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## REGULATING CONFLICTS OF INTEREST IN RESEARCH: THE PAPER TIGER NEEDS REAL TEETH

JESSE A. GOLDNER\*

### INTRODUCTION

[T]ell doctors that they have a “conflict of interest” in relation to a proposed protocol for research with human subjects, and they believe that you have accused them of unethical behavior. . . . [D]octors tend to assume that a conflict of interest exists only when they actually have made a “bad” decision motivated by their financial interest in the sponsor of their research. Lawyers . . . view conflicts as objective, structural, and rule-based. You could be a paragon of virtue, and you would be conflicted out of representing a client if a prohibited conflict of interest exists. Doctors, in contrast, view conflicts of interest as relating to the individual’s character and ability to resist temptation. We lawyers might say that doctors just don’t get it when . . . we get defensive at their response and fail to understand their starting point.<sup>1</sup>

The scope of conflicts of interest in research is broad and dynamic. As suggested in this introductory quote from an article by Sandra Johnson, the 2008 Richard J. Childress Memorial Lecture Keynote Speaker,<sup>2</sup> there is a fundamental disconnect between how conflicts of interest are viewed in law versus medicine.<sup>3</sup> Further, within the medical community itself, clinical researchers approach, perceive, and respond to conflicts of interest quite

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1. Sandra H. Johnson, *Five Easy Pieces: Motifs of Health Law*, 14 HEALTH MATRIX 131, 131–32 (2004) (footnote omitted).

2. This year’s Richard J. Childress Memorial Lecture, coinciding with Professor Johnson’s retirement from teaching, honored her esteemed career as a teacher and scholar. See Symposium, Saint Louis University School of Law Richard J. Childress Memorial Lecture: Still Crazy After All These Years: Is Regulating Physician Practice an Exercise in Futility? (Oct. 17, 2008), in Sandra H. Johnson, *Regulating Physician Behavior: Taking Doctors’ “Bad Law” Claims Seriously*, 53 ST. LOUIS U. L.J. 973 (2009).

3. Johnson, *supra* note 1, at 131; Michelle M. Mello & Troyen A. Brennan, *Demystifying the Law/Science Disconnect*, 26 J. HEALTH, POL. POL’Y & L. 429, 429 (2001).

differently. No doubt, the vast majority of researchers comply with whatever institutional or federal regulatory requirements apply to them. For many, the rationales are obvious: regulatory requirements both protect the integrity of the research process and help ensure public support of the research enterprise. For others, perhaps at times they comply reluctantly—because regulatory requirements are perceived as simply one more time-consuming effort in a large series of bureaucratic steps that seemingly must be followed to enable researchers to pursue their research. But when violations come to light at least publicly, the typical consequence for both the investigator (and sometimes to the institution) seems to be little more than embarrassment. One could readily describe the current regulatory regime as simply a paper tiger. In the absence of truly significant government regulation of these conflicts in research, the varied approaches pose unique challenges for institutions that support such research.<sup>4</sup>

This article will address the current state of conflicts of interest in research. Following a discussion in Section I of how the academic research environment has changed over the past twenty-five years, Section II will consider recent empirical research on such conflicts. The data suggests, contrary to beliefs held by many clinicians and researchers, that conflicts of interest can and often do, at least unconsciously, affect how they behave and the outcomes of their studies. Section II will also review additional recent empirical analyses, directed to the question of how potential research subjects view disclosure of conflicts of interest. Section III will touch on a number of widely publicized research “scandals” involving conflicts of interest that likely have had a negative effect on public support for the research enterprise, but also may well result in the delivery of lower quality of care when clinicians reject otherwise good science out of concern for the apparent conflicts of interest in published research.

Section IV will discuss current federal regulations and initiatives by institutions and professional organizations to further guide researchers. The nature of the historical resistance to placing any significant limitations on conflicts of interest stems from a wide variety of attitudes by researchers that affect their behavior. Such attitudes can be grouped into general categories, and Section V presents a “Taxonomy of Researchers,” based primarily on my own membership on a university conflict of interest committee over a four year period.

Section VI will discuss how, once identified, conflicts of interest are typically managed by institutions, and critiques by the Office of the Inspector General of the Department of Health and Human Services (OIG) of the federal

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4. “Research,” as it is used in this article, means “a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.” 45 C.F.R. § 46.102(d) (2008).

government's role in the current interplay between government agencies, sponsors, and institutions in regulating conflicts. Collectively, Sections I through VI will demonstrate that the existing world of conflict of interest regulations is shamefully inadequate. Section VII will, therefore, set forth a proposal for reform of the way conflicts of interest are managed at both the federal and institutional levels. As Section VII will argue, the conflict of interest picture is not entirely bleak, and the adoption of a critically necessary uniform set of governmental regulations could help minimize the likelihood of further scandals and help restore public confidence in research.

This article will not address non-financial conflicts presented by researchers' efforts to climb the academic ladder.<sup>5</sup> While real, these conflicts, arguably, are unavoidable given the nature of the academic enterprise. Also beyond the scope of this article are institutional conflicts of interest<sup>6</sup> and conflicts of interest that may be presented by membership on an Institutional Review Board (IRB).<sup>7</sup>

#### I. CHANGES IN THE RESEARCH ENVIRONMENT AND THE EFFECTS ON CONFLICTS OF INTEREST

Universities, prior to the 1970s, and through the 1980s, were governed to a significant extent by what can be termed the "collegial ethos." The institutions were perceived as having a public interest mission, whether they were public or private not-for-profits.<sup>8</sup> The relationship between the university and external institutions generally emphasized the former's financial independence from the latter.<sup>9</sup> Another aspect, internal relationships, also emphasized

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5. See Norman G. Levinsky, *Nonfinancial Conflicts of Interest in Research*, 347 NEW ENG. J. MED. 759, 759 (2002).

6. See Eric G. Campbell et al., *Institutional Academic-Industry Relationships*, 298 JAMA 1779 (2007); Michael M.E. Johns et al., *Restoring Balance to Industry-Academia Relationships in an Era of Institutional Financial Conflicts of Interest*, 289 JAMA 741, 741 (2003); Hamilton Moses III et al., *Collaborating with Industry—Choices for the Academic Medical Center*, 347 NEW ENG. J. MED. 1371, 1371 (2002); see also Nicholas H. Steneck, *Institutional and Individual Responsibilities for Integrity in Research*, 2 AM. J. BIOETHICS 51 (2002).

7. See Eric G. Campbell et al., *Financial Relationships Between Institutional Review Board Members and Industry*, 355 NEW ENG. J. MED. 2321, 2321 (2006).

8. See AM. ASS'N OF UNIV. PROFESSORS, 1940 STATEMENT OF PRINCIPLES ON ACADEMIC FREEDOM AND TENURE 3 (2006) [hereinafter AAUP, 1940 STATEMENT], available at <http://www.aaup.org/NR/rdonlyres/EBB1B330-33D3-4A51-B534-CEE0C7A90DAB/0/1940StatementofPrinciplesonAcademicFreedomandTenure.pdf> ("Institutions of higher education are conducted for the common good and not to further the interest of either the individual teacher or the institution as a whole. The common good depends upon the free search for truth and its free exposition." (footnote omitted)). For-profit institutions of higher education rarely have the conduct of research as part of their mission. See RICHARD S. RUCH, HIGHER ED, INC.: THE RISE OF THE FOR-PROFIT UNIVERSITY (2003).

9. See AAUP, 1940 STATEMENT, *supra* note 8.

independence, focusing on the central role of faculty rights to academic freedom that provide faculty with the autonomy and independence to define and control their work.<sup>10</sup> That academic freedom is essential to enable faculty to work in a way that fulfills the university's public mission and its social role as a public trust, free from the influence of third parties such as university administrators, the government, or commercial enterprises.<sup>11</sup> The government, to a large extent, and perhaps only until more recently, has trusted the universities to do the right thing and to govern themselves because, after all, the Ivory Tower was just that—relatively unaffected by the capitalist ethos of pursuing profit, especially in a particularly aggressive manner.<sup>12</sup>

Beyond ordinary salary support for research, there was little, perhaps other than tenure, promotion, and increased collegial recognition, which individuals could obtain through their research efforts within the university. Prior to the 1980s, little public attention was paid to pharmaceutical and device manufacturers and other corporate entities that offered the kinds of valuable financial incentives to engage in collaborative efforts with faculty members that they currently offer.<sup>13</sup> This is likely because, relatively speaking, little such behavior was occurring. The perception was that university researchers were people who had chosen to forgo greater financial rewards in the public sector for the noble, bucolic, but relatively poverty-stricken, academic environment. The external public had little interest in the financial aspects of the “research environment.”

The minimal focus on the research enterprise that existed dealt largely with the treatment of research subjects, courtesy of the Nazi experiments,<sup>14</sup> Henry

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10. Risa L. Lieberwitz, *Confronting the Privatization and Commercialization of Academic Research: An Analysis of Social Implications at the Local, National, and Global Levels*, 12 *IND. J. GLOBAL LEGAL STUD.* 109, 109–10 (2005).

11. *Id.* at 109–10, 114–15.

12. *Id.* at 113, 115–16; see DEREK BOK, *UNIVERSITIES IN THE MARKETPLACE: THE COMMERCIALIZATION OF HIGHER EDUCATION 185–98* (2003); LAWRENCE C. SOLEY, *LEASING THE IVORY TOWER: THE CORPORATE TAKEOVER OF ACADEMIA 5–15* (1995); JENNIFER WASHBURN, *UNIVERSITY INC.: THE CORPORATE CORRUPTION OF AMERICAN HIGHER EDUCATION 103–36* (2005).

13. See Dana Katz et al., *All Gifts Large and Small: Toward an Understanding of the Ethics of Pharmaceutical Industry Gift-Giving*, 3 *AM. J. BIOETHICS* 39, 39 (2003); see also, S. Madhavan et al., *The Gift Relationship Between Pharmaceutical Companies and Physicians: An Exploratory Survey of Physicians*, 22 *J. CLINICAL PHARMACY & THERAPEUTICS* 207, 211–13 (1997).

14. See generally ROBERT JAY LIFTON, *THE NAZI DOCTORS: MEDICAL KILLING AND THE PSYCHOLOGY OF GENOCIDE* (1986); *THE NAZI DOCTORS AND THE NUREMBERG CODE: HUMAN RIGHTS IN HUMAN EXPERIMENTATION* (George J. Annas & Michael A. Grodin eds., 1992) (suggesting that the trial of Nazi physicians in post-World War II Nuremberg, Germany can be used as a basis from which to question the permissible limits of human experimentation and the focus on universal ethical codes within the context of the criminal trial).

Beecher's article in the *New England Journal of Medicine* chronicling previously unidentified unethical activities by researchers in the United States,<sup>15</sup> and the Tuskegee Syphilis Study.<sup>16</sup> Congressional hearings on these concerns led to the passage of the National Research Act of 1974.<sup>17</sup>

The Act created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research<sup>18</sup> that issued the Belmont Report,<sup>19</sup> which set forth ethical principles for the conduct of human research. The Act also called for the issuance of federal regulations establishing certain requirements for institutions conducting such research.<sup>20</sup> Among these requirements was a mandate that institutions receiving federal funds enter into assurances with the federal government that research be conducted in an ethical manner. They also required that the institutions develop IRBs that would conduct a risk-benefit analysis of a research proposal and review both the proposed content of the information provided to obtain potential subjects in an effort to obtain informed consent and the method of doing so.<sup>21</sup> But there was precious little in the Belmont Report that even alluded to potential conflicts of interest, nor is there a single word about conflicts of interest in the federal IRB regulations, which have remained largely unchanged in the human subjects research context since the late 1970s.<sup>22</sup>

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15. Henry K. Beecher, *Ethics and Clinical Research*, 274 *NEW ENG. J. MED.* 1354, 1354 (1966).

16. See JAMES H. JONES, *BAD BLOOD: THE TUSKEGEE SYPHILIS EXPERIMENT*, at ix (New & Expanded ed. 1993).

17. National Research Service Award Act of 1974, Pub. L. No. 93-348, 88 Stat. 342 (codified as amended in scattered sections of 42 U.S.C. (2006)); see generally Jesse A. Goldner, *An Overview of Legal Controls on Human Experimentation and the Regulatory Implications of Taking Professor Katz Seriously*, 38 *ST. LOUIS U. L.J.* 63 (1993). For a history of the events that led up to the development of regulations on the conduct of research with human subjects, see COLEMAN ET AL., *THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS* §§ 1.03-2.01, at 16-61 (2005).

18. National Research Service Award Act of 1974 § 201; see COLEMAN ET AL., *supra* note 17, § 2.01, at 52.

19. COLEMAN ET AL., *supra* note 17, § 2.01, at 52; NAT'L COMM'N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, *THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH* (1979) [hereinafter *BELMONT REPORT*], available at <http://ohsr.od.nih.gov/guidelines/belmont.html>.

20. National Research Service Award Act of 1974, §§ 211-12.

21. *Id.* § 212.

