

# COMBATING THE FUNDING EFFECT IN SCIENCE: WHAT'S BEYOND TRANSPARENCY?

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## INTRODUCTION

Professional ethics in government and in fields such as law, engineering, and accounting have evolved to protect the public from employee abuses and misconduct. Among those protections are rules that define, manage, or proscribe conflicts of interest. The term “conflict of interest” has been defined by Thompson as “a set of conditions in which professional judgment concerning a primary interest (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>1</sup> Before 1980, little if any attention was given to conflicts of interest in science and medicine. Beginning around that time, a major shift was taking place in sector boundaries affecting the media, finance, banking, medicine, and academia. The missions of distinctive sectors of our society were blended or superimposed onto one another. This has led to a fusion of sector goals and the creation of hybridized institutions. As examples, the entertainment and news sectors have, at times, become indistinguishable; banks and investment houses have begun adopting each other’s roles. And, more to the point of this Article, universities have been investing in for-profit enterprises started by their faculty. The new partnership between academia and business was reinforced by the passage of the Bayh-Dole Act of 1980.<sup>2</sup> Under the new law, universities were accorded intellectual property rights from any discoveries that were made under government grants. Business and academia

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1. Dennis F. Thompson, *Understanding Financial Conflicts of Interest*, 329 NEW ENG. J. MED. 573, 573 (1993).

2. University and Small Business Patent Procedures Act, 35 U.S.C. §§ 200-212 (2006). For regulations promulgated under this Act, see 37 C.F.R. § 401 (2010).

became intertwined through a mutually reinforcing body of legislative acts fostering technology transfer. These changes were the cultural counterpart to what was happening in the biological sciences when species barriers were broken with the discovery of recombinant DNA molecule technology.<sup>3</sup> The well-established biological boundaries that distinguished different life forms and the special features that distinguished socioeconomic institutions were disappearing. The new blended institutions of academia raised questions about changes in the normative framework that guided research practice and the commercial ventures within academic-clinical medicine. Mark Cooper argues that the commercialization of the university affects the faculty's choice of research problems "by shifting the focus of academic life scientists to a greater interest in research that generates patents or commercializable findings and away from research based on scientific curiosity and potential contributions to scientific theory."<sup>4</sup> The Bayh-Dole Act, along with a series of new federal laws, state economic development initiatives, and Presidential executive orders supporting university-industry partnerships, provided incentives for the development of a new class of entrepreneurial faculty who held onto their academic positions while setting up independent companies.

This Article examines the evolution of the public's concerns over conflicts of interest (COIs) in science (including medical science and the practice of medicine). I discuss the ethical foundations of COIs and the remedies that have been proposed by government, academic institutions, journals, and professional societies to address these concerns. The "funding effect" in science, an outcome in which commercial sponsorship of research influences its findings, will be explored. The role of transparency as an antidote to conflicts of interest will be examined. Also, the Article will identify initiatives designed to prevent and proscribe conflicts of interest rather than accepting them as inevitable and adopting transparency as the primary response. The thesis of this Article is that disclosure of a conflict of interest is a necessary but not sufficient response to address the most serious problems arising from blending academic science with commerce. I shall argue that when the autonomy of the scientist, the independence of the university, or the public's trust in academic research is compromised, conflicts of interest should be prohibited.

## I. PUBLIC LAWS ON CONFLICTS OF INTEREST

Policies on conflicts of interest have slowly evolved in federal law and regulation from an initial emphasis on government employees, later extended to government contractors, and more recently covering academic scientists in

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3. See, e.g., SHELDON KRIMSKY, *GENETIC ALCHEMY: THE SOCIAL HISTORY OF THE RECOMBINANT DNA CONTROVERSY* (1982).

4. Mark H. Cooper, *Commercialization of the University and Problem Choice by Academic Biological Scientists*, 34 *SCI. TECH. & HUM. VALUES* 629, 647 (2009).

institutions that receive government funding. The Founding Fathers had some clear ideas about conflicts of interest in public life. They wrote three provisions into the Constitution that restricted the conflicts of interest of those who held posts in the Executive and Legislative branches of government. First, federal officials were prohibited from accepting gifts, holding employment, or receiving titles from foreign governments.<sup>5</sup> Second, members of Congress were denied the opportunity of being appointed to a federal office that was created, or whose salary was increased, during the member's term in Congress.<sup>6</sup> Third, members of Congress were prohibited from receiving an increase in salary until they stood for re-election.<sup>7</sup> Not until the infamous Watergate affair on June 17, 1972, during the presidency of Richard M. Nixon, when five men were arrested for breaking and entering into the Democratic National Committee headquarters at the Watergate Office complex in Washington, D.C., had Congress thought seriously about a comprehensive ethics law for government employees. In 1978 Congress passed the Ethics in Government Act, which required certain federal employees to disclose their finances, and established the Office of Government Ethics. Then, in 1989 the Ethics Reform Act was passed, which established post-employment restrictions for members of Congress and high-level congressional staff. It also banned honoraria for almost all government employees, and restricted federal employees from accepting gifts.

Scientists at academic institutions were largely outside the scope of federal conflict of interest regulations before 1972, when the Federal Advisory Committee Act was passed.<sup>8</sup> The main conflict of interest provisions applying to scientists serving on federal advisory committees (called Special Government Employees or SGEs) are found in 18 U.S.C. § 208(a). The statute prohibits SGEs from participating on federal advisory committees on a matter that could affect their financial interest or that of members of their family or an organization on which they serve. Waivers can be granted (and many have been) when an administrator finds that the need for the individual's service outweighs the potential for a conflict of interest.<sup>9</sup> In 1995 the National Institutes

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5. U.S. CONST. art. I, § 9 ("No title of nobility shall be granted by the United States: and no person holding any office of profit or trust under them, shall, without the consent of the Congress, accept of any present, emolument, office, or title, of any kind whatever, from any king, prince, or foreign state.").

6. U.S. CONST. art. I, § 6 ("No Senator or Representative shall, during the time for which he was elected, be appointed to any civil office under the authority of the United States, which shall have been created, or the emoluments whereof shall have been increased during such time: and no person holding any office under the United States, shall be a member of either House during his continuance in office.").

7. Kathleen Clark, *Regulating the Conflict of Interest of Government Officials*, in CONFLICT OF INTEREST IN THE PROFESSIONS 49, 49 (Michael Davis & Andrew Stark eds., 2001).

