Financial Conflicts of Interest in Human Subjects Research: Proposals for a More Effective Regulatory Scheme

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Karen A. Jordan

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I. Introduction

Human participants' need for protection in research received substantial attention in the late 1960s and early 1970s because of public disclosure of abuses in research. After substantial study, the National Commission for Protection in Human Subjects of Biomedical and Behavioral Research (NCPHS) made numerous substantive and procedural recommendations for a process that would help ensure that research projects involving human participants were appropriately designed and carried out. In response, the federal government enacted regulations that require institutions to assure federal agencies that their researchers will obtain both approval of research procedures by an institutional review board (IRB) before commencing the research project and written informed consent from research participants throughout the project. Those regulations were well received, and, as one commentator has noted, "everything seemed settled" by the 1980s.

However, the environment for biomedical/biotechnology research involving human participants has changed in the last two decades and the discussion of how to improve the process of protecting human research participants has again moved to the forefront of the debate. Indeed, a flurry of activity by

1. A well-known example is the Tuskegee syphilis experiment. See Kathryn A. Tuthill, Human Experimentation: Protecting Patient Autonomy Through Informed Consent, 18 J. LEGAL MED. 221, 231 n.71 (1997) (explaining that the United States Public Health Service studied hundreds of poor African American men in order to develop and understand the natural history of syphilis).

Concerns also grew out of stories of abuse revealed during the Nuremberg trials, the promotional distribution of thalidomide resulting in numerous children born with birth defects, the administration of cancer cells to chronically ill and senile patients at a hospital in New York, and others. See Dep't of HHS, Office of Inspector General, Institutional Review Boards: Their Role in Reviewing Approved Research, Doc. No. OEl-01-97-00190, at 3 (June 1998) [hereinafter IRB's Role] (describing roots of concern about the treatment of human subjects).


5. Additionally, numerous abuses to research subjects came to light in a recent examination of the records of several thousand experiments funded and conducted, mostly in secret, by different branches of the federal government. See Childress, supra note 4, at 106 (describing
federal regulators, the research community and scholars has recently taken place as concerns stemming from the changing research environment have come to light. The changes in the research environment include more competition for research money and an increased commercialization of research. Together, the changes have resulted in a more entrepreneurial approach to research and development of innovative medical treatments, techniques, drugs, and devices such as surgical or diagnostic instruments.

An entrepreneurial approach to research means that scientists conduct research with an emphasis on commercial applications and generating revenue for the institution as well as for individual researchers. Through cooperative arrangements with for-profit businesses and industries, university research is more quickly transferred into the private market, and institutions and researchers share in the profits. The approach leads to an environment that is competitive, fast-paced, and laced with more tangible financial conflicts of interest arising at multiple points throughout the research process. The existence of financial conflicts of interest is not unique to the biomedical/biotechnology research arenas. But, because biomedical/biotechnology research more often involves human participants, financial conflicts of interest in this arena and the incentives they create must meet a higher level of scrutiny.

Importantly, the entrepreneurial factor is present within the community of academic medical centers, where the majority of biomedical/biotechnology research has traditionally occurred, as well as in the growing for-profit experimentation industry. The for-profit experimentation industry, involving "human experimentation corporations" that aggressively recruit research participants and use independent for-profit IRBs, presents unique and pressing regulatory problems. However, this Article addresses the entrepreneurial factor within

the work of the Advisory Committee on Human Radiation Experiments from 1994-95).


7. Infra notes 10-31 and accompanying text.

8. The term "biomedical research" broadly encompasses research involving biological, medical and physical science. "Biotechnology" is but a subset of biomedical research and has been described as involving the application of engineering and technological principles to living organisms or their components to produce new inventions or processes. One distinction is that biotechnology research and biotechnology firms are geared toward discovering breakthroughs. Gina A. Kuhlman, Alliances for the Future: Cultivating a Cooperative Environment for Biotech Success, 11 BERKELEY TECH. L.J. 311, 314 (1996).

9. See generally Dep't of HHS, Office of Inspector General, Recruiting Human Subjects: Pressures in Industry-Sponsored Clinical Research, Doc. No. OEI-01-97-00195 (June 2000). The Office of Inspector General noted that industry-sponsored trials are shifting from academic medical centers to private practice settings and that the number of private practice-based investigators grew from 3,513 in 1990 to 11,588 in 1995. Id. at 12. See also Dep't of HHS,
academic medical centers. In particular, this Article focuses on the increasing concern about conflicts of interest arising from financial arrangements between commercial entities and university-based research centers and their researchers.

Financial conflicts of interest within the academic research environment present a more difficult regulatory dilemma because of the general integrity of the academic community. Regulatory agencies historically have trusted the academic research community to oversee the research process and to ensure protection for human research participants. The increasing use of the research process to generate profits for universities and their researchers does not mean that the academic community can no longer be trusted. However, it does mean that universities and their researchers are operating under significant conflicts of interest more frequently than they previously had. Accordingly, the key federal agencies overseeing research involving human participants—the Department of Health and Human Services and the Food and Drug Administration—have an obligation to the public to preserve complete integrity and objectivity in research involving human participants, as well as the perception of complete integrity and objectivity.

The federal agencies have recognized this need and initiated discussions with the academic research community. A consensus exists among agencies and universities that something should be done to temper any potential negative consequences flowing from the rampant financial conflicts of interest facing researchers and institutions. However, little consensus has emerged as to the proper way to address the problem. This Article hopes to advance the discussion. The Article first reviews the problem of financial conflicts of interest and the inadequacies of the current regulatory regime in relation to that problem. The Article then outlines some of the emerging initiatives at the federal and institutional levels. Finally, the Article identifies deficiencies in those initiatives and offers suggestions for more comprehensive and effective regulatory intervention.

More specifically, the Article advocates a stronger federal role in all aspects of the regulatory process, from standard setting to enforcement. The Article fleshes out standards that should be used and analyzes the appropriateness of proposed regulatory responses. Additionally, the Article provides a rough outline of a more streamlined system that rejects the idea of the overlapping "designated institutional official" and a "conflicts of interest committee," which virtually all proposals to date have included. The Article suggests instead an office akin to an Office of Financial Conflicts Management and an Office or Committee for Patient and Research Protection, the former with

expertise related to financial matters and the latter with expertise related to the scientific aspects of the research process. Importantly, the proposed system would eliminate the need to further burden IRBs, which most proposals to date inappropriately would do. This Article does not discuss the position that all research involving human participants—and not just studies subject to current federal regulation—should come within the scope of any new regulatory scheme. Rather, the focus of this Article is on standards, regulatory responses, and enforcement procedures.

II. The Shift to a More "Entrepreneurial" Research Environment

The environment for research involving human participants in the last two decades has undergone significant changes that have diminished the protections put in place in the 1970s. During the 1970s and the early 1980s, most research involving human participants took place under government funding in a university teaching hospital with established research-related controls. Clinical trials typically involved a small cohort of participants, and a single investigator at a single institution generally conducted them. IRB workloads were limited and allowed sufficient opportunities to deliberate research proposals. The environment is much different today because of more competition for research dollars and the increasing commercialization of research.

A. Reasons Underlying the Changing Focus of Academic Research

At the most basic level, the reason for the increased competition for research dollars and the commercialization of biomedical/biotechnology research is the need for funds to support a university's research mission and status. In part, this can be tied to the shift to managed care. Managed care, with its emphasis on cost control and efficiency-based reimbursement methodologies, has eliminated the subsidy for research inherent in the fee-for-service, reasonable cost reimbursement environment. In response, institutions have pressured their physicians and researchers to find outside funding. As physi-


11. Id.

12. See A Time for Reform, supra note 10, at 4-9 (describing criticism leveled against IRBs for their failure to protect human participants).

13. Until last year, ranking of universities (e.g., the highest level was a Research I university) was based on federal funding of research. Currently, ranking is based on a number of factors.
cians at university teaching hospitals have been pressured to generate income, especially research-related funding, the number of grant applications received by the National Institutes of Health has increased dramatically. At the same time, there has been a decrease in the rate of growth of federal research funding. The result has been an increasingly competitive environment for finite federal research funds.

Universities therefore have been motivated to find alternative financing methods to support research activities. Two primary sources have surfaced. First, private industry, in particular biomedical/biotechnology firms, has increasingly offered to sponsor university-conducted research to allow for expedited product development and marketing. Second, an additional source of revenue has arisen from the commercialization of intellectual property through university technology transfer offices (TTOs). Through technology transfer, a university makes an invention or discovery available to the for-profit sector for commercial development.

Both of these developments are in part a consequence of the Bayh-Dole Act of 1980. Before the passage of the Act, title to all discoveries or inven-


15. See James S. Fairweather, Academic Research and Instruction: The Industrial Connection, 60 J. HIGHER EDUC. 388, 393 (1989) (documenting the reduction in funding and the effect on academic facilities and laboratory equipment).

16. In the mid 1990s, industry provided approximately 7% of national university research funds in the form of sponsored research agreements. Steve L. Bertha, Intellectual Property Activities in U.S. Research Universities, 36 IDEA: J.L. & TECH. 513, 520 (1996). Universities rely on corporate sponsors for support of biotechnology research because they need funding sources, and biotechnology firms rely on university research because of the expertise and sophisticated lab equipment required to conduct biotechnology research, both of which are available at university research centers. See generally Kuhlman, supra note 8.

Additionally, it has been noted that commercial entities are increasingly looking to universities for new developments because of the realization that "technology is moving too fast for any one company to keep ahead on its own. For the biotechnology industry, and particularly for that segment concerned with therapeutics, the university is the primary source of new product ideas." Dueker, supra note 14, at 469.

17. The Association of University Technology Managers (AUTM) defines “technology licensing” as including “activities associated with the evaluation and marketing of technology (including trademarks but not the university’s insignia) and intellectual property management, and those of license administration.” The definition does not include activities associated with industry research agreements. ASS'N OF UNIV. TECH. MANAGERS, LICENSING SURVEY: FY 1994 SURVEY SUMMARY AND SELECTED DATA FY 1991–FY 1994, at 13 (1995).

tions developed with federal funding in whole or in part reverted to the federal government. Prior to 1980, the federal government funded more than two-thirds of academic research, and the majority of university-developed technologies became subject to government-held patents. The federal government had hoped that retaining title would spur innovation and development. However, few companies were willing to take licenses on government-held patents, especially small businesses, which lacked the resources and time to deal with the required bureaucratic red tape. The result of these federal policies was that valuable tax dollars were used to develop ideas that were inaccessible to those businesses that could put them to viable use.

Recognizing the problem, Congress passed the Bayh-Dole Act of 1980 and fundamentally altered the treatment of the university research product. Under the language of the Act, small businesses and nonprofit organizations may elect to take title to inventions conceived or first reduced to practice in the performance of work under federal funding agreements by filing for patents and complying with certain reporting and other requirements. The Act defines the term "inventions" as "any invention or discovery which is or may be patentable." Patenable discoveries include surgical and diagnostic instru-


19. The rationale underlying the prior practice was simple: if tax dollars paid for the research behind an invention, the government should own it. Government ownership was seen as a good thing because it would keep inventions in the public domain. See Ducker, supra note 14, at 459–60 (explaining that certain government policies contain a presumption of title resting in the federal government).

20. The goal was to support basic research in academia (as well as in national laboratories) with the expectation that researchers would publish their results in scientific journals. The resulting "free information" would then be used by industry to develop new products and processes that would benefit society. Bertha, supra note 16, at 514.

21. See Ducker, supra note 14, at 460 (stating that bureaucratic process discouraged many companies from working with the government).

22. In 1978, the year the Bayh-Dole Act was introduced, the federal government spent over $30 billion to develop 28,000 patents, but licensed only 5% of them. Id. at 461.

23. See 35 U.S.C. §§ 201–02 (2000) (describing requirements for taking title). A university must elect title by notifying the federal agency within a reasonable time after the initial disclosure. Id. § 202(e). Should the university not elect to retain title, the funding agency may grant title to the inventor (i.e., the university employee). 37 C.F.R. § 401.9 (1999); 35 U.S.C. § 202(d) (2000). The Act defines a "subject invention" as "an invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement." 35 U.S.C. § 201(e) (2000). It defines "funding agreement" as "any contract, grant, or cooperative agreement entered into between any Federal Agency . . . and any contractor for the performance of experimental, developmental, or research work funded in whole or in part by the Federal Government." Id. § 201(b).

ments, drugs, and devices, as well as medical procedures and techniques.\textsuperscript{25} Thus, biomedical/biotechnology research often leads to products or discoveries that are patentable.

The primary purposes of the Bayh-Dole Act were to ensure that the patent system promoted the use of inventions arising from university-supported research and development, to encourage maximum participation of small business firms in federally supported research and development efforts, and to promote collaboration between commercial concerns and nonprofit organizations, including universities.\textsuperscript{26} These purposes have no doubt been served. The likelihood that a scientific finding will quickly produce a useful and marketable product has greatly increased since the Bayh-Dole Act has provided incentives to those best able to develop biomedical advances.\textsuperscript{27}

At the same time, the ability to "take title" affords universities the opportunity to license patented or patentable technologies and to negotiate a share of the receipts generated by the commercial product.\textsuperscript{28} Universities have wholeheartedly embraced this opportunity to generate unrestricted funds. Indeed, a virtual explosion of interest and activity in intellectual property and technology transfer on university campuses has occurred. That explosion has been especially pronounced in the biotechnology/biomedical arena. The right to share in revenues conferred by the Bayh-Dole Act, when coupled with a university's need for funding sources, has created an incentive for universities to try to negotiate license terms that will maximize the share of the profits they receive.\textsuperscript{29} Indeed, the money-making aspect of today's biomedical research


\textsuperscript{26} 35 U.S.C. § 200 (2000). It was claimed that preferential treatment should be accorded to small businesses and universities because they had stronger incentives than large businesses to promote widespread commercialization of inventions, but needed exclusive rights in a discovery to motivate commercial development. Further, small businesses and universities typically would not have sufficient market power for the acquisition of title to raise antitrust concerns. Rebecca S. Eisenberg, \textit{Public Research and Private Development: Patents and Technology in Government-Sponsored Research}, 82 \textit{VA. L. REV.} 1663, 1695–99 (1996).


\textsuperscript{28} Universities can generate substantial revenue streams through both nonexclusive and exclusive licensing arrangements. See Eisenberg, \textit{supra} note 26, at 1710–12 (noting that the revenue motives of universities inevitably operate at cross-purposes with the larger patent policy goal of promoting product development by enhancing its profitability to businesses).

\textsuperscript{29} Eisenberg notes:
environment has led to the comment that the Bayh-Dole Act "is often used [by universities] as an excuse for making as much money as possible in as many possible ways."

Still, for many universities, the aggressive pursuit of technology transfer is not solely for the purpose of bringing unrestricted revenue into the university's coffers. Rather, the pursuit is also attributable to the demands from state and local governments and industry that universities become engines responsible for regional economic development. Because many universities depend on appropriations from state and local governments, these demands cannot be ignored. Regardless of the impetus, however, the result has been a more entrepreneurial approach to the university's research mission involving, to a much greater extent, financial relationships between commercial research sponsors, biomedical researchers, and the university. Those financial arrangements create very real conflicts of interest.

B. The Resulting Financial Conflicts of Interest

What does it mean to say that today's biomedical research environment has become more entrepreneurial in nature? Basically, it means that universities and researchers have supplemented their traditional focus on basic research geared towards increasing scientific knowledge of fundamental systems or mechanisms with a focus directed increasingly towards commercial applications of scientific advances that can earn money. It means that researchers and their affiliated institutions desire to create a market for new treatments, procedures, devices, or drugs, and they hope to become the recognized expert in those markets or to generate revenue for the university through the transfer of technology and innovation to the market.

Importantly, it also means that, as a result of the university-corporate interaction spawned by the Bayh-Dole Act, innovative approaches to financing

Nothing other than forbearance on the part of universities, and resistance on the part of potential licensees, prevents universities from striking deals that would extract the full amount of rents from development of a patented product to the universities themselves, which would leave the innovating firms in exactly the same position they would be in if the discovery had been placed in the public domain.

Id. at 1711.


and corporate partnering have emerged. As part and parcel of the emerging financial arrangements, academic researchers may receive cash, consulting fees or honoraria, stocks or other ownership interests, or intellectual property rights. Thus, individual researchers can benefit not only from the enhanced reputation and academic standing that may accompany a scientific breakthrough, but also from resulting financial incentives. Although these financial incentives have always existed to some extent, they are intensified in today's entrepreneurial environment in which researchers may assume the role not only of clinical investigators, but also of sponsors of investigations, inventors named on patents, and product manufacturers.

Perhaps more importantly, to satisfy the intensified institutional need for research monies—monies needed to help fund the university's research mission and to help elevate the university's standing among institutions—universities themselves are increasingly entering into arrangements with for-profit entities. These commercial entities either directly fund research projects or indirectly do so by channeling monies back to the university after university research has been transferred into a usable product. Although comprising only a small percentage of the revenue stream for most universities, those revenue streams are growing. Further, monies from technology transfers are cherished because the monies are unrestricted funds that a university can use in a discretionary manner. For example, the following diagram illustrates the types of arrangements increasingly entered into by universities and commercial entities.

33. Generally, the individual researcher/inventor receives a portion of the technology-transfer revenue. The Bayh-Dole Act mandates that the researcher receive some share, albeit an indeterminate one, of the royalties under agreements to which the Act applies. See generally Lynne J. Bowers & Vickie Leon, Patent Policies of 65 Education Institutions: A Comparison, SOC. RES. ADMIN. J., Spring 1994, at 5.

34. See generally Kuhlman, supra note 8, at 345; see also Diagram of Common Financial Arrangements, infra p. 26 (hereinafter Diagram A) (illustrating typical financial arrangements).

35. In 1991 and 1992, university revenue from royalties (e.g., from licenses granted to industries) was $130 million and $172 million, respectively. See Kuhlman, supra note 8, at 326. In 2000, university revenue from licensed inventions exceeded $1.26 billion. National Center for Policy Analysis, Bayh-Dole Act: Moving Innovations from the Lab to Patients, DAILY POL'Y DIGEST, May 13, 2002, at www.ncpa.org/iss/heal/2002/pd051302c.html. Further, "while the total number of patents issued each year doubled from 1970 to 1994, the number of patents issued each year to United States universities increased seven-fold, going from about 250 per year in the early 1970s to 1,761 in 1994 alone." John M. Golden, Biotechnology, Technology Policy, and Patentability: Natural Products and Invention in the American System, 50 EMORY L.J. 101, 143 (2001).

36. See Massaro, supra note 14, at 1735 (noting that unrestricted, discretionary funds are perhaps the most difficult monies to find and yet the most important in allowing a well-prepared president to shape the future of an institution).
Diagram A
Schematic Diagram of Typical Process to Identify and Manage Financial Conflicts of Interest

Faculty Members
- Detailed disclosure of financial/economic interests held by faculty member related to any research interest
- Submitted annually to University Official

University Official
- Review for potential conflicts (assesses extent and nature)
- Questionable conflicts forwarded to Conflicts Committee

Conflicts Committee
- Determines whether a conflict of interest exists
- Assesses the nature and extent of the conflict
- Identifies means of managing or eliminating the conflict

Technology Transfer Office
- Communicates with the Conflicts Committee to avoid arguments that pose difficult-to-manage conflicting interests

Human Research Policy Board & Administration
- Formulates institutional policies and procedures relating to research involving human subjects
- Ensures that faculty is informed of the policies and procedures
- Ensures that IRB members & staff, investigators, and the Conflicts Committee receive appropriate education, training, & resources
- Monitors the IRB and conflicts of interest processes & procedures

Investigators
- Detailed disclosure of financial/economic interests held by investigator AND the University related to specific research project
- Submitted with research protocol

Monitoring

Institutional Review Board
- Performs traditionally required review of the research protocol (risks, benefits, research design, etc.)
- Reviews public disclosure form re: the financial interests, the description of the conflicts and management techniques, and the recommended disclosure language for informed consent (veto power)

- Determines the appropriate content form and forum for the informed consent
- Performs traditional continuing oversight plus additional oversight if recommended

- Forwards the public disclosure form to the appropriate University office so it is available for public review
On the whole, such financial arrangements enable the kinds of knowledge transfer and technology transfer that Congress envisioned. From the perspective of the stream of products entering the healthcare marketplace, the public is clearly better off as a result of these new relationships. However, the arrangements create conflicts that may interfere with decisions made in the process of research involving human participants. Moreover, not only does there exist a greater potential that a researcher’s financial interest may influence his or her research, but the traditional institutional safeguards are arguably less effective because universities also hold financial interests that could be affected by research. As explained in Part III, IRB review has traditionally served as the primary check on the appropriateness of research involving human participants. But IRBs work for institutions. Because of the heightened importance of research funding to institutions, as well as the prestige associated with involvement in cutting edge research, IRBs want to accommodate researchers and the university by approving research proposals. Thus, university-held financial interests may hamper the protection traditionally afforded through the IRB review process.

The increasing presence of commercial research sponsors in the academic setting also has other ramifications bearing on oversight of research projects. Commercial sponsors want prompt reviews for their protocols and have adopted increasingly active roles, including negotiating research design, rights to data, and publication rights. Further, oversight is often more difficult because commercially sponsored research studies are often conducted at multiple sites; indeed, some research is spread across hundreds of sites.

Additionally, the objective of and demand for research studies has evolved. Researchers of course continue to pursue life-saving medical treatments, which can more readily justify the risks associated with experimental medical care, and there have been dramatic advances in the effort to find new therapies for cancer and other diseases. But, due to the incentives to innovate and to profit, researchers are increasingly pursuing biomedical inventions and technologies, as well as innovative treatments and procedures, that are

37. August 15 Conference Transcript, supra note 27, at 11 (statement of Dr. Raub, principal spokesperson on the Secretary’s new initiatives to strengthen human subject protection).
38. See id. at 12–18 (statement of Thomas Bodenheimer, Clinical Professor of Family and Community Medicine at the University of California-San Francisco) (citing examples of such conduct).
more elective in nature. When experimental procedures that are not necessarily life-saving are involved, it becomes more difficult for IRBs to strike the appropriate balance between risk and benefit.

In short, the biomedical/biotechnology research environment has become competitive and fast-paced, with less institutional and more commercial control. IRBs are facing tremendous pressures, are being asked to review projects presenting increasingly complex issues and, in many cases, are not receiving sufficient support. As a result, a plethora of ethical and practical concerns have arisen. A series of reports by the Office of the Inspector General have highlighted and identified these emerging concerns associated with the IRB process and made recommendations for improving the process.

The rampant financial conflicts of interest thus are but one consequence of the changing research environment. But it is one that the media has highlighted, thereby fueling public concerns. For example, the press highlighted violations that occurred during a clinical trial at the University of Pennsylvania in which Jesse Gelsinger died in September 1999. When the media reported the event, the public was appropriately concerned. However, the acknowledgment that medical research involves risks, and sometimes serious risks, tempered that concern. The public concern later intensified when it was revealed that the Food and Drug Administration investigation found protocol violations by the clinical investigators, including the failure to file serious adverse-event reports and to notify the National Institutes of Health; that concern turned to shock when it was discovered and reported that a financial conflict of interest existed. Observers raised questions concerning the

41. At the same time, today's health care consumers are often demanding to participate in clinical studies. A Time for Reform, supra note 10, at 5.

42. Id.; The Emergence of Independent Boards, supra note 9; IRB's Role, supra note 1; Dep't of HHS, Office of Inspector General, Institutional Review Boards: Promising Approaches, Doc. No. OEI-01-00191 (June 1998).