22. 45 C.F.R. § 46.101-409 (2008); see, e.g., Carol Mason Spicer, *Federal Oversight and Regulation of Human Subjects Research—An Update*, 10 *KENNEDY INST. ETHICS J.* 261, 263 (2000) (noting various statements released by the Department of Health and Human Services (HHS), including the need for additional guidance regarding conflicts of interest in research involving human subjects); see generally COLEMAN ET AL., *supra* note 17, § 2.01, at 51-61

At best, and only by inference, the issue of conflicts of interest might conceivably come into play in two ways. First, in an IRB's analysis of risk,<sup>23</sup> it may find that there is the attenuated possibility that a financial conflict of interest might lead an investigator to (a) cheat on inclusion and exclusion criteria when recruiting subjects, (b) inappropriately keep subjects on a protocol in order to complete the study, or (c) falsify data in an effort to make a test article<sup>24</sup> appear safer and more efficacious than the actual facts would suggest. A second, again inferential and related reference to conflicts of interest, might be seen in the section of the federal regulations that details the elements of informed consent that requires a description of "any reasonably foreseeable risks."<sup>25</sup>

The university academic environment has changed radically, yet there is no one cause to which this change can be attributed. Far more research, percentage-wise, is supported by private sources than by the federal government.<sup>26</sup> As of 2003, academic health centers performed nearly thirty

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(providing an overview of governmental oversight of research with human subjects from the 1960s to 1990s).

23. See 45 C.F.R. § 46.111(a)(1)–(2); accord 21 C.F.R. § 56.111(a)(1)–(2) (2008).

24. A "test article" is any drug, biological product, or medical device for human use. 21 C.F.R. § 56.102(1).

25. See 45 C.F.R. § 46.116(a)(2); accord 21 C.F.R. § 50.25(a)(2).

26. Although the federal government has been the primary source of funding for clinical research in the past, it has been superseded by private industry in the last decade. There is a pronounced trend toward a greater percentage of research being funded by the private sector. One study has shown that 28% of life sciences faculty received private sponsor funding. In 1986, the private sector funded 42% of health care research and development. By 1995, the private sector's allocation of research dollars had risen to 52%. This equated to a three-fold increase, from approximately \$6 billion to \$19 billion. Thus, although federal funding of research has incrementally increased over time, the private funding has increased exponentially.

Patricia C. Kuszler, *Curing Conflicts of Interest in Clinical Research: Impossible Dreams and Harsh Realities*, 8 WIDENER L. SYMP. J. 115, 118–19 (2001) (footnotes omitted).

Biomedical research funding increased from \$37.1 billion in 1994 to \$94.3 billion in 2003 and doubled when adjusted for inflation. Principal research sponsors in 2003 were industry (57%) and the National Institutes of Health (28%). Relative proportions from all public and private sources did not change. Industry sponsorship of clinical trials increased from \$4.0 to \$14.2 billion (in real terms) while federal proportions devoted to basic and applied research were unchanged. The United States spent an estimated 5.6% of its total health expenditures on biomedical research, more than any other country, but less than 0.1% for health services research. From an economic perspective, biotechnology and medical device companies were most productive, as measured by new diagnostic and therapeutic devices per dollar of research and development cost. Productivity declined for new pharmaceuticals.

Hamilton Moses III et al., *Financial Anatomy of Biomedical Research*, 294 JAMA 1333, 1333 (2005); see also David Blumenthal et al., *University-Industry Research Relationships in Biotechnology: Implications for the University*, 232 SCIENCE 1361, 1364 (1986).

percent of all the health care research and development in the United States and more than fifty percent of research supported by the National Institutes of Health (NIH).<sup>27</sup> Nonetheless, there has been a significant shift in research from academic centers to private hospitals and physicians in private practice.<sup>28</sup> Increasing costs of bringing drugs and devices to market<sup>29</sup> have led industry to look elsewhere in an effort to avoid the bureaucracy endemic to universities, and move research sites to private physicians and to for-profit contract research organizations and other independent research enterprises.<sup>30</sup> The Bayh-Dole Act, passed in 1980, encourages academic institutions, supported by federal grants, to patent and license new products developed by their faculty members and to share royalties with the researchers.<sup>31</sup> In many respects this legislation, though designed to facilitate the transfer of technology from academic institutions to bedside, has had the unintended consequence of blurring distinctions between academic entities and researchers on the one hand and commercial entities on the other.

Even while seeking non-academic research environments to conduct research, industry recognizes that academic clinicians remain the “thought leaders”<sup>32</sup> and are very willing to handsomely reward such individuals for giving continuing medical education talks that are likely to increase the sales of new products, or for putting their names on academic papers to which they may contribute little, if anything, substantively. The point to be made is that now there is money to be had—sometimes in such significant amounts as to dwarf an academic salary. In 1985, 2.6% of principal investigators had personal financial ties to their industry sponsors, but by 1999, that figure had been raised to 7.6%.<sup>33</sup> No doubt this figure has grown exponentially in the interim. In 2007, 60% of departmental chairs in academic medical centers had some form of personal relationship with industry.<sup>34</sup>

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27. THE COMMONWEALTH FUND TASK FORCE ON ACADEMIC HEALTH CTRS., ENVISIONING THE FUTURE OF ACADEMIC HEALTH CENTERS 3, 31 (2003), available at [http://www.commonwealthfund.org/usr\\_doc/ahc\\_envisioningfuture\\_600.pdf?section=4039](http://www.commonwealthfund.org/usr_doc/ahc_envisioningfuture_600.pdf?section=4039).

28. See generally Thomas Bodenheimer, *Uneasy Alliance—Clinical Investigators and the Pharmaceutical Industry*, 342 NEW ENG. J. MED. 1539, 1539 (2000).

29. *Id.* at 1540.

30. COLEMAN ET AL., *supra* note 17, § 2.03, at 77–86; see, e.g., Covance: The CRO for Drug Development Services, <http://www.covance.com/> (last visited July 30, 2009); INC Research, <http://www.incresearch.com> (last visited July 30, 2009); MDS Pharma Services, <http://www.mdsp.com> (last visited July 30, 2009), Pharmaceutical Product Development, <http://www.ppdi.com> (last visited July 30, 2009).

31. 35 U.S.C. §§ 200–212 (2006); see also 37 C.F.R. § 401 (2008) (implementing the Act).

32. See Nikolaos A. Patsopoulos et al., *Origin and Funding of the Most Frequently Cited Papers in Medicine: Database Analysis*, 332 BRIT. MED. J. 1061, 1061–63 (2006).

33. Elizabeth A. Boyd & Lisa A. Bero, *Assessing Faculty Financial Relationships with Industry: A Case Study*, 284 JAMA 2209, 2211 (2000).

34. Campbell et al., *supra* note 6, at 1783.



## II. EMPIRICAL STUDIES OF THE IMPLICATIONS OF CONFLICTS OF INTEREST

### A. *Definition and Types of Conflicts*

There are numerous definitions of conflicts of interest. For the purposes of this article, a conflict of interest is defined as a “set of conditions in which professional judgment . . . (such as a patient’s welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain).”<sup>35</sup> Examples in the research area include, but are not limited to: (1) various forms of payments to investigators in connection with the recruitment of subjects, such as per capita payments to investigators for recruiting subjects; (2) various forms of bonus payments for boosting subject enrollment or meeting enrollment deadlines; (3) finder’s fees to those who refer subjects to investigators; (4) gifts from industry sponsors, including discretionary funds, research equipment, and support for travel to professional meetings (often in exotic locales that more closely resemble vacations); (5) stock ownership; (6) highly paid consultant positions; and (7) excessive compensation for providing continuing medical education lectures.<sup>36</sup>

### B. *Empirical Research on Clinician Behavior and Study Outcomes*

Until recently there was a relative paucity of empirical research on conflicts of interest and clinician behavior. Today, a number of scholars are devoting significant efforts to examining issues such as physician behaviors in response to sponsor offers of various inducements;<sup>37</sup> the failure of journals to adhere to their own guidelines regarding the publication of research and

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35. Justin E. Bekelman et al., *Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review*, 289 JAMA 454, 454 (2003) (quoting Dennis F. Thompson, *Understanding Financial Conflicts of Interest*, 329 NEW ENG. J. MED. 573, 573 (1993)).

36. Jesse A. Goldner, *Dealing with Conflicts of Interest in Biomedical Research: IRB Oversight as the Next Best Solution to the Abolitionist Approach*, 28 J.L. MED. & ETHICS 379, 381–84 (2000); see Neal Dickert et al., *Paying Research Subjects: An Analysis of Current Policies*, 136 ANNALS INTERNAL MED. 368 (2002); Neal Dickert & Christine Grady, *What’s the Price of a Research Subject? Approaches to Payment for Research Participation*, 341 NEW ENG. J. MED. 198 (1999); Trudo Lemmens & Paul B. Miller, *The Human Subjects Trade: Ethical and Legal Issues Surrounding Recruitment Incentives*, 31 J.L. MED. & ETHICS 398 (2003); see generally COLEMAN ET AL., *supra* note 17, § 5.02, at 235–37.

37. Jason Dana & George Loewenstein, *A Social Science Perspective on Gifts to Physicians from Industry*, 290 JAMA 252 (2003); Madhavan et al., *supra* note 13; Bruce M. Psaty & Drummond Rennie, *Clinical Trial Investigators and Their Prescribing Patterns: Another Dimension to the Relationship Between Physician Investigators and the Pharmaceutical Industry*, 295 JAMA 2787 (2006); David M. Studdert et al., *Financial Conflicts of Interest in Physicians’ Relationships with the Pharmaceutical Industry—Self-Regulation in the Shadow of Federal Prosecution*, 351 NEW ENG. J. MED. 1891 (2004).

conflicts of interest;<sup>38</sup> relationships between financial conflicts of interest and voting patterns at Food and Drug Administration (FDA) advisory committee meetings;<sup>39</sup> and relationships between individuals reporting conflicts of interest and the likelihood that they would report positive results on the one hand,<sup>40</sup> and the extremely small likelihood, on the other hand, that authors with conflicts of interest would publish negative results.<sup>41</sup>

Data from empirical research examining conflicts of interest in clinical medicine and research is not at all surprising, but rather, it is disheartening. There is a statistically significant relationship between positive findings in studies funded by for-profit entities versus those funded by not-for-profit sources,<sup>42</sup> between industry sponsorship and pro-industry conclusions,<sup>43</sup> and between author conflicts of interest and the greater likelihood of reporting a drug to be superior to placebo.<sup>44</sup> Industry funding may result in study designs that are more likely to lead to favorable results, such as utilizing protocols that involve placebos or other poor comparators, doses that are inappropriate, carefully constituted experimental populations, inappropriate surrogate endpoints, trials whose lengths are sufficiently short so as to be unlikely to show side effects, and definitions that are unlikely to show activity or not likely to show side effects.<sup>45</sup> Industry sponsorship is also associated with

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38. Joel Lexchin et al., *Pharmaceutical Industry Sponsorship and Research Outcome and Quality: Systemic Review*, 326 BRIT. MED. J. 1167, 1167 (2003); Susan Mayor, *Surgery Journal Bans Authors Who Hide Conflicts of Interest*, 332 BRIT. MED. J. 135, 135 (2006).

39. Peter Lurie et al., *Financial Conflict of Interest Disclosure and Voting Patterns at Food and Drug Administration Drug Advisory Committee Meetings*, 295 JAMA 1921, 1921 (2006).

40. Bekelman, *supra* note 35; Mohit Bhandari et al., *Association Between Industry Funding and Statistically Significant Pro-Industry Findings in Medical and Surgical Randomized Trials*, 170 CAN. MED. ASS'N J. 477, 477 (2004); Lee S. Friedman & Elihu D. Richter, *Relationship Between Conflicts of Interest and Research Results*, 19 J. GENERAL INTERNAL MED. 51 (2004); Robert E. Kelly, Jr. et al., *Relationship Between Drug Company Funding and Outcomes of Clinical Psychiatric Research*, 36 PSYCHOL. MED. 1647 (2006); Lexchin et al., *supra* note 38; Patsopoulos et al., *supra* note 32, at 1061; Roy H. Perlis et al., *Industry Sponsorship and Financial Conflict of Interest in the Reporting of Clinical Trials in Psychiatry*, 162 AM. J. PSYCHIATRY 10 (2005); John Yaphe et al., *The Association Between Funding by Commercial Interests and Study Outcome in Randomized Controlled Drug Trials*, 18 FAM. PRAC. 565, 565–68 (2001). *But see* Thomas P. Stossel, *A Biopsy of Financial Conflicts of Interest in Medicine*, 143 SURGERY 193, 196 (2008).

41. Friedman & Richter, *supra* note 40, at 53, 55.

42. Paul M. Ridker & Jose Torres, *Reported Outcomes in Major Cardiovascular Clinical Trials Funded by For-profit and Not-for-Profit Organizations*, 295 JAMA 2270, 2272 (2006).

43. Bekelman et al., *supra* note 35, at 463; Bhandari et al., *supra* note 40, at 478–79; Friedman & Richter, *supra* note 40, at 55; Kelly et al., *supra* note 40, at 1653; Lexchin et al., *supra* note 38, at 1169.

44. Perlis et al., *supra* note 40, at 19.

45. Sergio Sismondo, *How Pharmaceutical Industry Funding Affects Trial Outcomes: Causal Structures and Responses*, 66 SOC. SCI. & MED 1909, 1910–12 (2008).

restrictions on publication and data sharing.<sup>46</sup> Such restrictions and the selective reporting of more favorable pro-protocol analysis can result in erroneous conclusions based on published data.<sup>47</sup> On the purely clinical side, for example, research has shown that a drug company's hosting of an all-expense-paid trip to a resort for a seminar had substantial effects on the attendee-physicians' prescribing patterns.<sup>48</sup> More generally, it has been shown "that favors and promotional items of negligible value can influence behavior of the recipient in ways the recipient does not often realize."<sup>49</sup> As Dr. Arthur Caplan, director of the Center for Bioethics at the University of Pennsylvania's School of Medicine, has noted:

Even small gifts can influence behavior . . . .