8. The Federal Advisory Committee Act, 5 U.S.C. app. 2 §§ 1-16 (2006).

9. For an analysis of waivers by FDA, see Dennis Cauchon, *FDA Advisors Tied to Industry*, USA TODAY, Sept. 25, 2000, at 1A. For a discussion of conflict of interest among

of Health (NIH) and the National Science Foundation issued guidelines to universities for managing and documenting faculty conflicts of interest.<sup>10</sup>

## II. ETHICAL FOUNDATIONS OF CONFLICTS OF INTEREST

There are four ethical grounds for managing or proscribing conflicts of interest among university faculty. They can be characterized by the terms stewardship, transparency, consequentialism, and integrity of science. Stewardship pertains to the responsibility for the proper management of public funds and resources used in carrying out research. Transparency requires that the methods, sources of materials, background literature, contributions of authors to the research project, and limitations to the study are made available to the reviewers, journal editors, and readers. Consequentialism refers to the link between a behavior (such as a COI) and the quality of the research outcome (such as bias). Finally, integrity of science speaks to the public confidence in the scientific enterprise, which could be compromised despite complete transparency and an outcome of objective science.

The ethical grounds for government conflict of interest policies can most readily be traced to the concept of “stewardship.” Because elected officials and government employees are the temporary stewards of the laws, lands, and properties that have been placed under the authority of government, and because they also bear the responsibility for promoting the health and welfare of the citizenry, it is in the public’s interest that these officials are devoid of conflicts of interest. Without laws prohibiting conflicts of interest for public officials, the citizenry could never be confident that “private gain” rather than “public interest” was the motivating force behind a decision.

The stewardship concept has only limited application to academic scientists, who, after all, are not public employees. But they do receive federal research funds, and therefore they have a responsibility for the proper use (stewardship) of the funds. In 1994, the NIH issued a proposed rule on “objectivity in research,” a term which became a euphemism for a conflict of interest policy. Under the rule, NIH stated: “prudent stewardship of public funds includes protecting federally funded research from being compromised by the conflicting financial interests of any Investigator responsible for the design, conduct, or reporting of PHS-funded research.”<sup>11</sup> The NIH rule, which became part of the *Code of Federal Regulations*, had as its explicit goal “to ensure there is no reasonable expectation that the design, conduct, or reporting of research funded under [Public Health Service] grants or cooperative agreements will be biased by any conflicting financial interest of an

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members of federal advisory committees, see SHELDON KRIMSKY, SCIENCE IN THE PRIVATE INTEREST 91-106 (2003).

10. *Id.*

11. Objectivity in Research, 59 Fed. Reg. 33,243 (proposed June 28, 1994) (to be codified at 42 C.F.R. pt. 50 and 45 C.F.R. pt. 94).

Investigator.”<sup>12</sup> Thus, the government had connected the concept of “stewardship” with research, and in doing so linked conflicts of interest with biased science.

Scientists are stewards of the funds they receive from the federal government, and it is their responsibility to use these funds to generate “objective” knowledge untainted by bias and personal interest. The consequences of the NIH rule, which applied to all institutions that received NIH funding, was that the institutions were responsible for managing or preventing research conflicts of interest that could compromise the objectivity of science. But unlike government employees, scientists are afforded considerable autonomy within their institutions to undertake multivested activities that include teaching, research, service on public and private advisory committees, and consultancies. While good stewardship of research funds includes engaging in proper management of those funds (scientists are forbidden to use research dollars for unauthorized purposes), as well as conducting “objective” research, there is more consensus over the criteria for the former than the latter. Misuse of federal research funds has resulted in strong punitive actions against institutions.<sup>13</sup> There are no comparable penalties for biased research arising from conflicts of interest.

Thus, the NIH left it to the institutions to manage conflicts of interest as they saw fit. As an ethical foundation for regulating conflicts of interest in scientific research, the concept of “stewardship” falls short. There are no guidelines for stewardship of the “knowledge commons,” namely, that the production of knowledge is protected from biasing commercial interests. If anything, the government has created incentives for scientists to partner with industry.

Science progresses through norms that are more relevant to a process that sociologist Robert Merton called “organized skepticism.” Those appropriately trained in the discipline must have as much information about a study as possible in order to fully exercise their skepticism over whether the data are sound, the conclusions are reliable, and an experiment is properly executed. Organized skepticism, according to Merton, “is both a methodological and an institutional mandate” involving “[t]he suspension of judgment until ‘the facts are at hand.’”<sup>14</sup> Whereas “most institutions demand unqualified faith . . . the institutions of science make skepticism a virtue.”<sup>15</sup> The exercise of skepticism over the reliability of scientific results is an essential quality control feature of science. The burden of proof in science is to demonstrate that a hypothesis or conjecture is true. Reviewers of a new study typically begin their review with

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12. 42 C.F.R. § 50.601 (2010).

13. See, e.g., Stacey Burling, *Jefferson to Pay \$2.6 Million to Settle Research-Fraud Case*, PHILA. INQUIRER, May 20, 2000, at A1.

14. ROBERT K. MERTON, SOCIAL THEORY AND SOCIAL STRUCTURE 560 (Free Press 1957) (1949).

15. *Id.* at 547, 560.

skepticism. We assume the claims are false until the results of the inquiry melt our skepticism away.

Because the conflicts of interest held by scientists in the subject matter of their research are potential biasing factors, conflicts of interest should be as transparent as any other aspect of research. Scientists may have potentially biasing intellectual interests, such as a predilection for a certain theory or an association with certain advocacy groups. These interests are usually expressed by the authors' own writings or public activities. Financial COIs, however, have been traditionally more secretive, and therefore their biasing effects are less transparent.<sup>16</sup> A journal reviewer with knowledge of a conflicting interest of an author can ratchet up his or her skepticism and as a result pay closer attention to the reliability of the findings. Anything that can potentially bias the methods or outcome of a scientific study must, on ethical grounds, be available to anyone who is part of the scientific peer community.

There are several distinct ways that transparency is built into the scientific enterprise. First, authors must cite the evidence for their claims in a paper. The evidence must be accessible to others in the field. In some fields, readers and reviewers can get access to original data. Second, the methods of the experiment or investigation must be stated in sufficient detail to enable another investigator trained in the discipline the opportunity, where possible, to replicate the results and reviewers to evaluate the plausibility of the results. Third, in fields like biology, created cell lines are made available to other researchers.

Once it became clear to journal editors that author conflicts of interest were a potential biasing factor in scientific studies, reviews, and commentaries, beginning in 1984 journals began adopting COI disclosure requirements.<sup>17</sup> Transparency also became an important requirement for publishers of clinical practice guidelines in medicine<sup>18</sup> and professional manuals that provide diagnostic criteria for assessing illness (such as the *Diagnostic and Statistical Manual for Mental Disorders* or DSM).<sup>19</sup>

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16. Cf. Sheldon Krinsky, *Autonomy, Disinterest, and Entrepreneurial Science*, SOCIETY, May-June 2006, at 22, 27 (noting that a scientist's financial interest is usually not in the public record).

17. The *New England Journal of Medicine* introduced its COI policy in 1984, and the *Journal of the American Medical Association* followed with its policy in 1985. Arnold S. Relman, *Dealing With Conflict of Interest*, 310 NEW ENG. J. MED. 1182, 1182 (1984); Elizabeth Knoll & George D. Lundberg, *New Instructions for JAMA Authors*, 254 JAMA 97, 97 (1985).