44. See August 15 Conference Transcript, supra note 27, at 32–33 (statement of Dr. Savio Woo, Professor of Medicine and Director of the Mount Sinai School of Medicine Institute of Gene Therapy and Molecular Medicine) (discussing heightened levels of concern as more information in Gelsinger case emerged). Reporters found that the University of Pennsylvania receive[d] substantial support from a company founded by the principal researcher and Institute director, and that the University's conflict of interest rules were altered to permit his ownership of 30% of the company's stock [, and that the] University itself opted for 15%. The University also gave the investigator the exclusive right to license patents derived from his institute to the company and its corporate sponsors.
financial interests of the investigators and whether those interests clouded judgment or influenced research designs. The increased potential for conflicts of interest that could affect professional judgment is therefore a very serious consequence of a more entrepreneurial approach to biomedical research. Although not intrinsically unacceptable, a more entrepreneurial research environment nonetheless raises concerns that the current regulatory framework may not adequately take into account.

III. The Current Federal Regulatory Framework

Currently, federal regulation of research involving human participants follows a model whereby the federal government provides guidance, but oversight and enforcement is largely left to research institutions therefore. Protection for human participants in research falls within the authority of two agencies: the Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA), an agency within HHS. HHS oversees research supported through funding from the National Institutes of Health (NIH). The FDA, as designee of the Secretary of HHS, has authority pursuant to the Food, Drug, and Cosmetic Act to regulate research conducted on products subject to FDA approval (namely drugs and devices).

As noted, the federal regulatory scheme is grounded in trust. Congress has directed the Secretary of HHS to require any entity that applies for a grant, contract, or cooperative agreement for any project or program that involves human participants to submit to the Secretary an "assurance" that it has established a board to review and monitor biomedical and behavioral re-


48. The Food, Drug, and Cosmetic Act (FDCA) defines "drug" to include "articles (other than food) intended to affect the structure or any function of the body." Id. § 321(g)(1)(c). It defines "device," in part, as "an instrument, apparatus, implement, machine, contrivance, . . . or other similar or related article, including any component, part, or accessory, which is . . . intended to affect the structure or any function of the body." Id. § 321(h). The FDCA also gives the FDA authority to regulate "combination products," which "constitute a combination of a drug, device, or biological product." Id. § 355(g)(1).
search—i.e., an IRB.49 In furtherance of this directive, the Secretary of HHS has promulgated regulations setting forth more specifically the criteria governing IRB activity.50 Like HHS, the FDA relies on the IRB process for protection of human participants.51 Additionally, seventeen federal agencies that are involved in research involving human research participants have agreed upon a set of governing rules. This set of rules is known as the "common rule."52 The agencies that adhere to the common rule have agreed that they will not modify their policies absent agreement by the other agencies.53

Each of these regulatory schemes—the HHS scheme, the FDA scheme, and the common rule—provides protection to human participants through the dual requirements of IRB approval and oversight and of informed consent. These schemes have also addressed to some extent the issue of conflicting interests. The following sections describe the basic IRB and informed consent requirements and the rules addressing conflicting interests.

A. The Basic Federal Protections: IRB Review and Informed Consent

Because the basic protections established by the HHS and FDA regulations and the common rule are substantially similar, this discussion will refer to and cite only the HHS regulations. As noted, the HHS regulatory scheme provides protection to human participants through the dual requirements of IRB approval and oversight and informed consent. The HHS regulations direct that an IRB "shall review and have authority to approve, require modifications in...or disapprove all research activities."4 In order to approve research, the IRB must determine that the risks to participants are minimized and that the procedures being used are consistent with sound research design.55 Additionally, the IRB must perform a risk-benefit analysis: it may approve research only if the IRB determines that the risks are reasonable in relation to antici-
pated benefits to individual participants and the importance of the knowledge that may reasonably be expected to result.\textsuperscript{56} The IRB must also ensure that the selection of participants is equitable,\textsuperscript{57} that privacy is maintained,\textsuperscript{58} and that data monitoring occurs when appropriate.\textsuperscript{59} Lastly, the IRB must ensure that the researchers will obtain written informed consent.\textsuperscript{60}

Importantly, the IRB is directed to oversee the informed consent process. The regulations specify that the informed consent must be obtained under circumstances that provide the prospective subject the opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.\textsuperscript{61} Generally, the informed consent process must include the following:

1. an explanation that describes the purpose and expected duration of the research and that identifies the procedures that are experimental;
2. a description of the reasonably foreseeable risks and benefits and, where appropriate, a statement that the procedure may involve unforeseeable risks;
3. a disclosure of alternative procedures that might be advantageous;
4. an explanation of whether confidentiality will be maintained;
5. an explanation of any additional costs to the subject that may result from participation;
6. an explanation of whether compensation or medical treatments are available if injury occurs;
7. a statement that participation is voluntary and that the subject may withdraw at any time and an explanation of the consequences of withdrawal;
8. a description of the approximate number of participants involved in the study; and

\textsuperscript{56} Id. § 46.111(a)(2). However, the IRB is not supposed to consider possible long-range effects of applying knowledge gained in the research. Id.

\textsuperscript{57} Id. § 46.111(a)(3).

\textsuperscript{58} Id. § 46.111(a)(7).

\textsuperscript{59} Id. § 46.111(a)(6).

\textsuperscript{60} See id. § 46.111(a)(4)–(5) (directing compliance with written consent regulations). An expedited review process is available when the research involves only minimal risk or only a minor change in previously approved research. Id. § 46.110.

\textsuperscript{61} Id. § 46.116.
(9) a statement that significant findings that may relate to the subject's willingness to participate will be provided to the subject.62

The IRB oversees the informed consent process primarily through its approval of the "informed consent form" that the researcher uses and the participant signs.63 The regulations provide that the IRB may approve a form that embodies the elements noted above that are generally necessary to satisfy the informed consent requirement,64 or the IRB can approve a short form stating that the elements have been presented orally to the participant.65

Thus, the key protections for human research participants are an assessment by the IRB of the risks, benefits, and design of the research project and the provision to potential participants of information deemed sufficient by the IRB to allow potential participants to make an informed decision regarding participation. Because the IRB's role is critical to protecting human research participants, it is important to consider the HHS requirements regarding the composition of the IRB.

The regulations emphasize professional competency and diversity. In order "to promote complete and adequate review of research activities commonly conducted by the institution," the IRB must be "sufficiently qualified

62. Id. § 46.116(a)-(b). The subject should also be informed whom to contact for answers to questions about the research and the subject's rights. Id. § 46.116(a)(7).

The IRB may approve a consent procedure that fails to include the above noted information—or may even waive the need to obtain informed consent—if the IRB makes the following four findings: (1) that the research involves minimal risk, (2) that the waiver will not adversely affect the rights and welfare of the participants, (3) that the research could not practicably be conducted without the waiver or alteration, and (4) that the participants will be provided with pertinent information after participation. Id. § 46.116(d). Informed consent may also be altered or waived if the research is to be conducted by or subject to approval of state or local government officials and is designed to study or evaluate public benefit or service programs. Id. § 46.116(c).

63. See id. § 46.117(a) (requiring general use of written consent form).

64. Id. § 46.117(b)(1).

65. Id. § 46.117(b)(2). If the short form is used, the IRB must approve a written summary of what is to be said to the subject. Id. Further, a witness must be present for the oral presentation. Id. The research subject signs only the short form; the witness signs both the short form and a copy of the summary. Id. A copy of the summary must be given to the research subject in addition to the short form. Id.

In addition to the informed consent itself, the IRB may waive the requirement that the researcher obtain a "signed" consent form. Id. § 46.117(c). The IRB may waive the "signing" requirement when the IRB finds either (1) that the consent document would be the only link between the subject and the research and the principal risk involved is the potential harm resulting from a breach of confidentiality or (2) that the research presents only minimal risk of harm and involves only procedures for which written consent is normally not required outside of the research context. Id.
through the expertise of its members." Specifically, the IRB must have at least five members "with varying backgrounds" and with knowledge of institutional commitments and policies, applicable law, and standards of professional conduct and practice. The regulations stress diversity of membership, considering race, gender, and cultural backgrounds, in order to promote respect for its determinations and recommendations. Further, if the institution regularly conducts research involving vulnerable categories of persons, such as children, prisoners, pregnant women, or the disabled, the regulations suggest including one or more individuals who are knowledgeable about and experienced in working with such individuals. The regulations specifically require each IRB to include at least one member whose primary concerns are in "scientific areas" and at least one member whose primary concerns are in "nonscientific areas." Further, each IRB must include at least one member who is not otherwise affiliated with the institution.

Although the federal regulatory schemes are substantially similar respecting the composition and operation of the IRB, their processes for oversight are somewhat different. HHS oversees the IRB process through two agencies within HHS: the Office for Human Research Protection (OHRP) and the FDA. The OHRP’s oversight of IRBs primarily is prospective. As noted, the regulations require each institution engaged in federally sponsored or supported research to provide a written "assurance" specifying that the institution is committed to the human-subject protections specified in the federal regula-

66. See id. § 46.107(a) (setting forth goals to be accomplished through membership criteria).
67. Id.
68. Id.
69. Id.
70. Id. § 46.107(c).
71. Id. § 46.107(d). Additionally, the IRB must operate in accordance with written procedures for conducting initial and continuing reviews. Id. § 46.108(a). Procedures must be written in order to fulfill the requirement of the assurance of compliance. Id. § 46.103(b)(4). IRBs may review research proposals only at meetings at which a majority of the members are present. Id. § 46.108(b). A member whose primary concerns are nonscientific must be present. Id. To secure approval, research must receive approval of a majority of those members present at the meeting. Id.
72. The OHRP replaces the Office for Protection from Research Risks. The change was part of the Secretary of HHS’s new initiatives to protect human research participants. The new office, OHRP, was also moved to the Office of the Secretary, thereby elevating its status within the Department.
73. The OHRP oversees the process as to research funded by NIH (or conducted or supported by any federal department or agency). The FDA oversees the process as to research conducted as part of the FDA approval process for drugs and devices.
The assurance outlines the organization and purview of the IRB in addition to its processes for reviewing research protocols and other procedural issues. OHRP evaluates all assurances for adequacy in light of the anticipated scope of the institution's research activities and may approve or disapprove the assurance or may work with the institution to develop an acceptable assurance. Thus, the focus is on whether the institution has developed appropriate policies and procedures, and the agency largely trusts the institution to ensure that its policies and procedures are followed.

In contrast, FDA oversight is largely retrospective. The FDA oversees such research through inspections of investigators, IRBs, and research sponsors. FDA's goal is to routinely inspect an IRB once every five years. The inspection focuses on a review of IRB records and an examination of written procedures. A goal is to conduct a file review of at least three actual research studies approved by the IRB to assess things such as timely continuing review, the use of the most current consent documents, and the submission and review of adverse-event reports. Although providing more oversight than a mere review of the institution's "assurance," a retrospective review is similarly premised on trust that the institution generally will have ensured that its policies and procedures were followed.

B. Current Safeguards Against Conflicts of Interest

The regulatory scheme described thus far provides few meaningful protections against the heightened concerns arising from conflicts of interests.

74. 45 C.F.R. § 46.103(a) (2001).
75. Id. § 46.103(b). The assurance must state the principles governing the institution in protecting human research participants, designate one or more IRBs that satisfy the federal requirements and for which meeting space and staff have been provided, list IRB members and their qualifications and information pertaining to their relationship with the institution, set forth the procedures that the IRB will follow in conducting initial and continuing reviews, and describe the procedures for ensuring prompt reporting to the IRB of unanticipated problems involving risks or noncompliance. Id.
76. Id. § 46.103(d).
77. Id. § 46.103(e).
78. While the assurances are the primary oversight tool, the OHRP may conduct an investigation based upon complaints by research participants. However, the OHRP rarely goes on site; rather, the investigations mostly occur through paper and phone communications. A Time for Reform, supra note 10, app. at C-2.
79. See id. app. at C-3 (noting that the goal of a routine inspection every five years is difficult due to workload constraints). However, an inspection may occur as part of the product-approval process or because of complaints of noncompliance. Id.
80. IRB's Role, supra note 1, app. at B-3.
81. The operation of the IRB process is also reviewed for the presence of a quorum during voting procedures. Id. app. at B-3, B-4.
The requirements for the composition of the IRB arguably could provide some measure of protection. IRB members who have knowledge of institutional policies and who are qualified to assess the scientific soundness of a proposed research design conceivably could monitor for signals indicating influence by financial interests. Similarly, a member not otherwise affiliated with the institution conceivably could monitor for signals that the university's interests are influencing IRB decisions. However, one noninstitutional voice can easily be ignored or outnumbered. Further, evidence shows that institutional IRB members historically have received insufficient education and training to serve as effective monitors of conflicts of interests.82

The basic IRB regulations do expressly specify that "[n]o IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest."83 This requirement provides some measure of protection: it helps ensure that the IRB review itself is not improperly influenced by a conflicting financial interest of an IRB member. But the requirement does not reach the more serious concerns arising from the increasingly entrepreneurial nature of medical research: the concerns that the financial interests of the researchers and the university may compromise a researcher’s professional judgment, thereby threatening the integrity of research design, conduct, or publication.

Importantly, neither the HHS regulations governing NIH-supported research nor the FDA regulations require IRBs to consider whether the investigators or the institutions have any financial interest that could be affected by a proposed research project. Moreover, they do not require that any conflicting financial interests are disclosed to research participants in the informed consent process.84

Recognizing the growing existence of financial conflicts of interest, HHS through the Public Health Service (PHS) in 1995 issued regulations that address financial conflicts of interest more specifically.85 The FDA followed suit shortly thereafter.86 Although the PHS and FDA regulations are substan-

82. A Time for Reform, supra note 10, at ii.
83. 45 C.F.R. § 46.107(e) (2001). The phrase "conflicting interest" is not defined.
84. The common law of some jurisdictions requires as a part of the informed consent process a disclosure of any personal interests, whether or not related to the patient's health, that may affect the physician's professional judgment. See, e.g., Moore v. Regents of the Univ. of California, 793 P.2d 479, 483 (Cal. 1990) (requiring physician to disclose personal economic interests that may affect his judgment regarding treatment of patient). Thus, while state law may require such disclosure, the federal regulations do not include such a requirement.
85. These regulations were codified at two locations, one set appearing in the PHS regulations and the other in the HHS regulations. As the two sets of regulations are substantially similar, this Article will cite the PHS regulations.
86. The FDA’s rules are codified at Subchapter A (General), Part 54 (Financial Disclosure
tially similar, this Article will discuss both. The purpose of both the PHS and FDA conflict-of-interest regulations is to promote "objectivity" in research by helping to ensure that the design, conduct, and reporting of research funded under PHS grants or agreements,87 or supporting applications for FDA approval,88 will not be biased by conflicting financial interests of the investigator. Hence, this Article will refer to the regulations as the "Objectivity Regulations."

The PHS Objectivity Regulations follow the IRB regulatory model: they impose on the institution an obligation to identify and manage significant financial interests that research conducted at or for the institution could affect. Specifically, the Objectivity Regulations impose three primary obligations on institutions applying for PHS support for research.9 Institutions must (1) maintain a written, enforced policy on financial conflicts of interest; (2) inform research investigators of the institution’s policy, of the associated reporting responsibilities, and of the regulations themselves; and (3) report to awarding offices the existence of any conflicting interests and assure that the institution has managed, reduced, or eliminated such interests.90

The institution is directed to accomplish these duties through the designation of an institutional official(s) who will be responsible for the solicitation and review of financial disclosure statements from any investigator who is planning to participate in PHS-funded research.91 The official(s) must identify whether a conflict exists and, if so, determine what action should be taken to manage, reduce, or eliminate the conflict. The institution must support the designated official(s) by providing guidelines for identifying conflicting

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87. 42 C.F.R § 50.601 (2001). The PHS Objectivity Regulations reach NIH-supported research because within the organizational structure of HHS, the NIH is under the auspices of the PHS. Notably, the regulations do not reach Small Business Innovation Research Program Phase I applications. Id. § 50.602. Further, when an individual, rather than an institution, is the grant applicant, applicability is determined on a case-by-case basis. Id.

88. Id. § 54.1(a)–(b) (2002).

89. Similarly to the previously discussed HHS regulations, the Objectivity Regulations define the term "research" to mean "a systematic investigation designed to develop or contribute to generalizable knowledge relating broadly to public health, including behavioral and social-sciences research." 42 C.F.R. § 50.603 (2001).

90. Id. § 50.604(a).

91. Id. § 50.604(b). By the time an application is submitted to PHS, each investigator who is planning to participate in the PHS-funded research must submit to the designated official(s) a listing of his/her known significant financial interests that the research for which the funding is sought might reasonably appear to affect. The listing must include any interests of the investigator’s spouse and dependent children and interests in any entity whose financial interests the research might reasonably appear to affect. Id. § 50.604(c).
interests, by taking actions necessary to manage, reduce, or eliminate the conflict, and by establishing adequate enforcement mechanisms. 92

Obviously, the effectiveness of the Objectivity Regulations depends in large part on the conflicts encompassed by the regulations. Investigators must disclose their "significant financial interests," as well as those of the investigator's spouse and dependent children. 93 The Objectivity Regulations define "significant financial interest" as anything of monetary value, including but not limited to:

(1) salary or other payments for services (such as consulting fees or honoraria), unless the payments, when aggregated for the investigator and the investigator's spouse and dependent children over the next twelve months, are not expected to exceed $10,000; 94

(2) equity interests (such as stock, stock options, or other ownership interests), unless (a) the applicant institution participates in the Small Business Innovation Research Program (SBIR) or (b) the equity interest, when aggregated for the investigator and the investigator's spouse and dependent children, does not exceed $10,000 and does not represent more than a five-percent ownership interest in any single entity; 95 and

(3) intellectual property rights (such as patents, copyrights, and royalties from such rights). 96

The list prepared by the investigator must include significant financial interests that "would reasonably appear to be affected by the research for which PHS funding is sought." 97 Applying the guidelines provided by the institution, the designated official(s) must determine whether the disclosed significant finan-

92. Id. § 50.604(d), (f). The institution must also maintain for three years records of all financial disclosures and all actions taken by the institution with respect to identified conflicts. Id. § 50.604(e).

93. See id. § 50.604 (explaining institutional responsibility regarding conflicting interests of investigators).

94. Id. § 50.603.

95. The value of the equity interest may be determined through reference to public prices or other reasonable measures of fair market value. Id. The Small Business Innovation Research Program (SBIR) is the PHS extramural research program for small businesses. Id.

96. Id. However, the provision expressly exempts the following: salary and other remuneration from the applicant institution; ownership interests in an SBIR applicant institution; income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities; and income from service on advisory committees or review panels for public or nonprofit entities. Id.

97. Id. § 50.604(c)(1)(i).
cial interests could "directly and significantly affect the design, conduct, or reporting of the PHS-funded research." As noted, the designated official(s) must then determine what action should be taken, and the institution must follow through with enforcement mechanisms.

Thus, as with the basic IRB and informed consent regulations, the PHS Objectivity Regulations are grounded in trust. The regulations provide guidance as to the types of interests that an institution must disclose and manage, but they leave oversight and enforcement to the institution. Further, enforcement of the Objectivity Regulations is comparable to the HHS assurance process. In each application for PHS funding, the institution need only certify that it has a written and enforced administrative process to identify and manage conflicting interests with respect to all research projects for which funding is sought. Additionally, the institution must certify that, prior to any expenditure of funds under the award, the institution will report the existence of any identified conflicting interest and must assure that it will manage, reduce, or eliminate the conflict. The regulations do not specify additional oversight, such as an OPHR check on whether an institution’s designated official(s) is properly identifying significant financial interests or even a review of an institution’s written policies and guidelines used in making the determination.

The FDA Objectivity Regulations in some ways go further in regulating financial conflicts of interest. First, the FDA regulations specify that an applicant seeking FDA approval of a human drug, a biological product, or a medical device must submit a list of all clinical investigators identifying those investigators who are employees of the applicant. Additionally, for each nonemployee investigator, the applicant must either (1) provide certification that certain financial arrangements do not exist or (2) disclose the nature of such financial arrangements and the steps taken to minimize any bias in the research process. The FDA reviews the disclosures during the course of the FDA approval process. The regulations specify that the FDA may consider clinical studies inadequate or unreliable if appropriate steps have not been

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98. Id. § 50.605(a).
99. Id. § 50.604(g)(2). The institution must certify in each application for funding that, prior to any expenditure of funds under the award, the institution will report the existence of any identified conflicting interest and assure that the conflict will be managed, reduced, or eliminated. Id.
100. Id. § 50.604(g)(1).
101. Id. § 50.604(g)(2).
103. Id. § 54.4. The FDA regulations define "clinical investigator" as "a listed or identified investigator or subinvestigator who is directly involved in the treatment or evaluation of research participants...[as well as] the spouse and each dependent child of the investigator." Id. § 54.2(d).
taken to minimize bias, including bias that may arise from an investigator's financial interest in the outcome of the research. The FDA regulations go further by departing from the PHS model of leaving oversight and enforcement to the IRB or to the institution conducting the research: the disclosures are made to the FDA, and the FDA assesses their impact.

The FDA Objectivity Regulations also define the financial arrangements or interests that must be disclosed more broadly, in some respects, than do the PHS regulations. The disclosure must include:

1. Any financial arrangement between the sponsor of the study and the clinical investigator whereby the value of the compensation to the clinical investigator for conducting the study could be higher for a favorable outcome than for an unfavorable outcome;

2. Any significant payments of other sorts from the sponsor, such as a grant to fund ongoing research, a retainer for ongoing consultation, or provision of equipment or honoraria, if the payments have a monetary value of more than $25,000;

3. Any proprietary interest in the tested product involved in the study, such as a patent, trademark, copyright, or licensing agreement, and

4. Any significant equity interest in the sponsor of the study, meaning (a) any ownership or financial interests or stock options in a non-publicly traded entity or (b) any equity interest in a publicly traded corporation exceeding $50,000, during the time the clinical investigator is carrying out the trial and for one year following completion of the trial.

These arrangements capture some financial interests that have less value than the interests targeted under the PHS regulations and some only if the value is significantly greater. For example, under the PHS regulations, payments for consulting or honoraria must be disclosed when they exceed $10,000, but under the FDA regulations, similar payments need not be disclosed until they exceed $25,000. On the other hand, any compensation arrangement that is tied to a favorable outcome must be disclosed under the FDA regulations, whereas the PHS regulations do not have a similar provision. Similarly, any equity

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104. Id. § 54.1(b).
105. Id. §§ 54.4(a)(3)(i), 54.2(a).
106. Id. §§ 54.4(a)(3)(ii), 54.2(f).
107. Id. §§ 54.4(a)(3)(iii), 54.2(c).
108. Id. §§ 54.4(a)(3)(iv), 54.2(b).
interest in a non-publicly traded entity must be disclosed under the FDA provisions, whereas the PHS regulations exempt any equity interest that does not exceed $10,000 or five-percent ownership interest and exempts ownership interests in SBIR entities entirely.\textsuperscript{109}

In assessing the financial interests disclosed, the FDA will consider the steps taken to minimize any bias that could impact the reliability of the study. The regulations specify that certain study design techniques, such as use of a sufficient number of investigators without any financial interest, may adequately protect against any bias created by a disclosed financial interest.\textsuperscript{110} However, if the FDA determines that a serious question regarding the integrity of the data exists, the FDA can take the steps it deems necessary to ensure reliability of the data, such as initiating an audit of the study, requesting further analysis of the data, requiring additional studies to confirm the results, or rejecting the data as support for FDA approval of the drug or device at issue.\textsuperscript{111} Thus, FDA enforcement of the Objectivity Regulations also appears more stringent.

