FROM BIRTH TO DEATH AND BENCH TO CLINIC

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for Journalists, Policymakers, and Campaigns

CHAPTER 7

Conflict of Interest in Biomedical Research

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conflict of interest in biomedical research

by Josephine Johnston

Framing the Issue

Traditionally, academic biomedical research institutions and for-profit companies have had different missions. Academic institutions have focused on teaching, research, and public service, whereas companies have focused on generating revenue through commercial activities. But the distinction between their missions is becoming blurred now that academic institutions and their employees have opportunities to make significant amounts of money—from research contracts, equity holdings, patents, and other relationships with industry, particularly pharmaceutical and biotechnology companies. These opportunities have been facilitated over the past quarter century by the Bayh-Dole Act of 1980 and significant public and private investment in biomedical research. Some of these new financial interests have raised concern about conflicts of interest.

The potential conflicts are between, on the one hand, the obligation of biomedical researchers to conduct, oversee, and assess studies according to scientific and ethical principles and, on the other hand, the desire for financial gain. The risk is that these conflicts could adversely affect the quality of research, possibly harming human subjects and anyone who relies on the research, including patients. It is difficult to prove that financial interests have caused researchers or their institutions to waiver in their commitment to producing quality studies, and there is considerable disagreement over which financial interests might inappropriately influence whom and under what circumstances. But studies of academic biomedical researchers have found troubling correlations between financial relationships with industry and problems with research, including a tendency to produce pro-sponsor results, increased secrecy, and poor study design.

Even in the absence of evidence that research quality has dramatically suffered, conflicts of interest can create the appearance of impropriety. The idea that money threatens impartial judgment has strong intuitive appeal. When researchers and research institutions take money from industry or have a financial stake in their own research, they risk undermining trust in the results of that research, as well as in individual researchers, their institutions, and the whole biomedical research system. Because of the complex nature of biomedical research, it is no exaggeration to say that trust is essential to its continued success.

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HIGHLIGHTS

- The Bayh-Dole Act of 1980, which encourages technology transfer from universities to industry, has facilitated financial relationships between academic biomedical researchers and the biotechnology industry.
- Financial relationships can create conflicts of interest between researchers' obligations to abide by scientific and ethical principles and their desire for financial gain.
- Studies have found correlations with results benefiting sponsors, poor study design, withholding negative data from publication, and other problems.
- The risk, therefore, is that conflicts could adversely affect the quality of research, possibly harming human subjects and patients along with public trust in the biomedical research enterprise.
- However, financial relationships with industry also carry benefits, including facilitating the development of new drugs and medical devices and increasing research budgets and opportunities.
- Policies to manage financial conflicts of interest need to be simplified, standardized, and better enforced.

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Prevalence of Conflicts of Interest

Studies on the extent and impact of financial interests in biomedical research have fueled concern. They have found that financial interests between academic researchers and industry are common, and are correlated with both results that favor sponsors and increased secrecy—scientists refusing to share data with colleagues, withholding negative data from publication, and delaying publication of research results.

- A 2007 survey in the *Journal of the American Medical Association* of medical school department heads found that nearly 60% of respondents had personal relationships with industry.
- A 2003 review article, also in the *Journal of the American Medical Association*, found studies suggesting that between 23% and 28% of academic investigators received research funding from industry, over 40% received research-related gifts, and about 33% had personal financial ties with industry sponsors.
- The same review also found "strong and consistent evidence" that industry-sponsored research tends to draw conclusions favoring industry, often uses an inactive control, and sometimes administers a higher dose of the sponsor's drug than of the comparison drugs or uses comparison drugs that are poorly absorbed. Industry sponsorship of research, as well as involvement with start-up companies and other commercial relationships, were significantly associated with delaying publication or withholding data.
- A 1999 survey conducted by the Association of University Technology Managers, a group that promotes academic technology transfer, found that 68% of academic research institutions held equity in companies that in turn sponsored research there.

Benefits Along with Risks

Despite the risks, financial relationships with industry can have a number of benefits. They help bring new drugs and medical devices to market and economic growth to surrounding regions and the nation as a whole. They also boost research budgets, whether directly through research funding or indirectly through gifts, sponsorships, royalty payments, dividends, and proceeds from the sale of start-up companies.

Researchers and students can also derive benefits from collaboration with industry, including the opportunity to access data, equipment, and materials, and the satisfaction of seeing basic research translated into commercial products. In addition, because average academic salaries have barely improved in real value for over 30 years and are lower than salaries of nonacademic scientists, health professionals, and engineers, opportunities for additional compensation can assist research institutions with recruitment and retention.