18. See Lisa Cosgrove, Harold J. Bursztajn & Sheldon Krinsky, *Developing Unbiased Diagnostic and Treatment Guidelines in Psychiatry*, 360 NEW ENG. J. MED. 2035, 2035-36 (2009).

19. Cf. Lisa Cosgrove et al., *Financial Ties Between DSM-IV Panel Members and the Pharmaceutical Industry*, 75 PSYCHOTHERAPY & PSYCHOSOMATICS 154, 155 (2006) (arguing that contributors to the DSM should reveal their financial conflicts of interest in light of the effect those conflicts of interest can have on their research).

Surveys of science and medical journals taken between 1997 and 2009 have shown a rapid growth over that decade in the adoption by journals of author COI requirements, from sixteen percent<sup>20</sup> to about eighty-five percent.<sup>21</sup> Currently, for English language journals in science and medicine, transparency of author COIs has become the norm. The disclosure policies among journals, however, vary significantly. Some are highly specific in what they request and cover a broad scope; others are vague and much narrower in scope.<sup>22</sup> For example, one journal requires that authors are responsible for submitting “[a] statement of financial or other relationship that might lead to a conflict of interest.”<sup>23</sup> Another journal requires that authors report all financial relationships, including employment, consultancies, stock ownership or options, paid expert testimony, grants or patents received or pending, and royalties.<sup>24</sup> With the reporting of COIs in journals, transparency in science has been extended from describing the methodology, materials, and science that supports the hypothesis to the commercial interests of scientists.

Consequentialism in ethics is the view that moral conduct can be evaluated by the consequences of one’s actions. Applied to scientists and physicians holding conflicts of interest in their research and practice, the moral significance of their actions should be gauged by the impact the COIs may have on the quality and integrity of the research. The relevant question is: are authors with COIs, whether revealed or not, compared to those without COIs, more or less likely to exhibit a deficiency in moral integrity such as bias, exaggeration, false claims, misconduct, and scientific fraud?

Before journals began requiring authors to disclose their COIs, questions about their impact on science were not being asked. By the early 1990s, social scientists began investigating the relationships between the source of funding in science (private versus public) and the outcome of studies. The purpose of this line of investigation was to determine whether there was a “funding effect” in science.<sup>25</sup> Can the difference in outcome in a group of similar studies be accounted for by the source of the funding? Within two decades, a body of research has confirmed the existence of the funding effect in certain fields that have been investigated.

The litigation by state attorneys general against the tobacco industry

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20. Sheldon Krinsky & L.S. Rothenberg, *Conflict of Interest Policies in Science and Medical Journals: Editorial Practices and Author Disclosures*, 7 *SCI. & ENGINEERING ETHICS* 205, 205 (2001).

21. Sheldon Krinsky & Erin Sweet, *An Analysis of Toxicology and Medical Journal Conflict-of-Interest Policies*, 16 *ACCOUNTABILITY RES.* 235, 235 (2009).

22. *See id.* at 252.

23. Journal of Internal Medicine, Journal Information, <http://www.wiley.com/bw/submit.asp?ref=0954-6820&site=1> (last visited Jan. 26, 2010).

24. Archives of Internal Medicine, Author Instructions, <http://archinte.ama-assn.org/misc/ifora.dtl#ConflictofInterest> (last visited Jan. 26, 2010).

25. *See, e.g.*, Sheldon Krinsky, *The Funding Effect in Science and Its Implications for the Judiciary*, 13 *J.L. & POL’Y* 43, 45-46 (2005).

produced a wealth of documents through discovery that shed light on how tobacco companies influenced research findings pertaining to smoking and health.<sup>26</sup> Tobacco companies hired public relations specialists who played the role of “sponsors of science.” Under the names of contracted academic scientists, they placed articles in the medical literature without revealing the source of support for the research.<sup>27</sup> Tobacco companies sponsored a large number of studies, literature reviews, and scientific conferences, which were conducted by pseudo-independent organizations sponsored by the tobacco industry.<sup>28</sup> One study found that “[s]cientists acknowledging tobacco industry support reported typically that nicotine or smoking improved cognitive performance while researchers not reporting the financial support of the tobacco industry were more nearly split on their conclusions.”<sup>29</sup> In another report by the World Health Organization (WHO), the authors revealed the extensive campaign by the tobacco industry against WHO’s scientific findings on tobacco health concerns.<sup>30</sup>

After learning about big tobacco’s influence on science, public health advocates issued a “call for policymakers to demand complete transparency about affiliations and linkages between allegedly independent scientists and tobacco companies.”<sup>31</sup>

The call for transparency by itself does not correct the scientific record for bias and distortion. At most it allows readers to label the record: industry sponsored versus non-industry sponsored research. Moreover, transparency just shifts the problem from one of “secrecy of bias” to “openness of bias.” Good public policy demands peer reviewed science. Once a study is published in a reputable refereed journal, it is not sorted out by its source of funding, nor

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26. See Richard Edwards & Raj Bhopal, *The Covert Influence of the Tobacco Industry on Research and Publication: A Call to Arms*, 53 J. EPIDEMIOLOGY & COMMUNITY HEALTH 261, 261 (1999).

27. See David B. Resnik, *Perspective: Disclosing Hidden Sources of Funding*, 84 ACAD. MED. 1226, 1226-27 (2009); Suzaynn F. Schick & Stanton A. Glantz, *Old Ways, New Means: Tobacco Industry Funding of Academic and Private Sector Scientists Since the Master Settlement Agreement*, 16 TOBACCO CONTROL 157, 161 (2006).

28. See, e.g., Comm. of Experts on Tobacco Indus. Documents, World Health Org., *Tobacco Company Strategies to Undermine Tobacco Control Activities at the World Health Organization*, at iii, (July 1, 2000), available at <http://www.escholarship.org/uc/item/83m9c2wt>.

29. Christine Turner & George J. Spilich, *Research into Smoking or Nicotine and Human Cognitive Performance: Does the Source of Funding Make a Difference?*, 92 ADDICTION 1423, 1423 (1997).

30. See, e.g., Comm. of Experts on Tobacco Indus. Documents, World Health Org., *supra* note 28, at 197 (“The tobacco companies planned an ambitious series of studies, literature reviews and scientific conferences, to be conducted largely by front organizations or consultants, to demonstrate the weaknesses of the IARC [International Agency for Research on Cancer] study and of epidemiology, to challenge ETS [environmental tobacco smoke] toxicity and to offer alternatives to smoking restrictions . . .”).

31. Derek Yach & Stella Aguinaga Bialous, *Junking Science to Promote Tobacco*, 91 AM. J. PUB. HEALTH 1745, 1747 (2001).

perhaps should it be. We should expect the scientific community to do the sorting and quality control before the article gets into print. The question remains: will transparency improve the quality of review and thus result in less bias?

