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Clinical Research: Financial Conflicts of Interest

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What Are Financial Conflicts of Interest in Clinical Research?

Financial conflicts of interest (FCOIs) in clinical research are external interests held by the research investigator, and in some cases by the institution, that are financial in nature that could directly and significantly affect and/or appear to affect the design, conduct, and or reporting of research. Individual FCOIs are specifically defined in federal regulations that apply to Public Health Service (PHS)-funded research as external interests of the research investigator that reasonably appear related to their institutional responsibilities and are considered significant financial interests (SFIs).[2] FCOIs can be complex, considering that interactions have become increasingly more common among academia, industry/private sector, and government agencies in pursuit of advancing scientific discoveries using cutting-edge science and technology. The Bayh–Dole Act enacted in 1980 was the key piece of legislation that changed the landscape at academic institutions by allowing institutions and faculty to retain rights to inventions from federally funded research.[3] This provided a pathway toward commercialization through technology licensing and transfer and also opened up a wider door for interactions with industry. Therefore, it is critical to understand where FCOI risks may occur in such interactions and employ strategies to ensure that research remains objective and is ethically conducted.

In clinical research, FCOIs are important to detect and effectively manage in order to prevent bias from negatively or inappropriately affecting the design, conduct, or outcome of the research. These steps are also essential to maintaining the public's trust in the research produced by healthcare or research institutions and individual researchers. Healthcare institutions often participate in clinical research through government, industry, or internal funding mechanisms. The federal government funds clinical research at healthcare institutions through the form of grants that require recipient institutions and research investigators to comply with the terms and conditions of the award, including FCOI disclosure and management. Industry-sponsored clinical research is governed by contracts between the institution and company developing or marketing the drug, device, or biologic under study, and is often bound by disclosure and reporting requirements pursuant to the Food and Drug Administration (FDA) financial disclosure regulations. There may also be other state and local laws or institutional policies that govern conflict of interest (COI) disclosure and management pertaining to business interactions and transactions. Clinical researchers and institutions have a shared responsibility in ensuring compliance with regulatory and other local requirements to promote objectivity in the research conducted at their organizations, which is why this remains an important and complex risk area for compliance professionals.

A number of factors that affect institutional FCOI risk and risk tolerance in clinical research include the overall maturity of compliance and research integrity programs; leadership support and investment; nature and breadth of research programs, including funding sources; degree of interactions with industry and commercialization activity; institutional culture; reporting mechanisms; and reputational impacts. The increasing pressures and complexities of the academic and scientific environments combined with heightened public scrutiny regarding FCOIs require more sophisticated oversight programs to ensure transparency, accountability, and effective management of conflicts.

A comprehensive lens should be applied when evaluating FCOI risks associated with clinical research. This is because other types of individual conflicts (e.g., conflict of commitment, role-based conflicts, conflict of conscience) may arise or be comingled with FCOI in the context of clinical research. Researchers in healthcare environments often have multiple roles, including that of a healthcare provider, faculty member or student, administrator, and institutional official, or serve on institutional review committees. They may have external interests (e.g., start-up companies) and collaborations or relationships (e.g., advisory board roles) that may intersect or conflict with their institutional responsibilities. Growing concerns by the US government over inappropriate influence by foreign governments on federally funded research have led to reinforcement by the National Institutes of Health (NIH) of appropriate disclosure by researchers and review by institutions of foreign support, relationships, and activities that represent an FCOI or conflict of commitment.[4] Institutional FCOIs may also arise from institutionally held investments or equity, royalties, significant donations from or interactions with industry, or from institutional officials who have substantial purchasing or business decision-making authority. There are currently no federal regulations that govern FCOIs on an institutional level, which are often left up to institutional policies. Despite this, there have been mounting concerns over increased institutional FCOIs at academic institutions and the need to ensure effective oversight and management of this particular risk area.[5] Therefore, healthcare institutions should be attuned to the various types of conflicts that may occur and employ ways to comprehensively review and manage these risks in clinical research.

