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Drafting a Policy for Research Conflicts of Interest

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Research institutions must ensure that the integrity of their research is not compromised by financial interests or the pursuit of professional or personal gain.[1,2] Given the complexity of universities, hospitals and other research institutions, and their relationships to other organizations and individuals in the biomedical research community, effective research conflict of interest ("RCOI") policies and procedures are essential for protecting the integrity of such research.

Potential vs. Actual RCOI

Potential RCOIs exist when an outside, independent observer would see the presence of a conflict of interest that could affect the quality or integrity of a clinical study, or the study subjects' safety or welfare.[3] An actual RCOI occurs when a researcher, other person, or the institution itself acts upon an RCOI to the detriment of the research or study subject. Potential RCOIs are extremely common, existing wherever a person or entity has financial, professional or other interests that could influence their actions. In contrast, actual RCOIs are uncommon, or at least seldom detected. Researchers and their team members can easily appreciate the direct negative consequences of an actual RCOI. Actual RCOIs can affect research conduct, reporting, publishing and supervision, as well as human subject protection, by investigators, study personnel, IRB members, and institutional officials acting within their authority on behalf of the institution. However, there must also be sensitivity to the impact of any perceived RCOI (or "potential RCOI") by the public and regulatory agencies.[4]

Guidance from regulatory agencies and professional organizations suggests that both potential and actual RCOIs must be effectively managed.[5] Both potential and actual RCOIs can be managed preventively, e.g., with education, transparency, policy control and policy compliance. It is far less desirable, though also necessary, to manage potential and actual RCOIs after commission, e.g., with self-reporting, restrictions, study suspension, and possible penalties.

RCOI Policy Questions

Creating and implementing an RCOI policy is a major undertaking. Before starting the project, the following questions need answers:

- What categories of research team members and which types of RCOIs will be covered? It is not necessary to start with an all-encompassing policy that addresses every possible situation. For example, the first priority may be investigator financial COIs, which is the motivating force behind investigator financial disclosure regulations.[6]
- Will there be one policy or multiple policies? For example, there may be separate policies for investigators, research staff, and IRB members. Alternatively, a single

comprehensive policy has the advantage of consistency and general coverage. On the other hand, separate specialized policies can be fine-tuned for specific needs and situations. For example, some institutions may favor having a general policy for all research team members and other policies that assure adherence to the investigator-focused requirements of the FDA and Public Health Service.

- How will the RCOI policy fit with other, non-research conflict of interest policies at the institution? There should be some consistency and cross-referencing to assure awareness of and compliance with multiple policies. This goal may be difficult, given the differing regulations for disclosure and management of RCOIs and other conflicts of interest.
- Who will participate in the time-consuming and perhaps contentious process of creating the RCOI policy, RCOI management department, and reporting/enforcement mechanisms? The group must be small enough to make decisions, large enough to represent the stakeholders, expert enough to make the right decisions, and unburdened enough to spend the necessary time. Adequate administrative support is also required.
- How committed (or opposed) are the various stakeholders to implementing an RCOI policy? In particular, senior leadership support is essential for implementation, especially to add credence to the time-consuming and repetitive disclosure requirements investigators and research team members will experience.
- How will real-world support and compliance from the stakeholders, including investigators and research team members, be obtained for implementation of the RCOI policy? Support at the conceptual level may not translate into support for day-to-day self-evaluation, disclosure obligations, and implementation of RCOI management plans — details that some will consider onerous, unnecessary and insulting.

Laws, Regulations, Case Law, and Guidance

A comprehensive RCOI policy will take into consideration applicable laws, regulations, case law and guidance. "Customers," such as the National Institutes of Health (NIH) and the Public Health Service (PHS), have requirements that can affect RCOI policies. For example, the PHS's regulation, "Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding Is Sought,"[7] focuses on investigator RCOI and includes specific directives for the institution's RCOI policies and procedures. The Food and Drug Administration (FDA) requires a party who submits a marketing application for the approval of a drug, device or biologic product to disclose certain financial relationships with clinical investigators performing the applicant's clinical trials.[8] As a practical matter, this reporting obligation is often passed on from the applicant to the investigator. The FDA has published guidance to clarify and elaborate on such financial disclosure requirements.[9]

Some research institutions may find that they are subject to case law, which adds additional rules and considerations to RCOI management. For example, the Supreme Court of California ruled that a physician who is seeking a patient's consent for a medical procedure must, in order to satisfy his or her fiduciary duty and to obtain the patient's informed consent, disclose his or her personal interests unrelated to the patient's health, whether research or economic, that may affect his or her medical judgment.[10] The Court also held that "a physician's failure to disclose such interests may give rise to a cause of action for performing medical procedures without informed consent or breach of fiduciary duty."[11] This ruling likely applies to much clinical research in California, since it is common for physician-

investigators to ask their patients to participate in studies. Other institutions may find such laws instructive where the case law in their state is underdeveloped.