C. The Inadequacies of the Current Safeguards

As explained in Part II, multiple conflicts of interest arise in today's entrepreneurial research environment, including conflicts affecting IRBs, the institutions, and the researchers. The basic rules regarding IRB composition temper only conflicts that may impair the IRB review process itself. The regulations state that IRB members with a conflicting interest cannot participate in the approval of a research project that may affect that interest. However, the regulations provide neither guidance regarding when an interest should be considered sufficient to create a conflict requiring recusal, nor guidance for implementing or enforcing the requirement. Rather, the agencies have elected to trust that IRB members will know when it is appropriate to remove themselves, and will do so. Further, the requirement of one IRB member with no affiliation with the institution is likely insufficient to counter the tensions faced by the other IRB members who are affiliated with the university and thus who likely feel some obligation to approve research projects to help the institution. Thus, the basic regulations do little to ensure the independence of IRBs from the pressures of the institution. Moreover, they do not require disclosure to human research participants.

\textsuperscript{109} See infra notes 114–15 and accompanying text for a discussion of the exemption of SBIR entities.

\textsuperscript{110} 21 C.F.R. § 54.5(b) (2002).

\textsuperscript{111} Id. § 54.5(c).
The Objectivity Regulations also contain several deficiencies. Most significantly, the regulations only require disclosure of financial interests of the investigators. They do not address financial interests of the university. Additionally, the regulations use terms that are not only ambiguous, but that suggest disclosure and management are necessary only if the financial interests and their potential effect on research reach a fairly high threshold. Under the PHS regulations, investigators need only disclose "significant" financial interests, and conflict-of-interest management is necessary only if the interest is deemed to affect research "directly and significantly." The FDA regulations use the terms "significant equity interest" and "significant payments of other sorts."

A related deficiency of the PHS regulations is the exemption for ownership interests in SBIR applicant institutions. An SBIR applicant institution is one that participates in the Small Business Innovation Research Program. The SBIR program is the PHS extramural research program for small businesses. Yet, the emerging financial arrangements often include SBIR-qualifying small businesses, some of which faculty members own and operate. Thus, the exemption encompasses interests that would seem to pose very significant financial conflicts. Although the FDA regulations go further in some respects—for example, the FDA is involved in disclosure, assessment, and enforcement, and the FDA terms capture some interests arising from some arrangements no matter how de minimis—deficiencies still exist. Foremost, the requisite disclosure does not occur until application for FDA approval—and thus after researchers have performed studies involving human participants.

In addition, neither set of Objectivity Regulations provide any guidance regarding how to manage conflicts that have been identified. The PHS regulations simply state that institutions must assure that they will "manage,

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113. 21 C.F.R. § 54.2(b), (f) (2002).
114. See 42 C.F.R. § 50.603 (2001) (listing six exemptions from "significant financial interest[s]" including exemptions for ownership interests in SBIR applicant institutions).
115. Congress has expressly recognized that the expense associated with research and development is beyond the means of many small business concerns and that small businesses are handicapped in obtaining federal funds to support research. Accordingly, Congress established the policy of giving assistance to small businesses to enable them to undertake and obtain the benefits of research. 15 U.S.C. § 638(a) (2000). Pursuant to that policy, federal agencies must help small business concerns obtain government contracts for research and development. Id. § 638(b). Under the SBIR program, a portion of a federal agency's research monies must be reserved for award to small businesses. Id. § 638(e)(4). The qualifying criteria for a "small business concern" are set forth at 15 U.S.C. § 632.
reduce or eliminate" conflicts, but provide no guidance as to how much a conflict must be "reduced." 117 Similarly, the FDA regulations require the FDA to determine whether the interests raise a "serious question" regarding the integrity of the data, but fail to provide any further guidance. 118 Finally, neither set of regulations has expressly required any disclosure to research participants of financial interests that have the potential to influence objectivity.

Thus, although the Objectivity Regulations were a step in the right direction, additional federal safeguards and guidance arguably are necessary. The inadequacies of the conflict-of-interest regulations have been highlighted by the recent reports issued by the Office of Inspector General (OIG) of HHS, as well as by recent media reports questioning the financial interests of investigators and whether those interests may influence decisions made in the process of clinical trials. These reports have generated significant response.

IV. Emerging Initiatives Relevant to Financial Conflicts of Interest

The response to the OIG reports and media attention has been swift and fairly voluminous. First, the OIG itself made several recommendations, relating mostly to conflicts in the IRB process. The HHS quickly followed with a series of initiatives relating to financial conflicts of interest. The private sector has also responded, perhaps hoping to head off a stronger federal role by invigorating the self-regulatory process. These initiatives are a step in the right direction, but have been insufficient to provide the comprehensiveness and uniformity essential to protect human research participants and to preserve the public trust in the research endeavor.

A. Federal Regulatory Initiatives

1. The Recommendations of the Office of Inspector General: Help IRBs Do Their Job

In June 1998, the Office of Inspector General extensively studied the role of IRBs in protecting human research participants and reported that, although widespread abuses were not found, the IRB system for protecting human research participants has numerous vulnerabilities that threaten its effectiveness. The OIG was especially concerned with rising pressures stemming from the increased commercialization of research and the shift to managed care. The OIG found that IRBs review "too much, too quickly, with too little

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118. 21 C.F.R. § 54.5(c) (2002).
expertise," conduct minimal continuing review of approved research, provide little training for investigators and board members, and devote scant attention to evaluating IRB effectiveness.

Additionally, the OIG found that IRBs face serious conflicts of interest, specifically conflicts resulting from financial interests held by the institution. The OIG recognized the importance to institutions of research-related revenue and prestige and the resulting impact on the IRB process. The report noted that "[t]he institutions expect IRBs to support these interests at the same time that they protect human participants. The resulting tension can lessen the IRBs' focus on their basic mission. The minimal 'outside' representation that typically exists on IRBs deprives them of an important counterbalance to the institutional interests." As noted, the current regulatory framework does little to ensure the independence of IRBs from the pressures of the institution. Accordingly, the OIG made several recommendations. Because the focus of the OIG study was on the IRB process, the OIG recommendations relevant to conflicts of interest address the concern arising from conflicts affecting the IRB itself and the IRB approval and oversight process.

First, the OIG made two recommendations regarding explicit federal IRB criteria. The OIG recommended that federal agencies explicitly require greater representation on IRBs of nonscientific and noninstitutional members in order to ensure that their voices and concerns will carry weight in the review process. Additionally, because the OIG found that most institutions did not have a formal policy regarding an IRB member with a financial conflict of interest, the OIG recommended that the regulations be strengthened to prohibit explicitly IRB members with equity interests related to proposed research from participating in the IRB process relating to that research.

Second, in line with the regulatory model used by the agency—the scheme of leaving oversight and enforcement with the institutions—the OIG

119. The OIG pointed to expanded workloads, resource constraints, a rushed atmosphere in which sufficient deliberation is often not possible, and insufficient access to scientific expertise needed to reach informed judgments. A Time for Reform, supra note 10, at ii.
120. The OIG noted that IRBs have little time for continuing reviews other than superficial reviews of annual reports, adverse-event reports, and protocol amendments. IRB's Role, supra note 1, at ii. Further, the OIG noted that IRBs rarely visit the research site to determine how the informed consent process works or to review research protocol. Id.
121. The OIG noted that IRBs judge their effectiveness based mainly on the number of protection lapses or complaints that are brought to their attention. A Time for Reform, supra note 10, at iii.
122. Id. at ii.
123. Id.
124. Id. at 17–18.
125. Id. at 18.
urged the agencies to reinforce to universities with IRBs the importance of ensuring that IRBs have sufficient independence. This recommendation is premised on the theory that institutions will modify their policies in light of concerns expressed by the funding agencies. More specifically, the OIG recommended that IRBs be shielded from pressures to approve protocols by ensuring that IRBs do not report directly to that part of the institution responsible for bringing in research funds, that members are not compensated based on the outcome of the review, and that recourse is available should the IRB feel subject to any institutional pressure. If implemented, these practices would provide a welcome level of independence for the IRB.

The OIG reports created a sense of urgency regarding the need to improve protections for human participants participating in research studies. The federal agencies responded in several ways. First, the OIG noted in a June 2000 report that the OHRP and the FDA had stepped up their enforcement activities. Between April 1997 and May 1998, on-site presence at research institutions significantly increased. Further, since June 1998, OHRP has conducted off-site investigations (document reviews) at more than 140 institutions and has required seven of them to suspend some or all of their federally funded research. The OIG has noted that the temporary suspension of research had a "strong sentinel effect," causing many institutions to reassess their policies and procedures. More significantly, however, HHS responded with a number of initiatives of its own.

2. The HHS Initiatives

On May 23, 2000, HHS Secretary Donna Shalala announced several new initiatives to further strengthen protections for human research participants in

126. Id.
127. Id.
129. The report notes:

Between April 1997 and May 1998, the OHRP had conducted an on-site investigation at only 1 institution. Between June 1998 and March 2000, it conducted on-site investigations at 10 institutions. FDA's number of routine on-site investigations of IRBs increased from 213 in fiscal year 1997, to 253 in fiscal year 1998, and 336 in fiscal year 1999.

Id. at 9–10.
130. Id.
131. Id. at 10 (noting that many major medical journals and newspapers gave prominent attention to OHRP's enforcement actions).
PROPOSALS FOR A MORE EFFECTIVE REGULATORY SCHEME

clinical trials. Importantly, the Secretary's initiatives would go further than the OIG recommendations and address conflicts of interest held by the universities and the researchers themselves. In announcing its initiatives, HHS publicly acknowledged the legitimacy of the concerns raised by the media regarding the conflicting interests of institutions and of individual researchers.

To address these concerns, HHS made two moves. First, the Secretary elevated the status of OHRP by relocating it from NIH to the Office of the Secretary. Second, HHS announced that it would issue additional guidance to clarify the Objectivity Regulations and, further, that it would develop new policies for the broader biomedical research community that would require, for example, "that any researcher's financial interests in a clinical trial be dis-

132. The initiatives, which are designed to heighten government oversight of biomedical research and to reinforce to research institutions their responsibility to oversee their clinical researchers and IRBs, include:

(1) Education and Training. HHS will take steps to require that clinical investigators, IRB members, and associated IRB and institutional staff undergo continuing education in issues relating to human participants. Training will be a requirement of all clinical investigators receiving NIH funds and will be a condition of the NIH grant award process and of the OHRP assurance process.

(2) Informed Consent. NIH and FDA will issue specific guidance on informed consent, clarifying that research institutions and sponsors are expected to audit reports for evidence of compliance with informed consent requirements. Further, for particularly risky clinical trials, IRBs will be expected to take additional measures, such as third-party observation of the process.

(3) Improved Monitoring. NIH will require clinical trial monitoring plans for smaller-scale early clinical trials (Phase I and Phase II) and will expect investigators to share the plans with IRBs. Additionally, FDA will issue guidelines for Data and Safety Monitoring Boards (DSMBs), detailing when they should be required, when they should be independent, their responsibilities, and other issues.

(4) Civil Monetary Penalties. HHS will pursue legislation to enable FDA to levy intermediate sanctions, namely, civil monetary penalties—up to $250,000 per clinical investigator and up to $1 million per research institution—for violations of informed consent and other important research practices. See Press Release, Shalala Bolsters Protections, supra note 40 (summarizing HHS initiatives).

133. Secretary Shalala noted that "the explosion in biomedical research has also brought new challenges, as more researchers are becoming involved in commercial ventures that may create new ethical dilemmas." Id.

134. At the same time that the Secretary of HHS was calling attention to the need to strengthen protections for human research participants, some members of Congress were also ready to respond. In June 2000, the "Human Research Subject Protections Act of 2000" was introduced in the House of Representatives. The legislation stalled and has not been addressed recently.

135. The effective date for the reorganization of the OHRP was June 18, 2000. 65 Fed. Reg. 37, 136 (June 13, 2000).
closed to potential participants.136 Thus, the Secretary explicitly recognized the inadequacy of the current informed consent regulations and, more generally, that the Objectivity Regulations can and should be strengthened.

However, the Secretary was careful to appease constituencies. First, HHS signaled that it continued to believe that the primary regulatory responsibility should lie with the institutions. In the announcement, Secretary Shalala stressed the responsibilities of the leaders of universities and academic medical centers in safeguarding the integrity of the research process. Secretary Shalala stated:

I want to urge university presidents, leaders of our academic medical centers, and others involved in biomedical research to take a hard look at oversight of clinical trials, their partnerships with the private sector, their own ethical guidelines, and the support and guidance they give their IRBs.137

Because the current regulatory model allows each university to formulate and implement its own policies and procedures, within the parameters set by federal regulations, institutions can do more even without agency action to address the identified deficiencies.

Second, HHS sought institutional input in developing the more stringent policies. HHS promised to undertake an extensive "public consultation" to identify new or improved means to manage financial conflicts of interest that could threaten the safety of research participants or the objectivity of the research. To that end, HHS held a conference August 15–16, 2000, primarily to discuss current approaches being taken for dealing with real and potential financial conflicts of interest at the institutional, IRB, and clinical investigator level.138 HHS presented a number of issues relating to conflicting financial interests and established a period for public comment that was extended to September 30, 2000. The following subsection reveals the tenor of the comments presented at the Conference.

a. The Conference on Financial Conflicts of Interest: August 2000

The Conference on Human Subject Protection and Financial Conflicts of Interest was held at the National Institutes of Health in Bethesda, Maryland, on August 15–16, 2000. At the Conference, the various perspectives of the following groups were presented: the NIH and FDA, the biomedical academic

137. Id.
community, the biomedical industry, proponents of greater regulation, and persons who recognize the concerns arising from financial conflicts, but who question the prudence of greater federal regulation.\textsuperscript{139} Interestingly, the overriding message delivered via the Conference was twofold: (1) financial conflicts of interest are a very serious problem that must be addressed, but (2) any initiatives must continue the practice of self-regulation to allow for diversity in policies and procedures and flexibility in selecting case-by-case management strategies. The proposals offered in this Article are starkly contradictory to the latter message of the Conference.

Most Conference participants expressed the view that further federal guidance on financial conflicts of interest would be appropriate and welcomed. However, several speakers noted that the federal government should continue its approach of entrusting institutions with the tasks of formulating policies and procedures and of providing oversight and enforcement.\textsuperscript{140} It was stressed that federal guidance should be flexible and should establish only minimum standards, thereby allowing individual institutions to devise a process consistent with unique university cultures and resource constraints. The importance of the latter was underscored by the uniform recognition that identifying and managing financial conflicts of interest is an extraordinarily labor- and resource-intensive endeavor.

Despite the general view that oversight and enforcement should remain the responsibility of the institutions, participants recognized that leaving these tasks to the institutions is not a perfect solution given the increasing existence of conflicting financial interests held by the institution. However, participants could not envision any effective alternative.

At the Conference, several academic institutions explained the policies and procedures that they had put in place to monitor and manage conflicting financial interests. Although the procedures varied considerably, all included the following key elements:

1. Disclosure of some or all financial interests held by investigators and the university;
2. Review for the purpose of identifying and assessing the nature of conflicts; and
3. Management of any conflicts, involving some disclosure through informed consent plus additional measures when appropriate.

\textsuperscript{139} August 15 Conference Transcript, \textit{supra} note 27 (statement of Dr. Stuart Nightingale).

\textsuperscript{140} The paragraphs in the text represent the author's summary of the many and varied comments and views expressed at the Conference. Transcripts from the two-day Conference are available at http://ohrp.osphps.dHHS.gov/coi/ntu.
Some recognized disclosure to and review by a person or entity charged with identifying financial conflicts as the crux of any procedure designed to address the problem of conflicts of interest. As aptly noted by the Acting Director of NIH in discussing the risks posed by financial conflicts, "[Disclosure] is at the heart of the matter . . . . It takes more than one person, especially one interested person, to decide on the innocence of a transaction."  

The institutions also all agreed that a variety of management tools should be available to temper the effect of a financial conflict. All agreed that disclosure was appropriate in every case, although variations regarding the form of and forum for the disclosure existed. Suggested forums included the informed consent process, the IRB review process, and public records. Further, all agreed that strategies in addition to disclosure would likely be necessary in many cases. Common management tools beyond disclosure include the following: placement of an equity interest or stock into escrow, limitation of the role of the individual with the conflict, greater oversight of the research study, and divestiture of the interest or outright prohibition of the arrangement.

Conference participants generally recognized that determining when and how to use these management tools will be a difficult task involving the consideration of a multitude of factors. For example, whether an institution can manage a conflict through greater oversight of the study will depend on the complexity of the study and the resources available to the institution. Whether a conflict can be managed by limiting the role of the researcher with the interest will depend on the extent to which the researcher's technical knowledge is essential to the conduct of the study. Accordingly, participants recognized that the determination of how to manage conflicts should be made on a case-by-case basis.

Lastly, because of the complexity of the endeavor, participants recognized that institutions should affirmatively share information about their policies and procedures and about their experiences in implementing them. The academic community collectively could then develop workable models for conflict identification and management.

b. The HHS-OHRP Draft Interim Guidance: January 2001

Following the August 2000 Conference, the HHS Office of Human Research Protection (OHRP) issued a "Draft Interim Guidance" relating to the issue of financial conflicts of interest. Notably, OHRP recognized that institutions should affirmatively share information about their policies and procedures and about their experiences in implementing them. The academic community collectively could then develop workable models for conflict identification and management.

141. August 15 Conference Transcript, supra note 27 (statement of Dr. Ruth Kirschstein).
"there are as yet 'no best practices,' and that there is little consensus on what is 'right' and what is 'wrong' at this time." Further, OHRP reiterated that the Guidance would not replace or modify any current HHS regulations, policies, or guidance covering financial conflicts of interest. However, OHRP decided it was important to offer assistance to institutions, researchers, and IRBs and to stimulate further development of policies and approaches in the area.

Much of the OHRP Guidance is unremarkable. Indeed, it begins with what is largely a recitation of the PHS objectivity regulations. First, the Guidance adopts the PHS's narrow view of the concept of "conflict of interest." Under that view, a conflict of interest exists only when a two prong test is satisfied: when a designated institutional official(s) reasonably determines that (1) a "significant financial interest" exits and (2) that interest could "directly and significantly affect the design, conduct, or reporting of PHS-funded research." The Guidance does not expressly define "significant financial interest," but presumably the drafters of the Guidance intended to incorporate the PHS regulation definition. Under the PHS regulations, a significant financial interest includes (1) salary and other payments for services that exceed $10,000 over twelve months, (2) equity interests exceeding $10,000 or representing more than a five-percent ownership interest in any single entity, and (3) all intellectual property rights.

Second, like the PHS objectivity regulations, the Guidance arguably continues to allow researchers themselves to apply the first prong in determining whether a particular financial interest falls within the category of significant financial interests and thereby must be disclosed. The Guidance notes that the institutional policies should be clear regarding who determines whether a "significant" financial conflict of interest exists. However, given the definition, this recommendation suggests only that the policy should be clear regarding the second prong of the test—namely, who determines whether a disclosed significant financial interest "could directly and significantly affect [research] design, conduct or reporting."

The Guidance goes further than the PHS regulations in two ways. First, it suggests that institutions consider extending the disclosure requirements to

143.  Id. § 1.
144.  Id. § 2.
145.  Id. § 1.
146.  Id. § 1.1.
148.  See supra notes 94–96 and accompanying text (reviewing PHS definitions of "financial interest").
149.  OHRP Guidance, supra note 142, § 1.1.
150.  Id.
researchers conducting studies of FDA-regulated articles, expanding the category of who must comply with the FDA objectivity regulations that require disclosure at the time of application for FDA approval. Second, the Guidance goes further than the PHS objectivity regulations by implying that a "financial relationship of any kind" between a clinical investigator and a commercial sponsor may create a conflict of interest. In addition to the disclosures of "salary or other payments for services" and "equity interests" that create a significant financial interest, the Guidance states that the conflicts of Interest Committee should review "any agreements between investigators and a sponsor" (other than a federal funding agency), including commitments for financial support unrelated to the study in question.

The Guidance also offers structural recommendations. As to both individual researcher and institutional conflicts, HHS suggests that institutions establish independent "conflicts of interest committees" to determine whether financial arrangements pose conflicts and, if so, how the conflicts should be managed. The Guidance also envisions a strong role for IRBs in dealing with institutional and individual conflicts. Specifically, the Guidance notes that "the IRB should review the Institution's financial relationship to the Sponsor and determine whether the trial should be permitted to be carried out at the Institution." Moreover, as to clinical investigators, the Guidance suggests that IRBs should repeat the scrutiny conducted by the "designated institutional officer.

The Guidance includes several suggestions regarding institutional structuring of IRB activity. HHS stresses that institutions should ensure that the composition of IRBs is such that IRBs can act autonomously, free from institutional pressures. Specifically, HHS emphasizes "broad participation of members from outside the institution, who will have no interest in the outcome of

151.  Id. § 1.2.
152.  Id. § 2.1.
153.  Id. §§ 2.1–2.2. Other relationships described in the Guidance include receiving financial incentives, serving as a paid consultant or speaker on behalf of a commercial sponsor, and accepting nonmonetary inducements or rewards to investigators or their family members. Id. § 2.1.
154.  Id. § 1.7.
155.  Id. § 4.1.
156.  Id. § 4.3. The Guidance states:

[The IRB] should consider all the elements that a designated Institutional Official would need to consider under the PHS policies, requirements, guidelines and guidance as well as FDA Financial Disclosure requirements that are the basis for submissions to sponsors and then to FDA, and then decide if the protocols and Consent documents should be modified accordingly.

Id.
the research or the business interests of the institution.\textsuperscript{157} HHS also suggests a greater institutional role in monitoring IRB members' potential conflicts of interest and in educating IRBs and researchers on the issue of financial conflicts of interest.\textsuperscript{158}

In addition to these fairly unremarkable suggestions, the HHS includes in the Guidance two more striking, prohibitory statements. First, the Guidance broadly states that "if there are any financial conflict-of-interest issues on the part of the Clinical Investigator, he or she should not be directly engaged in aspects of the trial that could be influenced appropriately by that conflict."\textsuperscript{159} The breadth of this prohibitory statement is affected by the decision to adopt the PHS's relatively narrow definition of financial conflict of interest, but to include financial relationships of any kind with commercial sponsors as a potential conflict. Moreover, the ambiguity of the statement mitigates its force. It is not clear what constitutes a financial conflict-of-interest "issue," thereby triggering the prohibition on involvement in research.

Second, the Guidance includes prohibitory language relating to institutional conflicts that is also remarkable, albeit less strongly stated. The Guidance suggests that institutions with a financial interest in the outcome of a research project should "carefully consider whether a clinical trial to evaluate safety and efficacy should be performed at that site, and if it should, what special protections would be needed."\textsuperscript{160} The Guidance notes that the integrity of the research and thus of the institution

may be best protected by having the clinical trial performed and evaluated by independent investigators at sites that do not have a financial stake in the outcome of the trial, or carried out at the institution but with special safeguards to maximally protect the scientific integrity of the study and the research participants.\textsuperscript{161}

B. Private "Self-Regulatory" Initiatives

As stated above, the representatives from the academic institutions strongly opined at the August Conference that, although federal guidance would be welcomed, the government should continue its approach of entrusting institutions with the ultimate task of formulating policies and procedures and of providing oversight and guidance. They also stressed that federal guidance should establish only minimal standards, thereby allowing individual institu-

\begin{itemize}
\item 157. \textit{Id.} § 1.3.
\item 158. \textit{Id.} §§ 1.4–1.5.
\item 159. \textit{Id.} § 4.4.
\item 160. \textit{Id.} § 1.6.
\item 161. \textit{Id.}
\end{itemize}
tions to devise a process consistent with unique university culture and resource constraints. However, given the complexity of the endeavor, the academic institutions suggested that they collectively could develop workable models for conflict identification and management. The academic community has made some progress toward that goal. First, a group of leading medical schools agreed on guidelines pertaining to financial conflicts of interest policies. Second, a leading academic organization, the Association of American Medical Schools, has issued guidelines and policies addressing individual financial interests and is drafting guidelines and policies addressing institutional financial interests.