The doctors who say, "I can't be bought for a piece of pizza or a free box of doughnuts," aren't paying attention to what empirical science shows influences people . . . . It isn't just a drug company giving out \$25,000 to give a talk and go on a nice vacation—that would certainly influence you. But even if (a drug rep) shows up with a free lunch every week for 50 weeks, it tends to build a sense of reciprocity on the part of the people who get the free gift.<sup>50</sup>

C. *Empirical Studies of the Effects of Disclosures of Conflicts of Interest on Research Participants*

Another area of empirical research related to conflicts of interest in the research enterprise has been the reactions and perceptions of research subjects to disclosures regarding conflicts of interest. For the most part, these studies have demonstrated little concern on the part of participants with the nature of the disclosures made.

Thus, for example, in one study patients with diabetes or asthma were read descriptions of a hypothetical clinical trial with one of five financial disclosure

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46. Bekelman, et al., *supra* note 35, at 454; Jerome M. Stern & R. John Simes, *Publication Bias: Evidence of Delayed Publication in a Cohort Study of Clinical Research Projects*, 315 BRIT. MED. J. 640, 644 (1997).

47. Frank Peinemann et al., *Negative Pressure Wound Therapy: Potential Publication Bias Caused by Lack of Access to Unpublished Study Results Data*, 8 BMC MED. RESEARCH METHOD. 4, 4 (2008), <http://www.biomedcentral.com/1471-2288/8/4>.

48. James P. Orłowski & Leon Wateska, *The Effects of Pharmaceutical Firm Enticements on Physician Prescribing Patterns: There's No Such Thing as a Free Lunch*, 102 CHEST 270, 270–71 (1992); *see also* Sarah Boseley & Rob Evans, *Drug Giants Accused Over Doctors' Perks*, THE GUARDIAN, Aug. 23, 2008, <http://www.guardian.co.uk/society/2008/aug/23/health.pharmaceuticals>.

49. Katz et al., *supra* note 13, at 42; *see also* COLEMAN ET AL., *supra* note 17, § 2.02, at 61–77.

50. Janet Moore, *U Plan: Ban All Gifts to Doctors*, MINN. STAR TRIB., Oct. 21, 2008, at 1A (quoting Arthur Caplan, Dir., Ctr. for Bioethics at the Univ. Penn. Sch. of Med.) (internal quotation marks omitted).

statements: (1) a generic disclosure that the principal investigator might benefit financially; (2) the principal investigator would receive per capita payments from the sponsor to support salaries of research staff and supplies; (3) the study is supported by the sponsor, and the principal investigator receives additional money for consulting, giving speeches, or writing reports; (4) the principal investigator has an investment in the sponsor's stock and therefore could gain or lose money depending on the results; and (5) the institution conducting the study has an investment in the sponsor's stock.<sup>51</sup> The study results indicated respondents were sensitive to some of the financial interest disclosed, and that, in particular, they viewed ownership of equity interests less favorably than receiving per capita payments,<sup>52</sup> with other financial conflicts falling between these two extremes.<sup>53</sup> Nonetheless, patients' willingness to participate did not substantially differ among other types of disclosure, as 45% to 59% were very willing to participate.<sup>54</sup> Other factors, such as potential benefits and risks and the purposes of the research were deemed to be more important in making a decision.<sup>55</sup> Some respondents were surprised to learn about the equity interests and expressed concern if they were not disclosed.<sup>56</sup> Some 59% felt that the possibility that the researcher or institute might benefit financially did not change their trust in the researcher or institution.<sup>57</sup> Over a third of the respondents, however, were less trusting in the researchers and institutions as a result of the disclosures.<sup>58</sup> For some, of course, the disclosure might have increased trust based on the potential participants' perception of increased honesty.<sup>59</sup> In general, however, changes in trust did seem to be related to variations in an individual's willingness to participate in a study, but there was a perception that financial interests lowered the scientific quality of the hypothetical trial.<sup>60</sup> Other similar studies showed that types of disclosures had little or no influence.<sup>61</sup>

In another study, involving patients in cancer-research trials, nearly 90% expressed little or no worry about financial ties of researchers or institutions,

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51. Kevin P. Weinfurt et al., *Effects of Disclosing Financial Interests on Attitudes Toward Clinical Research*, 23 J. GEN. INTERNAL MED. 860, 861 (2008).

52. *Id.*; accord Lindsay A. Hampson et al., *Patients' Views on Financial Conflicts of Interest in Cancer Research Trials*, 355 N.ENG. J. MED. 2330, 2336 (2006).

53. Weinfurt et al., *supra* note 51, at 862.

54. *Id.* at 864.

55. *Id.* at 862.

56. *Id.*

57. *Id.*

58. Weinfurt et al., *supra* note 51, at 862, 864.

59. *Id.* at 864.

60. *Id.* at 863–64.

61. Jeffrey N. Gibbs & Gregory A. Guagnano, *Investigator Financial Disclosures and Its Effect on Research Subjects*, 62 FOOD & DRUG L.J. 727, 735 (2007).

including researchers receiving speakers' fees (82%), consulting fees (75%), royalty payments (70%), and stock ownership (77%).<sup>62</sup> Less than 15% of patients indicated that knowledge of a financial tie would have kept them from participating.<sup>63</sup> Eighty-one percent believed it was ethical for a researcher whose drug was being evaluated in the trial to receive speaking fees, and 82% thought it was ethical to receive consulting fees.<sup>64</sup> Seventeen percent of the participants thought that no disclosure to patients was even necessary, while some 40% said they wanted disclosure of the oversight system for the researcher, and 31% believed that there should be a requirement to disclose all financial ties.<sup>65</sup>

In one further study, using focus groups of potential research participants, the individuals wanted to know about financial interests, irrespective of whether or not those would affect their participation.<sup>66</sup> The study indicated that potential research participants varied in both the desire and ability to understand the nature and implications of information provided.<sup>67</sup> It further concluded that as a result of the group sessions, participants were better able to identify information they would want to obtain.<sup>68</sup>

Finally, in what the authors, Christine Grady and her colleagues, indicated was the first published qualitative study reporting research participants' views regarding financial interests of investigators,<sup>69</sup> the study design involved a face-to-face, semi-structured interview with patients with serious, life-threatening, or chronic conditions.<sup>70</sup> Most were long-term participants in clinical studies.<sup>71</sup>

They were presented with a hypothetical clinical trial "in which the principal investigator [either] . . . 1) held a patent on the intervention being tested . . . , 2) held stock in the company that made the investigational intervention, 3) received consulting fees from [that] company . . . , or 4) received funding from the sponsoring company over and above per participant costs of the study."<sup>72</sup>

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62. Hampson et al., *supra* note 52, at 2333, 2335 tbl.3.

63. *Id.* at 2333.

64. *Id.* at 2334, 2335 tbl.4.

65. *Id.* at 2336 tbl.5.

66. Kevin P. Weinfurt et al., *Views of Potential Research Participants on Financial Conflicts of Interest: Barriers and Opportunities for Effective Disclosure*, 21 J. GEN. INTERNAL MED. 901, 903-04 (2006).

67. *Id.* at 903-05.

68. *Id.* at 904.

69. Christine Grady et al., *The Limits of Disclosure: What Research Subjects Want to Know About Investigator Financial Interests*, 34 J.L. MED. & ETHICS 592, 597 (2006).

70. *Id.* at 592-93.

71. *Id.* at 593.

72. *Id.*

After reviewing the scenarios, almost all of the interviewees indicated that they trusted the researchers and the research team and would recommend the study to others.<sup>73</sup> Responses to each of the scenarios ranged from “concerns about data integrity and ‘conflicts of interest’” to an acceptance of the idea that the principal investigator’s expertise and hard work deserved financial awards, to indifference or ambivalence, recognizing the financial rewards’ legitimacy “but worrying about money’s potential corrupting influence.”<sup>74</sup>

The more educated the individual, however, the more concern was expressed about financial interests having a potential for manipulating or fudging data.<sup>75</sup> As was noted with the prior study described above, most wanted to know both about the existence of an investigator’s financial relationship and the fact that safeguards had been put in place by the institution to monitor financial interests and protect data integrity.<sup>76</sup> But, “[o]nly a few wanted full disclosure, including” details regarding “the amount of money an investigator might receive.”<sup>77</sup> Most significantly, nearly two-thirds said that receiving information such as that in the four scenarios would have no impact on their decisions or willingness to participate, again, typically because other factors were more important or because they trusted institutional safeguards that they assumed were in place to oversee the financial conflicts.<sup>78</sup> Some did not want financial information “because it did not matter to them or was perceived as a burden” they did not want to shoulder.<sup>79</sup> “Several acknowledged that concerns about the financial interests depended on the severity of their clinical condition,” alternative treatment options, and “hope in the possibility of benefit from a trial.”<sup>80</sup> More serious illnesses and limited options were associated with less concern about financial interest.<sup>81</sup>

It is not surprising that there are indications that potential research subjects generally are not terribly troubled when they review consent documents disclosing conflicts of interest information (perhaps other than ownership of equity interests),<sup>82</sup> in the sense that conflicts of interest are unlikely to cause them to refuse to participate in a study. An ill individual often is unaware of what scholars have identified as the “therapeutic misconception.”<sup>83</sup> Nor do

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73. *Id.* at 594.

74. Grady et al., *supra* note 69, at 594, 595 tbl.3.

75. *Id.* (internal quotation marks omitted).

76. *Id.* at 596; *see supra* text accompanying notes 62–65.

77. Grady et al., *supra* note 69, at 597–98.

78. *Id.*

79. *Id.* at 597.

80. *Id.*

81. *Id.*

82. *See supra* text accompanying notes 52–54.

83. *See, e.g.*, Paul S. Appelbaum et al., *False Hopes and Best Data: Consent to Research and the Therapeutic Misconception*, HASTINGS CENTER REP., Apr. 1987, at 20; Lisa M. Arkin et

potential participants necessarily understand the related concept of “clinical equipoise.”<sup>84</sup>

The therapeutic misconception is a fundamental confusion among research subjects between the goals of clinical care (improving the health of an individual patient) and the goals of research (generalizable knowledge).<sup>85</sup> Despite clear information to the contrary that may appear in consent documents, a patient frequently will believe that the project in which he or she has consented to participate was designed to benefit the patient directly, and not to contribute to generalizable knowledge.<sup>86</sup> Of course, this simply is not true. Patients, when asked why they agreed to be in a study, often will indicate that “the medication [they] will receive, they believe[ ], will be the one most likely to help [them].”<sup>87</sup> The patient will, incorrectly, “rule[ ] out the possibility that he might receive a placebo” as that “would not be likely to do him much good,” thus denying that there may be major disadvantages to participating in research.<sup>88</sup> In so doing, the patient would also be denying the possibility that the patient’s interest could well be “secondary to other demands on the physician-researcher’s loyalties.”<sup>89</sup>

This confusion typically will occur because the patient may not adequately comprehend the nature of clinical research. Such research generally involves techniques of randomization and the use of control groups.<sup>90</sup> Each of these may result in the patient being placed on a placebo or perhaps on a drug that he or she would have received by virtue of the then existing standard of care without being on a protocol. This absolute belief that the individual will receive the test article can be seen in comments made by respondents in some of the studies discussed above.<sup>91</sup>

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al., *Confronting the Issues of Therapeutic Misconception, Enrollment Decisions, and Personal Motives in Genetic Medicine-Based Clinical Research Studies for Fatal Disorders*, 16 HUM. GENE THERAPY 1028, 1029–30 (2005); Charles W. Lidz & Paul S. Appelbaum, *The Therapeutic Misconception: Problems and Solutions*, 40 MED. CARE, at V-55, V-57 (2002); Franklin G. Miller & Howard Brody, *A Critique of Clinical Equipoise: Therapeutic Misconception in the Ethics of Clinical Trials*, HASTINGS CENTER REP., May–June 2003, at 19, 20.

84. See Miller & Brody, *supra* note 83.

85. Appelbaum et al., *supra* note 83, at 20; see also Lidz & Appelbaum, *supra* note 83, at V-57.

86. See Appelbaum et al., *supra* note 83, at 20.

87. *Id.*

88. *Id.*

89. *Id.*

90. *Id.* at 20–21.

91. See, e.g., Grady, et al., *supra* note 69, at 593–94, 596–97 (noting that “[a]lmost all” subjects in the study of participant attitudes toward disclosure “said they enrolled because the . . . study offered what looked like the *best treatment option for them*,” that some did not want to be informed because “[i]t is just too much. . . . I already know what I want. And I don’t want to read anything or hear anything *that’s going to deter me from getting what I came to NIH for*,” that

Under standard of care treatment, off-protocol, the patient might well not have to deal with inconvenient or uncomfortable aspects of the study. In addition, and perhaps of greater importance, the physician-researcher's obligation to adhere to the study protocol might well mean that alterations in the care of the individual patient, from which he or she could potentially benefit, might well not occur if doing so would violate the study protocol's strict requirements.<sup>92</sup> Off-protocol, the alteration would be made. The point here is that researchers

are not offering personalized medical therapy for individual patients. Rather, they seek to answer clinically relevant scientific questions by conducting experiments that test the safety and efficacy of treatments in *groups* of patients. . . . Protocols governing [randomized controlled trials] frequently restrict flexibility in dosing and use of concomitant medications. These features of research design are implemented to promote scientific validity, not to promote therapeutic benefit.<sup>93</sup>

Some evidence both of confusion regarding the research enterprise and of possible examples of therapeutic misconceptions can be found in accounts of recently conducted empirical research.<sup>94</sup> There also is some evidence that disclosure of conflicts of interest may actually encourage potential subjects to agree to participate in a study. In Dr. Grady's study, for example, one of the subjects observed that knowledge of a patent interest would be a positive factor in encouraging the researcher to be accurate with study data: "that [consulting] would make me think, oh, he's really on board with this . . . it would be a positive . . . [and] make me a little more [interested in participating]."<sup>95</sup> One of the other studies concluded that participants to whom financial interests were disclosed, believed the researcher would "do a better job," and would not "cut corners or try to do it the easy way instead of doing it the way it should be done."<sup>96</sup> Such financial disclosures were interpreted "as an indication of the integrity of the study or researcher. . . . Implicit in many comments was the notion that the researcher who discloses a financial interest will be more likely to conduct the study in an ethical fashion."<sup>97</sup> One could well imagine potential participants, in considering financial conflicts of interest, particularly equity interests, going even further and concluding that the researcher must really

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"[m]y primary reason that I participate is because of the drug;" and that "[i]f I am ill and he's got a drug that could help me, I don't care about [the investigator's financial interests]" (emphasis added)).

