HRPP POLICY APPROVAL & IMPLEMENTATION

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

Policy Number: 102

SOP Title: Investigator Conflict of Interest and Government Royalties

Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB Chairs, IRB Administrators, Protocol Navigators

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NIH Intramural Research Program		
Office of Human Research Subjects Protections	Effective Date: 12/21/2020	
Investigator Conflict of Interest and Government Royalties	Policy 102	Version: 1.0

POLICY

A. PURPOSE

1. Describe 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.
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, 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 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 to the reviewing IRB along with the name(s) of any investigators (i.e., any NIH employee investigator on the 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 the COI outcome letter to the reviewing IRB as an assurance that all

applicable legal and NIH policy requirements related to Conflicts of Interest have been satisfied.

D. DEFINITIONS

1. *Appearance of Conflict of Interest* – Occurs when an individual's impartiality in clinical research, particularly clinical research involving commercial interests, might reasonably be questioned because the interests of a member of the individual's household would be affected by the matter, or because certain persons or entities (i.e. those with whom the individual has a "covered relationship") are involved in or will be affected by the research, including close relatives or household members of the individual or others with whom the individual has or recently had (within the past year) certain personal or business relationships, or with whom the individual's spouse, parent or dependent child has certain personal or business relationships. (5 C.F.R. § 2635.502)
2. *Conflict of Interest* – A conflict of interest (COI) occurs when a government matter, including clinical research, will have a direct and predictable effect on the financial interests of an individual or the individual's spouse, minor children, general partner(s), or certain other organizations the individual serves as officer, director, trustee, general partner or employee, and entities with which the individual is negotiating for or has an agreement regarding prospective employment (18 U.S.C. § 208, 5 C.F.R. Part 2640).
3. *Covered Research Protocol* – Covered research protocols (and covered substudies) include: (1) studies of investigational drugs and devices, (2) studies with a research question about a commercially available drug or device, and (3) studies involving collaborations with a substantially affected organization (SAO) or other for-profit entities when the entity is receiving data or specimens from the NIH for the purpose of developing a product. Most interventional protocols will be Covered Research Protocols unless the intervention does not involve the criteria listed above (e.g. a behavioral intervention might not meet the criteria for a covered research protocol).
    a. *Non-covered research protocols* – Non-covered research protocols include any NIH research protocols that do not meet the criteria for *covered research protocols* listed above.
4. *Disqualifying Financial Interests for Federal Employees* – These include:
    a. Ownership and other financial interests in publicly traded SAOs involved in or that will be affected by the research unless the values are within regulatory *de minimis*

levels (see 5 C.F.R. Part 2640). At present, the *de minimis* exemptions provide there is no conflict where:

I. The aggregate value of the interest of an investigator and his/her spouse and minor child(ren) in the SAO(s) whose products are being/may be evaluated in the research does not exceed $15,000;

II. The aggregate value of the interests of an investigator and his/her spouse and minor child(ren) in all SAOs that may be directly or indirectly affected by the research (including those whose products are being/may be evaluated) does not exceed $25,000;

III. The aggregate value of the interest of an investigator and his/her spouse and minor child(ren) in health-related sector funds does not exceed $50,000; and/or

IV. The otherwise disqualifying financial interest arises from ownership of shares in a widely-diversified mutual fund.

b. Ownership and other financial interests, regardless of value, in privately-held companies whose products are/may be evaluated by the research and/or that might be indirectly affected by the research.

c. Proprietary interests and royalty sharing rights derived from work done outside of the federal government that are related to or may be affected by research performed at/by the NIH including, but not limited to, a patent, trademark, copyright or licensing agreement. (Note: under federal law, neither royalty payments received nor the right to receive such payments from the Federal Government based on work done as a federal employee constitutes a disqualifying financial interest.

d. A Board or other fiduciary relationship to a commercial sponsor of the research, regardless of compensation. (Note: NIH employees are subject to legal and policy limitations on such activities and need prior approval consistent with NIH and IC procedure(s); such activities with commercial entities generally are prohibited.)

5. *Engaged in human subjects research* – For the purposes of this policy, an individual is engaged in human subjects research if that individual, for research purposes, either:

a. Obtains information or biospecimens through intervention or interaction with a living individual, and uses, studies, or analyzes the information or biospecimens; or

b. Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens from a living individual; or

c. Obtains informed consent from a prospective subject for the purposes of research participation.