Academic researchers may also have a strong reluctance to give their time, expertise, or resources—including inventions—to industry without being compensated, even if compensation risks creating a conflict of interest. This reluctance may stem from what one commentator writing in the *New England Journal of Medicine* in 2005 called the "no conflict, no interest" principle, according to which a financial stake increases an individual's commitment to a project and, therefore, its chances of success. This attitude may also reflect a belief that it is unfair to prevent individuals from profiting from their effort and that restrictions are intrusions on privacy and freedom of association. Finally, the Bayh-Dole Act explicitly encourages commercialization activity by federally funded institutions and mandates that institutions share royalties with individual inventors.

Safeguarding Research Quality and Trust

Currently, most conflict-of-interest policies are to some extent self-regulatory systems: while federal regulations require that research institutions monitor, report, and sometimes resolve financial conflicts of interest, the institutions are free to create their own policies to achieve these goals. In addition, many medical journals require contributors to disclose some or all conflicts of interest, and professional organizations issue guidelines and recommendations. All these policies generally rely on individuals to be honest in their disclosures. A third party (such as a conflict-of-interest committee at a university or an editor at a scientific journal) then assesses the disclosures and decides whether to prohibit a financial interest, allow it, or allow it subject to additional measures. Most of these policies apply only to financial interests held by individual researchers—few extend to financial inter-

High-Profile Cases

Conflicts of interest have been alleged or documented in several widely reported incidents involving clinical trials, government research, and government oversight of drugs.

- After 19-year-old **Jesse Gelsinger** died in a gene transfer study at the University of Pennsylvania in 1999, conflicts of interest were among the allegations leveled at the research team and the university. The lead investigator and university held equity stakes in a company with a financial interest in the experiment, and the lead investigator and medical school dean held patents on processes used in the trial. Although no causal relationship was established between these financial interests and the irregularities associated with Gelsinger's death, the financial interests raised the suspicion that money clouded judgment.
- More than half of the scientists involved in testing **Rezulin**, a type-II diabetes drug, had received funding or other compensation from Parke-Davis/Warner-Lambert, its manufacturer. The drug was fast-tracked through Food and Drug Administration approval in 1997 on the basis of their research but was withdrawn from the market three years later when it was shown to have caused liver failure in at least 90 patients. Newspaper reports and academic commentaries expressed concern that the financially conflicted scientists may have concluded that the drug was safer and more effective than the evidence warranted.
- In late 2004 and early 2005 the *Los Angeles Times* published a series of articles detailing financial relationships between the pharmaceutical industry and senior scientists at the **National Institutes of Health** (NIH). The investigation revealed that some staff members collected hundreds of thousands of dollars from companies whose products were the subject of NIH research, and that the NIH failed to disclose these payments to human research subjects. Although no problems were reported with the scientists' work, the revelations lead some commentators and politicians to question the NIH's objectivity and commitment to public health.
- Potential conflicts of interest extend to government advisors. In 2005, an FDA advisory panel voted to allow the painkillers **Celebrex**, **Bextra**, and **Vioxx** to remain on the market, despite data showing that they increased the risk of heart attacks. A week later, the Center for Science in the Public Interest reported that 10 of the 32 panel members had recently provided consultations to the manufacturers of the drugs, leading to speculation that if these conflicted researchers had been left off the panel, the drugs would have been withdrawn from the market.

ests held by institutions—and many appear to be inadequately understood, followed, enforced, and assessed.

Nevertheless, most commentators—including several committees convened by professional organizations—remain committed to self-regulation within the biomedical research community. But for such self-regulation to successfully safeguard the quality and trustworthiness of biomedical research, conflict-of-interest policies must be improved. These important questions should be considered when crafting conflict of interest policies:

- Whose financial interests should be disclosed, and to whom?
- Which interests pose a risk to research quality or trustworthiness?
- What are the management options following initial disclosure?
- Who decides and who enforces the rules?

Despite some agreement on the basic issues to be addressed in policies, however, much of the devil is in the details. Details of conflict-of-interest policies vary considerably among, and often within, institutions, journals, professional societies, and other organizations. For instance, some policies require disclosure of financial interests over $10,000 while others require disclosure of interests over $25,000. Some policies strongly recommend that a financially conflicted individual not be involved in human subject research, while others are silent on that question. Some policies urge public disclosure in all publications and presentations, but others do not specify if or when public disclosure is necessary.

In addition, policies may not be clearly written or understood by those who must comply with them. Many could be improved through streamlining, simplification, unification, and better enforcement. Furthermore, to achieve the kind of "buy-in" that these policies desperately need, education for and outreach to those who must comply with and enforce them should be strengthened. Otherwise, conflict-of-interest policies will be seen as pesky rules rather than important safeguards to research quality and trust. A lack of faith in the prospects for improving self-regulation lead to the Physician Payments Sunshine Acts of 2007 and 2008, legislation introduced to both houses of Congress that would require drug and device makers to report to

the federal government payments made to doctors and their employers.