92. See Appelbaum et al., *supra* note 83, at 21.

93. Franklin G. Miller & Howard Brody, *What Makes Placebo-Controlled Trials Unethical?*, 2 AM. J. BIOETHICS 3, 4-5 (2002).

94. See generally Weinfurt et al., *supra* note 66; Weinfurt et al., *supra* note 51, at 860.

95. Grady et al., *supra* note 69, at 596 (alterations in original).

96. Weinfurt, *supra* note 66, at 903 (internal quotation marks omitted).

97. *Id.* at 903.



believe in the efficacy of the test article if he or she owns stock in the company that manufactures it.<sup>98</sup> Another respondent in Dr. Grady's study, for example, commented on the possibility that, as a result of an investigator's equity investment, the investigator might be "afraid he's going to lose [money], then I think he will put his best foot forward to make this a good drug . . . to make sure you have the right data on it," thus making it more likely that the participant would join the study.<sup>99</sup>

A first cousin to the concept of therapeutic misconception is the concept of clinical equipoise. This generally means that "the various arms of a study not only must be in a position of equipoise vis-à-vis one another, but that they also be in a position of equipoise with respect to other interventions the subjects could receive outside of the study."<sup>100</sup> Therefore, the 2008 revised version of the Declaration of Helsinki states: "The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention . . ."<sup>101</sup> Consequently, it could be argued that the only time a placebo controlled trial, for example, is appropriate would be when no effective treatment exists or when existing treatments are inadequate for the patient.<sup>102</sup>

As noted, some data suggests that information about conflicts of interest presented to potential research participants may increase the likelihood that they will participate. However, the increased willingness to participate may well be based on two factors, neither of which may necessarily be true.

The first is that the researcher's financial interests suggest that the researcher has a strong belief in the test article's efficacy or greater efficacy than other treatment approaches. But, the potential subjects are not likely to understand that this concept of clinical equipoise, so critical to the conduct of

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98. See Grady et al., *supra* note 69, at 594, 598; see also Hampson et al., *supra* note 52, at 2334, 2336 tbl.4 (reporting that the majority of patients believed it was acceptable for researchers or the health center where the trial was being conducted to each "own stock in the drug company whose drug is being used" (internal quotation marks omitted)).

99. Grady et al., *supra* note 69, at 595 tbl.3 (second alteration in original).

100. COLEMAN ET AL., *supra* note 17, § 6.02(B)(4), at 262.

101. World Med. Ass'n, Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects ¶ 32, at 5 (adopted 1964) (2008) [hereinafter Declaration of Helsinki], <http://www.wma.net/e/policy/pdf/17c.pdf>; COLEMAN ET AL., *supra* note 17, § 6.02(B)(4), at 262 (providing a similar discussion and analysis of the 2000 revisions to the Declaration of Helsinki).

102. See Declaration of Helsinki, *supra* note 101, ¶ 32, at 5 ("The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists . . ."); see also Trudo Lemmens & Paul B. Miller, *Avoiding a Jekyll-and-Hyde Approach to the Ethics of Clinical Research and Practice*, 2 AM. J. BIOETHICS 14 (2002) (discussing the ethical tension inherent in the use of placebo controls when the clinical researcher is bound by conflicting moral commitments—the researcher to research itself and the medical clinician to upholding the duty of care).

research, cuts precisely against any such notion.<sup>103</sup> By its very definition, the concept of clinical equipoise requires that the researcher believe that the test article is, in fact, not more likely to be a better alternative.<sup>104</sup>

The second possibility that emerges from the fact that disclosure may actually increase willingness to participate, may well be based on the potential subject's idea that the mere fact that the disclosure was made serves to significantly increase his or her level of trust in the researcher. Yet, the disclosure may well have been required of the researcher by third parties such as conflict of interests committees or IRBs and over the strong objection of the researcher.

Moreover, other psychological factors may well undermine the effectiveness of disclosure as a remedy for problems caused by conflicts of interest. A number of investigators conducted a study of the "perverse effects" of disclosing conflicts of interest.<sup>105</sup> The study design did not involve healthcare.<sup>106</sup> Instead, it required individuals, or "estimators," to estimate the value of coins in several jars and paid them according to the accuracy of their estimates.<sup>107</sup> Some information was provided to the estimators by "advisors," (who were also study participants), but the advisors were paid, depending on the experimental condition, on the basis of either how accurate or how high (relative to actual values) the estimators' estimates were.<sup>108</sup> Advisors carefully examined the jars and wrote reports containing their suggestions of the value of the jar in question, which were then shared with the estimators.<sup>109</sup> In the condition where both estimators and advisors would be paid based on the estimator's accuracy, this fact was prominently noted in the advisor's report to the estimators.<sup>110</sup> In the other condition, where payment to advisors would be based on how high the estimators' estimate was, no such information regarding the basis of payment was provided to the estimator in the advisor's report.<sup>111</sup> Before making an estimate, estimators could only briefly look at the jars, which were placed some distance from where they sat.<sup>112</sup>

The analogy to conflicts of interest in a research protocol is apparent. The estimators are the potential research participants, the advisors are the investigators, and the information provided by advisors to estimators is akin to

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103. See Lemmens & Miller, *supra* note 102, at 15–16.

104. *Id.*

105. Daylian M. Cain et al., *The Dirt on Coming Clean: Perverse Effects of Disclosing Conflicts of Interest*, 34 J. LEGAL STUD. 1, 20 (2005).

106. *Id.* at 9.

107. *Id.*

108. *Id.* at 8.

109. *Id.* at 9.

110. Cain et al., *supra* note 105, at 10.

111. *Id.*

112. *Id.* at 9–10.

that in a consent document or discussion between research participants and investigators. Such information, of course, in the human research context, would include information about conflicts of interest.

The results of the study indicated that there was a general tendency to underestimate jar values when incentives were aligned (i.e., both would be paid on the basis of the accuracy of the estimator's report), but where the advisor's reward would be based on how high the estimator's stated valuations were, there was a clear tendency on the part of advisors to exaggerate jar values.<sup>113</sup> The authors concluded that "[a] superficial analysis of disclosure helps to explain the popularity of this purported remedy for conflicts of interest: all parties appear to benefit."<sup>114</sup> But, the "more complex analysis" questions this conclusion, and it indicates that the providers of information benefited the advisors but not the estimators, thereby challenging "the belief that disclosure is a reliable and effective remedy for the problems caused by conflicts of interest."<sup>115</sup>

The authors suggest that disclosure can fail because "(1) disclosure gives advisors strategic reason and moral license to further exaggerate their advice" (for our purposes, be it in a consent document or in the one-on-one discussion between the patient and the researcher regarding participation in the study), and "(2) [disclosure] may not lead to sufficient discounting to counteract this effect."<sup>116</sup> That is, people generally do not discount advice from biased advisors as much as they should because disclosure may increase trust. This might well occur when advisors' (or researchers') conflicts of interest are disclosed.<sup>117</sup> Moreover, disclosure can actually increase the bias in advice because it "leads advisors to feel morally licensed and strategically encouraged to exaggerate their advice even further. . . . [D]isclosure may fail to solve the problems created by conflicts of interest and may sometimes even make matters worse."<sup>118</sup> As one of the studies noted above suggests, for example, knowledge of a researcher's investment in a company sponsoring the study, or the researcher's affiliation as a consultant to the company, only serves to promote confidence that the test article or drug is likely to improve the study participant's condition.<sup>119</sup>

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113. *Id.* at 12–14.

114. *Id.* at 18.

115. Cain et al., *supra* note 105, at 20.

116. *Id.* at 22.

117. *Id.* at 6.

118. *Id.* at 1, 22.

119. *See supra* text accompanying notes 93–99.

### III. RESEARCH SCANDALS

Several prominent research scandals involving conflicts of interest, a number of which are particularly infamous, began to surface in 1998.<sup>120</sup> Among the more notable situations are those described in *Moore v. Regents of the University of California*,<sup>121</sup> as well as the facts surrounding the story of the death of Jesse Gelsinger in 1999,<sup>122</sup> and the events at the Fred Hutchinson Cancer Research Center in 2001.<sup>123</sup> Newer ones, such as the PRODISC clinical trial in 2008, are disclosed with some frequency.<sup>124</sup>

Recently, four of the largest manufacturers of artificial joints paid a total of \$310 million in penalties to settle federal accusations that they used fake consulting agreements and other means to persuade surgeons to use their products.<sup>125</sup> Researchers at NIH accepted hundreds of thousands of dollars in consulting fees, failing to inform agency officials, with “NIH doctors [seeing] requirements to disclose outside consulting as ‘basically a bureaucratic nuisance.’”<sup>126</sup> Lately, there has been a spate of disclosures regarding previously unidentified earnings by academic researchers from study sponsors. Many of these came to light in response to congressional demands that the sponsors produce lists of actual payments made. These responses indicated significant payments to researchers who failed to report such payments to their own institutional officials when they had been required to do so.<sup>127</sup>

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120. See generally COLEMAN ET AL., *supra* note 17, § 2.01, at 57–61; Goldner, *supra* note 36, at 379, 382, 389.

121. 793 P.2d 479 (Cal. 1990). In 1999, the California Supreme Court held that a treating physician developing a cell line from the blood of a patient was required to tell the patient of the physician’s personal interests that may affect his professional judgment. *Id.* at 484–85. The court found that the physician’s failure to do so could render him liable for malpractice based on breach of informed consent. *Id.*

122. See Goldner, *supra* note 36, at 379–80 (describing the death of an eighteen-year-old in a gene therapy trial in which the lead scientist had a financial interest in a positive trial outcome).

123. Duff Wilson et al., *Congress Takes on Medical-Trials Controversy*, SEATTLE TIMES, May 30, 2001, at A1 (reporting that 80 out of 82 subjects died in a clinical trial in which three lead researchers and a Hutch-affiliated foundation held stock in a firm that held the commercial rights to some of the drugs tested); see also COLEMAN ET AL., *supra* note 17, § 5.01, at 207, 225.

124. Reed Abelson, *Financial Ties Cited as Issue in Spine Study*, N.Y. TIMES, Jan. 30, 2008, at A1 (noting doctors at approximately half of the seventeen research centers involved in the study stood to profit financially if the device was successful).

125. Press Release, U.S. Dep’t of Justice, Five Companies in Hip and Knee Replacement Industry Avoid Prosecution by Agreeing to Compliance Rules and Monitoring (Sept. 27, 2007), available at <http://www.usdoj.gov/usao/nj/press/files/pdf/hips0927.rel.pdf>.

126. Rick Weiss, ‘*Serious Misconduct*’ by NIH Expert Found, WASH. POST, June 14, 2006, at A6.

127. Gardiner Harris & Benedict Carey, *Researchers Fail to Reveal Full Drug Pay*, N.Y. TIMES, June 8, 2008, at A1; see also Gardiner Harris, *Top Psychiatrist Didn’t Report Drug Makers’ Pay, Files Show*, N.Y. TIMES, Oct. 4, 2008, at A1.

The public has only recently learned that Dr. Charles B. Nemeroff, the chairman of the psychiatry department at Emory University, apparently violated both University rules and federal reporting regulations when he told the institution's administrators that he would earn under \$10,000 in consulting fees in 2004 from any single drug manufacturer.<sup>128</sup> In fact, congressional investigators learned that Nemeroff had already earned in excess of \$98,000 from a sponsor at the time of the disclosure, and the sponsor paid him a total of \$170,000 that year.<sup>129</sup> In both 2005 and 2006, Nemeroff also greatly exceeded the federal regulations' \$10,000 threshold from any one source such that reporting is required.<sup>130</sup> From 2000 through 2006, Nemeroff earned \$960,000 from one sponsor alone, but he declared less than \$35,000 on his disclosure forms.<sup>131</sup> In fact, he earned a total of \$2.8 million from sponsors between 2000 and 2007 and failed to disclose \$1.2 million of it.<sup>132</sup> In response, he claimed that "to the best of my knowledge, I have followed the appropriate university regulations concerning financial disclosures."<sup>133</sup>

Between 2003 and 2006, Nemeroff was the principal investigator on a \$3.9 million NIH study.<sup>134</sup> Had Emory known about his higher income, the University would have been required to inform NIH of his potential conflict or remove him as principal investigator.<sup>135</sup>

The federal government froze funds for his then current \$9.3 million project and now requires more of Emory in the way of checks and documentation on researchers' outside activities and potential conflicts of interest before awarding any additional funding.<sup>136</sup> After the congressional investigation became public, Nemeroff voluntarily resigned his department chairmanship on a temporary basis.<sup>137</sup>

Internal Emory documents indicated that on a number of prior occasions the University questioned Nemeroff's outside activities and relationships with drug companies.<sup>138</sup> In 2004, for example, there was a similar investigation of

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128. See Mike King, *Time to Disinfect Research Dollars*, ATLANTA J. CONST., Oct. 12, 2008, at A15.