1. Guidance by Premier Medical Schools: January 2001

In early 2001, the leaders of eight of the nation’s top ten NIH-funded medical schools and another six nationally prominent leaders in academic medicine issued a set of guidelines intended to "clarify, strengthen, and add structure" to financial conflicts of interest policies of research institutions. More specifically, the leaders intended the proposals to guide individual institutions as they revamped their own conflict-of-interest policies and procedures relating to conflicts of researchers, as opposed to institutional conflicts. The guidelines are a combination of a few specific recommendations and a number of ideals or guiding principles. The following is a summary of the most meaningful guidelines on policy issues.

Policies should do the following:

1. Apply to persons directly involved in the conduct, design, or review of research.
2. Prohibit involvement in the conduct, design, or reporting of research involving human participants by persons having more than a clearly defined minimal personal financial interest in a company that sponsors the research or owns the technology being studied.
3. Define financial interests clearly and broadly to include any form of remuneration or special relationships having the potential for personal material gain.
4. Clearly delineate the activities and levels and kinds of financial interests that are and are not permissible and/or that require review and approval.

(5) Require all individuals who participate in research (of any kind) to periodically and prospectively disclose all related financial interests to specifically designated institutional offices and to the research funder.

(6) Require all individuals who participate in clinical research to disclose related financial interests to IRBs.

(7) Require disclosure to multiple levels within institutions, such as the Dean (or equivalent individual) and department chairs.

(8) Establish an advisory policy oversight committee (such as a conflicts of interest committee), with broad representation of faculty, administrative staff, and possibly lay representatives, that is charged with providing oversight of the policies, reviewing individual cases involving conflicts, and recommending monitoring procedures (final authority for monitoring should be the responsibility of the Dean or equivalent individual).

(9) Impose on IRBs the responsibility for ensuring, as the IRBs determine appropriate, that patients are informed of financial relationships.

(10) Include an explicit policy on disclosure to outside entities.

(11) Require disclosure by all individuals of all related financial interests in any publications or presentations.

(12) Clearly state procedures for disclosure, review, sanctioning, and the like.

(13) Ensure coordination amongst offices of the institution dealing with research and conflicts of interest, including IRBs, offices of technology transfer, and the like.

(14) Ensure overall institutional compliance through monitoring by the institution's internal audit mechanisms.  

Although the guidelines issued by the premier medical schools (PMS Guidelines) lack specificity, they are nonetheless meaningful. Foremost, the guidelines recognize that any financial interest may be problematic. The guidelines therefore recommend mandatory disclosure of "all related financial interests" by all who participate in research of any kind and recommend a definition of financial interests that broadly encompasses "any form of remu-

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neration or special relationships"—even those having only the "potential" for material gain. The recommendations thus appear to allow an institutional representative, rather than the researchers themselves, to decide whether a conflict of interest exists. Moreover, like the OHRP Guidance, the PMS Guidelines take the position that prohibiting involvement in research may be the best regulatory safeguard when a researcher has more than a "clearly defined minimal personal financial interest." The PMS Guidelines are weakened by their continued reliance on traditional academic culture—namely the notion that each institution must be free to develop its own specific conflict-of-interest policies—even as to identifying which financial interests create conflicts of interest. The PMS Guidelines leave crucial decisions in the hands of individual institutions, including the specific definition of financial interests that must be disclosed and the specific delineation of activities and levels and kinds of financial interests that warrant prohibition, rather than mere management. Similarly, the PMS Guidelines suggest that compliance and enforcement can be effectively monitored "by the institution's internal audit mechanisms." The PMS Guidelines contain no suggestion of greater enforcement or monitoring by persons or entities external from the institution.

2. Guidance by the Association of American Medical Colleges: December 2001

In October 2000, the President of the Association of American Medical Colleges (AAMC) established a Task Force to respond to the growing public concern over financial conflicts of interest in the academic research community. The Task Force represented a broad range of interests: the Task Force was comprised of not only leaders of academic medicine, but also prominent clinical researchers, patient representatives, former legislators, drug and device company executives, and journalists. Similar to the product of the academic community leaders, the product of the Task Force was intended to serve as a

164. Id.
165. Id.
166. Id.
167. Id.
168. Id.
170. Id.
"model for baseline standards and practices," thereby allowing individual institutions to implement policies consistent with their unique cultural and self-governance practices. The initial product of the Task Force dealt only with financial interests of individual researchers and administrators. In contrast to the sketchy principles outlined by the leaders of the premier medical schools, the guidelines issued by the Task Force (AAMC Guidelines) are more comprehensive and provide greater substantive guidance through both general and specific recommendations.

The AAMC Guidelines provide the most specific recommendations regarding three practices that it found should be prohibited. The AAMC Guidelines provide that medical school policy should prohibit the following:

1. Payments from the institution or the sponsor to a researcher that are conditioned upon a particular research result or are tied to successful research outcomes;

2. Agreements that permit a sponsor or other financially interested company to require more than a reasonable period of prepublication review or that interfere with an investigator's access to the data or ability to analyze the data; and

3. Agreements that permit a sponsor or other financially interested company to place restrictions on the activities of students or trainees or that bind students or trainees to non-disclosure provisions.

The Task Force likely believed it could be specific regarding these prohibitions because they involve practices on which it may be fair to say that consensus exists. As to the remainder of the recommendations, it is probably fair to say that a consensus has not emerged.

171. Id.
173. AAMC Guidelines, supra note 169, at 19–20. However, the AAMC Guidelines do not present this as an absolute prohibition. "When deemed unavoidable, such agreements should be subjected to close scrutiny ...." Id. at 20. The AAMC Guidelines further note that "[u]nder no circumstance should a student or trainee be permitted to participate in research if the terms and conditions of participation would prevent him or her from meeting applicable institutional degree requirements." Id.
174. Indeed, one member of the Task Force declined to endorse the AAMC Guidelines due to her concern that the recommendations therein would present a serious impediment to research
One key difference between the AAMC Guidelines and the principles articulated by the leaders of the premier medical schools is the Task Force's decision not to recommend an absolute prohibition on involvement in research when an impermissible conflict of interest is found to exist. Instead, the AAMC Guidelines suggest the use of a "rebuttable presumption." At first blush, the presumption appears very rigorous. The AAMC Guidelines suggest that institutions establish a "rebuttable presumption that an individual who holds a significant financial interest in research involving human participants—whether funded by a public agency, a non-profit entity, or a commercial sponsor, and wherever the research may be carried out—may not conduct such research." Closer scrutiny, however, reveals a fairly low level of rigor.

The AAMC Guidelines start from the premise that "significant financial interests" are only "potentially problematic." That is, a conflict of interest does not arise upon the existence of "any" conflicting financial interest, but rather only in those cases in which the financial interest is "significant" (as that term is narrowly defined below). Moreover, the AAMC Guidelines suggest that even a significant financial interest creates only the "perception of a conflict of interest." The Task Force acknowledged in the AAMC Guidelines that "opportunities to profit from research may affect—or appear to affect—a researcher's judgments...[and that] financial interests...threaten scientific integrity when they foster real or apparent biases" in the research process. However, that is as close as the Task Force came to characterizing the presence of "any" financial interest as an "actual" conflict.

Another limitation on the rigor of the standard relates to the definition of "significant financial interest." According to the Task Force, a significant financial interest includes the following:

(1) Consulting fees, honoraria, gifts, or other emoluments, or in-kind compensation from an entity with financial interests that would reasonably appear to be affected by the conduct or outcome of the research (i.e., a "financially interested company")—but only to the extent the aggregate amount thereof exceeds $10,000.
(2) Equity interests in a publicly-traded financially interested company (or entitlements to the same, including stock or stock options) — but only to the extent that they exceed $10,000 in value or represent more than a five percent ownership interest (and excluding interests in publicly-traded, diversified mutual funds);\(^{181}\)

(3) Equity interests (including stock options) of \textit{any amount} in a non-publicly traded financially interested company,\(^{182}\)

(4) \textit{Any} royalty income or the right to receive future royalties under a patent, license, or copyright;\(^ {183}\)

(5) \textit{Any} payments (or entitlements thereto) in connection with the research that are \textit{not} directly related to the reasonable costs of the research, including any bonus or milestone payments in excess of reasonable costs incurred (and thus excluding payment for reasonable costs incurred or salary and other payment for services from the institution);\(^ {184}\) and

(6) Serving as officer or director for a financially interested company, regardless of compensation.\(^ {185}\)

The Task Force elected to track the current PHS regulations as to the magnitude of certain financial interests that should be deemed significant. However, the AAMC Guidelines are more specific than the PHS regulations in that they make finer distinctions among equity interests and, importantly, characterize some equity interests as significant regardless of the monetary amount involved. Further, they designate some additional financial interests as problematic, for example, receiving any payments not related to reasonable costs and serving as an officer or director. Thus, the AAMC Guidelines extend beyond the current regulations.

A more troublesome limitation on the rigor of the AAMC Guidelines relates to use of the rebuttable presumption against involvement in research. The AAMC Guidelines suggest that institutions allow a researcher to override the presumption in "compelling circumstances."\(^ {186}\) However, it does not

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181. \textit{See id.} (same).
182. \textit{See id.} (same).
183. \textit{See id.} (same).
184. \textit{See id.} (same).
185. \textit{See id.} (same).
186. \textit{Id.} at 7.
appear that it would be very difficult to show that circumstances are compelling. The Guidelines suggest that whether circumstances should be deemed compelling should depend on "the nature of the research, the magnitude of the interest . . . the degree to which it is related to the research, [and] the degree to which the interest [may be] affected by the research." Yet the guidelines also explain that even "direct" and "lucrative" financial interests may be justified when, for example, "the individual holding such interests is uniquely qualified by virtue of expertise and experience and the research could not otherwise be conducted as safely or effectively without that individual." Given the type of research and innovation frequently involved when potentially lucrative financial interests are at stake, it would seem that researchers could often make a showing of compelling circumstances to a conflicts of interest (COI) committee: often it is the researcher with the financial interest who also has the expertise necessary to conduct the research most "effectively." The AAMC Guidelines attempt to temper this apparent loophole by stating that the COI committee might approve the involvement of a researcher with a significant financial interest by imposing "conditions that ensure effective management and credible oversight of the research." The AAMC Guidelines offer nothing new in the area of oversight and management. They state the obvious: if a financially interested researcher is allowed to conduct research involving human participants, the interests and research "must be managed through rigorous, effective and disinterested monitoring undertaken by individuals with no financial or professional ties to the research or direct reporting relationships to the researchers." But the examples that the AAMC provides—such as regular audits of the informed consent and enrollment process, the involvement of patient representatives during recruitment and consent, escrow of the financial interest, and use of data safety monitoring boards—have well-recognized shortcomings.

187. Id. at 10–11. In the definitions section, the AAMC Guidelines state that "compelling circumstances are those facts that convince the institution's COI committee that a financially interested individual should be permitted to conduct human participants research." Id. In addition to those listed in the text, the AAMC Guidelines suggest that other factors to consider are the degree of risk to the human participants involved that is inherent in the research protocol and "the extent to which the interest is amenable to effective oversight and management." Id. at 11.

188. Id. at 7.

189. Id. at 8.

190. Id. at 9.

191. Id.

192. See, e.g., infra text accompanying notes 353–54 (explaining shortcomings of Data Safety Monitoring Boards).
Further, the AAMC Guidelines suggest that the oversight and monitoring might be performed solely by institutional representatives. 193

Just as importantly, the AAMC Guidelines recommend the practice of allowing the individual researchers themselves to determine whether a significant financial interest exists. The guidelines state that "[i]nstitutional policies should require full, prior reporting of each covered individual's significant financial interests that would reasonably appear to be affected by the individual's research." 194 The guidelines define "reporting" as the "provision of information about significant financial interests . . . to responsible institutional officials and to the institutional COI committee." 195 Given the more refined and inclusive definition of "significant financial interests," less discretion lies with the individual researcher in making the determination of what to report. The AAMC Guidelines go on to recommend updated reporting. 196 In addition, the AAMC Guidelines state that "[p]rior to executing a technology licensing agreement, the Office of Technology Licensing must determine whether the agreement would create a significant individual financial interest . . . , and if so, inform the institution's COI committee of the proposed terms of the agreement." 197 Thus, the AAMC Guidelines provide at least one independent check on the discretion accorded to individual researchers to disclose financial interests that should be characterized as "significant."

The AAMC Guidelines also continue to recommend the involvement of the IRB in the process of evaluation and management of financial conflicts of interest. The guidelines state that the COI committee findings and determinations about significant financial conflicts of interests should "inform the IRB's review of any research protocol or proposal." 198 The AAMC Guidelines also suggest that IRBs be allowed a type of veto power by empowering them to "require additional safeguards or demand reduction or elimination of the financial interest." 199 The guidelines suggest, however, that, between the

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193. AAMC Guidelines, supra note 169, at 9. The AAMC Guidelines suggest that participation of individuals from outside the institution might only become necessary when the institution itself holds a financial interest. Id. The shortcoming of monitoring as a risk management technique is discussed infra subsection V.C.3.b.

194. Id. at 8.

195. Id. at 12. Reporting also includes "transmission of such information within institutional channels (e.g., from the COI committee to the IRB)." Id. in the section on "process," the AAMC Guidelines state that institutions "should require covered individuals to report to the institution all significant financial interests that would reasonably appear to be affected by the individual’s current or anticipated human participants research." Id. at 17.

196. Id. at 8.

197. Id. at 17–18.

198. Id. at 8.

199. Id.
findings of the IRB and the COI committee, the "more stringent determination should be dispositive," and they recommend that institutional policies clearly designate which institutional officials or committees have the power to make final and binding decisions.\textsuperscript{200}

The AAMC Guidelines also require additional disclosures of the existence of significant financial interests. First, the guidelines recommend requiring disclosure to patients in informed consent forms, but leaving the precise wording of the disclosure to the IRB.\textsuperscript{201} Second, the guidelines recommend disclosure to research funders or sponsors, to editors of any publications to which manuscripts relating to the research are submitted, and in any substantive oral or written public communication of the research results.\textsuperscript{202}

\textbf{C. Reprise of Key Deficiencies in the Recent Initiatives}

A number of specific deficiencies exist in the approaches outlined by the OHRP and representatives of the academic community, and those deficiencies were highlighted in the foregoing discussion. Two are most troublesome. First, the recent initiatives fail to outline a means of accurately or sufficiently identifying conflicts of interest that should warrant a regulatory response. Second, the initiatives lack a clear signal as to the most appropriate regulatory response when a problematic interest is identified. The initiatives suggest that researchers with significant financial interests should not conduct research involving human participants. But the guidance also suggests that IRBs and conflicts of interest committees, or deans or department heads, may stop short of exclusion of a researcher and select other responses to reduce the effects of a conflict of interest.

Even more global deficiencies exist. These deficiencies stem from the adherence to the traditional culture of self-regulation in the academic and medical arenas. Each set of guidelines issued to date, even that of HHS issued through OHRP, has been presented as a "model" of recommended practices and standards, intended to allow individual institutions to implement policies consistent with unique cultural and self-governance practices and policies. The result is a wealth of ambiguities, inconsistencies, and variability in standards and regulatory responses. Moreover, there exists considerable overlap in the responsibilities of the designated institutional officer, the conflicts of interest committee, department heads, and IRBs.

\textsuperscript{200} Id.
\textsuperscript{201} Id. at 18.
\textsuperscript{202} Id.
Diagram B
Diagram of Common Financial Arrangements

Dr. Jones
UNIVERSITY
RESEARCHER

- Basic Research leading to new technology
- "Principal Investigator" for Research at University on the technology

$  

- Company funds part of research
- Company holds patents, royalties to University

$  

Separate Not-for-Profit Corporation (University Foundation)

UNIVERSITY

License for Technology without "fees"

$ Equity in Co.

Biotech Company – Small start-up for profit

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Separate For-Profit Corporation Research Center

Rents office space and support staff (when company is successful, will move to adjacent research park)

- Pres., CEO, major shareholders
  - Venture capitalist
  - Dr. Jones (or spouse)
- Senior Scientific Officer or consultant, etc.: i.e., Dr. Jones
The result is a recommendation for a complex, confusing, resource-intensive, yet potentially ineffective system. Even if the system actually reduced the chance that financial conflicts of interest would influence research, the recommendations would do little to promote the public trust in the research endeavor. As some have noted, perhaps the concerns arising from financial conflicts of interest cannot be entirely eliminated given the incentives created by the Bayh-Dole Act and other technology-transfer acts. But we can surely do a better job of limiting their negative consequences than the proposals outlined to date suggest.

V. Proposals for a More Effective Regulatory System

The recent suggested policies from the OHRP, the leaders of premier medical schools, and the AAMC are a move in the right direction. Each has advanced the discussion and resolution of the concern over the increasing presence of financial conflicts of interest in the arena of biomedical research involving human participants. However, more satisfactory and complete guidelines can be built—ones that draw on the strengths of the recommendations that have emerged thus far, but that also go further to minimize variability and overlapping responsibilities.

It is beyond the scope of this Article to flesh out all aspects of a regulatory system for financial conflicts of interest. Rather, this Part of the Article strives to advance the rulemaking and policy making process by clarifying and exploring in greater detail selected key issues relevant to regulating financial conflicts of interest and by highlighting a fundamental structural change that could greatly improve the process of addressing financial conflicts of interest. The key issues relate to the degree of federal control, the standards governing disclosure and management, the appropriateness of various regulatory responses, and oversight and enforcement responsibilities.

A. Deviate from the Traditional Model of Self-Regulation

The recent guidance from both the OHRP and the academic communities adhered to the traditional culture of self-regulation. Traditionally, both the medical and academic communities have been regulated largely through various models of "self-regulation." In the medical arena especially, various types of self-regulation exist. For example, state and local governments typically designate a board of appointed private citizens to certify entry into

and to restrict practice of the profession; these boards have relatively plenary authority to articulate standards and to police and enforce those standards.\textsuperscript{204} A less formal type of self-regulation is the voluntary adoption of codes of ethics by professional associations; such standards are aspirational, policing is informal, and sanctions are often limited to expulsion from the group.\textsuperscript{205} A more formal type is sometimes referred to as "audited self-regulation," wherein the federal government delegates power to a "self-regulatory organization" to implement rules, subject to review by a federal agency.\textsuperscript{206} Programs of audited self-regulation include use of Joint Commission accreditation as a condition for hospital participation in Medicare and Medicaid and use of various types of peer-review organizations to assess whether Medicare services are "reasonable and necessary." Although many reasons underlie the dominance of "self-regulation" in the health care community, it stems largely from the expertise involved in the practice of medicine and the deference courts and legislatures traditionally have accorded the exercise of medical judgment.

Similarly, regulation of institutions of higher education has largely followed the model of self-regulation. Historically, "[t]he federal government's major function regarding post-secondary education has been to establish national priorities and objectives for education spending and to provide funds in accordance with those decisions."\textsuperscript{207} Federal aid to post-secondary institutions is available only to institutions accredited by one of the accrediting bodies recognized by the Secretary of Education; therefore, the federal government could have been active in establishing the standards used by the accreditation bodies. Instead, the federal government opted for an audited self-regulatory approach. The standards used by the accreditation bodies have been formulated by the private accrediting organizations, subject to a limited oversight role of the federal government. Moreover, the focus of accreditation today is on whether an institution complies with its own standards and progresses toward its own goals. The result has been regulation that has continued higher education's long tradition of "diversity in and local control over academic programs."\textsuperscript{208} The decision to follow the self-regulatory model in


\textsuperscript{206} See Michael, \textit{supra} note 204, at 175 (defining self-regulation in traditional context).

\textsuperscript{207} WILLIAM A. KAPLAN, THE LAW OF HIGHER EDUCATION 511 (2d ed. 1985).

\textsuperscript{208} Michael, \textit{supra} note 204, at 229 (citing WILLIAM K. SELDON, ACCREDITATION: A STRUGGLE OVER STANDARDS IN HIGHER EDUCATION 17–20 (1960)).
higher education similarly stems from the perceived expertise needed in making academic decisions, the historical deference to local control over basic educational decisions, and the existence of expert and reliable accrediting organizations.209

Regulation of biomedical research involving human participants, including the regulations addressing financial conflicts of interest, has neatly continued the tradition of self-regulation. The PHS Objectivity Regulations provide some guidance as to the types of interests that should be disclosed and managed, but oversight and enforcement policies and procedures are left to the institution. Further, enforcement of the PHS regulations is part and parcel of the HHS assurance process. In each application for PHS funding, the institution need only certify that it has in place a written and enforced administrative process to identify and manage conflicting interests with respect to all research projects for which the institution seeks funding from the PHS.210 Additionally, the institution must certify that, prior to any expenditure of funds under the award, the institution will report the existence of any identified conflicting interest and will assure that the conflict will be managed, reduced, or eliminated.211 The regulations do not specify additional oversight, such as an OHRP check on whether an institution’s designated official(s) is properly identifying significant financial interests or even a review of an institution’s written policies and guidelines used in making the determination.

The FDA Objectivity Regulations deviate from the traditional model of self-regulation, but only to a limited extent. The FDA regulations specify that an applicant seeking FDA approval of a human drug, a biological product, or a medical device must submit, along with the application, a list naming all clinical investigators and identifying those investigators who are employees of the applicant.212 Additionally, for each nonemployee investigator, the applicant either must provide a certification that certain financial arrangements do not exist or, if they do exist, must disclose the nature of the financial arrangement and the steps taken to minimize any bias in the research process.213 The FDA reviews the disclosures during the course of the FDA

209. See id. at 229–30 (discussing move from standardization in higher education).
211. See id. § 50.604(g)(2) (describing institutional responsibilities).
213. See id. § 54.4 (furthering the discussion of certification and disclosure requirements). The FDA regulations define “clinical investigator” as meaning “a listed or identified investigator or subinvestigator who is directly involved in the treatment or evaluation of research participants . . . [as well as] the spouse and each dependent child of the investigator.” Id. § 54.2(d).
approval process. The regulations specify that the FDA may consider clinical studies inadequate or unreliable if appropriate steps have not been taken to minimize bias, including bias that may arise from an investigator's financial interest in the outcome of the research.\textsuperscript{214} Thus, the FDA regulations depart from the PHS model of leaving oversight and enforcement to the institution conducting the research or to the IRB: applicants must make disclosures to the FDA, and the FDA assesses their impact.\textsuperscript{215} However, neither the FDA nor the PHS regulations provide any guidance regarding how to manage conflicts that have been identified. The PHS regulations simply state that institutions must assure that they will manage, reduce or eliminate conflicts,\textsuperscript{216} but provide no guidance, for example, as to how much a conflict must be "reduced." Similarly, the FDA regulations provide that if certain financial conflicts exist, the applicant must take steps to minimize any bias—but do not direct how the institution should control the conflict.