Some may argue that the tobacco industry is unique as a rogue industry that has stopped at nothing to promote its products. The pattern of bias in industry-funded research, however, can also be found in biomedical studies. In 2003, Bekelman et al. undertook a meta-analysis of thirty-seven original articles that investigated the extent, impact, and management of financial conflicts of interest in biomedical research. The authors concluded that “financial relationships among industry, scientific investigators, and academic institutions are widespread. Conflicts of interest arising from these ties can influence biomedical research in important ways,”<sup>32</sup> and that “evidence suggests that financial ties that intertwine industry, investigators, and academic institutions can influence the research process.”<sup>33</sup> They summarized their results by stating that “strong and consistent evidence shows that industry-sponsored research tends to draw pro-industry conclusions.”<sup>34</sup> Among the original research supporting the funding effect, Kjaergardet and Als-Nielsen found an association between competing interests and authors’ conclusions in epidemiological studies of randomized clinical trials published in the *British Medical Journal*.<sup>35</sup> Stelfox et al. studied the relationship of funding and authors’ views about the safety of calcium channel blockers. They found a strong association between the source of funding and the reporting of drug risks.<sup>36</sup> Djulbegovic et al. found a near balance in the effectiveness between new therapies and traditional ones in studies funded by non-profit organizations, whereas the balance was tipped in the significant favor of new therapies for studies funded by profit-making institutions.<sup>37</sup> Rothman et al.

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32. Justin E. Bekelman et al., *Scope and Impact of Financial Conflicts of Interest in Biomedical Research*, 289 JAMA 454, 454 (2003).

33. *Id.* at 463.

34. *Id.*

35. Lisa J. Kjaergardet & Bodil Als-Nielsen, *Association Between Competing Interests and Authors’ Conclusions: Epidemiological Study of Randomized Clinical Trials Published in the British Medical Journal*, 325 BRIT. MED. J. 249, 249 (2002) (“Authors’ conclusions . . . significantly favoured experimental interventions if financial competing interests were declared. Other competing interests were not significantly associated with authors’ conclusions.”).

36. Henry Thomas Stelfox et al., *Conflict of Interest in the Debate over Calcium-Channel Antagonists*, 338 NEW ENG. J. MED. 101, 101 (1998) (“Our results demonstrate a strong association between authors’ published positions on the safety of calcium-channel antagonists and their financial relationships with pharmaceutical manufacturers.”).

37. Benjamin Djulbegovic et al., *The Uncertainty Principle and Industry-Sponsored Research*, 356 LANCET 635, 635 (2000) (“[S]tudies funded by non-profit organizations maintained equipoise favouring new therapies over standard ones (47% vs. 53%; p=0.608) to a greater extent than randomized trials supported solely or in part by profit-making organisations [sic] (74% vs. 26% p=0.004).”).

assert that “both quantitative and qualitative research demonstrates [sic] the power of gifts to bias physicians’ choices.”<sup>38</sup>

Other journal articles cited an association “between funding and conclusions in randomized drug trials,”<sup>39</sup> “between competing interests and authors’ conclusions in randomised clinical trials,”<sup>40</sup> between “researchers acknowledging tobacco industry support” and conclusions favorable to the tobacco industry,<sup>41</sup> between favorable results in drug studies and pharmaceutical company support,<sup>42</sup> and between for-profit financial support and positive outcomes for drugs in random clinical trials.<sup>43</sup>

Once the funding effect in science is established (at least for tobacco research and drug experiments), the ethical concerns about conflicts of interest reach beyond transparency as the sole norm of commercially funded science. Without conclusive evidence of a funding effect, transparency is little more than political correctness, and there is no reason to believe that the quality of science is affected by conflicting interests, particularly financial interests. Once the quality of science is at stake, transparency takes on a different meaning. Awareness of the multivested interests of authors and of the source of funding can guide reviewers, editors, regulators, and readers on how to weigh the significance of a study. Consequentialism and the “funding effect” warn us that not all studies are equal. But even without evidence of the “funding effect,” there is one other factor that should be considered in examining the ethical foundations of conflicts of interest.

The appearance of objectivity is an important value in the scientific enterprise. Conflicts of interest in science distort that appearance even when the results of science are beyond reproach in their validity. Disinterestedness is the antipode of conflict of interest. Robert Merton cited “disinterestedness” as one of the pillars of the normative structure of science.<sup>44</sup> Others have extended the concept to a contemporary scientific milieu. Disinterestedness in science “requires that scientists apply the methods, perform the analysis, and execute the interpretation of results without considerations of personal gain, ideology, or fidelity to any cause other than the pursuit of truth.”<sup>45</sup>

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38. David J. Rothman et al., *Professional Medical Associations and Their Relationships with Industry*, 301 JAMA 1367, 1368 (2009).

39. Bodil Als-Nielsen et al., *Association of Funding and Conclusions in Randomized Drug Trials: A Reflection of Treatment Effect or Adverse Events?*, 290 JAMA 921, 921 (2003).

40. Kjaergard et al., *supra* note 35, at 249.

41. Turner & Spilich, *supra* note 29, at 1426.

42. Mark Friedberg et al., *Evaluation of Conflict of Interest in Economic Analyses of New Drugs Used in Oncology*, 282 JAMA 1453, 1453 (1999).

43. John Yaphe et al., *The Association Between Funding by Commercial Interests and Study Outcome in Randomized Controlled Drug Trials*, 18 FAM. PRAC. 565, 565 (2001).

44. MERTON, *supra* note 14, at 558.

45. SHELDON KRIMSKY, *SCIENCE IN THE PRIVATE INTEREST: HAS THE LURE OF PROFITS CORRUPTED BIOMEDICAL RESEARCH?* 77 (2003).

Of course, scientists have intellectual interests. They may show partiality to a hypothesis or theory. Or they may be partial to obtaining a positive outcome in demonstrating an effect, such as the efficacy of a drug, because it is easier to publish positive results. But you cannot remove passion, predilection toward a hypothesis, or the impulse to believe in an outcome from the practice of science. In contrast, there is nothing essential to doing science that impels one to have a commercial investment in a process or product. Scientists can just as easily cross the frontiers of stem cell research without having a patent on a cell line or equity in a company poised to commercialize stem cells.

The widely recognized Mertonian norms of science arose from observations the acclaimed sociologist of science made in the 1930s and 1940s when U.S. science was situated primarily in academic centers that were self-consciously independent of the industrial economy. Those norms are: universalism (certified scientific knowledge transcends the particularity of cultures), communalism (common ownership of the fruits of scientific investigation), disinterestedness (institutional requirements that keep personal interests from influencing one's work), and organized skepticism (suspension of judgment until the facts are at hand). Fifty years later, the model of academic business partnerships in medicine and science changed the social norms of practice. In this evolution, some have argued that "disinterest" has been supplanted by "multi-vested interest."<sup>46</sup> A single academic scientist may also be a consultant to a private company, a patent holder of an invention, or a principal in a startup company.

