

9 Biomedical Research: HHS Direction Needed to Address Financial Conflicts of Interest

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Recently we have seen tremendous growth in biomedical research funding and collaborative relationships between private industry and researchers. As the boundary between academia and industry has become less distinct, concerns have been raised about the potential for financial conflicts of interest in investigators' as well as institutions' relationships with private industry. The Department of Health and Human Services (HHS) has regulations that address aspects of financial interests in federally funded or regulated research. These include: a Public Health Service (PHS) regulation on promoting objectivity in research (42 CFR pt. 50, Subpart F), a Food and Drug (FDA) regulation on disclosing financial interests (21 CFR pt. 54), and the HHS human subjects protection regulations (45 CFR pt. 46).

Objectives

Because of Congress' concerns about the risks that financial conflicts of interest pose to the integrity of biomedical research and the well-being of human research subjects, the U.S. General Accounting Office (GAO) was asked by Senator William Frist (R-TN) to review these regulations and see how they were being implemented by academic research institutions. Our specific objectives were to examine:

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- how academic research institutions are implementing HHS regulations governing *individual investigators'* financial conflicts of interest;
- the types of policies and procedures these institutions have to minimize and manage *institutional* conflicts of interest; and
- the adequacy of the HHS regulations and oversight intended to ensure that financial conflicts of interest do not affect the integrity of research findings or the safety of human research subjects.

Methodology

To implement our objectives, we conducted case studies at five academic research institutions: the University of California, Los Angeles; the University of North Carolina at Chapel Hill; the University of Washington; Washington University in St. Louis; and Yale University. We selected these five universities because, in part, they receive the most National Institutes of Health (NIH) funding and have extensive technology transfer activities. We also wanted to include both public and private universities, and we wanted geographic diversity. To ease administrative burdens, we selected universities that had not been observed recently by either NIH or the Office for Human Research Protections (OHRP). We also interviewed officials at HHS, experts at academic associations, and other stakeholders and reviewed the HHS regulations on financial interests, as well as the HHS human subjects protection regulations.

Findings

Our report had three major findings. The first was that the five universities had developed broad individual investigator conflict of interest policies that varied in implementation. The second was that, although not required, the universities had policies and procedures that addressed aspects of institutional conflicts of interest. Third, we

found that the current regulations and oversight have limitations for promoting research integrity and human subjects protection, but that HHS was taking some action to address these limitations.

Discussion

Individual Investigator Conflict of Interest Policies and Implementation

The PHS regulation on promoting objectivity in research pertains to individual investigator conflicts of interest. Promulgated in 1995, it requires PHS-funded organizations or institutions (which include all NIH-funded organizations) to maintain and enforce written policies on financial conflicts of interest; inform their investigators of these policies; and require investigators to disclose any “significant financial interests” in entities whose financial interests may be affected by the research. The PHS regulation is flexible to allow institutions to implement it in ways that meet their individual circumstances. Because of this, and because an institutions’ policy can reflect the history of the university, its organizational structure, state laws, and other factors, we found some variation in the specific details of institution’s policies, procedures, and management of financial conflicts of interest. However, we also found some similarities. For example, we found that all five universities had policies that covered both the publicly funded research that was being conducted at their institutions and the privately funded investigators.

In addition, all five of the universities had conflict of interest committees that were responsible for the development and implementation of their financial conflict of interest policies and procedures. The configuration of these committees and the extent of their involvement in the review of disclosures varied.

All five universities allowed self-certification by investigators of their compliance with the university policy. We did not observe active oversight of investigators. We also found that research administration and financial relationship information was kept in multiple locations and formats, making it difficult to ensure that conflicts of interest were managed and not overlooked. Our own experience il-

illustrates this. Before we visited the universities, we asked them to provide data on research that involved human subjects where the investigator(s) had a significant financial interest that was determined to be a conflict of interest, and how it was managed. Four of the five universities were able to give us some information, but it took a great deal of effort to organize the information for us by the time of our site visits. One university could not give us this information at all. University officials told us that they learned from this exercise that they needed to develop better systems.

Institutional Conflicts of Interest

Although not required, the universities we visited had policies and procedures that addressed aspects of institutional financial conflicts of interest. We found that all five universities manage their institutional investments separately from their academic affairs. They had what we characterized as a “fire wall” between their institutional investments and their academic research and teaching activities. Some separated their technology transfer offices from their academic affairs to minimize potential conflicts. The five universities all had or were developing policies on accepting equity in start-up companies. We also found that they placed varying limits on their equity holdings and their roles in start-up companies.

Review of Current Regulations and Oversight

We found no direct link between the HHS financial interest regulations (PHS and FDA regulations) and the HHS human subjects protection regulations. Such a link would help ensure that institutional review boards (IRBs) are aware of financial conflicts of interest that might pose risks to study subjects and would help minimize those risks. The PHS and FDA financial interest regulations require disclosure of financial interests to institutional officials and to sponsors, but there is no mechanism to ensure that the disclosed information reaches IRBs. And although the HHS human subjects protection regulations require IRB members to disclose their own financial interests, they contain no explicit provision that investigators disclose

to IRBs their financial interests. In our review of the five universities, we found that some had developed their own ways to ensure that the IRB had information about individual investigator financial conflicts of interest, such as making sure that reports from the university's conflict of interest committee went to the IRB.

We also found that the PHS and FDA financial interest regulations are not uniform in their disclosure thresholds or timing. PHS regulations state that a significant financial interest is one that exceeds \$10,000, but the FDA threshold is \$25,000 in income or \$50,000 in equity. Under PHS regulations, institutions set up a conflict of interest policy and then report and manage any financial conflicts of interest. The PHS policy applies *before* the research is funded and initiated, and while it is being conducted. In contrast, under FDA policy, disclosure of the financial interest is made *after* the research is conducted. Sponsors who are submitting a marketing application to the FDA have to certify that investigators who have already conducted the research did not have a significant financial interest.

Finally, we found that NIH, FDA, and OHRP had taken some steps to improve oversight and monitoring of financial conflicts of interest. NIH has centralized institutions' reports of conflicts of interest at its Office of Extramural Research (OER). OER also conducts site visits of institutions, and is taking an inventory of institutions' financial conflict of interest policies. FDA has recently provided guidance on financial disclosures to reviewers of drug marketing applications. OHRP has developed draft guidance on financial relationships in clinical research.

Conclusion

In conclusion, we found that the institutions we visited needed and wanted information about best practices. In fact, we put the five universities in contact with one another, so that they could share what they are doing and learn from one another. The institutions felt that if they had information from other institutions across the country, it would help them develop their policies and procedures. In addition, although OHRP developed draft guidance on financial relationships in clinical research, we found that this guidance needs revi-

sion in a number of ways, particularly in fully addressing the issue of institutional conflicts of interest. Finally, as more biomedical research is conducted outside of universities by entities that are not operating under broad conflict of interest policies and procedures, potential financial conflicts of interest in these settings will need to be considered.

We made two recommendations to the Secretary of HHS. The first was to develop and communicate information on best practices and the second was to develop specific guidance or regulations concerning institutional conflicts of interest.¹

Endnote

1. To obtain a copy of our report, call (202) 512-6000 or visit <http://www.gao.gov> (the report number is GAO-02-89).