Moreover, the recently issued guidance envisions continued self-regulation. Even the guidance of HHS, issued through OHRP, has been presented as a "model" of recommended practices and standards, intended to allow individual institutions to implement policies consistent with unique cultural and self-governance practices and policies.\textsuperscript{217} Indeed, the leaders of the premier medical schools even favor allowing each individual institution to define fundamentals, such as which financial interests must be disclosed and/or further managed or prohibited.\textsuperscript{218}

The time has come to move away from the traditional models of self-regulation to ensure sufficient and uniform protections from the influence of financial conflicts of interest. As shown by the contributions of the leaders of the premier medical schools and the AAMC Task Force, it is probable that many academic research centers will, even without additional regulation or guidance, bolster their conflicts of interest policies. However, because academic research institutions benefit from current technology-transfer policies, some may be reluctant to provide the vigorous management, oversight, and enforcement necessary to preserve integrity and the perception of

\textsuperscript{214} See id. § 54.1(b) (stating purpose for financial disclosure by clinical investigators).

\textsuperscript{215} As explained above, the requisite disclosure does not occur until after an application for FDA approval of the drug, biological product, or device. Thus, disclosure occurs after research studies involving human participants have been performed. Supra text accompanying notes 102–04.

\textsuperscript{216} 42 C.F.R. § 50.604(g)(2) (2001).

\textsuperscript{217} See supra text accompanying note 137 (describing HHS belief that regulatory responsibility should lie with institutions).

\textsuperscript{218} See supra text accompanying notes 163–68 (enumerating and discussing guidelines for conflict-of-interest policy from premier medical schools).
integrity. Additionally, rigorous protections for human research participants should be uniform across the spectrum of academic institutions. Federal regulations can more readily ensure sufficient and uniform rigor at all academic research institutions.

Additionally, the regulated conduct falls outside the sphere of activity requiring traditional medical and academic expertise. The conduct is performing research activity involving humans while holding related financial interests, as opposed to the practice of medicine or academic decisions related to curriculum. As to research activity and the ability of academic researchers to make a profit from research being conducted at their academic institutions, less deference is justifiable. Importantly, the federal government has deviated from models of self-regulation in the academic and medical arenas when traditional medical and academic expertise were not at the heart of the regulated activity. For example, the federal government directly regulates physician referrals to entities in which the physician has a financial interest (the Stark laws), physician billing practices (fraud and abuse laws), and gender discrimination in athletic programs (Title IX).

Notably, representatives of the academic community who have opined that the federal government should continue using the audited self-regulatory approach largely have been concerned with the resource issues. Institutional resources vary considerably. However, as long as the federal regulations dictate a streamlined process, all academic institutions should be able to handle the resource demands. Further, regulation of financial conflicts of interest will have a weightier impact on institutions that are more heavily involved in technology-transfer arrangements, but those institutions will also likely have larger revenue streams resulting from the transfers, thereby mitigating the resource concern. A portion of the profits from research endeavors could be used to enhance patient protections.

Thus, although the private sector should continue its active involvement in the development of more rigorous protections against contemporary financial conflicts of interest, the protections should come primarily in the form of federal regulations. These regulations should shift away from the traditional model of self-regulation, clearly specify standards and regulatory responses, and grant federal agencies more responsibility for monitoring and enforcement.

220. See id. §§ 1320a-7, 1320a-7a, 1320a-7b (providing Medicare and Medicaid "fraud and abuse laws").
221. See Section 901(a) of Title IX of the Education Amendment of 1972, Pub. L. No. 92-318, 86 Stat. 235 (providing the educational program or activity anti-discrimination law).
222. See supra text accompanying note 140 (describing consensus view at the August 2000 Conference on Human Subject Protection and Financial Conflicts of Interest).
activities. Of course, these regulations should bring within their protective ambit all research involving human participants, not merely studies currently subject to federal regulation. However, the focus of this Article, and thus of the following sections, is on standards, regulatory responses, and enforcement procedures.

B. Standards

As noted above, a key deficiency of the recent initiatives is the failure to outline a means of accurately or sufficiently identifying conflicts of interest that should warrant a regulatory response. Both the PHS and FDA Objectivity Regulations turn on the presence of "significant financial interests," as narrowly defined by the regulations. Only significant financial interests need be disclosed, and only significant financial interests warrant steps to minimize bias or to reduce, manage, or eliminate the interest. A sufficiently rigorous regulatory system would use federal standards that are broader and more precise, including standards for disclosure and standards for determining whether any additional regulatory response, beyond initial disclosure, is appropriate.

1. The Standard for Disclosure

a. The "Actual v. Potential" Issue

Regulators and institutions agree that disclosure is the first step in a regulatory process addressing financial conflicts of interest. However, the recent initiatives and the responses thereto reveal that little consensus has been reached as to what information researchers should initially disclose. This debate reflects a fundamental issue underlying the problem of financial conflicts of interest: whether "any" financial interest should be characterized as creating a "conflict of interest," or whether a conflict arises only when the financial interest reaches a certain threshold. For example, this debate was an important aspect of comments made by the National Human Research Protections Advisory Committee (NHRPAC) in response to interim guidance issued by HHS. The NHRPAC stated:

NHRPAC encourages the Department to be careful in distinguishing between a duty to disclose or a process of disclosure of financial interests, on the one hand, and identification of a financial interest as a conflict of

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224. See generally Letter from Mary Faith Marshall, Ph.D., Chairperson, NHRPAC, to Arthur J. Lawrence, Ph.D., Acting Principal Deputy Assistant Secretary for Health (Aug. 23, 2001). The OHRP Interim Guidance is discussed supra notes 142–61 and accompanying text.
interest, on the other. In many cases, ... the term "conflict of interest" has been used, for example, to signify the presence of any financial interest. This seems to NHRPAC an inappropriate, inexact and overly broad use of the term, since mere presence of a financial investment or relationship does not necessarily result in a meaningful or significant conflict of interest that must be managed.\textsuperscript{225}

The NHRPAC went on to suggest that three categories of interests be recognized: (1) at one end of the spectrum, "mere financial relationships;" (2) at the other end, "well-established conflicts of interests;" and (3) between those two, "complicating financial relationships," "troubling financial relationships," or "relevant financial relationships."\textsuperscript{226} While NHRPAC's categorization may be relevant at some point in the regulatory scheme, its premise—that it is not accurate to equate "any financial interest" with a "conflict of interest"—is flawed. In the context of human subject research, any financial interest constitutes a "conflict of interest" and should be subject to regulation, although, as explored below, different levels of conflicts may merit different regulatory responses.

Importantly, none of the recent initiatives strongly favor this broad view of "conflict of interest." The leaders of the premier medical schools impliedly suggest that a broad view of conflicts of interest is appropriate through their recommendation that institutions define "financial interests" broadly to include any form of remuneration or special relationships having the potential for personal material gain.\textsuperscript{227} But the PMS Guidance then recommends allowing each institution to delineate for itself the activities and levels and kinds of financial interests that are or are not permissible.\textsuperscript{228} And the OHRP and the AAMC Guidelines merely follow the lead of the current conflict-of-interest regulations by requiring disclosure and management only if the financial interests and their potential impact on research reach a fairly high threshold.\textsuperscript{229} Under the PHS and FDA regulations, investigators need only

\textsuperscript{225} Letter from Mary Faith Marshall, \textit{supra} note 224, at 4. The letter continues: "Some financial relationships are so trivial or so attenuated that they cannot be thought of as posing any significant risk of 'conflict of interest.' Similarly, moral and regulatory scrutiny is required ... not for any and all 'financial relationships,' but only for those that pose some significant risk of conflict of interest." \textit{Id.} at 4–5. This statement seems to blur the issue. A financial interest can result in a conflict of interest even if that conflict is not "significant."

\textsuperscript{226} \textit{Id.}

\textsuperscript{227} \textit{Supra} text accompanying note 163.

\textsuperscript{228} See \textit{supra} text accompanying notes 163–68 (enumerating and discussing PMS guidelines).

\textsuperscript{229} Compare \textit{supra} text accompanying notes 142–61 (discussing the requirements of OHRP Guidelines) \textit{with supra} text accompanying notes 169–202 (discussing the requirements of AAMC guidelines).
disclose "significant" financial interests, and management is necessary only if the interest is deemed to "directly and significantly" affect research. As noted, by following this course, the OHRP and the AAMC Guidelines operate on the premise that a conflict of interest does not arise upon the existence of "any" conflicting financial interest, but rather only in those cases in which the financial interest is significant.

The broad premise that any financial interest creates a conflict of interest flows from the legal concept of conflict of interest. The concept of conflict of interest is associated with persons who, by law, are in a position of trust. Generally, a "conflict of interest" is defined as an interest that is inconsistent with the official responsibilities of a person in a position of trust. Institutions and researchers who carry out federally funded research are persons in a position of trust. Indeed, the current federal regulations governing research are based on trust. As explained, the federal regulations require institutions to "assure" federal agencies that their researchers will comply with the agencies’ rules by obtaining approval of research procedures by an IRB before commencing the research project and obtaining written informed consent from research participants throughout the project. The requisite "assurance" is a promise that the institution and investigators can be trusted to review research prospectively and to follow the rules that have been put in place.

Similarly, the Nuremberg Code, the Declaration of Helsinki, and the Belmont Report are premised on the principle that all persons involved in

230. See supra text accompanying notes 112–13 (describing deficiencies in PHS and FDA regulations).

231. See August 15 Conference Transcript, supra note 27 (statement of Dr. Thomas Bodenheimer, Clinical Professor of Family and Community Medicine at the University of California-San Francisco) (defining conflict of interest). See generally MARC A. RODWIN, MEDICINE, MONEY, AND MORALS: PHYSICIANS’ CONFLICTS OF INTERESTS (1993). It has been noted that "the phrase ‘conflict of interest’ is applied in so many and varied contexts that providing a single, unitary definition may be impossible." Pilar N. Ossorio, Pills, Bills, and Shills: Physician-Researcher’s Conflict of Interest, 8 WIDENER L. SYMP. J. 75, 81 (2001). Professor Ossorio described two slightly different conceptions of the phrase: (1) situations in which two interacting parties have opposing interests and (2) situations in which one individual has interests in opposition to other interests, such that both sets of interests cannot be advanced simultaneously. Id. at 81–82. Ossorio then notes that "[i]n all or nearly all cases, either of the two different conceptualizations or formulations . . . can be applied to the same set of facts." Id. at 83.

232. See supra text accompanying notes 74–77 (describing the "assurance" process used by NIH).

233. See August 16 Conference Transcript, supra note 30 (statement of Dr. Sugarman, Associate Professor of Medicine and Philosophy and Director of the Center for the Study of Medical Ethics and Humanities at the Duke University School of Medicine) (discussing development of ethical foundations in conflict-of-interest problems).
research involving human participants—investigators, research staff, institutions, federal and commercial sponsors—are fiduciaries.\textsuperscript{234} As persons in positions of special trust, these fiduciaries have special fiduciary duties. In the context of research, the fiduciary duty imposed would seem to be a duty to act for the benefit of current and future research participants and for other individuals who use the knowledge generated by the research.\textsuperscript{235} If a "conflict of interest" is defined as an interest that is inconsistent with the official responsibilities of a person in a position of trust, then a conflict of interest in the research context is an interest that is inconsistent with conducting research for the benefit of research participants and users of generated knowledge.

Conducting research for the "benefit of participants and users" means ensuring that studies are conducted only when they both provide benefit to the individual human research subject and contribute to the reservoir of knowledge needed to make scientific advances.\textsuperscript{236} IRBs, through their role of assessing risks and benefits and the soundness of a research design,\textsuperscript{237} have traditionally ensured the scientific and medical soundness of a research project. Additionally, however, conducting research for the benefit of participants and users means ensuring the integrity and objectivity of the research process. As the NIH has stressed, "[O]bjectivity of researchers is an essential value in scientific research and the basis for public trust. Researchers should be led by their data, not by other interests that might undermine the scientific integrity of their work."\textsuperscript{238}

\textsuperscript{234} See, e.g., \textit{Belmont Report}, supra note 2 (identifying basic ethical principles underlying research with human participants).

\textsuperscript{235} See August 16 Conference Transcript, supra note 30 (statement of Dr. Sugarman, Associate Professor of Medicine and Philosophy and Director of the Center for the Study of Medical Ethics and Humanities at the Duke University School of Medicine) (discussing fiduciary obligations in context of research).

\textsuperscript{236} Professor Pilar N. Ossorio has compiled a more specific list of duties owed to research participants, as well as to the colleagues of physician-researchers. See Ossorio, supra note 231, at 87–88 (compiling list of obligations of physician-researchers). Duties to research participants include engaging patients and research participants in honest and comprehensible informed consent processes, designing experiments with attention to minimizing harms and risks, engaging in continuing medical education, and informing proper oversight entities of unexpected adverse events that occur during an experiment or in response to a prescription drug. \textit{Id.} Duties to colleagues include refraining from knowingly, recklessly, or negligently injecting false or misleading data into the scientific literature, refraining from knowingly, recklessly, or negligently engaging in activities that could undermine the public’s trust in a department or institution, and contributing to the growth of scientific knowledge through publication and participation in professional conferences. \textit{Id.}

\textsuperscript{237} See supra text accompanying notes 54–65 (discussing the IRB review process).

\textsuperscript{238} Financial Conflicts of Interests, supra note 46.
From the perspective of objectivity, a conflict of interest exists whenever an investigator has more than the normal scientific preference in one outcome of his research over another outcome. Arrangements that give an institution or an investigator a financial interest in the success of a study would readily seem to create a situation in which the investigator would prefer one outcome over another. Thus, financial arrangements of the sort illustrated in the foregoing sections of this Article readily create "actual" conflicts of interest, not "potential" conflicts of interest. As noted recently, "The only thing potential about it is whether the conflict leads to bad research." Thus, one should recognize that any financial interest inherently creates a conflict.

The recognition that an actual conflict of interest creates only the potential for lack of objectivity does not weaken this conclusion. The existence of any financial interest, and thus the existence of a conflict of interest, always creates a probability or likelihood that the researcher will breach a fiduciary duty. Importantly, that likelihood exists largely as a result of unconscious bias rather than intentional breach of trust. As Professor Ossorio has noted, "[C]onflicts would not present much of a dilemma if they only affected a few 'bad apples.' It is because conflicts can influence the many professionals who have good intentions and good will that we must consider how to minimize and manage them.

Unconscious breaches can occur and are difficult to detect because many decisions in the research process—for example, decisions about study design, inclusion criteria, and adverse-event reporting—require judgment and discretion. And regulators agree that conflicts can undermine judgment. For example, commentators have recognized that conflicts can lead to "self-deception, excessive credulity, and selective attention [and that r]esolution of the cognitive dissonance created by a conflict may lead a scientist’s intuition to accept results she would otherwise have rejected, or vice versa.

See August 16 Conference Transcript, supra note 30 (statement of Marcia Angell, former Editor-in-Chief of The New England Journal of Medicine) (defining conflict of interest); see also Ossorio, supra note 231, at 91 (noting that "conflicts of interest are particularly problematic when they enhance the attractiveness or desirability of one outcome from the domain of all possible outcomes").

August 16 Conference Transcript, supra note 30 (statement of Marcia Angell, former Editor in Chief of The New England Journal of Medicine).

Ossorio, supra note 231, at 90.


Ossorio, supra note 231, at 90 (citing Bernard Barber, Resistance by Scientists to Scientific Discovery, in THE ETHICAL DIMENSIONS OF THE BIOLOGICAL SCIENCES 67 (Ruth Ellen Bulger et al. eds., 1993)). See generally William Broad & Nicholas Wade, Self-Deception and
Moreover, the existence of financial arrangements that give the researcher a financial interest has given rise to public concern about the integrity of the research process. As noted in the introduction, federal agencies with authority over federally funded research have an obligation to preserve not only actual objectivity, but also the perception of complete integrity and objectivity in research involving human participants. Thus, because concerns are raised by any financial arrangement that creates an interest in the outcome beyond the normal scientific preference, it is reasonable to posit that "any" financial interest should be characterized as a conflict of interest.

b. More Encompassing Initial Disclosure Requirements

As part and parcel of the recognition that "any" financial interest creates a "conflict of interest," the new federal regulations should follow the suggestion of the PMS Guidance and require disclosure, initially, of all financial interests held by academic researchers that are related to research being conducted by the researcher (research in which the researcher participates in a significant way). The goal should be to allow someone other than researchers themselves to conduct the initial scrutiny of a financial interest's impact on research.

Institutional policy should take the decision of whether to disclose a particular financial interest out of the hands of the researchers themselves. As the Acting Director of NIH stated at the August 2000 conference, "[Disclosure] is at the heart of the matter . . . . It takes more than one person, especially one interested person, to decide on the innocence of the transaction." Experts recognize that having a financial interest is not in itself wrong. Rather, the point is that a researcher possessing a financial interest is likely to be unconcerned, or at least less concerned, because it is likely that the researcher truly, subjectively believes that his financial interest is not going to impact the study. Yet as noted, the probability that the researcher will breach

244. The AAMC Task Force determined that the phrase "conducting research" should broadly include "designing research, directing research or serving as the principal investigator, enrolling research participants (including obtaining participants' informed consent) or making decisions related to eligibility to participate in research, analyzing or reporting research data, or submitting manuscripts concerning the research for publication." AAMC Guidelines, supra note 169, at 11.

245. August 15 Conference Transcript, supra note 27 (statement of Ruth L. Kirschstein, M.D., Principal Deputy Director, NIH).
a fiduciary duty arises upon the existence of any financial interest, due largely to unconscious bias rather than intentional breach of trust. Thus, the objective should be the disclosure of all financial interests related to research the researcher is conducting.

In practice, of course, this may be a difficult objective to achieve. One difficulty involves defining and identifying a "financial interest." The view recommended by the leaders of the premier medical schools should be followed, and institutions should define financial interests broadly, but simply, as including any form of "remuneration, benefit, arrangement, or relationship that creates a potential for personal material gain." To enhance responses, institutional policy should also define the term "potential for personal material gain." For example, the phrase could be defined as "any possibility that you or your spouse or dependent children could attain a pecuniary or status-related benefit (other than personnel/academic benefits related to job security or promotion or tenure)." Not only is this definition more encompassing than the definition of "significant financial interest" used by the PHS, FDA, OHRP, and AAMC Task Force, but the definition is easier to comprehend because it omits technical terms such as equity interests, intellectual property rights, emoluments, or entitlements.

246. See AAMC Guidelines, supra note 169, at 3 (explaining that public confidence in research is undermined by any financial conflict of interest).

247. This proposed definition represents the author's adjustments to the broad formulation advanced by the leaders of the PMS. The "financial" prong of this concept is probably easier to articulate than the "interest" prong. As Professor Ossorio queried, "Is an interest merely a desire or the object of a desire? Is it a need? Is it something to advance one's overall welfare or happiness? What is the relationship of values to interests? Must a person recognize an interest as something related to her good?" See Ossorio, supra note 231, at 84 (speculating on the notion of "interests"). Professor Ossorio noted that physician-researchers have numerous interests that may come into play in a conflict of interest situation and concluded that a theory stating how to prioritize interests is needed for the resolution of conflicts among them. See id. at 85–86 (listing and discussing competing interests). "Simply describing interests as organizing in or attached to the roles of physician and researcher does not necessarily suffice to make them normatively more important or primary than other interests a physician-researcher might have." Id. at 87.

248. This proposed definition also represents the author's idea of how to solicit appropriate disclosures from researchers.

249. This author serves as a member of a conflicts of interest committee at her institution, which is attempting to draft more comprehensive conflicts of interest policies. Several faculty on the committee voiced their concern about the detailed and complex definition of "significant financial conflicts" that must be disclosed. The committee suggested that the complicated technical information could be provided as additional guidance for those who may be interested, but felt that most faculty would better understand a broad and simple concept, thereby enhancing responses.
A second difficulty is that regulators must take the assessment of whether a financial interest "relates to research" from the researcher. The only way to take the assessment completely out of the hands of the researcher would be to require disclosure of all of the researcher's financial interests, even those not related to research being conducted by the researcher. Some institutions appear to have taken such an approach. However, such expansive disclosure could create substantial burdens for the institution, and faculty researchers likely would perceive it as an unwarranted invasion of privacy. Thus, some institutions have used language requiring disclosure of financial interests that "to an independent observer would reasonably appear to be affected by research in which the individual is involved; or that exist in entities whose financial interests to an independent observer would reasonably appear to be affected by the research." This does not take the assessment of the "relation to research" entirely out of the hands of the researcher because the researcher makes the determination whether an "independent observer" would view the financial interests as being affected by the research. But use of the "independent observer" language emphasizes more clearly that the researcher should consider how others might perceive the relationship between the research and the financial interest.

The combination of phrases should enhance disclosure of information that the appropriate institutional personnel can then assess for purposes of identifying whether an additional regulatory response is necessary. The institutional personnel selected to conduct the initial review of disclosures should possess enough resources and expertise to make the requisite assessment. Most proposals to date have suggested that institutions should make two distinct types of appointments: first, appointment of an official, a "designated institutional official," whose primary job is the initial assessment of

250. For example, State University of New York (SUNY) uses a disclosure statement that appears to require disclosure of all special relationships (i.e., "any office, trusteeship, directorship, partnership, position or consultancy of any type, whether or not compensated, held by you or your spouse . . . with any firm, corporation, association, partnership, or other organization other than the State University of New York."). Disclosure Statement for Academic Employees upon Application for a Sponsored Program Grant or Contract, State University of New York (Sept. 2001) (on file with author). The statement also asks for disclosure of all "warrants or stocks, and other investments [sic] interests in limited or general partnerships owned by you or your spouse at time of filing for research grant. DO NOT LIST AMOUNTS." Id. (emphasis added).

251. University of Louisville, Draft Policy on Financial Conflicts of Interest: Statement of Principles and Purpose, Definition of "Statement of Financial Interests" (on file with author). This language has been suggested for the policy being developed at the University of Louisville. Id. Other institutions use similar language, but substitute the phrase "that could be perceived as being affected," for the phrase "that would reasonably appear to be affected." See, e.g., Texas A&M University, "Significant Financial Interest Certification" (on file with author).
disclosed interests;\textsuperscript{252} second, appointment of a committee, frequently referred to as a "conflicts of interest committee," to scrutinize those financial interests requiring a more complex assessment.\textsuperscript{253} As depicted in Diagram B,\textsuperscript{254} the proposals suggest ambiguous and overlapping responsibilities. In contrast, this Article advocates a more streamlined and less resource-intensive approach, which is discussed in more detail in Part V.\textsuperscript{255} Accurately identifying those financial interests that could or should lead to prohibition or management and determining when an exception should be granted can be complex tasks. Thus, because a certain degree of financial or scientific expertise is required, institutions should be charged not only with the responsibility of designating a specific official, office, or committee to review financial interests, but also with the responsibility of ensuring that the designated personnel possess the necessary competence or qualifications to make a valid assessment.\textsuperscript{256}

2. The Standard for Additional Regulatory Responses

After disclosure, identifying financial interests that warrant a regulatory response, interests that this Article will refer to as "problematic interests," constitutes the next step. The guidance to date falls short as to the assessment process. Although the leaders of the premier medical schools recognized that "any" financial interest should be disclosed\textsuperscript{257} (and thereby implicitly acknowledged that any financial interest creates a conflict of interest with the potential to affect research), they elected not to take a position on what types or levels of financial interests should warrant a regulatory response.

\textsuperscript{252} See supra text accompanying notes 146–61 (discussing HHS-OHRP proposals).