129. See *id.*

130. *Id.*

131. *Id.*

132. Harris, *supra* note 127.

133. Gayle White & Craig Schneider, *Psychiatrist as Divisive as He Is Gifted*, ATLANTA J. CONST., Oct. 12, 2008, at A1 (internal quotation marks omitted).

134. King, *supra* note 128.

135. *Id.*

136. See Harris, *supra* 127; see generally S. Van McCrary et al., *A National Survey of Policies on Disclosure of Conflicts of Interest in Biomedical Research*, 343 NEW ENG. J. MED. 1621 (2000) (discussing models proposed by the Institute of Medicine for managing conflicts of interest).

137. King, *supra* note 128.

138. White & Schneider, *supra* note 133.

Nemeroff's consulting relationships with outside companies.<sup>139</sup> The University's conflict of interest committee identified multiple "serious" and "significant" violations of University procedures that were intended to protect patients.<sup>140</sup> *The New York Times* concluded that "the university apparently took little action against Dr. Nemeroff and made no effort to independently audit his consulting income."<sup>141</sup> Moreover, the *Times* noted that in conjunction with a 2000 investigation, Nemeroff wrote a letter to the University that explicitly noted his membership on some dozen corporate advisory boards, pointing out that one company donated an endowed chair and another was likely to do so.<sup>142</sup> The letter further observed that one funded a career development award in the department and two others had been asked to do so.<sup>143</sup> Thus, part of the University administration's lack of response could well be that it had its own conflicts of interest and stood to gain mightily by these kinds of corporate relationships. The entire attitude regarding these conflicts could also be explained by an unusually minimalistic attitude of federal agencies, research institutions, and professional organizations toward regulating conflicts of interest in research.<sup>144</sup>

Two critical facts emerge from these examples. First, in some of these instances research participants were injured, at least indirectly, but perhaps directly, as a result of the intervention. Second, these scandals damaged public support for the research enterprise.<sup>145</sup>

#### IV. EXISTING CONFLICT OF INTEREST REGULATIONS

Several empirical studies demonstrate clinical researchers' lack of knowledge of conflict of interest issues and guidelines,<sup>146</sup> inaccurate reporting of financial conflicts,<sup>147</sup> and the very limited extent to which institutions

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139. Harris, *supra* note 127.

140. *Id.*

141. *Id.*

142. *Id.*

143. *Id.*

144. Harris, *supra* note 127.

145. See, e.g., ADIL E. SHAMOO & DAVID B. RESNIK, RESPONSIBLE CONDUCT OF RESEARCH 192 (2009) ("[Conflicts of interest] not only can affect the integrity of the research process, but also can undermine the public's trust in the science by creating the perception that research is biased, unreliable, or morally tainted."); Catherine D. DeAngelis, Editorial, *Conflict of Interest and the Public Trust*, 284 JAMA 2237 (2000); Richard R. Sharp & Mark Yarborough, *Informed Trust and the Financing of Biomedical Research*, 34 J.L. MED. & ETHICS 460 (2006); *Research Scandals: Public Wants to Know Who's Minding the Store?*, MED. ETHICS ADVISOR, July 1999, [http://www.ahcpub.com/hot\\_topics/?htid=1&httid=1424](http://www.ahcpub.com/hot_topics/?htid=1&httid=1424).

146. Sharmon Sollitto et al., *Intrinsic Conflicts of Interest in Clinical Research: A Need for Disclosure*, 13 KENNEDY INST. ETHICS J. 83 (2003).

147. Harris, *supra* note 127; Anthony Tweedale, Letter to the Editor, *Accuracy of Declared Conflicts of Interest*, 114 ENVTL. HEALTH PERSP. 267, 267 (2004).

engage in effective management of conflicts and practically never penalize violations of disclosure requirements.<sup>148</sup> As Senator Charles E. Grassley (R-Iowa), who has been leading the congressional inquiry into these unreported or underreported conflicts of interest, commented, “[a]fter questioning about 20 doctors and research institutions, it looks like problems with transparency are everywhere . . . . The current system for tracking financial relationships isn’t working.”<sup>149</sup> After reviewing the results of the congressional investigation, the *Times* article concluded: “The findings suggest that universities are all but incapable of policing their faculty’s conflicts of interest. Almost every major medical school and medical society is now reassessing its relationships with drug and device makers.”<sup>150</sup> The existing world of regulation of conflicts of interest in research is woefully inadequate.<sup>151</sup>

#### A. *Federal Regulations and Guidance*

At the federal level,<sup>152</sup> the only formal regulations adopted through the notice-and-comment rulemaking process come from the Food and Drug Administration (FDA)<sup>153</sup> and the Public Health Service (PHS).<sup>154</sup> There is a reporting “policy” for the National Science Foundation (NSF) that was not subject to the notice-and-comment rulemaking process.<sup>155</sup> But the rules for NSF are practically identical to those for the PHS. Federal regulations to protect human subjects apply to research funded by the seventeen government agencies that have adopted the “Common Rule,”<sup>156</sup> and to research seeking FDA approval of drugs, biological agents, or devices.<sup>157</sup>

Health and Human Services (HHS) regulations<sup>158</sup> apply to research involving human subjects conducted by HHS or to research that is funded in

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148. See, e.g., Harris, *supra* note 127.

149. *Id.* (internal quotation marks omitted).

150. *Id.*

151. See generally Karen J. Maschke, *Human Research Protections: Time for Regulatory Reform?*, HASTINGS CTR. REPORT, Mar.–Apr. 2008, at 19; Anna C. Mastroianni, *Sustaining Public Trust: Falling Short in the Protection of Human Research Participant*, HASTINGS CENTER REP., May–June 2008, at 8.

152. For a detailed discussion of federal regulations regarding financial conflicts of interest in human subjects research, see Mark Barnes & Patrik S. Florencio, *Investigator, IRB and Institutional Financial Conflicts of Interest in Human-Subjects Research: Past, Present and Future*, 32 SETON HALL L. REV. 525, 531–39 (2002).

153. See Financial Disclosure by Clinical Investigators, 63 Fed. Reg. 5,233 (Feb. 2, 1998) (codified at 21 C.F.R. § 54 (2008)).

154. See Objectivity in Research, 60 Fed. Reg. 35,810 (July 11, 1995) (codified as amended at 42 C.F.R. § 50.601–.607 (2008)).

155. See Investigator Financial Disclosure Policy, 59 Fed. Reg. 33,308 (June 28, 1994).

156. See COLEMAN ET AL., *supra* note 17, § 3.02, 106–07.

157. See 21 C.F.R. § 50.1; COLEMAN ET AL., *supra* note 17, *passim*.

158. See Protection of Human Subjects, 45 C.F.R. § 46 (2008).

whole or in part by HHS.<sup>159</sup> But these regulations, as noted earlier, do not address in any direct way the issue of conflicts of interest.<sup>160</sup> FDA regulations pertaining to human subjects research apply to research involving products regulated by the FDA.<sup>161</sup> One portion of the FDA regulations essentially mirrors these HHS regulations, but again, the federal support is not necessary for the FDA regulations to be applicable.<sup>162</sup> When research involving products regulated by the FDA is funded, supported, or conducted by the FDA and/or HHS, both the HHS and FDA regulations apply.<sup>163</sup>

FDA regulations are relatively narrow in scope. They are directed at study sponsors, such as pharmaceutical and device manufacturers, at the time that there is a submission of clinical data to support claims of safety and effectiveness of products that the agency regulates.<sup>164</sup> The agency's principal concern is whether such financial relationships might jeopardize the reliability of the data submitted.<sup>165</sup> Specifically, what must be disclosed are "significant payments of other sorts" from the sponsor of over \$25,000 in payments beyond the costs of the study while the study is being carried out and for one year thereafter.<sup>166</sup> In addition, the sponsor must disclose any significant equity interests held by the investigator in the sponsor, which is defined as any equity of a privately held entity or over \$50,000 in a public company.<sup>167</sup>

Further, prior to an investigator becoming involved in a study, the sponsor of a "covered clinical study"<sup>168</sup> that is the basis of an Investigational New Drug (IND) or Investigational Device Exemption application, must obtain financial information before the study begins so as to possess the data that will be required when applying to market the test article.<sup>169</sup> There is no requirement that the FDA, the sponsor of the study, or the institution where the study is being conducted review the financial data, disclose the data to study

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159. 45 C.F.R. § 46.101(a).

160. See *supra* text accompanying notes 22–25.

161. 21 C.F.R. §§ 50, 54, 56, 312, 812.

162. See JOHN D. MAHONEY, NAT'L INST. OF HEALTH, NIH INITIATIVE TO REDUCE REGULATORY BURDEN: IDENTIFICATION OF ISSUES AND POTENTIAL SOLUTIONS § V (1999), <http://grants.nih.gov/grants/policy/regulatoryburden/humansubjectsprotection.htm>; see also sources cited *supra* note 159.

163. See 45 C.F.R. § 46.101(a); see also U.S. Food & Drug Admin., Frequently Asked Questions: Protection of Human Subjects Research, <http://www.fda.gov/oc/ohrt/IRBS/faqs.html> (last visited June 14, 2009) (follow "Frequently Asked Questions" hyperlink; then follow "IRB Organization" hyperlink).

164. See 21 C.F.R. § 54.

165. *Id.* § 54.1; see also Financial Disclosure by Clinical Investigators 63 Fed. Reg. 5,233 (Feb. 2, 1998).

166. 21 C.F.R. § 54.2(f).

167. *Id.* § 54.2(b).

168. See *id.* § 54.2(e) (defining "covered clinical study" for the purposes of FDA regulation).

169. See *id.* §§ 312.53, 812.43.



participants, or otherwise put in place a management plan while the study is being conducted. The only possible implication of such financial conflicts of interest is the remote possibility that the FDA might ultimately refuse to allow the test device to be marketed, based on its conclusion that the data was unreliable due to the conflicts.<sup>170</sup>

For the PHS, which includes NIH and the Small Business Innovation Research Program, the arrangement is significantly different. To apply for a grant the *institution* has to certify that it enforces a written institutional conflict of interest policy.<sup>171</sup> The policy must require that investigators disclose known “Significant Financial Interests,” which would “reasonably appear to be affected by the research,” to the institution’s “designated official.”<sup>172</sup> The designated official could be an individual or something like a conflict of interest committee. Here, the term Significant Financial Interest means “salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights),” in excess of \$10,000 in value, more than a five percent ownership interest in a single entity, or similar interests expected to exceed \$10,000 during the next twelve-month period.<sup>173</sup>

The institution itself does not need to further disclose any details regarding the conflict of interest, unless it is unable to “manage, reduce or eliminate” the conflict.<sup>174</sup> While the PHS agency does not define “manage, reduce or eliminate,” the rules provide some examples of conditions or restrictions that the institution may impose to do so.<sup>175</sup> These include: “[p]ublic disclosure of significant financial interests; [m]onitoring of the research by independent reviewers; [m]odification of the research plan; [d]isqualification from participation in all or a portion of the research funded by the [agency]; [d]ivestiture of significant financial interests; or [s]everance of relationships that create actual or potential conflicts.”<sup>176</sup> If an institution determines that the investigator’s failure to comply with its conflicts of interest policy resulted in a “biased design, conduct, or reporting of the PHS-funded research,” it is to notify the awarding agency of “the corrective action taken or to be taken.”<sup>177</sup> The agency will then “consider the situation and, as necessary, [either] take appropriate action [itself], or refer the matter [back] to the Institution for

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170. *Id.* § 54.1.

171. Institutional Responsibility Regarding Conflicting Interests of Investigators, 42 C.F.R. §50.604 (2008).

172. *Id.*

173. *Id.* § 50.603.

174. *Id.* § 50.604.

175. *Id.* § 50.605.

176. 42 C.F.R. § 50.605.

177. *Id.* § 50.606(a).

further action,” including directing the institution on “how to maintain appropriate objectivity in the funded project.”<sup>178</sup> The agency has a variety of other remedies, including the suspension of funding.<sup>179</sup> Still, there are no other specific standards in place to guide institutional behavior.<sup>180</sup> There are no limitations, per se, on dollar amounts that may be received, or on the maximum amount of percentage of equity interests that an investigator may hold. The government simply delegates responsibility to the institution which, itself, may have a conflict of interest in the research being conducted, or in maintaining the goodwill of an employee who brings significant resources to the institution.<sup>181</sup> There is no requirement of disclosure to potential research participants.

The Office of Human Research Protections (OHRP), the enforcement agency for regulations regarding the treatment of human subjects, provides investigators with a “guidance document” (notably not a regulation) which raises “points to consider” regarding financial relationships.<sup>182</sup> OHRP’s “points to consider” include “suggesting” (1) the possible establishment of conflict of interest committees, (2) the need for potential management of conflicts of interest by the institution, and (3) the determination of whether particular individuals should report financial interest to such a committee.<sup>183</sup>

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178. *Id.*

179. *Id.* § 50.606(b).