Risk Area Governance

FCOI federal regulations were promulgated in 1995 by the Office of the Secretary of the U.S. Department of Health & Human Services (HHS) to promote objectivity of PHS-funded research. HHS revised the regulations and issued a final rule on August 25, 2011, requiring compliance by institutions applying for or receiving PHS funding by August 24, 2012.[6]

Codified at:

- 42 C.F.R. §§ 50.601-50.607 (Subpart F), Responsibility of Applicants for Promoting Objectivity in Research for which Public Health Service Funding is Sought and Responsible Prospective Contractors[7]
- 45 C.F.R. §§ 94.1-94.6 , Responsible Prospective Contractors[8]

The FCOI regulations apply to institutions and research investigators that are recipients of funding from PHS funding agencies such as the NIH. Research investigators are defined by the regulations as the "project director or principal Investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS, or proposed for such funding, which may include, for example, collaborators or consultants."[9] These regulations do not apply to Phase I Small Business Innovation Research (SBIR) and Small Business Technology Transfer Research (STTR) applicants.[10]

Investigators are responsible for complying with their institutional FCOI policy and disclosing any external interests (including those of their spouse and dependent children) that are reasonably related to their professional responsibilities at their institutions and considered SFIs. Review of SFI disclosures must occur no later than at the time of applying for PHS funding, at least annually during the period of the award, and within 30 days of acquiring or discovering a new SFI.[11] Investigators must also complete FCOI training before engaging in PHS-funded research, at least every four years and under certain circumstances. Institutions have additional responsibilities under the regulations, including review of SFIs disclosed by investigators, identifying any COIs that require management or reduction or elimination of the interest as appropriate, and reporting FCOIs to the PHS awarding component prior to expenditure of funds and subsequently as required. Part of this process

involves a designated institutional official(s) that determines that the investigator's SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded research and therefore represents an FCOI. There are other oversight, policy, education and training, and handling of noncompliance requirements that institutions must comply with per the regulation.

SFIs are defined in the PHS regulations, which include the aggregate amount of remuneration received or value of equity interest from publicly traded entities in the past 12 months preceding the disclosure of $5,000 or more. SFIs also include those from non-publicly traded entities where remuneration exceeds $5,000 or any equity interest, intellectual property rights and interests upon receipt of income and reimbursed or sponsored travel from certain entities. Since industry interactions between industry and researchers may be sporadic or ongoing, new information representing an SFI should be disclosed to institutions within 30 days during the period of the research.

Institutions must be aware of any other applicable federal regulations, state or local laws, funding agency requirements, and institutional policies, especially if they differ from PHS rules, impose additional requirements, or govern other types of COIs and transactions. For example, the National Science Foundation, which is a federal agency that provides research funding, requires investigator disclosures of certain external interests in accordance with a higher SFI threshold amount of more than $10,000.[12] The FDA also requires clinical investigators (including their spouse and dependent children) to disclose certain financial interests, payments, or arrangements to the sponsor of a covered clinical study; however, their threshold amounts differ from PHS rules.[13] Investigator interests that require reporting and disclosure to the FDA include equity interests in the sponsor and, for publicly held companies, any interest of more than $50,000 in value, any significant payments of other sorts of more than $25,000 from the sponsor, proprietary interests in the tested product, and other compensation that could be affected by the study outcome.

Requirements for other conflict review and management areas may depend on the institution (e.g., state-funded institutions, nonprofits) and type of individuals covered (e.g., state employees, healthcare providers, institutional officials, key employees). The Physician Payments Sunshine Act, which was passed in 2009 and embedded within the Affordable Care Act, requires applicable drug, device, biological, or medical supply manufacturers and group purchasing organizations (GPOs) to report annually to the Centers for Medicare & Medicaid Services (CMS) any payments or transfers of value to physicians and teaching hospitals worth more than 10 dollars.[14] The legislation was meant to increase transparency of financial relationships between physicians and teaching hospitals and industry. CMS publishes this information on its website.[15]

Certain institutions apply PHS regulations to a subset of research funded by PHS, whereas others apply it to all research activities, regardless of funding source and per institutional policies. Extending regulatory requirements more broadly depends on the risk strategy that an institution takes depending on the type of institution, makeup of researchers, funding, and type of research that is conducted. Many institutions also have policies that cover both individual and institutional FCOIs and include other types of conflicts that may occur within the clinical research environment.