

# Research Compliance Overview for CRA Certification

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# Focus of Discussion

## Responsible Conduct of Research (RCR)

- Research Misconduct Requirements
- Conflict of Interest (COI) Requirements
- Human subjects requirements (IRB)
- Animal subjects requirements (IACUC)

# Research Misconduct

\*On December 6, 2000, the OSTP in the White House published the Federal Research Misconduct Policy which required all federal agencies or departments supporting intramural or extramural research to implement within one year.

The following agencies or departments have done so: DHHS, DOD, DOL, DOT, VA, EPA, NASA, NEH, NSF, and the Smithsonian Institution.

\*From <https://ori.hhs.gov/federal-policies>

# Research Misconduct

## Definitions:

*Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.*

*Fabrication is making up data or results and recording or reporting them.*

*Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.*

*Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit. Research misconduct does not include honest error or differences of opinion.*

# Finding of Research Misconduct

*A finding of research misconduct requires that:*

- *There be a significant departure from accepted practices of the relevant research community; and*
- *The misconduct be committed intentionally, or knowingly, or recklessly; and*
- *The allegation be proven by a preponderance of evidence.*

# Requirements for institutions

*Agencies and research institutions are partners who share responsibility for the research process. Federal agencies have ultimate oversight authority for Federally funded research, but research institutions bear primary responsibility for prevention and detection of research misconduct and for the inquiry, investigation, and adjudication of research misconduct alleged to have occurred in association with their own institution.*

# Research Misconduct

Agencies rely on research institution to perform review, inquiry, investigation, and adjudication whenever possible.

Initial review generally is performed by Research Integrity Officer (RIO) – is the allegation credible and specific?

Inquiry – determines whether the allegation has substance and if an investigation is warranted.

Investigation – the formal development of a factual record, and the examination of that record leading to dismissal of the case or to a recommendation for a finding of research misconduct or other appropriate remedies

# Research Misconduct

Adjudication - recommendations are reviewed and appropriate corrective actions determined.

Agency follow-up to institutional action.

Reviews report from institution, takes additional oversight/investigation steps if needed, and levies penalties.



# Financial Conflicts of Interest



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# FCOI NIH Requirements

- Applies to each institution that is applying for, or that receives, NIH research funding (excluding Phase I SBIR/STTR).
- Applies to all Investigators – the PD/PI and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the NIH, or proposed for such funding.
- Includes subgrantees, contractors, consortium participants, collaborators, and consultants.

# What is an SFI?

- (1) A financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:
  - (i) With regard to any publicly traded entity, a *significant financial interest* exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds \$5,000. For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;
  - (ii) With regard to any non-publicly traded entity, a *significant financial interest* exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds \$5,000, or when the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or
  - (iii) Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

# What is an SFI

- (2) Investigators also must disclose the occurrence of any reimbursed or sponsored travel (*i.e.*, that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), related to their institutional responsibilities; provided, however, that this disclosure requirement does not apply to travel that is reimbursed or sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education. The Institution's FCOI policy will specify the details of this disclosure, which will include, at a minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. In accordance with the Institution's FCOI policy, the institutional official(s) will determine if further information is needed, including a determination or disclosure of monetary value, in order to determine whether the travel constitutes an FCOI with the PHS-funded research.

# What is NOT an SFI?

- (3) The term *significant financial interest* does not include the following types of financial interests: salary, royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution, including intellectual property rights assigned to the Institution and agreements to share in royalties related to such rights; any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for-profit organization; income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles; income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education; or income from service on advisory committees or review panels for a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

# What is an FCOI?

Financial Conflict of Interest (FCOI): means an SFI that could directly and significantly affect the design, conduct, or reporting of the NIH-funded research.

# Investigator Duties

Disclose all SFIs:

- Prior to submission of a proposal;
- Within 30 days of obtaining a new SFI;
- Updated at least annually

# Institutional Duties

- Compliant policy (made publicly available via a website)
- Review SFI disclosures and determine if any SFIs pose an FCOI
- Manage FCOIs
- Submit initial and annual reports to NIH for all FCOIs
- Retrospective reviews when required
- Public disclosure of FCOIs



# Training

- Training prior to expenditure of funds and at least every 4 years. Also when:
  - Institutional FCOI policies change in a manner that affects Investigator requirements
  - An Investigator is new to an institution
  - An Institution finds that an Investigator is not in compliance with the Institution's FCOI policy or management plan

# Public Disclosure of Information

- Public disclosure of information upon request:
  - name,
  - title/role,
  - name of entity in which SFI is held,
  - nature of SFI, and
  - approximate dollar value

# Retrospective review of noncompliance (PHS)

## Required in the following circumstances:

- Failure by the Investigator to disclose an SFI that is determined by the Institution to constitute an FCOI;
  - Failure by the Institution to review or manage such a FCOI; or
  - Failure by the Investigator to comply with a FCOI management plan;
- “The Institution shall, within 120 days of the Institution’s determination of noncompliance, complete a “retrospective review” of the Investigator’s activities and the NIH-funded research project to determine whether any NIH-funded research, or portion thereof, conducted during the time period of the noncompliance was biased in the design, conduct, or reporting of such research.”