The late John Ziman, a physicist, fellow of the Royal Society, and erstwhile sociologist of science, characterized the changes in academia by coining the term "post-academic university." According to Ziman, "disinterestedness" as an internal norm of scientific practice was no longer viable in the new milieu of the entrepreneurial (post-academic) university. Moreover, he wrote, it was not needed to protect scientific objectivity, which was sufficiently protected by other norms. "The production of objective knowledge then depends less on genuine personal 'disinterestedness' than on the effective operation of other norms, especially the norms of communalism, universalism and skepticism. So long as post-academic science abides by these norms, its long-term cognitive objectivity is not in serious doubt."<sup>47</sup> Ziman was persuaded that the self-correcting function of science would overcome any bias, distortion, or misconduct arising from post-academic science. But in addition to "cognitive objectivity," Ziman also recognized the importance of "social objectivity," or the public's trust in science. The loss of disinterestedness could, he believed, have an irreversible effect on "social objectivity," and therefore

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46. Sheldon Krinsky, *Reforming Research Ethics in an Age of Multivested Science*, in *BUYING IN OR SELLING OUT?* 133, 133 (Donald G. Stein ed., 2004).

47. JOHN ZIMAN, *REAL SCIENCE: WHAT IT IS, AND WHAT IT MEANS* 174 (2000).

public trust in science.<sup>48</sup> An ethical argument can be made that the reestablishment of such trust is morally obligatory and cannot be accomplished merely by the transparency of interests.<sup>49</sup> Without the public's trust in science, people will be inclined to support policies that disregard rational scientific conclusions in favor of less reliable sources of belief. The first step, however, is exposing COIs in medicine and science at the time of publication, since postpublication media revelations of commercial interests are likely to create suspicion and mistrust.

### III. PHYSICIAN DISCLOSURE OF GIFTS AND HONORARIA

The pharmaceutical industry (Big Pharma) has a symbiotic relationship with research scientists and practicing physicians. Pharmaceutical companies hire academic clinicians to recruit and oversee patients for clinical trials in order to test the safety and efficacy of their new drugs. They also engage with practicing physicians to showcase and market their approved drugs through direct contact with "detail men" and through industry-funded programs in Continuing Medical Education.<sup>50</sup> Much has been reported of gift vacations and lucrative honoraria for service on speakers bureaus of companies. U.S. Senator Chuck Grassley (R-IA) has taken on the challenge of creating greater transparency in the financial relationships between physicians and the drug, device, and biologic industries. He and Senator Herb Kohl (D-WI) have introduced the Physicians Payment Sunshine Act.<sup>51</sup> Grassley described his goal in backing the legislation:

I'm working to shed light on financial relationships between drug companies and doctors. I've conducted oversight, and I'm working for passage of legislation that would require public reporting by drug companies of the money they give to doctors for consulting, travel, speeches, meals and other activities. The public interest is clear. We all rely on the advice of doctors and leading researchers influence the practice of medicine. Taxpayers spend billions of dollars each year on prescription drugs and devices through

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48. See John Ziman, *No Conflict*, NEW SCIENTIST, Oct. 4, 2003, at 34 ("This sentence [The production of objective knowledge thus depends less on genuine personal 'disinterestedness' than on the effective operation of other norms, especially the norms of communalism, universalism and skepticism] refers to the supposed philosophical objectivity of scientific knowledge. I do not believe this has much changed in the transition to 'post-academic' science. As I explain in my book, the conventional notion that it is entirely independent of human thought and action is epistemological codswallop. Throughout the book, however, I make it clear that the decline of disinterestedness in science gravely compromises its social objectivity—its hard-won reputation for a reasonable degree of impartiality, political neutrality and fairness. That's the key point.").

49. See, e.g., Benny Haerlin & Doug Parr, *How to Restore Public Trust in Science*, 400 NATURE 499, 499 (1999).

50. See Arnold S. Relman, *Separating Continuing Medical Education From Pharmaceutical Marketing*, 285 JAMA 2009, 2009 (2001).

51. S. 301, 111th Cong. (2009).

Medicare and Medicaid. The National Institutes of Health distributes \$24 billion annually on federal research grants. So the public has a right to know about financial relationships between doctors and drug companies.<sup>52</sup>

Several states, including Minnesota, Vermont, Massachusetts, Maine, the District of Columbia, and West Virginia have already passed legislation with similar objectives.<sup>53</sup> One of the strongest of these laws was passed by Vermont, which not only requires public transparency for the payments that the pharmaceutical industry makes to physicians, but also bans drug companies and manufacturers of medical devices and biological products from paying for gifts, such as meals and travel, to physicians, hospitals, nursing homes, pharmacists, and health plan administrators. There are some allowable payments drug companies would be able to make to doctors that pertain to education. Starting in 2011 those payments have to be posted in a database on a public website hosted by the Vermont Attorney General. The goal of both the transparency provisions and the prohibitions established by the law is to limit the influence of drug companies on prescription behavior and treatments by physicians.

The federal Physician Payments Sunshine Act, if passed, would override physician sunshine laws at the state level by establishing preemptive national rules and regulations.<sup>54</sup> The federal law would require drug, biological, and medical device manufacturers with \$100 million or more in annual gross revenue to participate in a national registry listing drug company payments to physicians. The registry would disclose the names and office addresses of every physician who receives a gift valued at more than \$25 from one of these participating companies.

But what will these registries do besides create a public record of the mutually reinforcing quid pro quo relationships between physicians and drug companies? The media and the general public will have an opportunity to learn about physician honorarium, capitation payments for recruiting patients into clinical trials, vacation junkets, free drug samples, etc.—but to what end? Will disclosures contribute to better, more consumer-oriented, or more accessible health care?

For example, the Vermont Attorney General issued a report for the 2007 fiscal year on the state's Physician Sunshine Act, which noted that seventy-eight pharmaceutical manufacturers spent \$2.9 million on fees, travel expenses, and other direct payments to Vermont's physicians, hospitals, and universities as part of their marketing plan, and that from fiscal years 2004 through 2008, "there has been a decrease of nearly 30% in the amount of expenditures and an increase of over 40% in the number of manufacturers who have reported

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52. Press Release, Sen. Chuck Grassley, Disclosure of Drug Company Payments to Doctors, available at <http://grassley.senate.gov/about/Disclosure-of-Drug-Company-Payments-to-Doctors.cfm>.