\textsuperscript{253} See supra text accompanying notes 189 and 195–200 (summarizing AAMC Guidelines conflict-of-interest committee proposal).

\textsuperscript{254} Supra p. 61.

\textsuperscript{255} As discussed in Part V of this Article, the author suggests that initial disclosures be made to an "institutional office," named, for example, the "Office of Financial Conflict Management" (OFCM). In contrast to the "designated institutional official" envisioned by the current regulations and recent initiatives, the OFCM would have primary responsibility and authority in the assessment, management, and oversight of financial conflicts of interest. Indeed, the author proposes that a separate "conflicts of interest committee" is not needed. Rather, the proposed system would have a "Patient and Research Protection Committee" (PRPC). In contrast to the "conflicts of interest committee" envisioned in the recent initiatives, the role of the PRPC would be limited to determining whether the rare exception should be granted to the prohibition on a participation in research by a researcher with a FI/FR.

\textsuperscript{256} Further, although beyond the scope of this Article, the appointments should take into account the need to safeguard against institutional conflicts of interest.

\textsuperscript{257} Supra text accompanying note 164.
The OHRP and AAMC Task Force provided greater guidance. The AAMC recommendations describe financial interests and explicitly identify certain permissible and impermissible financial interests. Under both the OHRP and AAMC recommendations, regulatory action is triggered when a financial interest can be deemed a "significant financial interest." In addition, OHRP recommends scrutiny of a "financial relationship of any kind" between a researcher and a commercial sponsor. These recommendations, however, fail to outline a means of accurately or sufficiently identifying conflicts of interest that should warrant an additional regulatory response beyond the initial disclosure.

An initial task in identifying such conflicts is to articulate a standard for problematic financial interests. The standard should reflect the underlying reason why financial conflicts of interest are cause for concern. As explained, a conflict of interest exists whenever a researcher has more than a normal scientific preference for one outcome over another, and any financial interest constitutes a conflict of interest because a financial interest creates a possibility that a researcher will breach the research fiduciary duty. However, different levels and types of financial interests create different probabilities of a breach. An appropriate standard for use at the assessment stage, then, is whether the financial interest creates a reasonable likelihood that the researcher may fail to fulfill the research fiduciary duty, even if the failure is unconscious. If a "reasonable likelihood" does not exist, the financial interest should not be considered problematic, and a regulatory response beyond initial disclosure should not be necessary.

As with any "reasonableness" standard, many factors would seem to be relevant. This vagueness highlights an important shortcoming of the recent initiatives' approach to identifying problematic financial interests, even as

258. See supra text accompanying notes 173 and 180–85 (detailing, for example, consulting fees, honoraria, gifts, and permissible interests in publicly traded, diversified mutual funds).

259. See supra text accompanying note 176 (discussing AAMC Guidance); supra text accompanying note 147 (discussing OHRP Guidance).

260. Supra text accompanying note 152.

261. See supra text accompanying notes 239–43 (describing conflict of interest from the perspective of preserving the objectivity of researchers).

262. See supra text accompanying notes 239–41 (explaining the argument that the existence of any financial interest always creates a possibility that the researcher will breach her fiduciary duty).

263. The phrase "reasonable likelihood" of breach of fiduciary duty has been used by Professor Ossorio, but not in the context of a standard for identifying financial interests warranting a regulatory response. Ossorio, supra note 231, at 87. Rather, Professor Ossorio has used the phrase to describe when conflicts of interests become morally or legally problematic. Id.
refined by the AAMC Task Force: the failure to consider the multitude of factors relevant in assessing the seriousness of a conflict and determining whether it is, in fact, a problematic interest. For example, the current PHS regulations and the AAMC recommendations predominantly base the determination of "significant financial interest" on a single factor: the amount or size of the interest (for example, consulting fees and honoraria exceeding $10,000, equity interests exceeding $10,000, or equity interests exceeding a five-percent ownership interest).264 A single factor test results in a fairly clear standard, and clarity is important. Indeed, the PMS Guidance emphasizes that point.265 This, however, sacrifices accuracy. Branding as a conflict of interest only payments that in the aggregate exceed $10,000 fails to identify problematic interests that arise even when payments, in the aggregate, amount to less than $10,000. Surely, for some (and perhaps many), a sum of less than $10,000 may be a sufficiently significant financial interest to warrant a regulatory response. Realistically, then, the seriousness posed by any financial interest depends on a number of factors. Relevant factors to consider would seem to include:

(1) The nature of the relationship between the researcher and the entity creating the interest (e.g., arms-length v. close and personal, the extent to which the remuneration depends on certain findings or outcomes, etc.);

(2) The magnitude of the interest, considering both the amount of money or remuneration and the researcher's total income otherwise; and

(3) The discretion to be exercised by the researcher (e.g., decisionmaking authority in the research enterprise, amount of oversight provided, and accountability expected).266

Those possessing greater financial expertise than this author likely could identify other relevant factors as well.

Consideration of a number of factors, such as those outlined above, would more accurately identify those situations in which a financial interest warrants a regulatory response. However, because a multifactored "reasonableness" approach is less clear cut, it would be more resource intensive for

264. Supra text accompanying notes 94–95 (describing PHS Objectivity Regulations); supra text accompanying 180–81 (describing AAMC Guidelines).
265. See supra text accompanying note 162 (quoting PMS guidelines).
266. See Ossorio, supra note 231, at 90–91 (summarizing factors for determining significance of a financial interest).
the institution. As in so many regulatory situations, a balance must be struck. Two options exist to strike that balance.

Given the resource limitations of many academic institutions, one option would be to use a more clear-cut and, thus, less resource-intensive test initially to identify financial interests that could or should be "presumed permissible," thereby reserving the more resource-intensive scrutiny for financial interests that create a higher likelihood of influence on researcher judgment. Financial interests could be "presumed permissible" when they would seem to create only a de minimis potential to influence researcher judgment. Such interests could include, for example, payments or remuneration not exceeding, in the aggregate, $500 rather than $10,000 or, as suggested by the AAMC, interests of any amount in publicly traded, diversified mutual funds.

The importance of preserving objectivity and human research protections could justify the resources necessary to conduct a multifactored, and thus more accurate, assessment of conflicts of interest. Further, academic

267. This perspective of financial conflicts is consistent with that proffered by the NHRPAC when it urged HHS to acknowledge and clarify that three categories of interests should be recognized: (1) at one end of the spectrum, "mere financial relationships"; (2) at the other end, "well-established conflicts of interests"; and (3) between those two, "complicating financial relationships," "troubling financial relationships," or "relevant financial relationships." Supra text accompanying note 226 (discussing different categories of conflicts of interests). However, NHRPAC advocated that some financial interests simply do not create "conflicts of interest." Supra note 225. Here the author is operating from the premise that all financial interests create a conflict, but advocating that some may be too insubstantial to warrant regulatory action.

268. The monetary amount selected as the cut-off could even be lower. In the Stark II Final Rule, the de minimis exception to the physician self-referral ban (the ban on physician referrals of Medicare and Medicaid beneficiaries to entities with which the physicians have a financial relationship) applies only as to compensation in the form of items or services (not including cash or cash equivalents) that does not exceed an aggregate of $300 per year. 66 Fed. Reg. 856 (2001). See generally Stark II Final Rule—Phase I: A Kinder and Gentler Stark? 2001 HEALTH LAW 1.

269. On the other hand, it is perhaps possible to identify certain financial interests that could be presumed impermissible. For example, the AAMC Task Force expressly recommended that institutional policies prohibit payments to a researcher that are conditioned upon a particular research result or tied to successful research outcomes. Supra text accompanying note 173. It is unclear what this means since many if not most interests are tied, at least indirectly, to success (e.g., equity interests, royalties). The Task Force Guidelines also recommended prohibiting agreements that permit a sponsor or other financially interested company to require more than a reasonable period of pre-publication review or that interfere with an investigator’s access to the data or ability to analyze the data. See supra text accompanying note 173 (describing AAMC Task Force recommendations). As noted, the guidelines do not present these as absolute prohibitions. "When deemed unavoidable, such agreements should be subjected to close scrutiny . . . ." AAMC Guidelines, supra note 169, at 20. But, if specific arrangements, such as these, can be identified as particularly objectionable due to their enor-
research institutions ought to be able to allocate (or reallocate) funds to the process. Although regulations emerging from current conflict-of-interest discussions may curtail the profits associated with financial interests and financial relationships, institutions and their researchers will continue to reap monetary benefits as contemplated by the Bayh-Dole Act and other technology-transfer acts. Greater benefits will likely flow to those institutions more heavily involved in financial arrangements, thereby requiring assessment of a greater number of financial interests. Thus, existing funds could be tapped to help offset the costs incurred due to the need to protect research participants as a result of those monetary benefits. Other resources could also be found. For example, the regulations could require commercial entities that benefit from ventures with academic research institutions to contribute towards the costs of greater human subject protections.

However, an alternative exists. Rather than using a multifactored approach, any financial interest not "presumed permissible" could be "deemed problematic." This approach would solve much of the resource problem by providing a more bright-line test. For example, payments or remuneration exceeding, in the aggregate, $500 rather than $10,000 or equity interests of any amount (aside from interests in publicly traded, diversified mutual funds) would merit the "deemed problematic" designation. A possible downside to this approach could be additional regulatory responses imposed due to nonsignificant financial interests or relationships that have been "deemed problematic." Given that potential drawback, the feasibility of this alternative approach depends on the extent to which the regulatory response unduly burdens innovation. If, as the following analysis suggests, the emerging regulatory responses likely would have a minimal impact on innovation, using a "deemed problematic" approach would result in a more streamlined regulatory system.

C. The Additional Regulatory Response

Once "problematic conflicts" are identified, such as those financial interests determined or "deemed" to create a reasonable likelihood of influencing research judgment, the issue becomes one of choosing the appropriate additional regulatory response. The current regulations do not articulate this response with any specificity. The PHS regulations require institutions to report identified conflicts of interest and assure that the conflicts will be managed, reduced, or eliminated. The FDA regulations require applicants

mous potential to influence researcher judgment, those arrangements could be deemed "pre-

270. Supra text accompanying notes 92 and 101.
to disclose the nature of financial arrangements and the steps taken to minimize any bias in the research process, but they do not spell out particular techniques that the applicants should use.\textsuperscript{271}

The recent guidance is more specific. The OHRP Guidelines suggest that agreements between researchers and institutions concerning commercial funding of research should be scrutinized to ensure that no other financial relationships or interests exist.\textsuperscript{272} In addition, the guidance issued by OHRP states that "if there are any financial conflicts of interest issues on the part of the Clinical Investigator, he or she should not be directly engaged in aspects of the trial that could be influenced inappropriately by the conflict."\textsuperscript{273} The reports issued by the leaders of the premier medical schools and by the AAMC Task Force use substantially similar language: both advise prohibiting researchers with problematic financial interests from conducting research.\textsuperscript{274} The reports provide little explanation for this regulatory choice. The question is whether these types of prohibitions represent an appropriate regulatory response.

At the broadest level, the options for regulatory safeguards are prohibition or management.\textsuperscript{275} This Article considers the appropriateness of both. Selecting an appropriate regulatory response requires consideration of three main factors. The first is effectiveness: does the response tend to protect human research participants and reduce the potential for breach of the research fiduciary duty? The second factor is cost: will the response be too resource intensive to be considered a feasible option? The third is the impact on innovation: will the response significantly hinder the key ingredients necessary for innovation in the biomedical/biotechnology arena?

\textsuperscript{271} See supra notes 102–11 (describing FDA Guidelines and various requirements they impose, none which prescribes how to handle financial interests).

\textsuperscript{272} See supra text accompanying 151–53 (describing how OHRP guidance goes further than PHS regulations).

\textsuperscript{273} OHRP Guidance, supra note 142, § 4.4. The OHRP recommends a similar risk management technique as to financial interests held by the institution. Id. § 1.6. The OHRP Guidance recommends that institutions with financial interests should "carefully consider whether a clinical trial to evaluate the safety and efficacy should be performed at that site . . . ."; it further notes that the integrity of the research and thus of the institution "may be best protected by having the clinical trial performed and evaluated by independent investigators at sites that do not have a financial stake in the outcome of the trial." Id.

\textsuperscript{274} Supra text accompanying notes 163 and 176.

\textsuperscript{275} Further disclosures, for example, through informed consent, are often considered as an additional regulatory response. However, further disclosures are a subset of conflict management. See infra subsection V.C.3.a (characterizing further disclosures as subset of conflict management).
Although a total prohibition on any financial interest held by individual researchers is not the appropriate regulatory response, a less stringent prohibition would be workable—namely, a prohibition on participation in relevant aspects of a study by researchers holding related problematic financial interests. Such a prohibition would be more effective than other conflict management strategies, without unduly burdening innovation.

1. Prohibition

Some believe that the emerging financial arrangements present such serious conflicts that prohibition is appropriate. For example, it has been suggested that investigators who receive grant support from industry simply should have no further financial ties to those companies or that institutions accepting support from industry should simply prohibit any industry-imposed restrictions on research design, analysis, or publication.

However, these suggestions reveal yet another definitional problem. The first suggestion purportedly refers to prohibition of any financial interest or financial relationship between a researcher and a commercial entity sponsoring research being conducted by the researcher. However, the fact that a commercial entity sponsors the research creates a financial relationship and thus a financial interest. Indeed, the OHRP guidelines recommend scrutiny of "financial relationships of any kind between a researcher and a commercial sponsor." The second suggestion similarly does not refer to prohibition of a financial interest, but instead refers to prohibition of certain activity when a financial interest exists. Thus, both suggestions actually refer to conflict or risk management techniques.

More accurately, the term "prohibition" would mean prohibition of any financial interest held by a researcher or an academic institution related to the success of any research study (beyond the traditional financial interests, such as promotion, tenure, and reputation). This definition would include the interest created when a commercial entity sponsors research, as well as any financial interest or financial relationship arising due to an interest in, or relationship with, a commercial entity that will benefit from the research. Defined as such, prohibition would obviously be effective in protecting human research participants and in reducing the injection of bias into the research.

276. See, e.g., August 16 Conference Transcript, supra note 30, at 37 (discussing suggestions for prohibitions on investigators).

277. See id. (same).

278. See supra text accompanying note 153 (suggesting scrutiny of researchers and commercial sponsors).
endeavor. If no financial interests exist beyond the traditional ones, contemporary concerns about research integrity would mirror the traditional concerns. 279

However, there are problems associated with total prohibition. First, some commentators suggest that, rather than resolving the problem presented by conflicts, a total prohibition could actually exacerbate the problem by driving the formation and existence of financial arrangements underground. 280 Intertwined with this concern is the notion that financial conflicts of interest realistically cannot be eliminated. Indeed, where there is a will, there is a way.

But more importantly, a total ban on financial interests would arguably have too great a negative impact on innovation. As noted by the Acting Director of NIH,

Profit is what operates a market economy . . . . It is also the prime motivator for producing the drugs that improve human health and reduce suffering. Profit, or making money, generally is not the problem, nor will it ever be. The problem is the collision of financial considerations, including the desire for personal or institutional profit, with the essential objectivity of science. 281

A total ban or prohibition on any financial interests held by a researcher or academic institution related to the success of any research study involving human participants would hinder innovation. Several ingredients are central to continued biomedical/biotechnology development. As is discussed in more detail below, innovation depends on the generation of ideas, research and development, and funding. 282 Academic researchers are a prime source of research ideas. Even without the profits existing in today's more entrepreneurial research environment, academic researchers have and will continue to formulate ideas. Other incentives, such as promotion and tenure and reputation, have long existed and continue to exist. However, the ability to profit through currently allowable financial interests likely spurred the recent biomedical and biotechnology explosion, leading to more and better research ideas. 283 Logically, a prohibition on any financial interests, and thus on the

279. In addition, this total prohibition would not be an overly costly regulatory option. Researcher disclosures would need to be reviewed for evidence of any financial interest, but if found, the institution would only need to direct the researcher to divest the interest.

280. E.g., August 15 Conference Transcript, supra note 27, at 56 (statement of Kenneth Trevett, General Counsel and CEO of a biomedical research organization in Boston).

281. August 15 Conference Transcript, supra note 27, at 7 (statement of Dr. Kirschstein, Acting Director of NIH).

282. See supra subsections V.C.2.b.(2), (3) (arguing that prohibition on participation in research will have minimal impact on innovation, generation of ideas, and conduct of research).

283. Kuhlman, supra note 8, at 342.
ability to profit from biomedical or biotechnology developments, likely would hinder innovation.

Moreover, a total prohibition on any financial interests held by a researcher or academic institution related to the success of any research study involving human participants would hinder innovation much more drastically than simply prohibiting participation in the research by those with problematic financial interests. As this Article discusses below, prohibiting participation in related research only reduces profits. In contrast, a total prohibition would eliminate the ability to profit from new advances. If the ability to profit is eliminated, no incentive would exist for academic researchers to participate in the risk associated with developing an idea. Yet, academic researchers often are the persons most likely to understand the potential for profit associated with new ideas. Indeed, it has been estimated that most breakthroughs and new devices come on the market as a result of small start-up companies that may be comprised of, say, a physician and an engineer working together to develop an idea, rather than as a result of large companies investing large sums of money in research.

The negative impact on innovation caused by a total prohibition would hurt the public generally, as well as individual patients who depend on scientific advances. In many areas of medicine, the interventions offered in the context of controlled clinical trials are the best health care available. Thus, even if all financial interests could be eliminated, patients and the scientific process, rather than becoming better off, would arguably ultimately lose out. Thus, prohibition, in its most technical sense, fails as an appropriate regulatory response.

2. Prohibition as a Conflict Management Tool

Any response other than total prohibition is more accurately characterized as conflict management. Thus, the prohibitions espoused in the recent guidance constitute conflict management. For example, the OHRP Guidelines suggest that agreements between researchers and institutions concerning commercial funding of academic research should be scrutinized to ensure that

284. See infra text accompanying notes 330–33 (describing spin-out entities).
285. August 15 Conference Transcript, supra note 27, at 38 (statement of James Benson, Executive Vice President for Technology and Regulatory Affairs at the Advanced Medical Technology Association); Golden, supra note 35, at 115–20.
286. August 15 Conference Transcript, supra note 27, at 12 (statement of Dr. Raub, principal spokesperson on the Secretary's new initiatives to strengthen human subject protection).
no other financial relationships or interests exist. This is not prohibition in its most technical sense because the financial interests created by the funding continue to exist, but the risk is managed by prohibiting any additional financial interests. Similarly, the guidance issued by OHRP, the reports issued by the leaders of the premier medical schools, and the AAMC Guidelines recommend prohibiting researchers with problematic financial interests from conducting research. These recommendations are also better viewed as conflict management. The existence of a financial interest is managed by limiting or preventing participation in research by those holding financial interests related to the research.

Conflict or risk management is premised on the fact that the presence of a conflicting financial interest does not automatically lead to bad research. Rather, a conflict of interest constitutes a "risk factor" for biased research. However, because a conflict creates "only a risk," albeit one that can be deemed "problematic," many believe that "risk management" is a sufficient regulatory response. At the same time, some believe that even risk management will inappropriately hinder innovation if the risk management techniques used are inappropriate. The question thus becomes whether the prohibitions

287. See supra text accompanying note 153 (summarizing OHRP Guidelines).
288. The OHRP recommends a similar risk management technique as to financial interests held by the institution. The OHRP Guidance recommends that institutions with financial interests should "carefully consider whether a clinical trial to evaluate the safety and efficacy should be performed at that site" and further notes that the integrity of the research and thus of the institution "may be best protected by having the clinical trial performed and evaluated by independent investigators at sites that do not have a financial stake in the outcome of the trial." OHRP Guidance, supra note 142, § 1.6.
289. But see supra text accompanying notes 239-43 (arguing that any financial interest automatically creates conflict of interest).
290. The following analogy to smoking was made at the August 2000 Conference:

Not everyone who smokes has coronary artery disease. Not everyone with coronary artery disease smokes. But people who smoke have a greater chance of having coronary artery disease. Similarly, not all conflict of interest situations create scientific misconduct. Not all misconduct is associated with a conflict of interest . . . . But conflict of interest situations may increase . . . . the chance of scientific misconduct . . . . [such as] designing studies to insure a desired result, making statements that are not justified by the evidence, publishing only part of the evidence, suppression of research, or [perhaps] outright fraud or fabrication of evidence.

August 15 Conference Transcript, supra note 27, at 12 (statement of Dr. Thomas Bodenheimer, Clinical Professor of Family and Community Medicine at the University of California-San Francisco).
291. For example, one member of the AAMC Task Force declined to endorse the report primarily due to concern that its recommendations would impede research innovation. See
of the type recommended in the recent initiatives are appropriate risk management techniques.

The prohibitions in the recent guidance were noted above: (1) prohibition on financial interests or relationships between researchers and a commercial entity sponsoring or funding research (other than the relationship created by the funding itself) and (2) prohibition on participation, in those aspects of a study that could be influenced improperly, by researchers holding a financial interest or relationship related to such research. In reality, these two prohibitions constitute but one: Generally, researchers should not hold financial interests related to research they are conducting, beyond the financial relationship created when a commercial entity funds the research. For the reasons outlined, commercial sponsorship itself should not be prohibited, despite the fact that it at least arguably creates a problematic conflict. Accordingly, the issue becomes whether it is appropriate to prohibit a researcher holding a financial interest from participating in related research.

a. Commercial Sponsorship Should Not Be Prohibited

Commercial sponsorship can occur in two types of situations. First, when a commercial research company generates the innovative idea underlying a research project, that commercial entity can conduct the research itself or elect to contract with an academic research institution for all or part of the research. But commercial sponsorship is also possible when researchers within an academic institution generate the idea underlying the research.

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AAMC Guidelines, supra note 169, at (i) (noting that Susan Hellman, M.D., declined to endorse the report).

292. Supra Part IV.

293. See, e.g., Michael J. Malinowski, Institutional Conflicts and Responsibilities in an Age of Academic-Industry Alliances, 8 WIDENER L. SYMP. J. 47, 54 (2001) (noting that "teaching hospitals and acclaimed research centers are beginning to offer clinical research services to industry in a manner intended to allow them to compete commercially with" contract research organizations); see also Lita Nelsen, The Rise of Intellectual Property Protection in The American University, 279 SCIENCE 1460, 1460–61 (1999) (noting several reasons for industry interest), at http://www.sciencemag.org/cgi/content/full/279/5356/1460. Nelsen notes: Technology is developing too rapidly for in-house development to be sufficient; central research laboratories with cutting-edge scientists were closed down in the draconian down-sizing of the late 1980s and early 1990s, and companies are reluctant to rebuild them; universities have specialized faculties and staff that cannot readily be obtained elsewhere; and companies can experiment with new technologies and approaches at universities without committing to hiring permanently the expertise that will be needed to develop these technologies.

Id.

