PHS FCOI Regulations: A Closer Look

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What we'll cover:

I. Conceptual Underpinnings of the FCOI Rule

II. "Gray Areas" in the FCOI Rule
   a. Who is an Investigator?
   b. What should we do with travel?
   c. The problem of affiliated corporations
   d. Oversight of subrecipients

III. Implementation Challenges
   a. Training
   b. Retrospective Reviews
   c. FCOI Prevention

IV. Taking Stock of Where We Are
I. Conceptual Underpinnings

- Compelling Circumstances?
- Are conflicts wrong?
- Appearance of conflict?
Does Appearance Really Matter?

- Why doesn’t the PHS regulation read, “A financial conflict of interest exists when the Institution . . . reasonably determines that the significant financial interest could directly and significantly affect the design, conduct, or reporting of PHS-funded research, or could appear to directly and significantly affect the design, conduct, or reporting of PHS-funded research”?

- Is there a difference in:
  - Outcomes?
  - Moral judgment or blameworthiness?

- The explanation may lie in the interests being served. While PHS aims to protect research from bias, universities also aim to preserve their claim to public trust. For universities, therefore, even the appearance of a COI is problematic.
Do Compelling Circumstances Have a Place on the FCOI Scales?
The AAMC Approach:

“In the event of compelling circumstances, an individual holding significant financial interests in human subjects research may be permitted to conduct the research. . . . For example, when the individual holding such interests is uniquely qualified by virtue of expertise and experience and the research could not otherwise be conducted as safely or effectively without that individual, he or she should be permitted the opportunity to rebut the presumption against financial interests by demonstrating these facts to the satisfaction of an institution’s conflict of interest (COI) committee.”

• The PHS Approach:

A conflicted investigator’s participation in the project is possible, despite the conflict, so long as the conflict is appropriately managed – meaning that the management plan adequately ensures the objectivity of the research. The purpose of the regulation is not to eliminate conflicts, but to identify and manage them.

In theory, whether there are, in addition, “compelling circumstances” to justify the conflicted investigator’s participation in the project is irrelevant. PHS requires in all events that the conflict be sufficiently managed.

But consider: In actual practice, would PHS be more inclined to find a management plan acceptable if compelling circumstances were also present?
Are FCOIs wrong?

- FCOIs are not inherently bad, and the determination that an FCOI exists isn't an accusation of wrongdoing; PHS rule retains this philosophy.
- Disclosure forms and management plans are not punishments; disclosure forms are necessary even if someone has nothing to disclose.
- Compliance = safeguards = the seatbelt everyone wears just in case, whether or not you’re a good driver.
II. “Gray Areas” in the FCOI Rule
a. **Who exactly is an “Investigator”?**

How “responsible for the design, conduct, or reporting of research” does one have to be in order to be considered an Investigator?
• It is up to individual institutions to determine how to apply the definition. There is no one prescription.

• NIH FAQs: “Institutions should consider the role, rather than the title, of those involved in research and the degree of independence with which those individuals work. When the definition of investigator is limited to titles or designations (e.g., to principal investigators, key personnel, faculty) the risk that an unidentified FCOI may compromise the research enterprise increases.”
• One approach: Any individuals who conduct the following activities –
  – Designing or directing research
  – Serving as the principal investigator, co-investigator, or sub-investigator
  – Enrolling research subjects (including obtaining human subjects' informed consent, if applicable)
  – Making decisions related to enrollment criteria
  – Analyzing or reporting research data
  – Submitting manuscripts concerning the research for publication as a primary author or co-author

• Another approach:
b. What should we do with travel expenses?

How should reimbursed travel factor into the FCOI analysis? Is travel on its own ever enough to give rise to an FCOI?

Even when the travel is to here? In January? For a week? Every year?
• PHS has given institutions wide discretion in this area (“In recognition of the different needs and resources of the diverse Institutions funded by PHS, the regulation seeks to minimize administrative burden by deferring to the Institutions’ FCOI policies to prescribe . . . the protocol that Institutions should use to review Investigators’ sponsored or reimbursed travel disclosures[].”
  – NIH Frequently Asked Questions, FAQ E.31 (9/30/11, as revised 1/9/14)

• Institutions have discretion, among other things, to prescribe the timing of disclosures, what aspects of reimbursed travel will drive further review, and what other details concerning reimbursed travel need be disclosed (see FAQ E.24)

• Early presentations by Sally Rockey, PhD., NIH Deputy Director for Extramural Research, suggested that institutions might reasonably decide that reimbursed/sponsored travel expenses alone are not enough to constitute an FCOI
• The result is varying practices and continuing confusion:
  – Threshold amount -- $5000? Zero? It depends?
  – Scope of expenses – Transportation only? Meals?
  – Valuation of the financial interest – Gross amount? “Luxury” component only?
• Burdensome for investigators to update disclosures within 30 days
• Is it worth it? Was the decision to set up a separate SFI category for travel expenses warranted?
c. The problem of affiliated corporations

Are there 3 financial interests, or only one ($ + $ + $)?
The regulation speaks of SFIs in terms of singular entities, e.g., “With regard to any publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity . . . [etc.]”

When, if ever, might it be appropriate to “pierce the corporate veil”?