53. Liz Kowalczyk, *State Bans Drug Firm Gifts to Doctors*, BOSTON GLOBE, March 12, 2009.

54. S. 301.

marketing expenditures.”<sup>55</sup>

Will the physician sunshine laws change behavior? One consequence of the current bill pending in Congress is that it would allow officials at NIH to compare what companies say they are paying academic physicians with what doctors actually report they are receiving from consulting income. Investigations carried out by Senator Chuck Grassley’s staff have revealed a number of cases where physicians were underreporting their consulting income. In the case of prominent Harvard psychiatrist Joseph Biederman, Grassley’s investigation found that he received at least \$1.6 million in consulting fees by drug makers from 2000 to 2007, but alleged that most of this income was not reported to Harvard officials for several years.<sup>56</sup>

Would patients ask doctors about their relationship with drug companies? If this were to become a norm for patients, and if it were to affect their choice of physicians, it could change physician behavior. Negative media attention directed at physicians who accept drug company gifts could feed patient mistrust and eventually turn physicians away from drug company influence. Thus far, studies indicate that few patients will reject a physician because of his or her conflict of interest. In a survey taken by the Community Catalyst’s Prescription Project, a group funded by the Pew Foundation, about one thousand people were interviewed in 2008 and asked what the likelihood was that they would query their doctor to determine if he or she accepted gifts, free samples, speaking fees, or other financial support from pharmaceutical companies. About fifty-five percent of the respondents said that they were unlikely to directly ask their doctors about their relationship with drug companies. About sixty-eight percent responded that they were likely to support legislation requiring drug companies to disclose gifts to doctors.<sup>57</sup> While the public seems to support disclosure, few people would be inclined to act on the information. In a study of 470 cardiac patients, a mere five percent of those who were informed about a hypothetical investigator’s equity interest in the clinical trials said they would not participate in the trial for that reason alone.<sup>58</sup>

Among the states that have thus far passed physician conflict-of-interest laws, Massachusetts’ contains requirements that go well beyond transparency. Passed in 2008, the law states that a

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55. 2007-2008 VT. ATT’Y GEN., PHARMACEUTICAL MARKETING DISCLOSURES REPORT 4, available at <http://www.atg.state.vt.us/assets/files/2009%20Pharam%20Report.pdf>.

56. Pam Belluck, *Child Psychiatrist to Curtail Industry-Financed Activities*, N.Y. TIMES, Dec. 30, 2008, at A16.

57. Ben Comer, *Survey Says Most Want Disclosure of Gifts to Docs*, INT’L COMM’NS RESEARCH, June 19, 2008, [http://www.icrsurvey.com/Study.aspx?f=Community\\_Catalyst\\_Prescription\\_Project\\_061908.htm](http://www.icrsurvey.com/Study.aspx?f=Community_Catalyst_Prescription_Project_061908.htm).

58. Kevin P. Weinfurt et al., *Disclosure of Financial Relationships to Participants in Clinical Research*, 361 NEW ENG. J. MED. 916, 917 (2009).

pharmaceutical or medical device manufacturing company . . . shall disclose . . . the value, nature, purpose and particular recipient of any fee, payment, subsidy or other economic benefit with a value of at least \$50 . . . to any covered recipient in connection with the company's sales and marketing activities,<sup>59</sup>

and prohibits "financial support for the costs of travel, lodging, or other personal expenses of non-faculty health care practitioners attending any [Continuing Medical Education] event."<sup>60</sup> An ethical standard of preventing conflicts of interest, which is reflected in the provisions of the Act, does not depend on responses to COIs by the public or physicians for ending certain practices. It is conceivable that federal and state laws mandating the transparency of gifts to physicians could eventually lead to the prohibition of those gifts once public awareness grows. In small measure this has begun to happen in some medical schools as a result of ethics rules adopted by professional organizations.<sup>61</sup>

#### IV. LIMITS OF TRANSPARENCY

Transparency of COIs responds to one of the core ethical issues in science and medicine. But unless transparency results in behavior change, it does not address the issues of bias and public trust discussed previously. Consider the case of COIs in the judicial system. According to the American Bar Association's Code of Judicial Conduct, the appearance of a conflict of interest must be avoided.<sup>62</sup> In his essay *Law's Blindfold*, David Lisbon asks: why prohibit mere appearances of a conflict of interest? According to Lisbon,

The theory is that the appearance of impropriety is almost as bad as impropriety itself, because—as the old saw puts it—justice must not only be done, but be seen to be done. Unless judges avoid the appearance of impropriety, public confidence in the fair administration of justice will be undermined.<sup>63</sup>

Consider the case of a judge who makes the following declaration to his courtroom prior to announcing the prison term a convicted felon will receive:

I will be sentencing the defendant, who has now been tried by his peers, to be incarcerated in a for-profit prison in which I have an equity interest. The extra money I earn from this partnership between my court and a reputable penal institution helps to compensate my low salary and allows me to serve the public interest and render more thoughtful and objective decisions.

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59. 105 MASS. CODE REGS. 970.009 (2010).

60. 105 MASS. CODE REGS. 970.007 (2010).

61. See Duff Wilson, *Harvard Medical School in Ethics Quandary*, N.Y. TIMES, Mar. 2, 2009, at B1.

62. See AMERICAN BAR ASSOCIATION, MODEL CODE OF JUDICIAL CONDUCT (2008), available at [http://www.abanet.org/cpr/mcjc/canon\\_4.html](http://www.abanet.org/cpr/mcjc/canon_4.html).

63. David Luban, *Law's Blindfold*, in CONFLICT OF INTEREST IN THE PROFESSIONS 26 (Michael Davis & Andrew Stark eds., 2001).

## V. JUDGE I. D. CLARE

The reason most people would feel uncomfortable with Judge I.D. Clare's disclosure is that we expect judges to be fair and disinterested in applying the law. If a judge has an equity interest in a for-profit penal institution, he can no longer exhibit an appearance of disinterestedness. The fact that he chooses to disclose his financial interest does not ameliorate the conflict or assure the public that he can render a fair decision. There is no way we can understand whether his financial interest in the prison will affect his sentencing decision. The judge himself may not understand the effect his equity interest in the prison has on his choice of the venue of a prison or duration of the sentence for the convicted felon. As Andrew Stark noted, "Because we cannot prevent officials from mentally taking notice of their own interests, we prohibit the act of holding certain kinds of interests in the first place."<sup>64</sup>

Are there circumstances in science and medicine where disclosure does not resolve the ethical dilemma associated with conflicts of interest? In medicine we distinguish between medical research and clinical medicine, which does not involve research. The ethical issues pertaining to conflicts of interest differ between these roles in medicine, although both share the norm of the Hippocratic Oath ("Do no harm").

Among the ethical concerns involving physician and physician-scientists are the following: Should a physician who has a financial interest in a drug therapy he is studying be permitted to serve as clinical investigator on a clinical trial for that drug? Should conflicted scientists be permitted to write editorial and book reviews for journals? Should physicians be allowed to get capitation fees for finding candidates for clinical trials? Should conflicted scientists be permitted to serve on federal advisory committees?

## VI. THE JESSE GELSINGER CASE: PHYSICIAN-ENTREPRENEUR IN A CLINICAL TRIAL

This case exemplifies the conflicts of interest held by a clinical researcher and his host institution that were not adequately disclosed to the patient in a clinical trial. It raises the question of whether the COI should have even existed.

Human Gene Therapy Research (HGT) experienced rapid growth in the 1990s. The number of English language journal articles published in HGT grew steadily from 175 in 1990 to 1550 in 2000. Likewise, there was a spectacular rise in U.S. HGT grants from 159 in 1990 to 1932 in 2000.<sup>65</sup> As the medical

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64. ANDREW STARK, CONFLICTS OF INTEREST IN AMERICAN PUBLIC LIFE 23 (2003).