The professional research community offers additional guidance for RCOI policies. For example, the Association of American Medical Colleges (AAMC) advises its members to include in their RCOI policies methods to identify, evaluate and manage the RCOI of investigators, the institution's officers and administrators, and the institution itself.[12] The AAMC also recommends the creation of a neutral, expert and effective institutional RCOI committee.[13] This recommendation currently goes beyond current FDA and PHS regulations. However, institutions that are experienced and sophisticated in RCOI management have gravitated towards the creation and implementation of such a committee.

The Research Conflict of Interest Committee (COIC)

It is a good idea to create a research COIC as a neutral, knowledgeable and operational arbiter of RCOI evaluation and management. The COIC reviews and makes recommendations to the institutional official responsible for carrying out the decisions of the COIC.

The COIC, together as a group, should have expertise in the areas of RCOI management, research law, regulation, bioethics and the day-to-day conduct of research. The COIC should be structured so that it can make its decisions independently from inappropriate influence.

The membership of a COIC may include:

- An "independent member" who is separate from the institution and research conducted at the institution, such as an unaffiliated "community" member with no financial or professional connection to the institution or research conducted at the institution; the non-affiliated member of the IRB may be analogous to this COIC member
- A senior official at the institution, who can help give the COIC authority and liaise within the institution
- An attorney from the institution's legal or compliance department, who can contribute legal and regulatory expertise
- A bioethicist with expertise in research
- An experienced research administrator who is familiar with the day-to-day practices of the institution

Additional members may be added. All members should be educated in areas beyond their specialized expertise. Because the COIC is likely to have only a few members, each with a particular perspective, and only one member independent of the institution, consensus decisions are probably more appropriate than majority voting. Any decision opposed by the independent member should be viewed with particular scrutiny, given the possibility that an RCOI (such as an institutional RCOI) may have affected the committee's decision. This additional scrutiny is also prudent since regulatory agencies and the public will likely place the burden of proof that the committee's decisions are neutral and independent on the institution and the COIC.

Sample RCOI Policy Components

One possible approach for an institution developing an RCOI policy is to have a general RCOI policy for all research team members and then other RCOI policies that address the investigator-intensive requirements of applicable regulatory agencies. For example, the following theoretical sample components are intended to address the general research staff and then PHS regulatory requirements separately:

- (A) General COI Policy (for all staff):
    - Statement of purpose/expected outcome
    - Definitions
        - RCOI
        - COIC
        - Covered individual (research team members covered by the policy)
        - Research
        - Reportable financial interest
    - Scope of policy
    - Procedures
        - COIC review criteria
        - Disclosure of RCOI
        - COIC review procedures
        - Continuing disclosure obligations
        - Sanctions for noncompliance
        - Institutional RCOI
        - IRB member RCOI
        - IRB review & evaluation of RCOI
        - Retention of documents
        - COIC retention of experts
        - Expansion of COIC
        - COIC member RCOI
        - Reconsideration of RCOI decision & management plan
        - Contact for questions
- (B) PHS Grant, Cooperative Agreement & Contracts Policy
    - Statement of purpose, applicability & expected outcome
    - Definitions
        - Contractor
        - PHS & PHS awarding component
        - PHS Act
        - Significant Financial Interest (SFI)
            - Reportable Significant Financial Interest
        - Small Business Innovation Research Program (SBIR)
    - Procedures
        - RCOI official & duties
        - Review & management of SFIs
        - Certification in PHS applications for funding or contract proposals
        - Investigator RCOI reporting & compliance with management plans
        - Enforcement & penalties
        - Retention of records
        - Disclosure of SFI information to federal agencies
        - Contact information for questions

Conclusion

The drafting, finalization, approval and posting of the RCOI policy is only the beginning of a very long journey for research team members. It is important for those within the institution who are knowledgeable about RCOI to then turn their attention and energy toward getting the policy adopted and implemented by the many research departments and team members governed by such rules. It is imperative that the RCOI policy leads to real-world RCOI management and is not simply "tucked away" in a policy binder or database, rarely visited and infrequently applied.

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