– When the investigator’s research compares a class of compounds manufactured by Sub 1 and Sub 2 against classes of compounds manufactured by other, unrelated entities?
– When deciding whether an investigator’s ownership in stock of Parent Corp. is “related” to the investigator’s research on a device manufactured by Sub 1?
d. Oversight of Subrecipients

If the designated institutional official (DIO) at the prime institution under an NIH grant disagrees with an FCOI finding made by a subrecipient of the grant, is the DIO for the prime institution still required to report the FCOI for the subrecipient to NIH? What if the DIO is aware of facts that appear to give rise to an FCOI at the subrecipient level, but the subrecipient doesn’t report one?
• If the subrecipient has found an FCOI, the prime institution has no prerogative to question it. However, if the subrecipient has not found an FCOI where the prime institution believes one to exist, the prime institution could (must?) ask questions and get additional information.

• The prime institution is not permitted to require changes to the subrecipient’s management plan. If the subrecipient’s COI policy applies, the subrecipient will report the FCOI management plan to the prime institution, and the prime institution will simply relay that plan.

• Remember: If you have a federally compliant policy, and it is decided that the subrecipient will follow your policy, the subrecipient just needs to disclose all Significant Financial Interests that are directly related to the subrecipient’s work for your institution.

III. Implementation Challenges

a) Training Strategies

b) Retrospective Reviews

c) FCOI Prevention
a. Training Strategies

(Less rigorous) (More rigorous)

Handouts of COI Policy
Handouts with Attestation Form
Online modules with Tests
In-Person Instruction with Testing

• **Goal:** To make sure investigators understand their responsibilities. Choices will vary with institution size, resource limitations, risk tolerance philosophy, institutional culture/faculty resistance, etc.
The Inverse-U Curve of Training and Compliance

- Less detail → more risky
- More onerous → more risky

Y Axis = Investigator Understanding of Responsibilities

X Axis = Level of detail/complexity of COI policies and training materials
b. Retrospective Review

What do awarding agencies require for retrospective reviews?

What kinds of processes are sufficient?

Is a “review panel” (as mentioned in the regulations on reporting on retrospective reviews) required?
• There is no prescription for how to conduct a retrospective review; it just needs to be a reasonable process. But Office of Extramural Research takes this seriously and vigorously reviews every report received.

• “Review panel” language in the regulation was provided in the regulation as an example – not required.
## Should You Use Your Misconduct Process?

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<th>Reasons To Do So</th>
<th>Reasons NOT To Do So</th>
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<td>Forensic resources</td>
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<td>People and processes already exist</td>
<td>Unnecessarily burdensome (confidentiality safeguards, sequestration, etc.)</td>
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<td>Not reinventing wheels</td>
<td>More adversarial nature may inhibit disclosure of innocent omissions</td>
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<td>Rigor</td>
<td>Institutional panel has its own COI if institution at fault</td>
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Two Model Retrospective Review Processes:

- OHSU (Oregon Health & Science University)
- Northwestern
OHSU Approach (where there was a failure to comply with a MP)
1) Committee chair confirms non-compliance
2) Investigator answers questionnaire about what happened
   – Research activities during period of non-compliance? Related to the SFI?
   – Who was involved?
   – Data generated? If yes – what was done with it?
3) Investigation by Chair and co-chair - review of questionnaire, all documentation, investigator interview - to determine potential for bias.
4) Additional review by qualified, non-conflicted person – of research design and raw data (or experiments if raw data is not available).
5) Post-review – If no concerns, documented and end (happened in this instance); If potential for bias found – COI committee to decide next steps. If bias can’t be ruled out, a mitigation plan will be required -
   – Options: Retraction of publication, Submission of erratum, Retraction of grant application, Retraction of data presented at conference, Refer to office of misconduct?
Northwestern Approach
1) Documentation gathered by COI office, guidance for committee drafted
2) Independent ad-hoc committee appointed by Dean’s office to determine whether there is evidence of bias
   – Burden of proof: Is there clear and convincing evidence that the design, conduct or reporting of the research was biased due to the FCOI?
   – Considerations: What would bias look like in this context? In conduct and design - was the planned methodology and design followed? In reporting – articles underwent extensive review by co-authors; publications appeared to accurately represent results.
3) Committee members (a) reviewed documentation outside the meetings, (b) interviewed the investigator, and then (c) came to a determination
   – In this instance - conclusion --No evidence of bias
4) Final report sent to VP for Research and Dean; findings accepted
5) Notification to investigator of disposition
6) Reporting to sponsor occurred – but wasn't needed because no bias was found
Northwestern Approach: Lessons Learned:

- Need central resource to administer and facilitate the retrospective review process (COI Unit).
- Need guidance and facilitation for committee, parameters for review.
- Levels might be useful: a) administrative review, then if needed, b) committee review. Committee is not needed under law for retrospective reviews – perhaps designate an official instead.
- Educate the community to prevent the need for retrospective reviews – emphasize that it is critical investigators update SFIs within 30 days of a change, otherwise there is an onerous process where the research will be questioned.
C. FCOI Prevention

1. Educate your research community

2. Pre-research design conferences – design project protocols to include:
   a) Blinding* at every level – participant, trial investigators, assessors. “All activities should be blinded to minimize potential sources of bias, to the extent feasible, and the success of blinding should be assessed and reported…” (test to find out if blinding worked on participants)
   b) Budget item for independent reviewers, where needed

3. Pre-start-up conferences

* See The Money Blind: How to Stop Industry Bias in Biomedical Science, Without Violating the First Amendment
IV. Taking Stock of Where We Are

Evidence–based data collection initiatives - AAMC and COGR efforts:

- AAMC COI Metrics Project: Measuring the Cost and Outcomes of the NIH Rule on Financial Conflicts of Interest in PHS-funded Research Online at: https://www.aamc.org/initiatives/research/coi/metricsproject/


And gatherings like these! Where do you think we are in our efforts to implement effective programs to protect research from COI-related bias?
Thank you, and good luck staying on top of things!