65. Christine Crofts & Sheldon Krinsky, *Emergence of a Scientific and Commercial Research and Development Infrastructure for Human Gene Therapy*, 16 HUMAN GENE THERAPY 169, 173 (2005).

research subspecialty in HGT exploded, there was a parallel growth in its commercial interests. The number of patents awarded to HGT techniques grew from zero in 1990 to 111 in 2000. Twelve years after 1990, 156 biotechnology companies listed HGT as one of their primary research and development missions. Peak firm formations consisted of eighteen, twenty-four, and seventeen in 1992, 1997 and 1999 respectively.<sup>66</sup>

Heightened expectations for HGT can be found in the media and in scientific journals during the 1990s. Clinical trials involving somatic gene transfer were widely reported to have improved the conditions of children afflicted with X-linked Severe Combined Immunodeficiency Disease (SCID), a disease that strips away the immune system. To prevent deadly infection, SCID children must live in an artificial infection-free bubble.<sup>67</sup>

In 1999 Jesse Gelsinger reached his eighteenth birthday after surviving for sixteen years with a rare metabolic liver condition called “ornithine transcarbamylase (OTC) deficiency.” When functioning correctly, the OTC gene provides instructions for making the enzyme ornithine transcarbamylase. If the gene is mutated (as in Jesse’s case), excess nitrogen from protein sources is not converted to urea for excretion, which results in ammonia accumulating in the body. A high level of ammonia is toxic, especially to the nervous system. This accumulation can cause neurological problems such as seizures, poorly controlled breathing, and mental retardation. Jesse’s disease was somewhat under control by diet and extensive medication.

At his physician’s suggestion, Jesse entered a clinical trial conducted at the University of Pennsylvania Medical School. The trial involved a new gene therapy protocol that was not designed to help Jesse’s situation, which, in relative terms, was mild compared to the fatal form of the disease.<sup>68</sup> Tragically, within a few days after his HGT treatment in September 1999, Jesse fell mortally ill; his organs stopped functioning and he died. At first his father Paul Gelsinger considered his son’s death one of the tragic and unanticipated consequences in the heroic path toward advancing medical science. But after he investigated his son’s death, Paul Gelsinger learned some things that neither he nor his son had understood about the clinical trial. The director of the Human Gene Therapy Institute at the University of Pennsylvania was a founder and equity holder in a biotechnology company poised to benefit from a successful outcome of Jesse’s human experiment. The University of Pennsylvania also had an equity stake in the company. These relationships were not revealed to Jesse Gelsinger in the informed consent documents he signed prior to the initiation of the trial. Paul Gelsinger filed a wrongful death lawsuit against the

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66. *Id.*

67. See Donald B. Kohn & Fabio Candotti, *Gene Therapy Fulfilling Its Promise*, 360 *NEW ENG. J. MED.* 521 (2009); see also Marina Cavazzana-Calvo et al., *Gene Therapy of Human Severe Combined Immunodeficiency (SCID)-x1 Disease*, 288 *SCIENCE* 669 (2000).

68. KRIMSKY, *supra* note 46, at 133.

University of Pennsylvania, its private sector biotechnology collaborator, Genovo, and two local hospitals.<sup>69</sup> Based on claims of negligence and conflicts of interest, the complaint argued that the conflicts of interests of the clinical investigator and the university were not disclosed to Jesse prior to his involvement in the HGT trial.

The Gelsinger case raised questions about whether a university with an institutional conflict of interest in a therapy or drug should be permitted to host a clinical trial involving that therapy or drug. It also brought into debate whether clinical investigators with an equity interest in a drug or medical procedure (such as HGT) should be permitted to participate in any aspect of the human trial.

These issues were brought into the policy sphere in 2001 when an interim guidance document of the Department of Health and Human Services (DHHS) stated:

The financial interest of the institution in the successful outcome of the trial could directly influence the conduct of the trial, including enrollment of subjects, adverse event reporting or evaluation of efficacy data. In such cases, the integrity of the research, as well as the integrity of the institution and its corporate partner, and the well being of the research participants, may be best protected by having the clinical trial performed and evaluated by independent investigators at sites that do not have a financial stake in the outcome of the trial, or carried out at the institution but with special safeguards to maximally protect scientific integrity of the study and the research participants.<sup>70</sup>

Following the Draft Interim Guidance Policy, in 2004 DHHS issued a final guidance document which recommended that clinical investigators make their financial interests in a human experiment transparent, but left the responsibility of how to protect subjects to the individual institution.<sup>71</sup>

In the spring of 2009, the Institute of Medicine (IOM) issued a report that went beyond the disclosure of COIs in clinical trials. The IOM, a division of the National Academies of Science, emphasized the need for prevention of COIs by limiting financial interests in clinical trials rather than simply disclosing the interests to research participants. "The disclosure of individual and institutional financial relationships is a critical but limited first step in the process of identifying and responding to conflicts of interest."<sup>72</sup> The IOM was

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69. Jeffrey L. Fox, *Gene-Therapy Death Prompts Broad Civil Lawsuit*, 18 NATURE BIOTECHNOLOGY 1136, 1136 (2000).

70. Draft Interim Guidance, Advisory Comm. to Office of Human Research Prot., Dep't of Health & Human Servs., *Financial Relationships in Clinical Research: Issues for Institutions, Clinical Investigators, and IRBs to Consider when Dealing with Issues of Financial Interests and Human Subject Protection* (Jan. 10, 2001), available at <http://www.hhs.gov/ohrp/nhrpac/mtg12-00/finguid.htm>.

71. *Financial Relationships and Interests in Research Involving Human Subjects Protection*, 69 Fed. Reg. 26,393 (proposed May 5, 2004) (to be codified at 21 C.F.R. pts. 50, 56 and 45 C.F.R. pt. 46).