6. *Federal Employee (For Conflicts of Interest only)* – An individual who is appointed by and subject to the supervision of an individual named by paragraph (a)(1) in 5 U.S.C. § 2105 while engaged in the performance of the duties of his position. For the purposes of this policy, this includes Special Government Employees (SGEs), and may include certain Intergovernmental Personnel Act (IPA) appointees. However, Guest Researchers, Special Volunteers, contractors and Intramural Research and Cancer Research Training Awardees are not federal employees.

7. *Guest Researcher* – Guest Researchers (GR) are scientists, engineers, and students who are permitted to engage in scientific studies and investigations using NIH facilities. Under this program, these individuals further their own research by using equipment and resources that are otherwise unavailable to them. They provide no direct services to NIH. They may not have any patient contact. (See NIH Manual Chapter "2300-308-1 – Guest Researcher/Special Volunteer Programs.")

8. *Individual or Institutional Investigator Agreement (IIA)* – An agreement between the NIH and a non-NIH investigator that extends the NIH FWA to either an individual investigator or to institutional investigators who are not covered by an FWA (e.g., physicians in private practice or individuals who work at an institution that does not have an FWA).

9. *Principal Investigator* –The investigator with the overall responsibility for the design, conduct and reporting of the research, and assumes the responsibilities described by regulation and NIH policy, even when certain aspects of the research are delegated to other investigators.

10. *Reliance (Authorization) Agreement* – An agreement between institutions involved in the same multi-site research that provides a mechanism to delegate IRB review, and that sets forth the authorities, roles, and responsibilities of the IRB and participating institutions. The agreement may apply to a single study or to certain categories of studies.

11. *Special Volunteer* – A "special volunteer" is an individual who meets NIH requirements set forth in NIH Manual Chapter "2300-308-1 – Guest Researcher/Special Volunteer Programs" and has been designated as a Special Volunteer (SV) by the NIH. SVs are non-NIH employees who provide research services, direct patient care, clerical support, technical assistance, or any other necessary services for NIH using NIH facilities.

12. *Substantially Affected Organization (SAO)* – A biotechnology or pharmaceutical company, a medical device manufacturer; or a corporation, partnership, or other enterprise or entity significantly involved, directly or through subsidiaries, in the research, development, or manufacture of biotechnological, biostatistical, pharmaceutical, or medical devices, equipment, preparations, treatments, or products (5 C.F.R. § 5501.109(b)(10)).

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.

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, 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 an amendment 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 Sponsor.

III. At each relevant timepoint described in *E.1.b.II.* above, the NIH PI must:

i. Collect a signed 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 a federal employee, and submit such forms to his/her IC Ethics Office, or NEO as appropriate.

ii. Submit a *Clearance of NIH Employee Personal Financial Holdings by IC Ethics Office* (PFH) form, and any signed certifications, to the PI's IC Ethics Office for clearance.

IV. Provide the *COI Outcome Letter* received from the IC Deputy Ethics Counselor (DEC), to the reviewing IRB, including to an external IRB when the NIH is a relying institution.

c. 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 Conflict of Interest (COI) Certification for Non-NIH Federal Employees and NIH Employees Who Do Not File a Financial Disclosure Report.

V. NIH employees who do not file financial disclosure reports must sign a Conflict of Interest (COI) Certification for Non-NIH Federal Employees and NIH Employees Who Do Not File a Financial Disclosure Report.

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 and participation in U.S. Government work, including clinical and human subjects research, while holding a Disqualifying Financial Interest.

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 Conflict of Interest (COI) Certification for Non-Federal Employees (COI Certification for non-federal Employees).

III. Abide by the Conflict of Interest Policy of his/her non-federal employer.

3. **Ethics Office Responsibilities**

a. Upon receipt of a PFH form for 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), or the employing agency 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, cause the *COI Outcome Letter* to be issued via the electronic IRB system for submission to the IRB.

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, the COI Outcome letter has been received prior to IRB approval (or in the case of an active study, continued approval).

F. REFERENCES

1. Federal Regulations

   HHS: 45 C.F.R. Part 46

   FDA: 21 C.F.R. Part 54
   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
   Office of Technology Transfer (OTT)

G. APPENDICES: NA

H. REVISION HISTORY: NA

I. SUPERSEDES DATE: 12/21/2020

SOP 21 - Conflict of Interest Requirements for Researchers and Research Staff

NIH Intramural Research Program		
Office of Human Research Subjects Protections	**Effective Date: 12/21/2020**	
Investigator Conflict of Interest and Government Royalties	**Policy 102**	**Version: 1.0**

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   18 U.S.C. §§ 203, 205, and 207-209

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