# Further details

<http://grants.nih.gov/grants/policy/coi/>



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# NSF FCOI Policy

- Requires each grantee institution employing more than fifty persons to maintain an appropriate written and enforced policy on conflict of interest
- Each investigator must disclose all SFIs of the investigator (including those of the investigator's spouse and dependent children) (i) that would reasonably appear to be affected by the research or educational activities funded or proposed for funding by NSF; or (ii) in entities whose financial interests would reasonably appear to be affected by such activities.

# NSF FCOI Policy

The term “significant financial interest” means anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interest (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights).

# SFI Does NOT Include

1. salary, royalties or other remuneration from the applicant institution;
2. any ownership interests in the institution, if the institution is an applicant under the SBIR or STTR Program;
3. income from seminars, lectures, or teaching engagements sponsored by public or non-profit entities;
4. income from service on advisory committees or review panels for public or nonprofit entities;
5. an equity interest that, when aggregated for the investigator and the investigator's spouse and dependent children, meets both of the following tests: does not exceed \$10,000 in value as determined through reference to public prices or other reasonable measures of fair market value, and does not represent more than a 5% ownership interest in any single entity; or
6. salary, royalties or other payments that, when aggregated for the investigator and the investigator's spouse and dependent children, are not expected to exceed \$10,000 during the twelve month period.

# NSF FCOI Policy

A COI exists when the institutional reviewer(s) determine that an SFI could directly and significantly affect the design, conduct, or reporting of NSF-funded research or educational activities.

Institutions must maintain all records of disclosures, FCOIs, and management plans.



# EPA Interim FCOI Policy

In effect December 26, 2014

*Conflict of Interest (COI):* An actual or potential situation that undermines, or may undermine, the impartiality of an individual or non-Federal entity because their self-interest conflicts, or may conflict, with their duty and obligations to EPA and the public in performing an EPA financial assistance agreement. The term also includes situations that create, or may create, an unfair competitive advantage, or the appearance of such, for an applicant in competing for federal financial assistance from EPA.

# EPA Interim FCOI Policy

## 4.0 Situations Requiring Disclosure

- (a) COIs related to Competitive Assistance Agreements.
- (b) COIs related to the selection, award and administration of recipient contracts.
- (c) Recipient procurement actions raising organizational COIs with a parent, affiliate or subsidiary organization that is not a State, local government or Indian Tribe.
- (d) Subaward COIs.

# Human Subjects Protections



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# Human Subjects Protection History

Nuremberg Code (1946)

Declaration of Helsinki (1964)

National Commission for the Protection of  
Research Subjects in Biomedical and Social  
Behavioral Research (1974)

Belmont Report (1979)

- Respect for persons
- Beneficence
- Justice



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# Regulatory requirements

## Regulations

- Federal
- 45 CFR 46 – DHHS Policy for Protection of Human Subjects – Subpart A = the “Common Rule”
- Heavily influenced by the Belmont Report
- Adopted by 15 Federal departments and agencies

Subpart B – D = Additional protections for vulnerable populations

21 CFR 50 – FDA Protection of Human Subjects = requirements for clinical investigations regulated by the FDA

Code of Virginia (32.1-162.16)

# Oversight

HHS – Department of Health and Human  
Services

OHRP – Office of Human Research  
Protection

FDA – Food and Drug Administration

# Institutional Requirements

If you accept funding from federal agencies you likely have a Federalwide Assurance (FWA)

Also state codes

The institution is responsible for reviewing all human subjects research through use of and support for an Institutional Review Board (IRB).

The institution is also responsible for ensuring compliance with all requirements in our FWA and the regulations and providing education.

# Human Subjects Review

The IRB Reviews Human Subjects Research as  
Defined by the Regulations

What does this mean?

How do we approach projects?





# Step 1: Is it Research?

## What is Research?

A systematic investigation **designed** to develop or contribute to **generalizable** knowledge (includes research development, testing, and evaluation)

- This include biomedical, social, and behavioral research

## Step 2:

# Does the Research Involve Human Subjects?

Human Subject = a living individual about whom an investigator conducting research obtains

- data through intervention or interaction with the individual, or
- identifiable private information

# IRB Review

The IRB only reviews projects that meet the definitions of **BOTH** research and human subjects

The IRB is a peer review board consisting of at least 5 members of varying backgrounds who:

- Are sufficiently qualified
- Are not solely from one profession
- Are diverse

Additional IRB composition requirements:

- At least one non-scientist
- At least one non-affiliated member
- Expertise on vulnerable populations
- Outside consultants when needed

