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Research Compliance Professional's Handbook, Third Edition
2 Options for Identifying and Managing Financial Conflicts of Interest in Research: Flexible Compliance with the PHS Final Rule

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Introduction

Merriam-Webster Online defines conflict of interest ("COI") as: "a conflict between the private interests and the official responsibilities of a person in a position of trust."

Simply put, a COI arises when two different interests are at odds with one another. It is actually a conflict of interests. There can be no conflict unless there are at least two interests; thus, the term "conflict of interest" is illogical, because there is no conflict unless there is more than one interest. Nevertheless, the term conflict of interest has entered the vernacular, and the even-more illogical term: conflicts of interest (COIs), is also in common usage. For these reasons and until or unless common usage harmonizes with English grammar, this chapter reverts to the vernacular terms: conflict(s) of interest.

There is no wrongdoing in the existence of a COI. These conflicts are part of human existence. For example, nearly all parents who have routinely read bedtime stories to their children have experienced a situation where, on the one hand, they recognized the importance and value of reading to a child at night. But on the other hand, invariably, a night arrived where they also recognized how tired they felt, and how important their own sleep was to them. At that moment, they had a bona fide COI. Note that both interests are important and legitimate... and in conflict. That particular COI might be managed differently depending on the day. For example, spouses might take on the task of reading some nights. On other nights, children might have to be told that mommy or daddy is too tired to read.

In conducting research, a problem arises when a COI leads to bias. It's not just actual bias, however, that presents a problem for researchers. The appearance of bias is also a concern. In the realm of COI, it is sometimes said that perception is reality. This is an important concept to bear in mind whenever considering COI in research. The goals are to eliminate bias (because bias is not acceptable in research), and to either eliminate or manage the appearance of bias.

This chapter is focused on financial COI (FCOI) only. However, not all COI involves money. For example, nepotism is a form of COI that is not necessarily financial. There are also conflicts that arise because of (real or perceived) scientific bias. That is, many researchers have strong beliefs—built on a pet theory, for example. These beliefs can influence research design, analysis and reporting. There may also be beliefs related to religion and faith that have potential to lead to research bias. This chapter does not address any of these conflicts, however, because federal regulations do not address non-financial COI.

The focus of this chapter is on FCOIs that investigators (individual people doing research) may have. Please note that there are also FCOIs that are harbored by institutions. For example, a university, or academic medical center, or hospital may have a significant financial interest in a new technology, drug, or device (by virtue of a patent, for example), and may choose to pursue a research project related to that technology, or drug, or device. Such a situation creates an institutional FCOI. That FCOI may be unacceptable to the public. To date, however, there are

no federal regulations that address this issue, and likewise, it is not addressed in this chapter.

Financial Conflict of Interest in Federally-Funded Research

Visit the National Institutes of Health (NIH) home page for financial conflict of interest and you'll find a notable quote from the current Director of the NIH, Dr. Francis Collins, stating: "The public trust in what we do is just essential, and we cannot afford to take any chances with the integrity of the research process."[2] The interpretation of this quote gets to the heart of some of the greatest challenges faced by research compliance professionals with responsibility for identifying and handling financial conflicts of interest at institutions conducting research. As Director of the NIH and one of the country's strongest advocates for research, Dr. Collins was acutely aware of the risks to the public trust—and the associated public funding of the NIH's intramural and extramural research programs.

Reduction of research funding is not the only immediate concern over the public's perception of the loss of integrity in research. Another short-term pain point is the public scrutiny faced by the NIH, research institutions, and investigators at congressional hearings and by the popular and science press. The longer-term consequences are especially troubling: When too many people lose faith in the integrity of research, progress itself will be slowed.

In the aftermath of a series of high-profile cases questioning the integrity of research conducted by investigators at some of the finest research institutions in the US from 2008 to 2011,[3] two new/revised rules were enacted. One addresses giving: i.e., transfers-of-value (essentially payments) from corporate entities to physicians, including payments to physician-researchers. The other addresses receiving: income received by researchers given by outside entities, or ownership of outside interests by researchers. Although these seem, superficially, like two sides of a coin, they're actually more like two sides of two partially-overlapping coins. The first set of rules were incorporated into the Physician Payment "Sunshine" Provisions of the Affordable Care Act,[4] which describe the obligations of pharmaceutical companies and medical manufacturers to publicly report all transfers of value made to healthcare providers. Some of these are payments made to physician-researchers, and to healthcare organizations conducting research. But many of these payments are unrelated to research or researchers. This chapter does not address the Sunshine Provisions of the Affordable Care Act, which is covered in Chapter 1.

The second rule was published on August 25, 2011, and is known as the Final Rule on Financial Conflict of Interest Regulations—Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding is Sought and Responsible Prospective Contractors.[5] It is a revision of an older, less-prescriptive rule and is meant to increase transparency and to clarify perceived ambiguities in the older rule. At the time of its publication, the Federal Register notice provided applicable organizations (primarily those which received, are receiving, or have applied to receive PHS research support) up to one year to implement the rule. Note that the rule applies to all PHS-funded research, investigators and their institutions, regardless of whether they are also healthcare providers. Although the rule required compliance by no later than August 26, 2012, it is still referred to as the "Final Rule," and still the topic of much discussion.