180. In the spring of 2009, a letter was issued by the acting director of NIH in response to an inquiry from congressman concerned with ensuring that stimulus money going to the agency not be compromised by potential conflicts of interest. In it he indicated that NIH was considering the issuance of a notice of proposed rulemaking regarding extramural research conducted by the agency. Issues that would likely be addressed include (a) a requirement that grantees provide details on financial conflicts and how they are managed; (b) defining ‘significant financial interest;’ (c) requirements for the identification and management of conflicts by institutions; (d) addressing the issue of assuring institutional compliance; (e) requiring institutions to report additional information to the PHS; and (f) addressing institutional conflicts of interest.

*Forthcoming Proposed Rule on Conflicts to Include New Requirements, NIH Chief Says*, 8 Med. Res. L. & Pol’y Rep. 311 (May 6, 2009). Soon thereafter, however, NIH’s acting deputy director for extramural research indicated that the agency’s review of NIH policies “might end in a few months with a decision to leave regulations just as they are now.” Paul Basken, *NIH Makes No Promises As It Considers Regulations on Financial Conflict* CHRON. HIGHER ED., May 14, 2009, [http://chronicle.com/daily/2009/05/18090n.htm?utm\\_source=at&utm\\_medium=en](http://chronicle.com/daily/2009/05/18090n.htm?utm_source=at&utm_medium=en).

181. See 21 C.F.R. § 50.604 (2008).

182. Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection, 69 Fed. Reg. 26,393–97 (May 12, 2004).

183. *Id.* at 26,396.

### B. Private Organization Policies

In February 2008, the Association of American Medical Colleges (AAMC) and the Association of American Universities (AAU) together issued a helpful report, directed at institutions, which advocated the adoption of more consistent policies and practices in implementing comprehensive conflicts of interest programs.<sup>184</sup> Among the recommendations are ones to require the broadening of the definition of “covered individual” beyond the principal investigator, so as to include others who share responsibility for designing, conducting, or reporting of funded research and to the spouses and dependent children of each of these individuals.<sup>185</sup> In addition, the report recommends more carefully defining the “compelling circumstances” that would overcome AAMC’s earlier policy recommendation that required a rebuttable presumption against participation in research by conflicted investigators.<sup>186</sup> The purpose of enumerating compelling circumstances would be to define the stages of research and the specific activities for which there are compelling reasons to permit the conflicted researcher to be involved, and to structure and approve a management plan that would clearly restrict the investigator in accordance with a pre-determined policy.<sup>187</sup>

In addition, the report argues in favor of the notion that the reporting requirement pertaining to outside financial interests related to professional responsibilities should be extended to eliminate any *de minimis* threshold, even if, for example, the PHS \$10,000 line might still be used to define what is a “Significant Financial Interest” that would trigger the rebuttable presumption of non-participation.<sup>188</sup> It also notes that institutions might want to exempt certain kinds of income, such as well-defined types of consulting fees, honoraria for academic activities, and the like.<sup>189</sup> On the other hand, the report recommends that institutions make clear that reporting is required for *all* outside financial interests, directly or indirectly related to their professional responsibilities, irrespective of whether the individual believes that such

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184. AAMC-AAU ADVISORY COMM. ON FIN. CONFLICTS OF INTEREST IN HUMAN SUBJECTS RESEARCH, PROTECTING PATIENTS, PRESERVING INTEGRITY, ADVANCING HEALTH: ACCELERATING THE IMPLEMENTATION OF COI POLICIES IN HUMAN SUBJECTS RESEARCH (2008) [hereinafter AAMC-AAU, PROTECTING PATIENTS], available at [https://services.aamc.org/Publications/showfile.cfm?file=version107.pdf&prd\\_id=220&prv\\_id=268&pdf\\_id=107A](https://services.aamc.org/Publications/showfile.cfm?file=version107.pdf&prd_id=220&prv_id=268&pdf_id=107A).

185. *Id.* at 5–6.

186. *See id.* at 6–7; AAMC TASK FORCE ON FINANCIAL CONFLICTS OF INTEREST IN CLINICAL RESEARCH, PROTECTING SUBJECTS, PRESERVING TRUST, PROMOTING PROGRESS: POLICY AND GUIDELINES FOR THE OVERSIGHT OF INDIVIDUAL FINANCIAL INTERESTS IN HUMAN SUBJECTS RESEARCH 7 (2001) [hereinafter AAMC, POLICY AND GUIDELINES], available at <http://www.aamc.org/research/coi/firstreport.pdf>.

187. AAMC-AAU, PROTECTING PATIENTS, *supra* note 184, at 6–7.

188. *Id.* at 7–9.

189. *Id.* at 8.

interests might reasonably be affected by present or anticipated future research.<sup>190</sup> It specifically addresses instances involving pre-clinical research and suggests the disclosures should indicate if the research linked to the financial interest is “reasonably anticipated” either to be a component of a submission for an IND or to progress to research involving human subjects within the next twelve months.<sup>191</sup> If so, the conflict of interest committee should determine if management plan types of stipulations should be applied to the pre-clinical stage of the research.<sup>192</sup>

The report also recommends broadening the scope of disclosure of managed conflicts, both within and outside of the institution, so as to include within the scope of the individuals or organizations with which the disclosure is to be shared, among others: all researchers, students, and trainees working on the project; editors of publications to which a manuscript is submitted; and oral or written public communication of research results.<sup>193</sup> It also makes recommendations regarding institutional conflicts of interest and on the implementation of conflicts of interest policies.<sup>194</sup>

Several other groups have promulgated other voluntary guidelines regarding conflicts of interest in human subjects research.<sup>195</sup> For the most part, these guidelines have received less attention among academic institutions and in literature.

### C. Institutional Policies

Institutional conflict of interest policies are all over the board, as empirical research has noted.<sup>196</sup> They differ in the amount of a financial interest that would constitute a Significant Financial Interest with 68% of the 101 institution cohorts in the study using the PHS standard of \$10,000, 27% using a lower dollar amount, and one using the \$25,000 FDA limit.<sup>197</sup> Sixty-one

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190. *Id.* at 9.

191. *Id.*

192. AAMC-AAU, PROTECTING PATIENTS, *supra* note 184, at 9.

193. *Id.* at 9–10.

194. *Id.* at 13–35.

195. See PHARMACEUTICAL RESEARCH & MFRS. OF AM., PRINCIPLES ON CONDUCT OF CLINICAL TRIALS AND COMMUNICATION OF CLINICAL TRIAL RESULTS 2 (2004), available at <http://www.phrma.org/files/Clinical%20Trials.pdf>; INT’L COMM. OF MED. JOURNAL EDITORS, UNIFORM REQUIREMENTS FOR MANUSCRIPTS SUBMITTED TO BIOMEDICAL JOURNALS: WRITING AND EDITING FOR BIOMEDICAL PUBLICATION 4–5 (2008), <http://www.icmje.org/icmje.pdf>; Am. Soc’y of Gene Therapy, *Policy of the American Society of Gene Therapy Financial Conflict of Interest in Clinical Research* (adopted 2000), [http://www.asgt.org/position\\_statements/conflict\\_of\\_interest.php](http://www.asgt.org/position_statements/conflict_of_interest.php).

196. See SUSAN EHRLINGHAUS & DAVID KORN, ASS’N OF AM. MED. COLLS., U.S. MEDICAL SCHOOL POLICIES ON INDIVIDUAL FINANCIAL CONFLICTS OF INTEREST: RESULTS OF AN AAMC SURVEY 3 (2004), available at <http://www.aamc.org/research/coi/coiresults2003.pdf>.

197. *Id.* at 4.

percent include equity in companies that are not publicly traded regardless of the percentage share of equity, and 64% include equity in such companies regardless of estimations of value.<sup>198</sup> Thirty-eight percent include royalty income above a certain threshold, while 33% include it regardless of amount, and 64% include non-royalty payments not directly related to reasonable costs of research.<sup>199</sup> Eighty-one percent allow a researcher with a Significant Financial Interest to conduct human research in compelling circumstances.<sup>200</sup> While 76% had established conflict of interest committees, merely 21% had members from outside the institution serving on those committees.<sup>201</sup> Institutions varied widely on how royalty rights would be shared, and there was a variety of approaches used to review such agreements, specifically on the issue of whether the researchers (and perhaps their institutions) might be prohibited from being involved in future research on the technology that used human subjects.<sup>202</sup> In addition, the study indicated a broad range of management techniques addressed in the policies.<sup>203</sup>

## V. RESEARCHER PARADIGMS

Resistance to conflict of interest management plans generally stems from the wide variety of attitudes held by researchers toward the entire issue of conflicts of interest. Such resistance can range from what would appear to be outright lying on conflict of interest reports to the institution, such as that which appears in the case of Dr. Nemeroff from Emory discussed above,<sup>204</sup> to less troubling, yet nonetheless frustrating (at least to members of conflict of interest committees), forms of resistance to the process and to proposed management plans. One question that arises, but that may help provide some guidance on how to go about remedying the situation, pertains to what motivates researchers to take such an approach. My own experience on such a committee, and discussions with committee members at various institutions, has led me to develop a taxonomy of categories into which most researchers fall: (1) The Ideologue, (2) The Wild-Eyed Scientist-as-Hero, (3) The Entrepreneur, (4) The Naïve Careerist, and (5) The Legalist.

### A. *The Ideologue*

The Ideologue approaches conflicts of interest from laissez-faire economic perspectives and espouses the view of non-intervention, particularly in

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198. *Id.*

199. *Id.*

200. *Id.*

201. EHRINGHAUS & KORN, *supra* note 196, at 3.

202. *Id.*

203. *Id.*

204. *See supra* text accompanying notes 127–33.

commercial ventures, by the government, by the institution, or by both. The Ideologue favors self-interest, competition, and natural consumer (i.e., research participants') preferences as forces leading to optimal prosperity and freedom. She possesses a firm belief that the natural economic order, untouched by regulations or adjustments, was designed to produce maximum well-being for all. The Ideologue's emphasis stems from the profit motive and from an unyielding resolve that individual initiative, and only that, will make for economic progress. Perhaps, as a scientist, the Ideologue might be forced to concede the need for minimal regulation, but only if hard, irrefutable, empirical data establishes that such regulation is needed—maybe not even then!

*B. The Entrepreneur*

The Entrepreneur focuses on initiating, or perhaps partially financing (if he is able) new commercial enterprises, in large part to increase his own assets or perhaps those of members of his family. He generally believes that he has a right to act in an unrestrained fashion and may be adept at developing facile arguments that enable him to avoid or even evade generally applicable rules. He differs from the Ideologue in that there are no serious philosophical premises to his position.

*C. The Wild-Eyed Scientist-as-Hero*

The Wild-Eyed Scientist-as-Hero believes that if left unfettered he will cure diabetes, cancer, etc. His view is that no kind of interference (i.e., regulations) can appropriately be placed in his path. The end really does justify the means.

*D. The Naïve Careerist*

The Naïve Careerist's behavior is such that she single-mindedly fights regulatory efforts on a number of grounds. She perceives herself as an extremely ethical individual. She takes umbrage at any thought that she would ruin her reputation as a competent, ethical researcher and clinician by having what others perceive to be conflicts of interest that either (1) adversely affect her patients who participate in research, or (2) that would lead her to manipulate research data to positively influence the research outcome. Often the nature of the conflict is such that she can readily align her own pecuniary interest with that of her employer. Consequently, she can also justify resisting the effort to deal with a conflict of interest on the basis that it will positively influence not only her own bottom line but also that of the institution. She just wants to be a good citizen. If in an academic setting, she may perceive her SFI as helping to make up for financial sacrifices that she has made in choosing to enter academia.

*E. The Legalist*

This type of researcher is readily willing to follow the rules once he is made aware of them. The vast majority of researchers who have conflicts of interest fall under this category. They want to know what is required of them, and they generally respond properly without issue.

## VI. MANAGING CONFLICTS OF INTEREST

Most discussions of conflict of interest management begin with compelled disclosure to at least the institution where the research is being conducted and/or where the researcher has his or her principal ties.<sup>205</sup> What kinds of conflicts and the amounts below which disclosures need not be made varies on a case-by-case basis.<sup>206</sup> Other management strategies include, but are not limited to, divestiture of part or all of equity interests, modification of research plans, prohibition of participation in all or certain aspects of the research, and limitations or prohibitions of activities not involving equity interests. Non-equity interest limitations could include consulting or engaging in certain educational activities of the research sponsoring entity and/or not serving in certain positions within the sponsoring entity. Similarly, where the researcher has administrative responsibilities within the institution, such as chairing a department or division, limits may be placed on his or her activities in those capacities. Thus for example, the researcher might be prohibited from or limited in passing upon applications for promotion and tenure or annual evaluations, where individuals under the researcher's supervision, be they faculty members, staff, or students, might also be engaged in the research. Where the conflict involves issues such as the physical location where the research is being conducted (for example, using institutional space or equipment for a "start-up" entity),<sup>207</sup> a plan that includes fair market rental payments to the institution by the researcher or the entity in which he or she holds an equity interest may be required. In addition, where such start-up entities are involved, it may well be necessary to develop a timetable for moving the research outside the institution.

Even in the absence of a specific federal mandate, most research institutions have established and maintain conflict of interest committees that identify and attempt to manage conflicts of interest.<sup>208</sup> Often committee members will assist researchers in negotiating the terms of such a management plan. Several studies suggest, however, that the lack of uniform conflict of

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205. See Barnes & Florencio, *supra* note 152, at 544.