294. See, e.g., Mike Ashley, Ideas In, Cash Out, VIRGINIA BUS., DEC. 1998, at 4 (noting
Academic researchers may be able to solicit commercial funding, especially when an arrangement also exists between the institution and a commercial entity regarding future profits stemming from the research.\textsuperscript{295}

Although commercial sponsorship may create a problematic financial interest, prohibition of commercial sponsorship itself would not be appropriate. One reason that commercial sponsorship itself may not be problematic, at least when the commercial entity has merely elected to contract with an academic institution for research pertaining to an idea generated within the commercial entity, is that the contract between the commercial sponsor and the academic institution likely promises merely reasonable compensation for services rendered. However, it should be acknowledged that commercial sponsorship may create concerns because obtaining funding for research is key in the academic research environment. Little internal institutional money for research remains available today. Instead, federal agencies or commercial entities largely fund research, and, given the greater competition for the limited federal funds, institutions are relying more heavily on commercial sources.\textsuperscript{296} Although researchers know that future funding depends on quality research, researchers may also believe, at least unconsciously, that future funding may be more readily available if the outcome reached will benefit the commercial entity sponsoring the research.\textsuperscript{297} Ideally, the researcher’s professional integrity and the knowledge that quality research will keep future dollars coming will prevail, and in many cases it probably does prevail. But, as explained, a problematic financial conflict of interest exists when a finan-

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\textsuperscript{295} See id. (explaining an arrangement similar to that illustrated in Diagram B, \textit{supra} p. 61); see also Baram, \textit{supra} note 44, at 269 (describing that reporters found that, in the Gelsinger trial, the University of Pennsylvania received substantial support from a company founded by the principal researcher and institute director).

\textsuperscript{296} \textit{Supra} text accompanying notes 13–16.

\textsuperscript{297} E.g., Baram, \textit{supra} note 44, at 269. Professor Baram notes that evidence supports the inference that prospects for financial gain have been a root cause of breakdowns in FDA and NIH sponsored clinical trials:

The inferences are based on the assumption that such researchers and organizations believe it is in their financial and career interests to compromise safety requirements in order to speed trials to completion without safety-related interruptions, and to emphasize positive outcomes . . . [because such outcomes can] stimulate more private investment and public funding . . . [and enhance the researcher’s] . . . prospects for continued funding . . . .

\textit{Id.}
cial interest creates a reasonable likelihood that the researcher will fail to fulfill the research fiduciary duty—even if only unconsciously.²⁹⁸

Nonetheless, a prohibition on commercial sponsorship would be difficult to justify given the lack of certainty that commercial sponsorship by itself creates a problematic financial interest. However, the existence of any further financial interests between the researcher and the commercial sponsor would increase the probability of a breach of the research fiduciary duty and very likely would raise the probability to or above the level of a "reasonable likelihood." Prohibition of additional financial interests, therefore, is an effective risk management technique because it minimizes, to the greatest extent practical, the chance that a researcher's judgment will be compromised when research is commercially funded.

b. Prohibition on Participation in Research Is Appropriate

The prohibitions recommended in the recent guidance boil down to this: A researcher should not, generally, participate in those aspects of a study that could be influenced improperly by the researcher's own financial interests.²⁹⁹ This includes instances in which the researcher has a financial interest³⁰⁰ that reasonably could appear to be affected by the research or in which the researcher holds financial interests in entities whose commercial success reasonably could appear to be affected by the research.³⁰¹ This prohibition targets the financial interests created (other than funding the study itself) when academic researchers and institutions engage in innovative approaches to financing and corporate partnering in order to bring an innovation to the market. That is, the prohibition targets financial interests such as royalty payments, license fees, and equity interests held by researchers, as well as consulting fees and any other payments or remuneration related to the research. The question whether this type of prohibition constitutes an appropriate risk management technique

²⁹⁸. See supra text accompanying notes 261–63 (articulating standard for problematic financial interests).

²⁹⁹. The PMS Guidance provides that university policies should "prohibit involvement in the conduct, design, or reporting of research involving human participants by persons having more than a clearly defined minimal personal financial interest in a company that sponsors the research or owns the technology being studied." Consensus Statement, supra note 164. The AAMC Guidelines do not recommend an outright prohibition on participation when an impermissible conflict of interest exists; but instead suggest that institutions establish a "rebuttable presumption" that an individual who holds a related, significant financial interest may not conduct research. Supra text accompanying note 176.

³⁰⁰. That is, an interest beyond the financial interest created when the research is funded by a commercial entity. Cf. supra text accompanying notes 247–49 (discussing definition of financial interest).

³⁰¹. Supra text accompanying notes 261–63.
involves consideration of the three factors discussed above: effectiveness—whether the prohibition tends to protect human research participants and reduce the potential for breach of research fiduciary duty, cost—whether the prohibition will be too resource-intensive to be considered a feasible option, and impact on innovation—whether the prohibition will significantly hinder the key ingredients necessary for innovation in the biomedical and biotechnology arena.

(1) More Effective and Less Costly Than Other Strategies

A prohibition on participation would be an effective conflict management strategy for those aspects of a study that could be influenced improperly. Problematic financial interests are those that create a reasonable likelihood that a researcher will breach the research fiduciary duty. The potential for a breach of the research fiduciary duty occurs because a conflict of interest undermines a researcher’s exercise of judgment. Thus, the risk posed by holding problematic financial interests is that a researcher’s judgment may be undermined. Logically, then, the prohibition would be effective as it would therefore eliminate the risk: If the researcher conducting the research is not the researcher holding the financial interests related to the research, those financial interests cannot impact the aspects of a research study calling for an exercise of judgment. Further, the prohibition is arguably the most effective strategy available because other risk management strategies can only reduce the risk; they cannot eliminate the risk.302

Moreover, the cost associated with the prohibition is minimal and likely less than the costs associated with other risk management strategies. The key impact of the prohibition is structural: A researcher cannot hold a financial interest related to the research he or she is conducting beyond the financial relationship created if the research is funded by a commercial entity. The likely consequences would seem to be twofold. More researchers may become involved in the process, or more venture capitalists may become involved in the process. For example, university researchers will generate ideas and conduct the preliminary underlying research. Then, if the research produces a technology that is determined to have potential market value (and therefore to be worth further research and development), arrangements must be made regarding (1) funding for the requisite research and development and (2) profit-making from the technology, meaning ownership, patenting, and licensing considerations.303

302. See infra subsections V.C.3.a and V.C.3.b for a discussion of the effectiveness of other strategies such as disclosures and monitoring.

303. See generally Ashley, supra note 294 (describing various means of accomplishing technology transfer).
Without prohibition on participation in related research, a university researcher can become an integral part of a for-profit entity that will take the technology to the market using the very research conducted by that researcher. Imposition of a prohibition on participation in the research would mean that the researcher(s) who initially generated the idea and produced the potentially profitable technology would have to make a choice. One choice would be to continue participating in the research, thereby forgoing opportunities to become part of the commercial venture marketing the technology. This would mean that additional venture capitalists would have opportunities to become involved in the process. Another choice would be to become part of the commercial entity that will take the technology to the market and potentially reap profits, thereby foregoing participation in future research of the technology. This would mean that other university researchers, who do not hold a related financial interest, would become involved in the research.

Such structural modification would seem to involve relatively insignificant costs for the university. Additional researchers would be brought into the research process for a given technology, seeming to create an opportunity cost given that those researchers would then be limited in their work on other projects. But, those potential opportunity costs would be minimized because the researcher prohibited from participating due to her related financial interest can move on to new or different unrelated research projects. Of course, some opportunity costs may be unavoidable in those cases in which the additional researchers brought into the process may need to be trained or allowed some time to gain necessary expertise. However, such cost would seem to be manageable and, more importantly, less burdensome than the opportunity costs associated with other risk management techniques such as monitoring, which is discussed below. Because the prohibition on participation would be effective and likely would not be too costly, the key issue is the prohibition’s impact on innovation.

(2) Minimal Impact on Innovation

Several ingredients are central to continued innovation in the biomedical and biotechnology fields. Innovation depends on people generating ideas. These people are physician researchers, engineers, and others such as life science Ph.D.s. Additionally, innovation depends on research and development. Ideas must be converted into products that are tested for efficacy and

304. Supra text accompanying notes 35–37.
305. The term “innovation” herein is understood as referring to the process of commercializing invention. See Golden, supra note 35, at 166 (also using the term in this way).
306. See id. at 145 (describing bioscience Ph.D.s as biotechnology’s “inventor class”).
are refined until they are marketable or usable. Both ideas as well as research and development depend on funding. Moreover, money spent on innovation in the area of biotechnology is money that might be lost. Thus, arguably, the key ingredient of innovation is someone willing to take a risk—someone willing to put up the funds necessary to bring an idea to the market despite understanding the uncertainty of a profit. Overall, separating the researcher holding the financial interest from the research itself will not unduly hinder innovation.

(3) Minimal Impact on the Generation of Ideas and the Conduct of Research

Under a prohibition on participation, the structural modification is the separation of the researcher with a financial interest from the researcher conducting the research. The current regulations do not mandate separation. The researcher with the idea also may be the researcher with expertise to carry out the research and development. This same researcher may also have a financial interest in the success of the innovation and thus the outcome of research. In most cases, the separation of research duties should not have a significant impact on the generation of ideas or the conduct of the research, as long as the researcher with the idea still has the potential to make a profit and someone else can conduct the research necessary to transform the idea into a usable product or technology.

First, the prohibition likely would not have a negative impact on the source of ideas. Ideas fueling innovation have historically come from two

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307. See Kuhlman, supra note 8, at 316–19 (noting that the biotechnology industry has been identified as one of the most capital- and research-intensive manufacturing industries and that biotech firms average research expenditures of $59,000 per employee, compared with the corporate average of $7,106).

308. Id. (citing estimates and averages and noting, "The cost of developing and bringing a product to market is phenomenal.").

309. Id. (observing that research investment in the biotechnology arena is "an expensive and high-risk endeavor"); see also Golden, supra note 35, at 118 (noting that "[a]lthough some successful firms have developed profitable product lines, the typical small biotechnology company has little prospect of producing a commercial product in the immediate future," and that "it is generally accepted that most such firms will fail").

310. The investors in small biotech firms are often referred to as "venture capitalists." See, e.g., Golden, supra note 35, at 139 (noting that funding for basic research in the biotechnology industry likely comes from venture capital; and that "most biotechnology firms start out as venture-capital-financed 'spin-outs' from a university or research institute"). This private investment is essential to the biotechnology industry because "the industry is characterized by not yet having a base of revenue from existing product sales with which to reinvest into research and development." See Kuhlman, supra note 8, at 317 n.21.
primary sources: (1) nonacademic commercial research-and-development entities and (2) academic research institutions.\textsuperscript{311}

In nonacademic commercial research entities, the employees internally generate the ideas. In large traditional research companies, the incentive for generating ideas comes primarily from traditional employment and compensation considerations, e.g., retaining "scientific quality" as a primary criteria in personnel decisions and rewarding general employment performance through salary increases.\textsuperscript{312} In some instances, employees may share in the profits, typically through various types of stock ownership; however, the value of stock generally is tied to the success of the company as a whole, not to the success of any one innovation.\textsuperscript{313} The prohibition at issue would come into play only if the commercial entity elects to have academic researchers conduct the research. The prohibition would preclude any financial interests (beyond commercial sponsorship of the research) between the commercial entity and the academic researcher. Thus, although the prohibition would be effective in preventing possible bias in commercially-sponsored research, it would have no impact on the generation of ideas in the nonacademic arena because it would not impact the compensation of employees of commercial entities.

As noted, today's biomedical and biotechnology market promotes the establishment of small "start-up" companies.\textsuperscript{314} These companies often focus on one or a few ideas and/or technologies.\textsuperscript{315} To the extent the ideas are generated internally by nonacademic researchers (meaning the shareholders, officers and directors, or employees with scientific expertise—who are not also academic researchers), the analysis would be the same as in the foregoing paragraph. However, academic researchers are often the sole or major shareholders, officers or directors, or scientific officers of the small start-up company, and they are often the creators of the innovative ideas as well.\textsuperscript{316} In this

\textsuperscript{311}. See Golden, \textit{supra} note 35, at 132–36 (discussing the "three institutional players in the 'treble helix' of the United States system of innovation").

\textsuperscript{312}. See id. at 160 (noting that biotechnology firm practice suggests that they "do not believe that increasing individual rewards for obtaining patents is the best way to motivate potential innovators;" and citing also NIH practices).

\textsuperscript{313}. See id. (noting that employee-inventors may receive benefits through growth in the value of their equity interests in the company).

\textsuperscript{314}. See id. at 117–18 (explaining that "in contrast with most research universities and pharmaceutical companies, biotechnology firms are mostly young, small, and privately held"); id. at 139 (explaining that "most biotechnology firms start out as venture-capital-financed 'spin-outs' from a university or research institute").

\textsuperscript{315}. See generally Ashley, \textit{supra} note 294 (describing several small biotechnology firms).

\textsuperscript{316}. See Golden, \textit{supra} note 35, at 116–17 (noting that "[scientists from major universities] have played a crucial role in providing [biotechnology] firms with energy, expertise, and ... scientific legitimacy;" and that "even when not among the founders, [university researchers]
circumstance, the impact should be assessed as if the idea were generated in
the academic setting.

In the academic research setting, innovative ideas similarly are generated
by employees, primarily faculty of the institution. The historical incentive for
faculty to generate research ideas has been promotion and tenure, and perhaps
additional compensation. Additionally, it has been argued that bio-scientists
are primarily motivated by what have been called "public sector values,"
meaning that they are motivated foremost by the "ethic of contribution" and,
to a lesser extent, by the "economy of credit" in which research is stimulated
by reputational rewards for publication and priority.317 Typically, profits
stemming from research ideas being converted into marketable or usable
products played a negligible role in the generation of ideas.318 Today, promo-
tion and tenure continue to provide an incentive for research ideas. However,
the potential for profits resulting from transfer-technology acts has greatly
increased the incentive for ideas, thereby diminishing the influence of promo-
tion and tenure in spurring the generation of ideas.319 Further, as opposed to
the traditional commercial research entities—and more akin to the small start-
up commercial company—the potential for profits in today’s academic setting
is more directly tied to the success of a particular research idea.

Nonetheless, for those aspects of a study that could be influenced im-
properly by a financial interest, the prohibition on participation by an aca-
demic researcher holding a financial interest would not unduly hinder the
generation of ideas. Foremost, the premise that academic scientists are
primarily motivated by the "ethic of contribution" and the "economy of credit"
strongly suggests that elimination of the ability to profit significantly would
only minimally impact the generation of ideas.320 Moreover, researchers could

have been pervasive in their presence— as employees, consultants, or members of the firms’
scientific advisory boards".

317. Id. at 153–56. Golden also explains that the "public sector values" includes some
tendencies be motivated, at least in later stages of a scientist’s career, by a more materialist
economy of wealth and power, including the desire to "establish a small academic empire, one
that they seek to sustain and enhance through continual applications for funding and the
acquisition of new equipment and personnel" or to use "science as a route to personal wealth." 
Id. at 156–57.

318. Id. at 157 (noting that the potential to profit from patents seems subordinate).

319. See Kuhlman, supra note 8, at 337 (noting the growing concern that researchers
motivated by financial rewards may distort research priorities and that a respected survey
showed that thirty percent of biotechnology faculty with industry support reported that "their
choice of research topics had been influenced by the likelihood that the results would have
commercial applications"); id. at 342 (noting that profit incentive spurs development in
biotechnology).

320. Supra notes 317–18 and accompanying text. Golden describes the "ethic of contribu-
still realize profits, despite a separation of the conduct of the research from the interest-holding researcher. That is, academic researchers could continue to structure financial arrangements such that they benefit financially from developing ideas. For example, even if another researcher conducts the research, a researcher with an innovative idea could still arrange to be the sole or major shareholder of a small company that holds the patent or other resulting intellectual property rights, or that researcher could hold a license to market the product.

However, it must be acknowledged that limiting faculty researchers' roles in academic research would have some financial consequences. The prohibition would mean that academic researchers with financial interests would have to limit their roles in the research necessary to develop innovative ideas. To the extent other researchers serve as, for example, "principal investigators," the researchers with the ideas may receive less credit from the academic institution. They may also earn less prestige within the community of academic researchers. These factors play at least some role in generating ideas. Thus, the question becomes whether this negative impact on ideas means that the otherwise effective prohibition is rendered inappropriate.

Because the negative impact can be offset, the better view is that the prohibition should still be considered appropriate. The negative impact on ideas flows from the potential that the researcher with the idea may receive less credit from the academic institution or earn less prestige within the community of academic researchers. That impact can be offset by adjustments to academic policies and procedures. Thus, the federal regulations should include such a directive to academic institutions, though it would be appropriate on this issue to allow each institution to devise its own policies, regarding credit for ideas underlying research when the faculty member is unable to serve as the principal investigator due to a related financial interest. If appropriately structured, the prohibition would have a minimal impact on the generation of ideas.

Second, the prohibition generally should have little impact on the research endeavor itself, unless no other researcher within the institution can

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321. See Golden, supra note 35, at 156–57 (explaining that public sector values motivating academic researchers may include a desire to "establish a small academic empire" or a desire to achieve recognition and esteem).
conduct the research necessary to develop the idea or technology. The AAMC Guidelines explicitly recognize that such a circumstance might occur. Indeed, that was the premise underlying the AAMC's "rebuttable presumption" that the research should not be conducted by a researcher with a related financial interest. The AAMC Task Force recommended allowing the research to be conducted by a researcher with an interest only if compelling circumstances are present— for example, if the research could not occur or could not occur safely unless the researcher with a financial interest also conducted the research. Or, for example, if no other researcher within the institution could conduct the research and develop the idea. In those instances, an absolute prohibition on participation might inflict too great a burden on innovation.

However, this author believes that in many, if not most, cases research likely could be adequately conducted despite a separation of the researcher with a financial interest from the conduct of the research. The researcher with the idea who also holds the financial interest often has special expertise relating to the idea and the research. Yet, generally, other academic researchers should be capable of learning what is necessary to conduct those parts of a study from which the financially interested researcher should be excluded. Thus, although somewhat more time-consuming and labor-intensive, the research underlying an innovation generally could be conducted by someone other than the interest-holding researcher.

Nonetheless, in some rare instances, research perhaps could not occur or could not occur safely without the participation of the financially interested researcher. In either case, an exception to the prohibition would be appropriate. The AAMC Task Force suggested that an exception would be appropriate "when the individual holding [financial] interests is uniquely qualified by virtue of expertise and experience and the research could not otherwise be conducted as safely or effectively without that individual." The wording of the AAMC exception is far too expansive, as it would be relatively easy to show that the research could not be conducted as "effectively" if the researcher with the idea and the financial interest is prohibited from participating in the study. For example, it certainly could be considered less effective—given the additional time and study involved—to require the interested researcher to teach another researcher what may be necessary to conduct the research. Any exception to the prohibition should be narrowly worded and interpreted so as to maintain the protection of the research process and the

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322. See supra notes 186–88 and accompanying text (discussing AAMC Task Force recommendations).
323. See supra text accompanying notes 188–89 (same).
324. AAMC Guidelines, supra note 169.
safety of the human participants. Further, any case that qualifies for the exception should be coupled with additional risk-management techniques, such as disclosure and monitoring. However, if appropriately structured, the prohibition would have a minimal—or at least acceptable—impact on the ideas and research essential for biomedical and biotechnology innovation.

(4) The Potential for Profit Still Justifies the Capital Risk

As explained, the key ingredient of innovation arguably is someone willing to take a monetary risk—that is, someone willing to fund the research and development necessary to bring an idea to the market, despite the uncertainty of realizing any return on the investment. Historically, the risk inherent in biomedical/biotechnology research was borne by commercial entities such as pharmaceutical companies, federal funding agencies, and academic research institutions to the extent that cost shifting could be used to funnel money toward research. Today, academic institutions have fewer avenues for cost shifting, and greater competition for federal funding exists. Thus, increasingly the important risk takers are the commercial entities. This includes both traditional research-and-development companies, such as pharmaceutical companies, and the emerging small start-up companies whose necessary capital is often supplied by venture capitalists or other private investors. Academic institutions, which are increasingly involved in financial arrangements that create a potential for a revenue stream from a research idea, may also make investments resulting in equity interests for the institution.

The question remains whether the separation of the researcher with a financial interest from the researcher conducting the research will impact the availability of research funds from these sources. More stringent regulations pertaining to financial conflicts of interest are not likely to impact the availability of federal funding. The federal funding agencies have historically

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325. See generally Golden, supra note 35, at 136–43 (describing sources of funding for technology transfer).

326. The investors in small biotech firms are often referred to as "venture capitalists." See id. at 139 (noting that funding for basic research in the biotechnology industry likely comes from venture capital; and that "most biotechnology firms start out as venture-capital-financed 'spin-outs' from a university or research institute"). This private investment is essential to the biotechnology industry because "the industry is characterized by not yet having a base of revenue from existing product sales with which to reinvest into research and development." Kuhlman, supra note 8, at 317 n.21.

327. AAMC Guidelines II, supra note 172, at 6; see also Diagram A, supra p. 26 (illustrating typical arrangements between academic institutions and for-profit entities).
borne, and today still bear, the risk associated with innovation as a means of serving the public interest.

In contrast, commercial entities have always been profit oriented. They have historically borne, and today still bear, the research-and-development risk because of the potential for future profits. The prohibitions do not preclude commercial sponsorship. Thus, traditional commercial research entities will still use academic researchers when that is the more practical and feasible way to conduct needed research. The prohibition simply precludes additional financial interests or relationships with the researcher conducting the study. For example, this would preclude a commercial sponsor from hiring as a consultant the researcher conducting the research or from paying an honorarium for the researcher to speak. The impact of such a limitation may or may not make it more costly overall (and thus less profitable) to conduct the research and development. It may be more costly, for example, if the prohibition results in companies having to hire more expensive consultants. However, it would not be more costly if the consulting, speaking, and other arrangements served primarily as perks for the academic researcher. The bottom line is that, although the prohibition may have some effect on the cost of research, it would not create an undue effect on commercial sponsorship of research.

For the small start-up company without academic researchers as shareholders, officers or directors, and/or scientific employees, the analysis is comparable to that of the traditional research company. For small start-up companies with academic researchers as shareholders, officers or directors, and/or scientific employees, the analysis is different, but the conclusion remains the same. As noted, many biotechnology firms begin as venture-capital-financed spin-outs from universities, and academic research scientists are often key players in these firms. However, in the early stages of existence, these companies commonly "leverage relatively narrow technical expertise, as well as intellectual property, for both financing and limited amounts of revenue." That is, it is the patent or license rights that the company obtains from the university that are key to its success. The intel-

328. See Golden, supra note 35, at 133 (noting that the biotechnology industry and its investors "seek first and foremost to advance their capacity to generate revenues").

329. This is certainly a reasonable inference from the arrangements described in Diagram A, supra p. 26. See also notes 93–96 and 105–08 (defining significant financial interests in current federal regulations).


331. Id.

332. Id. at 104–05.
lectual property right is "the inducement and reward" for private investment notwithstanding the risk. It provides an assurance that if the technology is successful, the intellectual property rights will protect it from competitors. Thus, even in the small start-up company, separation of the researcher with the financial interest from the researcher conducting the research will not have a significant impact on funding and private investment. Profits can be made notwithstanding the prohibition given that it is the intellectual property rights that secure private venture capital. Additionally, as noted, researchers who wish to be a part of that potential profit-making venture can make that choice. That is, a researcher who initially discovers a potentially profitable technology can elect to forego further participation in the research and become a part of the company that holds the patent or other resulting intellectual property rights.

In sum, the prohibition on participation in research would not unduly hinder innovation. It would have a minimal impact on the generation of ideas, the conduct of the research itself, and the availability of funding sources. Therefore, it is a change that the medical research community should embrace.