# Exempt

Means that the IRB does not have to review (exempt under 45 CFR 46); does not mean that subjects shouldn't have protections

Must be determined by someone other than the investigator

# IRB Review

## Expedited

- Reviewed by one or more IRB member outside of committee meeting.
- Must fit in one of 9 categories

## Full

- Reviewed at full board

Must review annually or more frequently

Disapprovals are only allowed at full board meetings

# IRB Responsibilities

Review and approve, require modifications, or disapprove all covered research

Review informed consent practices and ensure compliance with regulations

Notify investigators of concerns, questions, and decisions

Conduct yearly (or more frequent) review of ongoing covered research

# IRB Approval

In order to approve a project the following must be met:

- Risks to subjects are minimized
- Risks are reasonable in relation to anticipated benefits
- Selection of subjects is equitable
- Informed consent is sought from each subject
- Informed consent is appropriately documented

In Addition – for certain projects:

- Data collection is monitored to ensure subject safety
- Privacy and confidentiality is protected
- Additional safeguards are included for vulnerable populations

# Special Protections for Vulnerable Populations

Subpart B: Additional Protections for Pregnant Women, Human Fetuses and Neonates involved in Research

Subpart C: Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

Subpart D: Additional Protections for Children Involved as Subjects in Research



# Substantive Informed Consent

Consent is a **PROCESS** – not a document



# Recruitment

Subject recruitment is part of the consent process

- Advertisements and other methods should be consistent with protocol
- Recruitment should not be coercive or make unfounded claims
- It should be clear from recruitment materials that Research is involved

# Substantive Informed Consent

Research participant is legally and mentally able to give consent or has a representative,

They are given sufficient time to consider participation and ask questions,

Coercion/undue influence is minimized,

The language is appropriate for the population and understandable to the individual subject

No exculpatory language – language in which the subject is made to waive or appear to waive legal rights OR releases or appears to release researchers from liability for negligence:

<http://www.hhs.gov/ohrp/policy/exculp.html>

# Substantive Informed Consent

It should include a full discussion and disclosure of:

- the nature of the research,
- any risks and benefits,
- subjects involvement is voluntary and they may withdraw from the study at any time,

Risks should be explained in the context of recognizable experiences

# Documentation of Informed Consent

Documentation may be waived when:

- (1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
- (2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

# Waiver or Alteration of Consent

## Government Program Evaluations

- The study is an evaluation of a public program of services, is subject to governmental approval, and is evaluating procedures for obtaining benefits, changes in the program, or methods or levels of payment to be made under the program, AND
- The research cannot practicably be carried out without the waiver or alteration.

## Other Research

- The research involves no more than minimal risk,
- The waiver or alteration will not adversely affect the rights and welfare of the subject,
- The research cannot practicably be carried out without the waiver or alteration; AND
- The subjects will be provided with additional pertinent information, if appropriate, after participation.

# Animal Care and Use



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# Animal Use

## Law

- USDA – Animal Welfare Act (certain species)

## Policy

- Public Health Service (Office of Laboratory Animal Welfare – OLAW) – all species at institutions that accept PHS funding

## Guidance

- Guide for the Care and Use of Laboratory Animals (not really guidance because it is adopted by both USDA & OLAW). Similar to the rDNA “guide”



# Oversight

NIH/OLAW – assurance + annual reports

USDA – registration + annual reports

Accreditation

- AAALAC – Association for the Accreditation and Assessment of Laboratory Animal Science International

# IACUC

## Institutional Animal Care and Use Committee

Members must be qualified through experience & expertise to provide oversight for the animal programs, facilities & procedures.

### Minimum of 5 members

- Veterinarian
- Practicing scientist experienced in animal research
- Non-affiliated member
- Non-scientist

# IACUC

Reviews all research involving **vertebrate** animals

Approves for up to 3 years with annual continuing reviews

Reviews facilities and program every 6 months

# IACUC Reviews

## Types of review

- Designated member reviews
- Full board reviews

## Actions

- Approve
- Find acceptable following revisions
- Disapprove (only at full board)

# IACUC Evaluates

Justification of need for the research, numbers and types of animals

Procedures to ensure appropriate species

Degree of discomfort or distress and if they are justified

Appropriate use of analgesia and anesthetics

Permits & licenses

Euthanasia and disposal practices

# Common to both committees

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The following standards are common to both  
IRBs and IACUCs

# Records

Copies of all protocols, evaluations, consent documents (HS), continuing reviews, progress reports, and unanticipated problems reported

Meeting minutes

IRB/IACUC-PI Correspondence

Committee membership & credentials

Written procedures

# Additional information

All investigators interacting with human or animal subjects must complete training prior to initiation of that work

Noncompliance with protocols is evaluated in the context of risk to subjects. If there are serious unanticipated problems or negligence/intentional harm the institution would need to report to the appropriate agency. Suspensions must also be reported.



# Questions?



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