206. *Id.*

207. See *id.* at 526.

208. PHS and NSF require that research institutions "report the existence of conflicts of interest to the funding agency but allow the institutions to manage conflicts internally. The regulations do not specify how to do so." McCrary et al., *supra* note 136, at 1621, 1624–25.

interest policies and the lack of clarity in those that do exist, allow many financial conflicts of interest to go undetected and unmanaged, or inadequately managed.<sup>209</sup> Another study reports that the manner in which an institution actually manages conflicts of interest in research often is not consistent with its written policies.<sup>210</sup>

In January 2008, the Office of the Inspector General of the Department of Health and Human Services issued in a report titled “National Institutes of Health: Conflicts of Interest in Extramural Research.”<sup>211</sup> The report, based upon empirical data collected by the HHS-OIG, highlighted several areas where it believes that the NIH’s oversight of grantee institutions’ financial conflicts of interest is insufficient. Specifically, the OIG noted that “NIH could not provide an accurate count of financial conflict-of-interest reports,”<sup>212</sup> that “NIH is not aware of the types of financial conflicts of interest that exist within grantee institutions,”<sup>213</sup> and that “[m]any NIH Institutes’ primary method of oversight is reliance on grantee institutions’ assurances that financial conflicts-of-interest regulations are followed.”<sup>214</sup>

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209. *See id.*; *see also* Elizabeth A. Boyd et al., *Implementation of Financial Disclosure Policies to Manage Conflicts of Interest*, 23 HEALTH AFF. 206, 213 (2004) (“In the absence of a clear and consistent definition of *conflict of interest*, individual committees have developed their own sets of standards in evaluating financial disclosures. Those standards appear to be based on specific institutional values that the committees felt were important to protect.”); Mildred K. Cho et al., *Policies on Faculty Conflicts of Interest at US Universities*, 284 JAMA 2203, 2208 (2000) (“Most policies on conflict of interest at major US research institutions lack specificity about the kinds of relationships with industry that are permitted or prohibited.”); Elizabeth A. Boyd & Lisa A. Bero, *Improving the Use of Research Evidence in Guideline Development: 4 Managing Conflicts of Interest*, 4 HEALTH RES. POL’Y & SYS. 16 (2006), <http://www.health-policy-systems.com/content/4/1/16> (“We recommend the development of specific, detailed, structured forms that solicit as much information as possible about the nature and extent of the competing interests.”).

210. Recent empirical studies have not addressed this issue directly. For the most current discussion of the topic, *see* Michaela A. Dinan et al., *Comparison of Conflict of Interest Policies and Reported Practices in Academic Medical Centers in the United States*, 13 ACCOUNTABILITY RES. 325, 338, finding that in a study of 123 U.S. academic medical institutions with internal IRBs, “in the absence of explicit language in formal policies, oversight officials did not always agree about the actual practices of the institution.”

211. DEP’T HEALTH AND HUMAN SERVS., OFFICE OF INSPECTOR GEN., NATIONAL INSTITUTES OF HEALTH: CONFLICTS OF INTEREST IN EXTRAMURAL RESEARCH (2008) [hereinafter OIG, NIH: CONFLICTS OF INTEREST], *available at* <http://www.oig.hhs.gov/oei/reports/oei-03-06-00460.pdf>.

212. *Id.* at 9.

213. *Id.* at 11.

214. *Id.* at 13.



Although under the applicable federal regulations some investigators must report financial conflicts of interest, this information is self-reported.<sup>215</sup> In particular, the OIG reported that because conflict of interest reports are not required to detail the nature of the conflict, NIH is not aware of the types of conflicts of interest that exist in grantee institutions.<sup>216</sup> Further, “[t]he majority of the Institutes do not have any proactive methods to ensure that grantees have financial conflict-of-interest policies,” and as a result the Institutes must rely solely on assertions by grantee institutions that they are properly managing financial conflicts of interests that exist in their research endeavors.<sup>217</sup> The OIG also found that systems tracking financial conflicts of interest are inadequate or do not exist at all, making it virtually impossible for the Institutes to follow up on identified conflicts of interest.<sup>218</sup>

Based upon these insufficiencies the OIG recommended that the NIH “increase oversight of grantee institutions to ensure their compliance with federal financial conflict-of-interest regulations,” that it “require grantee institutions to provide details regarding the nature of financial conflicts of interest and how they are managed, reduced, or eliminated”, and that it “require institutes to forward to [the Office of Extramural Research (OER)] all financial conflict-of-interest reports that they receive from grantee institutions and ensure that OER’s conflict of interest database contains information on all conflict-of-interest reports provided by grantee institutions.”<sup>219</sup>

In 2009 the OIG of HHS issued another report, entitled “The Food and Drug Administration’s Oversight of Clinical Investigators’ Financial Information.”<sup>220</sup> The purpose of the this report was “[t]o describe the extent and nature of clinical investigators’ disclosed financial interests reported to the Food and Drug Administration (FDA) for marketing applications approved in fiscal year (FY) 2007,” and “[t]o assess FDA’s oversight of clinical investigators’ financial information.”<sup>221</sup> The report does not assess problems involving individual researchers or institutional failures in the area of conflicts of interest, but rather those of the FDA itself in tracking potential conflicts with respect to applications by sponsors for authority to market test articles.

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215. Nat’l Inst. of Allergy & Infectious Diseases, NIH, Financial Conflicts of Interest for Awardee: Standard Operating Procedure, <http://www.niaid.nih.gov/ncn/sop/fcoi.htm> (last visited July 30, 2009).

216. OIG, NIH: CONFLICTS OF INTEREST, *supra* note 211, at 11.

217. *Id.* at 13.

218. *Id.* at 11.

219. *Id.* at 16–17.

220. See DEP’T OF HEALTH & HUMAN SERVS., OFFICE OF INSPECTOR GEN., THE FOOD AND DRUG ADMINISTRATION’S OVERSIGHT OF CLINICAL INVESTIGATORS’ FINANCIAL INFORMATION (2009) [hereinafter OIG, FDA REPORT], available at <http://oig.hhs.gov/oei/reports/oei-05-07-00730.pdf>.

221. *Id.* at i.

The report, nonetheless, is quite instructive for present purposes regarding the need for an expanded role for both the federal government and for institutions in regulating conflicts. The report points to inconsistency and a lack of uniformity of process as underlying reasons why (a) 42% of marketing applications had missing financial information, (b) no documentation of review of financial interests existed for 31% of marketing applications, and (c) “[i]n 20 [%] of marketing applications, FDA reviewers did not take action and sponsors did not indicate that they minimized potential bias during the clinical trials.”<sup>222</sup> The OIG found that “FDA cannot determine whether sponsors have submitted financial information for all clinical investigators because FDA does not have a complete list of clinical investigators,” nor does the agency use on-site inspections to confirm that the financial information submitted in the study is complete.<sup>223</sup> This certainly indicates that serious concerns about conflicts of interest exist regarding procedures in the government agency whose mission is to protect the public from drugs and devices, the testing of which needs to be beyond reproach.

The OIG recommended that the FDA take a more active role to ensure that “sponsors submit complete financial information for all clinical investigators.”<sup>224</sup> Specifically, the OIG suggested that the FDA include a requirement that sponsors submit researchers’ financial conflict of interest information as part of the agency’s already existing pre-trial application process.<sup>225</sup> The report noted that if the FDA “received financial information before clinical trials, [it] could ensure that sponsors are collecting financial information before trials and are taking action to ensure that disclosed financial interests do not threaten human subjects or compromise data integrity.”<sup>226</sup> To achieve similar goals at an institutional level, new federal regulations are needed that would vest conflict of interest committees with the ability to be more active in conflict of interest management. One possible approach would be to require that such a committee approve the conflict of interest management plan for a research protocol before the protocol is even sent to an IRB.<sup>227</sup>

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222. *Id.* at ii.

223. *Id.* at ii, 15.

224. *Id.* at 23.

225. OIG, FDA REPORT, *supra* note 220, at 25.

226. *Id.*

227. Similarly, IRBs should have “look back” authority to review the findings and decisions of the conflict of interest committee. *See id.* at 3. Presumably, for example, if an IRB is not satisfied with a particular management plan, it should have the authority to refuse to approve the research. It could require additional management techniques should it determine that, given the nature of a particular protocol, the plan worked out by the conflict of interest committee and the investigator insufficiently protected the rights of research participants. This might, on very rare

In response to the significant public attention being paid to conflicts of interest concerns over the past few years, as noted above, a variety of “trade associations” have developed suggested voluntary guidelines for regulating conflicts of interest.<sup>228</sup> Apart from the various substantive inadequacies presented by these proposals, a key difficulty simply is that they are “voluntary,” with no or very limited enforcement mechanisms.<sup>229</sup> Thus, would a pharmaceutical company be drummed out of the Pharmaceutical Researcher and Manufacturers of America (PhRMA) should it fail to adopt or enforce a suggested restriction? Likewise, would a university be banned from membership in the AAMC or AAU or from participation in those associations’ activities for similar failures? At least one relatively small “trade association,” the North American Spine Society (NASS), has developed disclosure requirements with a bit more teeth, but only in connection with participation in the Society’s activities, and without addressing other potential management techniques.<sup>230</sup>

As an historical matter, disclosure has been the primary and sometimes sole vehicle used to manage conflicts of interest. The resolution of dilemmas regarding disclosure also continues to plague those who write about the issue in the context of publication requirements.<sup>231</sup> Some of the very same questions arise in connection with disclosure of conflicts of interest to conflict of interest committees and to potential research subjects. Ongoing concerns include when disclosures should be made, what level of financial interest should be disclosed, what period of time should be covered by the disclosure, who should the disclosure cover, and once the conflict is identified, how it should be managed?

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occasions, necessitate holding a joint meeting of the two committees to arrive at a consensus approach.

228. See *supra* text accompanying note 195.

229. See, e.g., AAMC-AAU, PROTECTING PATIENTS, *supra* note 184, at 4 (describing the contents of the report as “guidance” and “recommendations” for member institutions to adopt); PHARMACEUTICAL RESEARCH & MFRS. OF AM., CODE ON INTERACTIONS WITH HEALTHCARE PROFESSIONALS 3 (2008) [hereinafter PHRMA CODE] (introducing its “updated and enhanced voluntary Code on relationships with U.S. healthcare professionals”).

230. “This disclosure policy applies to all participants in all NASS activities, including those who serve in committee and leadership positions within the society, speakers, and authors on NASS publications, including but not limited to *The Spine Journal (TSJ)*, *SpineLine*, *Contemporary Concepts and Clinical Guidelines*.” N. Am. Spine Soc’y, NASS Disclosure Policy, <http://www.spine.org/Pages/PracticePolicy/EthicsProfConduct/NASSDisclosurePolicy.aspx> (last visited July 30, 2009). Sanctions for violations under the policy included, but are not limited to, “one- or two-year suspensions of membership, membership expulsion, public letters of censure, and/or—in conjunction with the Education Council Chairs—barring the member from presenting at a specified number of future meetings.” *Id.*; see also Thomas M. Burton, *Spine Doctors Are Adopting Strict Rules on Payments*, WALL ST. J., Jan. 24, 2009, at A3.

231. See generally Boyd & Bero, *supra* note 209.

More significant is the fact that such disclosure requirements are now clearly insufficient even if the questions just raised have been sufficiently answered. As discussed earlier, disclosing conflicts of interest does not adequately prevent improper physician behavior that can result from a variety of sponsor inducements.<sup>232</sup> Before describing a necessary, though many will view it as painful, solution to the conflict of interest dilemma, consider the following tale.

For nearly eighteen years I was a member of an IRB that, at that time, reviewed biomedical, behavioral, and social science research conducted at a large university with an academic medical center. During the final approximately five years (1998 through December 2003) I served as the IRB's chair, resigning that position to assume a visiting professorship opportunity in another part of the country. Nearly at the end of my tenure, I put together a small, and what I thought to be adequately diverse and representative, subcommittee of the IRB to review the possibility of having it collect information and make judgments about researchers' conflicts (albeit three years after I had written an article arguing that this was necessary<sup>233</sup>). No such review activity on research protocols of any kind was occurring at the University at that time. I thought this subcommittee arrived at a relatively benign proposal, which largely involved requiring certain minimum disclosures with the possibility of some restrictions on researchers who held substantial equity interests in entities for which they were doing research. The proposal was largely based on the earlier issued AAMC report, discussed above.<sup>234</sup> When the proposal came before the full IRB, it was hit by a large chorus of dissenters who ultimately carried the day. The proposal did not fail because of concerns that the IRB already was overburdened. Rather, it failed because of the concern that making our own institutional policies go anywhere beyond merely requiring disclosure (either to the IRB or to potential research participants), such that a management plan for a conflict or a prohibition on a researcher conducting a study might result, would cause researchers to leave the institution in droves. In other words, the fear that won the day was that top researchers would simply go elsewhere, where conflict of interest policies either did not exist or were far less "intrusive." The majority of the IRB membership took the position that any such interference with researchers' abilities to conduct their research was unnecessary and unwarranted. Consequently, in essence, the IRB should not adopt any policy that would require investigators to go beyond the most minimal policy (if any) existing at other academic health centers.

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232. See discussion *supra* Part II.A–B.

233. Goldner, *supra* note 36, at 381–84.

234. AAMC, POLICY AND GUIDELINES, *supra* note 186.

The problem is that this “race to the bottom”<sup>235</sup> can be stopped only by the government imposing the obligation to effectively deal with conflicts on the institutions. What is needed is a uniform set of regulations—yes, a command and control approach, albeit administered locally. This is critically necessary to minimize conflict of interest scandals and to restore public confidence in research.