3. Other Risk Management Techniques Are Not as Effective

Additional disclosures and monitoring are two other key strategies identified to manage the risk of problematic financial interests. Neither strategy is likely to be as effective as a prohibition on participation.

a. Additional Disclosures

Other articles have considered whether additional disclosure of financial interests can serve as an effective risk management technique, and therefore this Article will not address the issue in any depth. As explained, a consensus exists that researchers' disclosure of financial interests to competent institutional personnel is appropriate. Greater debate exists, however, regarding additional disclosure as a regulatory response. The recent guidance recommends additional disclosure to IRBs, disclosure to research participants as

334. See, e.g., Janet Fleetwood, Conflicts of Interest in Clinical Research: Advocating for Patient-Participants, 8 WIDENER L. SYMP. J. 105, 112–14 (2001) (discussing reforms prohibiting financial conflicts of interest); Ossorio, supra note 231, at 76 (considering whether conflicts of interest undermine integrity and safety).
335. Disclosure to IRBs is appropriate. IRBs should have access to all information relating to risks involved in the study. However, it is inappropriate to turn the disclosure to IRBs into a burden imposed on IRBs. The responsibilities for assessing interests, implementing the regulatory response, monitoring, and enforcement should lie with entities other than IRBs.
deemed appropriate by IRBs, and disclosure to journals and accompanying public statements, including disclosure at presentations and conferences. All of these disclosures would seem to be appropriate in order to protect patients' autonomy rights, as well as the appearance of integrity in research.

However, several barriers prevent disclosure to human participants from being an effective risk-management technique. Disclosure regarding financial interests of physician researchers involved in research with human participants is fraught with all the problems associated with obtaining effective informed consent. In the context of research, the consent process includes discussion of the study's "nature, purpose, risks and benefits, along with alternatives, including standard treatment or non-treatment, and the proposed intervention’s probability of success." Nonetheless, in part because of their trust in physicians, it is recognized that patients mistakenly and unrealistically believe that every aspect of the research project will benefit them directly. Additionally, researchers recognize that patient-participants often fail to

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336. An enlightened view of informed consent suggests that patients should have access to information relating to financial interests held by physician-researchers. The OHRP guidance recommends disclosure of "the source of funding for the study and the payment arrangements ... during the consent process and in the Consent Form, whenever that information is considered to be material to potential participants' decision making process." OHRP Guidance, supra note 142, § 5.2. The problem is deciding when the information becomes material. Does the OHRP mean disclosure even if the funding source does not create a problematic financial interest? The nature of any disclosure to human participants is also problematic and this author will leave that discussion for another forum.

337. Disclosures to journals in conjunction with public statements, presentations, or conferences serve a preventative purpose. Public knowledge of financial interests will enhance the likelihood of greater scrutiny of research results, thereby providing a safeguard against breaches of research fiduciary duty. See generally Marcia Angell, Is Academic Medicine for Sale?, 342 NEW ENG. J. MED. 1516 (2000) (describing risks of blurred lines between academic research and for-profit entities). But see Kenneth J. Rothman, Conflict of Interest: The New McCarthyism in Science, 269 J. AM. MED. ASS'N 2782, 2782-84 (1993) (arguing that strict conflict-of-interest policies will reduce objectivity).

338. See Frances H. Miller, Trusting Doctors: Tricky Business When It Comes to Clinical Research, 81 B.U. L. REV. 423, 443 (2001) ("Disclosure pays the respect that is due to the autonomy of human participants.").

339. Fleetwood, supra note 334, at 107 (citing ADVISORY COMM'N ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT OF THE ADVISORY COMM'N ON HUMAN RADIATION EXPERIMENTS 523-25 (1996)).

understand the terms used in consent forms, rarely understand the underlying methodology of the study, and have difficulty assessing the benefits and burdens. As Dr. Janet Fleetwood has noted,

"As Dr. Janet Fleetwood has noted,

Even when conflicts of interests are disclosed in consent forms, patients may still be left wondering how to weigh the investigator’s involvement… It is difficult to imagine patients routinely assessing whether the financial gains disclosed in a consent discussion are sufficient to affect the objectivity of their physician. Moreover, if the patient believes there is a conflict of interest, the patient must then attempt to determine how to reassess the balance of benefits and burdens of participating in the study. It is difficult to imagine patients... being able to make these assessments."

Thus, many believe that additional disclosure of related financial interests to participants in human research, although arguably appropriate, is unlikely to serve as an effective conflict-management strategy. Devising an appropriate and effective manner and means of disclosure to human research participants will require greater exploration.

b. Monitoring

Similarly, monitoring as a risk-management technique is likely to be less effective than prohibiting participation in the research by the researcher.


342. Fleetwood, supra note 334, at 109. Dr. Fleetwood’s article includes the following quote: "[In most cases,] the process of obtaining ‘informed consent,’ with all its regulations and conditions, is no more than an elaborate ritual, a device that, when the subject is uneducated and uncomprehending, confers no more than the semblance of propriety on human experimentation." Id. (quoting F.J. Ingelfinger, Informed (But Uneducated) Consent, 287 NEW ENG. J. MED. 465, 466 (1972)).
holding a related financial interest. Monitoring can take several forms, two of which are currently used, albeit minimally. First, federal regulations require IRBs to conduct "continuing review" of research that is supported or regulated by the PHS and the FDA. However, the regulations do not define the term "continuing review" and provide little guidance beyond the directive to "conduct continuing review . . . at intervals appropriate to the degree of risk, but not less than once per year," and the grant of authority "to observe or have a third party observe the consent process and the research." Unfortunately, IRBs have faced considerable criticism regarding their handling of continuing review. Specifically, it has been noted that IRBs "routinely review only written reports that are submitted by investigators conducting clinical trials. IRBs do not visit research sites, oversee the informed consent process, or seek feedback from research participants." Further, IRBs lack the data and the expertise necessary to conduct meaningful continuing review. Given the resource limitations and burdens already imposed on IRBs, strengthening continuing review by IRBs is not likely to be a satisfactory regulatory response.

Another form of monitoring sometimes employed is use of a "Data and Safety Monitoring Board" (DSMB). As first conceived, DSMBs would consist of "experts . . . [with] no vested interests in the outcome" of research, who would provide oversight for double-blinded clinical trials. The DSMB would

1. have access to all data (particularly adverse event data) pertaining to each subject in the trial; 
2. establish "stopping rules" to be applied in the event that participants on one arm of the study fared much better or much

347. Hoffman, supra note 344, at 726–27 (noting also that only minimal progress had been made between 1998 and 2000) (citing Status of Recommendations, supra note 128, at 12–13).
349. See id. (describing role of DSMBs).
By providing continuous analysis of accumulating trial data, DSMBs can effectively monitor investigator performance and assess the safety of a clinical trial.\textsuperscript{351}

The use of DSMBs is still very limited although increasing, especially by NIH and private-industry sponsors of large, multicentered trials that are expected to involve significant risks to participants.\textsuperscript{352} This is due in large part to the expense involved. IRBs have authority to require approved research studies to utilize DSMBs. However, it has been noted that if an IRB required DSMB oversight, "the requirement would be tantamount to disapproval of the study."\textsuperscript{353} DSMBs typically consist of six to eight members (clinicians and biostatisticians, for example) who meet several times a year, but who spend numerous additional days examining data. They may be paid up to $2,000 per day.\textsuperscript{354} Accordingly, although DSMBs could provide risk management, they are unlikely to serve as an effective regulatory response as currently employed.

However, a variation on the idea of the DSMB may provide a more feasible approach to monitoring as a conflict-management strategy in the academic research community. This approach would use a rigorous review of those aspects of a research study that could be influenced by a financial interest, conducted by two or more institutional researchers without a financial interest. Like a more formal DSMB, these reviewers would study, from time to time throughout the trial, central aspects of the project: the research design, the enrollment process, the informed consent process, the data analysis and conclusions, and the reporting and publication. Alternatively, an institution could manage the risk by having a second principal investigator who would be more directly involved with the research on a day-to-day basis. The second principal investigator would take an active role in the central aspects of the research process.

\begin{itemize}
\item \textsuperscript{350} Id.
\item \textsuperscript{351} See Hoffman, supra note 344, at 762–63 (advocating use of DSMBs) (citing Janet Wittes, Behind Closed Doors: The Data Monitoring Board in Randomized Clinical Trials, 12 \textit{STAT. MED.} 419, 420 (1993)).
\item \textsuperscript{352} See Mica, supra note 348 (noting limited use of DSMBs).
\item \textsuperscript{353} Id.
\item \textsuperscript{354} See Hoffman, supra note 344, at 763–64 (describing composition and compensation of DSMBs).
\end{itemize}
All forms of monitoring discussed would seem to provide at least some risk-management benefits. The risk created by allowing research to be conducted by a researcher with a financial interest is that the researcher’s judgment may be undermined, thereby impacting the many decisions in the research process that require judgment and discretion. Monitoring by review of those aspects of a study that turn on the exercise of judgment and discretion will protect participants and the integrity of the research to the extent that bad judgment can be detected in time to protect the participants. However, researchers have noted that detecting errors in judgment by review of information is difficult unless the deviation is large. Further, harm to participants may have already occurred by the time a problem is identified. Thus, monitoring through the more direct involvement of a second principal investigator would seem to provide greater protections than other monitoring strategies. If a second principal investigator is involved in making judgment calls concurrently with the researcher with a financial interest, it would seem more likely that deviations in judgment could be detected, and detected earlier.

However, no form of monitoring would be as effective as prohibiting the researcher with the financial interest from participating in the central aspects of the research. As this Article has already explored, a prohibition on participation in research by a researcher holding a financial incentive helps eliminate the risk that the researcher’s judgment will be undermined by a conflict. In contrast, monitoring can at most reduce the risk. Further, monitoring arguably constitutes a more costly regulatory option. More formal DSMBs involve the additional expenses discussed above, and with less formal monitoring an opportunity cost arises because the time of one or more additional researchers must be devoted to the research affected by the financial interest, rather than being spent on other research studies. For the same reason, this regulatory option arguably would have a negative impact on innovation. If more researchers are tied up in the conduct of one research project, fewer research projects can be conducted.

\[D. \text{ Structural Enhancements for Disclosure and Management}\]

As explained, the global deficiencies in the recent initiatives stem largely from the adherence to the traditional model of academic and medical community self-regulation. This Article has advocated that, rather than allowing each academic institution to design its own conflict-of-interest system dependent

355. August 15 Conference Transcript, supra note 27.
356. Notably, these negatives could be minimized if the researcher serving as the second principal investigator, although possessing solid research knowledge and skills, perhaps lacks the creativity and the desire to be actively involved in innovation.
PROPOSALS FOR A MORE EFFECTIVE REGULATORY SCHEME

on the unique cultural and governance practices at the institution, the federal regulations should direct each institution to follow a largely uniform disclosure, management, and oversight system using mandated federal standards and regulatory responses as outlined in the foregoing sections. Protections for human research participants should be rigorous and uniform from institution to institution. Further, uniformity will also enhance the ability of the federal agencies to monitor compliance with the mandated protections. However, because resources do vary from institution to institution, the mandated system should be streamlined to minimize complexities.

Complexities can be minimized by using the suggestions already presented in this Article: (1) requiring disclosures of all financial interests related to research at the institution, (2) adopting the "deemed problematic" approach to assessing financial interests, and (3) using as the primary conflict-management technique the prohibition on research participation by researchers holding problematic financial interests (absent truly compelling circumstances).

The system can be streamlined by clearly establishing discrete responsibilities at each stage of the system and by ensuring that those responsibilities are delegated to entities with appropriate and focused expertise. As noted above, the recent initiatives suggest considerable overlap in the responsibilities of the "designated institutional officer," the "conflicts of interest committee," the department heads, and the IRBs. Importantly, it is beyond the scope of this Article to flesh out all aspects of a regulatory system for financial conflicts of interest. Rather, the mission of this subpart of the Article is to highlight a fundamental structural change that could improve and streamline the process of addressing financial conflicts of interest. The key differences between the regulatory schemes envisioned by the recent guidance and the system proposed herein are (1) the segregation of the responsibilities for financial assessments and oversight from the responsibilities for the scientific assessments and oversight and (2) the minimal imposition of additional responsibilities on IRBs.

1. Disclosure to the "Office for Financial Conflict Management"

As is currently required, initial disclosures by researchers of their financial interests should be made to an institutional office or officer. However, in contrast to the dual entities envisioned by the current regulations and recent initiatives (referred to as the designated institutional official and the conflicts of interest committee), a single entity—for example, an "Office for Financial Conflict Management" (OFCM)—would have primary responsibility and authority for the disclosure and assessment of financial interests.
The OFCM would oversee the disclosures from all institutional researchers of all financial interests related to institutional research at three points in time—annually, before the submission of a specific research proposal to an IRB, and periodically throughout the studies. Further, the OFCM would conduct any and all assessments of the nature and quality of the financial interests held and disclosed by researchers. Because of the magnitude of this administrative task, an adequately staffed office would be required. However, the complexity of the administrative task would be minimized by use of the "presumed permissible"/"deemed problematic" approach. The OFCM assessment would involve (1) determining whether a researcher holds a financial interest that is presumed permissible using fairly bright-line tests clearly established in federal regulations and (2) deeming any other financial interest as problematic.

Disclosures submitted with research protocols showing only presumed permissible financial interests could be forwarded to the IRB, along with a written description of the financial interests and an explanation of why the financial interests were presumed permissible. If the interests were presumed permissible, no additional action would be necessary.

Upon identifying any deemed problematic financial interest, the OFCM would impose the prohibition on research and ensure that the research protocol is in accord with the prohibition. Written findings relating to any prohibition on research would be forwarded to the IRB and reported to the researchers and the "Patient and Research Protection Committee" (PRPC), described in the following section. As explained therein, a researcher wishing to challenge the imposition of the prohibition would file an application for exception with the PRPC.

2. The Patient and Research Protection Committee

Under the scheme envisioned in the current regulations and recent guidance, the designated institutional officer forwards questionable conflicts to a conflict-of-interest committee for assessment and management. Use of the presumed permissible/deemed problematic approach eliminates the need for a separate conflicts of interest committee. What is needed instead is an entity to assess whether a particular circumstance warrants an exception from the usual regulatory response to a deemed problematic financial interest.

Thus, rather than a conflict-of-interest committee, a more streamlined and efficient system would have a PRPC with appropriate expertise to decide whether a researcher with a problematic financial interest should be permitted to participate in the research to preserve patient safety and innovation. Whether the PRPC is a committee that meets periodically or an office with daily duties will depend on the frequency of requests for exceptions, and the
number of exceptions granted (given that those cases then require ongoing oversight). The PRPC would constitute the heart of the management and oversight system.

As noted, a primary role of the PRPC would be to determine whether the rare exception should be granted to the prohibition on participating in research by a researcher with a problematic financial interest. Assessment of whether the exception should be granted would be triggered by an application by a researcher upon whom the OFCM imposes the research prohibition. Because the exception hinges on whether other academic researchers are competent to conduct the research safely, the review committee would be unconcerned with the extent or seriousness of the financial interest. Rather, the PRPC would consider factors such as:

- the thesis of the study;
- the methodology being used;
- the scientific or professional expertise required for determining eligibility, conducting the study, and analyzing data; and
- whether another researcher could conduct, or be trained to conduct, the research.

Thus, in contrast to the conflict-of-interest committee envisioned in the recent initiatives, the determinations made by the PRPC would be more scientific in nature.

If the PRPC determines that an exception should be granted, it would also detail the extent to which the researcher with a financial interest could participate in related research. That assessment would similarly hinge on the extent to which other academic researchers are competent to conduct certain aspects of the research. Additionally, the PRPC would determine what additional conflict-management strategies should be used. For example, the PRPC likely would find that the most effective additional safeguard would be some form of monitoring. If monitoring were appropriate, the PRPC would outline a monitoring plan, including the form of monitoring that would be appropriate (for example, review or direct involvement) and the extent of the monitoring. The formulation of a conflict-management plan is properly within the domain of the PRPC because the inquiry involves considering the research process and how to protect that process, rather than consideration of the nature or seriousness of financial interests held by the researcher. The federal regulations could specify that certain other conflict management strategies would be triggered automatically in every case in which an exception to the prohibition is granted.

All findings of the PRPC would be reported to the IRB and the OFCM. However, in contrast with the recently issued guidance, the IRB would have little responsibility relating to financial conflicts of interest. Rather, the OFCM and the PRPC would have responsibility for the oversight and monitoring of financial interests related to research.
3. Oversight by the OFCM and the PRPC

In addition to the responsibilities outlined in the foregoing sections, the OFCM and the PRPC would have certain responsibilities relating to the oversight and monitoring of financial interests related to research. Responsibilities for oversight should also be clearly delegated to entities with appropriate expertise.

Accordingly, the OFCM’s responsibilities would relate to disclosures. First, the OFCM would continue to review disclosures submitted by researchers with financial interests relating to research. Because the financial interests relating to ongoing research may change (that is, the financial arrangements relating to research may be modified), continuing review by the OFCM will be necessary. Additionally, the OFCM should require periodic reporting from researchers prohibited from research in order to verify compliance with the prohibition.

Second, the OFCM would oversee disclosures regarding researchers with financial interests who were granted an exception from the prohibition. As explained, the PRPC would forward to the OFCM a report from every challenge to the prohibition. If the PRPC granted an exception from the prohibition on research to a researcher with a financial interest, the report would also detail the conflict-management (monitoring) plan formulated by the PRPC and direct the OFCM to prepare any appropriate additional disclosures. Because of its financial expertise, the OFCM would have primary responsibility for preparing and overseeing the required additional disclosures. For example, the OFCM could require presentation reports and copies of all publications to ensure that proper disclosures of financial interests are being made. Similarly, if federal regulations require disclosure to human research participants of financial interests held by researchers conducting any part of the study, the OFCM, rather than the IRB, would draft the informed consent materials. However, the IRB also has responsibilities under federal law for overseeing the informed consent process. Accordingly, after drafting the informed consent materials, the OFCM would forward those materials to the IRB. The IRB would review the materials and ensure that the disclosures become properly integrated into the implementation of the research project.

An adequate oversight system would also involve PRPC monitoring of those projects in which an exception to the prohibition was granted. The PRPC would have the responsibility to assess periodically the effectiveness of the monitoring in reducing the potential for bias in the research process. This could be accomplished through periodic consultation with the researchers performing the monitoring strategies and through periodic review of the research itself. If concerns were raised, the PRPC would reformulate the monitoring plan, or, if necessary, the PRPC would reimpose the prohibition even if doing so would result in the discontinuation of the study.
4. Additional Enforcement Considerations: Monitoring Compliance and Sanctions

An effective regulatory system includes methods of ensuring compliance and sanctions for noncompliance. Under current regulations, the federal agencies have a limited role in ensuring compliance with financial conflicts of interest regulations. As explained, the system has largely been grounded in trust. However, given the problems that have come to light and the importance of regaining the public's trust in the research process, the enforcement process should be more vigorous and, as in other areas, involve a greater role for the federal agencies. Fleshing out the details of compliance and sanction considerations is beyond the scope of this Article. However, a few points should be beyond debate.

The assurance process is useful and can be maintained. But, in addition, the federal regulations should impose recordkeeping and reporting requirements, as well as an auditing process that would allow the federal agencies to ensure that academic institutions are in fact carrying out the responsibilities directed by the federal regulations. If the institutions are not carrying out these responsibilities, these regulations should provide an effective sanctions scheme.

**Recordkeeping:** Federal regulations should require academic institutions to document their compliance with the disclosure, management, and oversight process outlined in the foregoing sections. For example, based on the suggestions in this Article, records such as the following could be maintained:

- For the OFCM, researcher disclosure forms; findings of "presumed permissible" financial interests; findings of "deemed problematic" financial interests; periodic verifications regarding imposed prohibitions; reports from the PRPC regarding challenges.
- For any exception granted, the management (monitoring) plan formulated by the PRPC; informed consent materials drafted for any exception granted; and reports regarding and copies of additional disclosures.
- For the PRPC, reports of findings for all challenges to the prohibition on research; for any exception granted, the management (monitoring) plan; documentation of periodic consultation with monitoring researchers; any modifications to monitoring plans, including revocation of the exception.

**Auditing:** Auditing of an institution's implementation of a regulatory system is an effective means of ensuring compliance, especially if the auditing occurs frequently. However, federal agencies notoriously are unable to audit with the frequency necessary to instill public confidence regarding compliance. Accordingly, an effective compliance system will likely need to continue relying to some extent on self-auditing by the institution. The federal regulations could specify random and periodic audits by the federal agencies, supplemented by an annual, institutional self-audit of the financial conflict-of-
interest system. An audit committee designated by the institution could conduct the self-audit.

The self-audit could consist primarily of a review of the records relating to a specified number of research projects. Reviewing records could help an auditing committee determine the following:

- Are the initial disclosures from researchers adequate for identifying financial interests?
- Has the OFCM properly identified presumed permissible and deemed problematic interests?
- Is the OFCM properly enforcing the prohibition through periodic verifications?
- Has the PRPC properly determined when exceptions should be granted, and are exceptions properly supported?
- When an exception has been granted, are the conflict-management plans adequate?
- Is the PRPC conducting meaningful periodic consultations with monitoring researchers?
- Are required additional disclosures being made?
- Are informed consent materials on file?
- Has the IRB ensured that protocols are in compliance with findings of the OFCM and the PRPC?

While not a perfect means of ensuring compliance, auditing and recordkeeping can help ensure implementation of the system.

Reporting: The federal regulations should also require the institution to report the findings of the self-audit. Additionally, institutions should be required to report any exception to the prohibition granted, along with the conflict-management plan formulated by the PRPC.

Sanctions: A federal sanction system should be developed and implemented. In other areas of health care regulation, the effectiveness of intermediate sanctions has been recognized. That concept would seem to be a good one for this area as well. A total cut-off of federal funds for research for violations of financial conflicts of interest regulations would be a draconian sanction and one arguably not in the public interest.

VI. Conclusion

The presence of financial conflicts of interest in the arena of biomedical/biotechnology research at academic medical centers is sufficiently problematic to justify a strong federal role in addressing the issue. The time has come to move away from the traditional models of self-regulation to ensure sufficiently rigorous and uniform protections for human participants. The federal regulations governing financial conflicts of interest should clearly specify standards, require adequate responses, and strengthen monitoring and
enforcement activities. Researchers with problematic related financial interests should be prohibited from participating in those aspects of a clinical study that could be improperly influenced, absent compelling factors showing that the research could not be conducted without the researcher's participation. Further, the financial threshold triggering that response should be considerably less than what the regulations to date have considered to be significant financial interests. Whether a problematic financial interest exists should be determined by persons with the requisite expertise in financial matters, and whether an exception to the prohibition is justified should be determined by persons with the requisite scientific and research expertise.

Undoubtedly, some of the suggestions in this Article will not be popular among current university researchers who have significantly profited, or who envision future opportunities for significant profit, from technology transfer while at the same time fulfilling their academic responsibilities for research. And institutions may object to the labor and organizational requirements. But the risk is real, and the public trust must be respected. The obligation to the public is to preserve complete integrity and objectivity—as well as the perception of complete integrity and objectivity.

Moreover, innovation and technology transfer can continue to thrive without the troublesome financial arrangements and relationships that currently exist. This Article did not attempt to address the problem of financial conflicts of interest held by academic institutions themselves. It is possible that institutions can devise arrangements that continue to assist technology transfer of the university research product, thereby likely creating some financial interests related to research at the institution, but that do not raise substantial conflicts of interest concerns. This is especially possible if the institution is firm in eliminating problematic financial conflicts of interest of the researchers at the institution who conduct the related research. If the potential financial influence on the exercise of judgment by the researchers is eliminated, the ability of the interest of the institution to cause improper influence is substantially mitigated. Academic technology-transfer offices may need to work harder to attract nonacademic participants for the spin-out biotechnology firms, but that vision of transferring the university research product into the for-profit sector for commercial development may be more consistent with the congressional vision underlying the technology-transfer acts.