Because applicable organizations are now required to comply with the Final Rule, this chapter neither compares nor contrasts it with the older rule. Also, because the published rule can easily be referenced, we do not rehash it here (with the exception of a few small elements). Similarly, there are no model policies or procedures to be found here. For these, the reader is referred to The Institute on Medicine as a Profession, which has a public website compendium and searchable database of COI policies and processes from various organizations and organization types.[6] Instead, this chapter focuses on the major options inherent in the rule and the flexibility it

allows, including applicability and standards, disclosure and disclosure thresholds, tolerance and management, transparency, and technology.

Applicability and Standards

Who is required to follow the Final Rule? The rule is clear in stating that it applies to institutions that have PHS research support (or who have recently had it, or seek it), and to the investigator(s) receiving that support. Note that the terms "research" and "investigator" have clear, broad, and non-obvious definitions embedded in the rule. But even when it is crystal clear when and to whom the rule must apply, the institution has the option of widening the scope of the rule and applying it to others.

Why apply the PHS Final Rule where it is not required? The issue comes down to standards. That is, does the institution have a single standard for FCOI that it applies fairly to investigators across the board, or does it have a double-standard—one for PHS-funded investigators, and one for those who are not PHS-funded? Or does it have multiple standards? For example, one for PHS-funded investigators, one for National Science Foundation (NSF)-funded investigators,[7] another for another agency, and perhaps one for state-funded investigators?[8] The choice of whether to apply one standard or more can be made on the basis of three considerations: ethics, fairness, and practicality.

Ethics: If we accept the notion that bias in research as a result of a FCOI is bad, and that the FCOI rules are designed to reduce or eliminate bias, it may seem ethically unsupportable to set anything but a single standard. Whether or not research is funded by PHS, we would not want to accept bias in that research. For example, it is not unusual for a single investigator to have research projects funded by multiple sources. The idea that even the appearance of bias in the investigator's non-PHS-supported research would be acceptable, but disallowed for a PHS-funded project, seems unfathomable. For this reason, some institutions have adopted a single standard. Note that this approach may require harmonizing multiple regulatory requirements to "set the bar" high enough so that all hurdles are overcome together in one process (this issue is also addressed below under "practicality").

On the other hand, an institution might adopt a single ethical standard and believe that the different requirements of various federal, state, and local agencies and private sources are nuanced, regulatory in nature, and though they require compliance, are not ethically relevant. In this case, it is possible to set the ethical bar and as long as the differences in requirements do not allow any research to go under the bar, multiple regulatory standards are acceptable.

Fairness: The FCOI rules are often viewed by investigators as intrusive because considerable information about their personal finances is disclosed. The disclosure requirements under the Final Rule—and the ensuing administrative processes—are burdensome. In a university, academic medical center, or research hospital environment, no investigator wants to feel singled out for financial disclosure, for any reason. For this reason, some institutions have chosen to apply the same set of rules (and tools for analysis, such as disclosure forms) to all investigators, regardless of funding source. This levels the playing field and fairly distributes the burden among all investigators.

On the other hand, this approach might be viewed as "collective punishment." For example, some investigators may never seek or receive PHS funding, simply because their research is outside of PHS's mission (as in the case of most faculty of chemistry, physics, engineering, or mathematics). Is it really "fair" to burden them with all the complexities and requirements of the PHS Final Rule? Perhaps it would be more appropriate to acknowledge that the rules simply don't apply to them? With this perspective in mind, some institutions with mature programs, including research faculty in diverse disciplines, have chosen to apply the PHS Final Rule strictly when required, but no more.

The issue of fairness can also be linked to the alignment of incentives and the growth of the research institution. As described above, a mature organization may feel it is unfair to burden non-biomedical faculty with PHS requirements. But the opposite can be true in other institutions. For example, organizations seeking to establish/grow a PHS-funded portfolio of research may struggle to appropriately encourage the submission of grant applications. In this circumstance, those investigators aligned with organizational goals and who seek or obtain PHS support can interpret the situation as "no good deed goes unpunished," because they are burdened with disclosures and processes, while their less-productive colleagues are undisturbed. Thus, in the institution focused on research growth, the issue of fairness can be analyzed differently.

Practicality: What could be more practical and straightforward than a single policy with a single set of processes, one disclosure form, one set of analytical tools and standard operating procedures? From a utilitarian perspective, this approach may be more practicable than adopting two or more processes, forms, SOPs, etc. However, depending on the type of institution, its resources and its goals, there are circumstances where a single, consistent process is more challenging to implement, and multiple processes may actually be more practicable. For example, in a research hospital environment, where there may be only five PHS-funded investigators, but a cadre of 95 clinical investigators doing corporate-sponsored clinical trials, applying the PHS Final Rule to all investigators may generate much more work than the hospital is able to manage, especially if it uses manual workflows and document management, rather than dedicated electronic COI (eCOI) software (discussed further below).