director of the conflict of interest requirements allowing participation in the research under review. (18 U.S.C. § 208, see also E.3.b.III. above)
f. When the NIH is relying on an external IRB for the review of a covered research protocol, the reviewing IRB may request information as to whether any NIH investigator has received a conflict of interest waiver pursuant to 18 U.S.C. § 208 from the NIH Director by filing an Office of Government Ethics (OGE) form 201 with the NIH Freedom of Information Office.
g. When the NIH IRB is informed that an NIH investigator has or may receive royalty payments or licensing fees for intellectual property that is the object of the investigation, or has received a waiver from the NIH Director from the conflict of interest requirements related to the research under review, the NIH Protocol Royalty Analysis Committee (PRAC) will consider whether additional measures are required to protect human subjects. (See the guideline for *Management of real or apparent financial and other conflicts of interests or royalty payments for investigators conducting research being reviewed by the NIH IRB*.)

    I. Such measures may include, but are not limited to: 1) disclosure of government royalty rights related to this research in the informed consent document, or if other circumstances exist in which there may be a financial conflict of interest, a statement that an actual or apparent conflict of interest may exist without identifying any individual(s) or specifying the nature of that conflict, 2) restrictions on performing specific study activities such as obtaining informed consent from subjects, or 3) establishment of an independent data monitoring committee, as appropriate, and consistent with applicable federal law, regulation and policy, including NIH policy.

h. When the NIH IRB is informed of a financial conflict of interest for an investigator of a relying institution, the NIH PRAC will review the summary of the management plan, if one has been provided, to determine if additional measures (see E.4.g.I. above) are needed to protect human subjects, consistent with the terms of the reliance agreement. If additional measures are determined to be needed, the NIH will consult with the relying institution.

F. References

1. **Federal Regulations**

HHS: 45 C.F.R. Part 46

FDA: 21 C.F.R. Part 56

5 C.F.R. Parts 2634, 2635, 5501, and 5502

18 U.S.C. §§ 203, 205, and 207-209

2. **NIH Policy and Resources**

NIH Manual Chapter 2300-308-1 – Guest Researcher/Special Volunteer Programs

NIH Ethics Program

NIH Ethics Program policy page

IC Ethics officials

Office of Technology Transfer (OTT)

Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Clinical Research at the NIH

Information sheet for PROTECT question on Investigator inventions (document download)

Management of real or apparent financial and other conflicts of interests or royalty payments for investigators conducting research being reviewed by the NIH IRB (document download)