Setting Effective and Ethical Policies

An important barrier to improving conflict of interest policies is surely the mixed message to the biomedical research community on the propriety of financial interests. On the one hand, an outcry often accompanies revelations of financial interest because of a strong suspicion that money can cause bias. On the other hand, technology transfer and receipt of industry research funds are encouraged and expected, and carry significant benefits. As long as this mixed message persists, cultural change may be extremely difficult. There is no simple solution to this problem. Institutions, policymakers, and professional organizations will need to acknowledge the benefits and risks of the financial relationships and the care required to navigate them. A sympathetic response to the bind some institutions and individuals feel themselves to be in—and tools for avoiding or managing financial conflicts of interests—will surely prove more useful than condemnation or cavalier disregard.

Finally, continued discussion about the relationships among incentives in research, funding, and financial conflicts of interest is important. As much as possible, this discussion should reach outside the biomedical community to include policymakers, advocacy and professional organizations, and the media. Otherwise, the management of financial conflicts of interest runs the risk of being seen simply as window dressing—a way to make research-industry financial relationships appear innocuous without assuring that they really are.

RESOURCES

Web sites

- http://ori.dhhs.gov/ – Office of Research Integrity of the Department of Health and Human Services. Includes guidance, policies and regulations, and publications on research misconduct.
- www.hhs.gov/ohrp – Department of Health and Human Services Office of Human Research Protections. Includes the complete Code of Federal Regulations on protection of human subjects (Title 45, Part 46), as well as a guidance document on conflicts of interest in human subjects research.
- www.aamc.org/research/coi/start.htm – the Association of American Medical Colleges page on financial conflicts of interest in academic medicine. Includes reports of the AAMC Task Force on Financial Conflicts of Interest in Clinical Research (guidelines on policy, and principles and recommendations).
- www.aau.edu – Association of American Universities. Research issues page includes conflicts of interest and misconduct as a topic, with several reports and guidance documents.

Recent news

- Gardiner Harris and Benedict Carey, "Researchers Fail to Reveal Full Drug Pay," *New York Times,* June 8, 2008.
- David A. Shaywitz and Dennis A. Ausiello, "Scientific Research with an Asterisk," *Boston Globe*, April 29, 2008.
- "Should They Send a Thank-You Note?" (editorial), *New York Times*, April 29, 2008.
- Gina Kolata, "Citing Ethics, Some Doctors Are Rejecting Industry Pay," *New York Times*, April 15, 2008.
- Philip Shenon, "New Guidelines Ahead of Ashcroft Testimony," *New York Times*, March 11, 2008.

Further reading

- Eric G. Campbell et al., "Institutional Academic-Industry Relationships," *Journal of the American Medical Association*, October 17, 2007.
- Eric G. Campbell et al., "A National Survey of Physician-Industry Relationships," *New England Journal of Medicine*, April 26, 2007.
- Laura M. Brockway and Leo T. Furcht, "Conflicts of Interest in Biomedical Research—The FASEB Guidelines," *The Federation of American Societies for Experimental Biology (FASEB) Journal*, December 2006.
- Sheldon Krimsky, *Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research?* Rowman & Littlefield, 2003.

See online-only campaign appendix at www.thehastingscenter.org/briefingbook

The contributors also address conflicts of interest, paying particular attention to the growing commercialization of medical research, as well as the legal liability of scientific investigators, research institutions, and governmental agencies. Legal liability is a growing concern in medical research and this fascinating study is, in the international context, one of the first to explore the liability of various parties involved in the research enterprise. eISBN: 978-1-4426-7659-6. Subjects: Health Sciences. Financial conflicts of interest in academic biomedical research first entered the public consciousness during the 1980s, along with a series of widely publicized episodes of scientific misconduct. In some of these episodes, faculty investigators were accused of having fabricated or falsified research data on therapeutic products in which they had substantial financial interests. conflict with the topic he/she is researching. Not all relationships represent a true conflict of interestâ€“conflicts can be potential or actual.1,2 Some considerations that should be taken into account include: whether the person's association with the organization interferes with their ability to carry out the research or paper without bias; and whether the relationship, when later revealed, make a reasonable reader feel deceived or misled.3.Â Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Ethical Considerations in the Conduct and Reporting of Research: Conflicts of Interest. Available at: http://www.icmje.org/ethical_4conflicts.html. Accessed on September 2, 2012.