## VII. A PROPOSAL FOR REFORM

Are attempts to reform how financial conflicts of interests in human subjects research are managed doomed to be a Sisyphean struggle? Certainly not if an abolitionist position is adopted for financial conflicts of interest, and such a policy is enforced with vigor and with meaningful and appropriately severe sanctions for serious violations that would have a significant deterrence effect.<sup>236</sup> Despite all of the increased attention to such conflicts, as I argued some nine years ago,<sup>237</sup> I continue to believe that abolition, absent a clear federal requirement, is unlikely. Moreover, such a federally mandated abolition flies directly in the face of more than twenty-five years of other clear federal policies, such as the entire scheme envisioned by the Bayh-Dole Act, designed to foster the very kind of research that often gives rise to such potential conflicts.<sup>238</sup> Consequently, the likelihood of a federally imposed ban

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235. Cf. Marcia Angell, Former Editor of THE NEW ENG. J. MED., Address at the NIH Conference on Human Subject Protection and Financial Conflicts of Interest (Aug. 16, 2000) (transcript available at <http://hhs.gov/ohrp/coi/8-16.htm>) (“[I]nstitutions need to [work together] on this issue [of financial conflicts of interest] and develop a common policy. As it now stands, investigators may threaten to leave institutions with stringent policies and go to more lenient ones. That race to the bottom can be stopped only by the major academic medical centers joining together to do the right thing.”).

236. Institutions rarely prohibit financial conflicts of interest outright. For example, a 2000 study analyzing the conflict of interest policies of the ten U.S. medical schools receiving the largest amount of research funding from NIH found that one university “prohibited faculty from having any financial interests, including stock options, consulting agreements, and decision-making positions that involved a company sponsoring the study,” that another university “prohibited faculty and research staff from trading in stock or stock options in a company sponsoring the research or selling the product or device being investigated,” but that policies at the other universities in the study generally “stopped short of prohibitions.” Bernard Lo et al., *Conflict of Interest Policies for Investigators in Clinical Trials*, 343 NEW ENG. J. MED. 1616, 1618 (2000). While in the intervening time, given the increased attention to conflict of interest issues, many institutions have placed some kinds of limitations on conflicts, there appear to be no recent reports of institutions imposing a total ban on them for its researchers, nor have leading professional organizations called for such a ban. See generally AAMC-AAU, PROTECTING PATIENTS, *supra* note 184; INST. OF MED., CONFLICT OF INTEREST IN MEDICAL RESEARCH, EDUCATION, AND PRACTICE (2009).

237. Goldner, *supra* note 36.

238. 35 U.S.C. §§ 200–212 (2006); see COLEMAN ET AL., *supra* note 17, § 2.02(c)(1), at 67–69; *supra* text accompanying notes 28–31.

appears to be nil. Still, if the research community and the government alike are serious about addressing financial conflicts of interest in research, a fundamental change in the way conflicts of interest are viewed and ultimately managed will be required.

Thus, I have concluded that the appropriate response to concerns about conflicts of interest is to develop new federal conflict of interest regulations promulgated through administrative law procedures that involve notice and comment.<sup>239</sup> The principal advantage of such a new federal regulatory regime is that it could be constructed so as to be practically universal in its applicability, thus overcoming concerns about the “race to the bottom,” which, no doubt, still exists. To ease implementation, many of the new regulations could be modeled after existing IRB regulations under which institutions have worked for many years.

New federal conflict of interest committee regulations should require that institutions develop, through an assurance process similar to that established for IRBs,<sup>240</sup> conflict of interest committees that meet certain membership criteria, again similar to those applicable for such boards and including non-affiliated members. Federal regulations require that each IRB have “at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution.”<sup>241</sup> The regulations further require that each IRB include “at least one member who is not otherwise affiliated with the institution.”<sup>242</sup> In its February 2008 report, AAMC-AAU recommended that an institution’s conflict of interest committee

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239. A movement for uniform national conflict of interest rules is gaining strength. *See, e.g.*, Ted Agres, *FASEB: Nationalize Conflict Rules*, THE SCIENTIST, July 17, 2007, [www.the-scientist.com/news/display/53381/](http://www.the-scientist.com/news/display/53381/) (on file with *Saint Louis University Law Journal*).

240. For example, 45 C.F.R. § 46.103(a) (2008), states: “Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency *shall* provide written assurances satisfactory to the department or agency head that it will comply with the requirements set forth in this policy.” (emphasis added). In an earlier article, I argued for IRB review of conflicts of interest. *See* Goldner, *supra* note 36. In the intervening years, however, I have become convinced that (a) IRBs already have too much on their plates and typically are both understaffed and overworked, and that (b) the level and type of expertise required to engage in appropriate regulation of financial conflicts of interest is such that, except at institutions engaging in a minimal level of research, it would be wiser to establish a separate body that focuses on conflicts of interest alone. Also, if the research site is not affiliated with an institution having such a committee, the site would have to find a duly established conflict of interest committee to review and manage any conflicts that are identified. Finally, any conflict of interest committee that is established under such an assurance must have the authority, similar to that vested in existing IRBs, *see* 45 C.F.R. § 46, to delay the initiation of research until the committee’s concerns are adequately addressed, and irrespective of the desire of institutional officials given the potential for institutional conflicts of interest.

241. 45 C.F.R. § 46.107(a).

242. *Id.* § 46.107(d).

be composed of at least seven members, “of whom at least two [are] members of the public with no active transactional relationships with the institution.”<sup>243</sup> Additionally, AAMC-AAU recommended that “[o]ne of the public members should have no institutional affiliation at all.”<sup>244</sup> The purpose of a conflict of interest committee is to provide an ethical analysis of the effect of a conflict on research and the appropriate way to remedy it when necessary. A majority of members without institutional ties would be preferable.<sup>245</sup> This is something that intelligent lay members of a conflict of interest committee would be qualified to do.

The new regulations should also establish requirements for disclosure of all financial conflicts of interest of any amount to the conflict of interest committee,<sup>246</sup> provide a non-exclusive list of potential management techniques, grant the conflict of interest committee the authority to prohibit research from commencing or continuing until conflict of interest concerns are resolved,<sup>247</sup> and require that serious or continuing violations are reported to appropriate

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243. AAMC-AAU, PROTECTING PATIENTS, *supra* note 184, at 39.

244. *Id.*

245. In Denmark, for example, it is required by law that there always be one more lay member than professional member on IRB or Research Ethical Committees. Søren Holm, *How Many Lay Members Can You Have in Your IRB?—An Overview of the Danish System*, 14 IRB 8 (Nov.–Dec. 1992). A majority of members without institutional ties would be preferable since the conflict of interest committee should, ideally, be divorced from institutional politics. Holm notes that “[o]utside observers at committee meetings have found that the most valuable contributions are often made by lay members, who often seem better able to spot . . . an inappropriate trade off between risks and benefits.” *Id.*; *see also* Goldner, *supra* note 17, at 63, 107.

246. As noted earlier, PHS and NSF require that research institutions report the existence of financial conflicts of interest over certain thresholds to the funding agency but allow these conflicts to be managed internally. *See supra* note 208. As recommended by the AAMC-AAU, financial conflicts of interest of any amount should be reported to the institution, and the PHS de minimis thresholds should continue to guide disclosure to the appropriate non-institutional entities. *See* AAMC-AAU, PROTECTING PATIENTS, *supra* note 184, at 8 (“The requirement for reporting a covered individual’s outside financial interests that are directly or indirectly related to professional responsibilities to the institution should be extended to eliminate any de minimis threshold. . . . However, the PHS de minimis thresholds may continue to be used to define significant financial interest for the purpose of applying the rebuttable presumption against participation by a conflicted investigator in human subjects research.”).

247. Under 45 C.F.R. § 46.113, IRBs have “the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to subjects.” Conflict of interest committees should have the same power to suspend or terminate approval of research where, for example, a researcher is non-compliant with a conflict of interest management plan, or where a conflict is so egregious as to appear to cause serious harm to the research.

governmental agencies.<sup>248</sup> Violations of such regulations, that is the failure of an institution to deal with conflict of interest concerns appropriately and in accordance with the federal guidelines, should result in suspension of federal funding of research for some or all projects at the institution.<sup>249</sup> Conflict of interest committees should be federally mandated to review and approve research proposals prior to submission to external funding agencies or, if no external funds are involved, then certainly prior to commencement of research. Similarly, researchers who fail to report conflicts or who otherwise violate conflict of interest regulations should be subject to a range of sanctions, including limitations on participation in research projects, debarment from receiving federal funding, and other penalties.<sup>250</sup>

New federal regulations should also require public disclosure of investigator conflicts of interest, both on the NIH-sponsored internet site, [www.clinicaltrials.gov](http://www.clinicaltrials.gov),<sup>251</sup> and in informed consent documents provided to participants. In particular, such a requirement should apply where the conflict involves equity interests<sup>252</sup> or in other situations where the conflict of interest committee determines disclosure to be appropriate.

Institutions should be required to mandate training of all investigators in both the ethical norms that underlie appropriate conflict of interest reporting and management prior to the submission of any research protocols for institutional approval. Such educational efforts should include instruction in the proper completion of reporting documents.

To make clear why potential research participants should carefully consider the effects of such conflicts of interests on their willingness to participate, conflict of interest committees should have the power to require descriptions of particular conflicts in the portion of the consent document regarding risks of participation; albeit set out in a separate paragraph from other types of risks. This would be in accord with the IRB regulations that require informed consent documents to include “[a] description of any

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248. *Id.* (“Any suspension or termination of approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly to the investigator, appropriate institutional officials, and the Department or Agency head.”).

249. *Cf.* 45 C.F.R. § 46.123.

250. Similar to AAMC-AAU’s recommendations, a presumption of the need for disclosure should exist. For an analogous discussion of sanctions for scientific misconduct, see Goldner, *supra* note 36, at 298–307. *See also supra* text accompanying notes 129–41.

251. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 810, 121 Stat. 823, 904–22 (to be codified at 42 U.S.C. § 282) (requiring that a “responsible party,” for example the sponsor or principal investigator, register and report results of certain “applicable clinical trials”); *see* Protocol Registration System (PRS) and U.S. Public Law 110-85, ClinicalTrials.gov, <http://prsinfo.clinicaltrials.gov/fdaaa.html> (last visited July 30, 2009).

252. *See supra* text accompanying notes 48–99 (discussing potential research participants’ particular concerns about researchers’ equity interests versus other types of conflicts).



reasonably foreseeable risks or discomforts to the subject.”<sup>253</sup> Certainly, conflicts of interest have caused a variety of serious problems to research subjects; problems that could be characterized as risks or causing discomfort.<sup>254</sup>

Beyond the baseline federal regulations suggested, research institutions should retain the power to develop additional policies that may limit or prohibit conflicts of interest so that standards remain “based on specific institutional values that the committees [feel are] important to protect.”<sup>255</sup> Existing federal IRB regulations provide a valuable framework for restructuring and improving the current conflict of interest committee scheme. While few would argue that the IRB regime has been entirely successful, it is important to recognize that the perfect is the enemy of the good.

### CONCLUSION

Financial conflicts of interest are no longer research’s dirty little secret. Widespread publicity and several notable research scandals, among other factors, have brought this issue to the forefront of discussions of regulatory and legislative reform. In fact, financial conflicts of interest have been tabbed the most important issue for medical research in 2009.<sup>256</sup> Senator Grassley and other lawmakers are actively investigating a variety of individual and institutional conflicts of interest in research.<sup>257</sup> It would not be surprising if, in the near future, prosecutions were brought. The NIH is in the process of revising its external conflict of interest policy and regulations.<sup>258</sup> In January 2009, the OIG concluded that “[f]inancial relationships between researchers

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253. 45 C.F.R. § 46.116(a)(2).

254. See discussion *supra* Part III; see also Goldner, *supra* note 237.

255. Boyd & Bero, *supra* note 209, at 2213.

256. *Conflict of Interest Said Top Issue in 2009*, 8 Med. Res. L. & Pol’y Rep. 5 (BNA) (Jan. 7, 2009).

257. Press Release, U.S. Senate Comm. on Fin., Grassley Calls on Congress and NIH Leaders to Identify Conflicts of Interest in Taxpayer Sponsored Medical Research (June 25, 2008), <http://finance.senate.gov/press/Gpress/2008/prg062508CEG%20urges%20NIH.pdf>; Press Release, IowaPolitics.com, U.S. Sen. Grassley: Grassley, Kohl Continue Campaign to Disclose Financial Ties Between Doctors and Drug and Device Companies (Jan. 22, 2009), <http://www.iowapolitics.com/index.ihtml?Article=146479>; see also John Fauber, *Doctors Face Pressure to Disclose All Side Pay*, JSONLINE (Wis.), Jan. 11, 2009, <http://www.jsonline.com/features/health/37397284.html>; Andis Robeznieks, *Curbs Put on Mass. General Researcher’s Activities*, MODERNHEALTHCARE.COM, Dec. 31, 2008, <http://www.modernhealthcare.com/article/20081231/REG/312319975> (on file with *Saint Louis University Law Journal*); David Wahlberg, *UW Hospital Surgeon Properly Received Millions from Medical Company*, WIS. ST. J., Jan. 16, 2009, <http://www.madison.com/wsj/topstories/433229>.

258. *Conflict of Interest Said Top Issue in 2009*, *supra* note 256.

and medical companies may compromise the safety of human subjects and the integrity of research data.”<sup>259</sup> The time is ripe for regulatory reform.

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259. OIG, FDA REPORT, *supra* note 220, at 1; see *Conflict of Interest Said Top Issue in 2009*, *supra* note 256.