72. INST. OF MED., *CONFLICT OF INTEREST IN MEDICAL RESEARCH, EDUCATION, AND*

perhaps responding to the rising tide of commentaries that spoke critically of conflicts of interest in academic medicine and proposed that medical schools sever their commercial ties. However, another cohort of medical science researchers spoke of the unavoidability of physician-industry relationships and advocated proper management of COIs.<sup>73</sup>

Even as the counterattack proceeded against advocates of stronger conflict-of-interest rules, a group of eighteen prominent physicians published a statement in the *Journal of the American Medical Association* proposing that professional medical associations (PMAs) wean themselves from industry funding. PMAs are private associations of medical specialties and subspecialties that offer continuing medical education courses, set diagnostic and treatment guidelines, and promote ethical norms for their members. In their recommendations, Rothman et al. wrote that “PMAs should work toward a complete ban on pharmaceutical and medical device industry funding (\$0), except for income from journal advertising and exhibit hall fees.”<sup>74</sup> Another recommendation of the physicians is: “Industry should not be allowed to provide a grant [to PMAs] for a project of its choosing or be associated with a specific project. Research funds from industry, like educational support from industry, should go to a PMA’s central repository or committee . . . .”<sup>75</sup> This group of physicians also would prohibit PMAs from accepting funding from industry for journal supplements or for developing practice guidelines or outcome measures. “Disclosure of industry relationships by committee members is not sufficient protection.”<sup>76</sup> Rothman et al. ended their recommendations to physician-centered PMAs by drawing on the public trust argument as the rationale for zero dollar tolerance. “Professional Medical Associations have such an important role to play in speaking for medicine, defining best practices, and promoting evidence-based decision making that they cannot allow relationships with industry to diminish the public’s trust.”<sup>77</sup>

Those advocating a strict financial firewall between academic science and medicine and commerce were once thought to be a fringe group with naïve views about the progress of medicine and the role of industry-university partnerships. But there may have been a sea change when IOM issued its report

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PRACTICE 5 (Bernard Lo & Marilyn J. Field eds., 2009).

73. Laurence J. Hirsch, *Conflicts of Interest, Authorship, and Disclosures in Industry-Related Scientific Publications: The Tort Bar and Editorial Oversight in Medical Journals*, 84 MAYO CLINIC PROC. 811, 811-21 (2009) (“Conflicts of interest are widespread and represent a state of affairs, not a behavior or misconduct. They should be managed, rather than vainly attempting their elimination.”); Andrew P. White et al., *Physician-Industry Relationships Can Be Ethically Established, and Conflicts of Interest Can Be Ethically Managed*, 32 SPINE 53, 53-57 (2007) (“Many conflicts of interest are inevitable, and management is the optimal strategy to eliminate bias.”).

74. Rothman et al., *supra* note 38, at 1368.

75. *Id.* at 1370.

76. *Id.*

77. *Id.* at 1372.

in April 2009 recommending an end to industry support for medical refresher courses.<sup>78</sup> The prestige of the National Academies of Science was now behind the idea that some COIs in medicine and science should be diminished or avoided. Writing in the *New England Journal of Medicine* (NEJM), Steinbrook describes two of IOM's new recommendations. First, "academic medical centers, research institutions and medical researchers should *restrict participation of researchers with conflicts of interest in research with human participants*, except where an individual's participation is essential for the conduct of research."<sup>79</sup> Second, "groups that deliver clinical practice guidelines should restrict industry funding and conflicts of panel members."<sup>80</sup>

The terms "restricted participation" and "restrict industry funding" leave room for interpretation and balancing. While it is not a categorically zero-tolerance prohibition, it nevertheless rejects transparency as the sole ethical response to conflicts of interest. This is a first step in creating a firewall between certain medical activities and drug company gifts and funding. It is premised on two ideas: first, even small gifts can bias scientist-physicians; second, the appearance of objectivity is every bit as important as objectivity itself in protecting public trust in medical science.

#### VII. PREVENTING COI AUTHORSHIP

In medical publishing, the *New England Journal of Medicine* is among a few high profile medical journals to have taken a leadership role in first establishing a COI policy and subsequently in elevating the standards of that policy. Between 1996 and 2002, NEJM had a policy that prohibited editorialists and authors of review articles from having any financial interest with a company that could benefit from a drug or device discussed in the article.<sup>81</sup> The distinction made between original research articles versus reviews and commentaries was based on the fact that, in the latter submissions, authors have broader discretion to make editorial choices that open up opportunities for bias. Jeffrey Drazen, Editor-in-Chief of NEJM, revised the policy in 2002, eliminating a zero-tolerance prevention in favor of a *de minimis* COI requirement. Drazen informed readers and contributors that with regard to original articles and special articles, the policy was the same as it was in 1996. But he indicated that his editors were having difficulty finding expert reviews from the "small and shrinking pool of authors eligible to evaluate drugs for the

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78. Gardiner Harris, *Institute of Medicine Calls for Doctors to Stop Taking Gifts from Drug Makers*, N.Y. TIMES, Apr. 29, 2009, at A17.

79. Robert Steinbrook, *Controlling Conflict of Interest—Proposals from the Institute of Medicine*, 360 NEW ENG. J. MED. 2160, 2160-63 (2009) (emphasis added).

80. *Id.*

81. Marcia Angel & Jerome P. Kassirer, *Editorials and Conflict of Interest*, 335 NEW ENG. J. MED. 1055, 1055-56 (1996).

journal.”<sup>82</sup> His revised policy gives the NEJM editors the authority to use a “significant conflict of interest” standard. He wrote: “Because the essence of reviews and editorial is selection and interpretation of the literature, the journal expects that authors for such articles will not have any *significant financial interests* in a company (or its competitor) that makes a product discussed in the article.”<sup>83</sup> Drazen argued that the change from zero tolerance of COIs to “significant COIs” will enable the editors to recruit the best authors, i.e., people who have experience with new treatments, to write editorial and review articles. Physicians writing reviews for the journal could accept up to \$10,000 a year from each drug company in speaking and consulting fees. In contrast, another leading journal, *The Lancet Oncology*, prohibits authors with financial interests in or contracts with a relevant company within the past three years from publishing any review, personal view, or health care paper in the journal.<sup>84</sup>

#### VIII. INDUSTRY-SPONSORED ACADEMIC RESEARCH WITH STRINGS ATTACHED

It has been a standard practice in the biomedical sciences for authors to disclose in publications the sources of funding for their research. However, grants and contracts that commercial entities negotiate with universities contain provisions that are rarely transparent. Some of these provisions give sponsors control over the data, veto power over publication, or some degree of editorial control over the interpretation of results.

After a few highly publicized cases in which the research sponsor took editorial control away from the investigator, a number of universities adopted a zero-tolerance standard for secret contract covenants that gave the commercial sponsor control over the research methods, data, or interpretation of results. In one notable case, Betty Dong of the University of California at San Francisco (UCSF) was the principal investigator of a drug company-sponsored contract to evaluate the bioequivalency of the generic and trade versions of a drug. When Professor Dong completed her study, her data showed that the two drugs were bioequivalent for the medical conditions they were approved to treat. In the small print of the contract, the sponsoring company was given the right to exercise control over publication. Under threat of personal litigation and left by her university to her own devices, Professor Dong had little option but to withdraw the paper from the galley of JAMA after the paper had been refereed and was awaiting publication.<sup>85</sup>

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82. *Relaxing The Rules*, TUFTS E-NEWS, June 19, 2002, <http://enews.tufts.edu/stories/1095/2002/06/19/RelaxingTheRules>.

83. Jeffrey M. Drazen & Gregory D. Curfman, *Financial Associations of Authors*, 346 NEW ENG. J. MED 1901, 1901 (2002).

84. Astrid James et al., *Commentary, The Lancet's Policy on Conflicts of Interest*, 363 LANCET 2, 2-3 (2004).

85. Drummond Rennie, *Thyroid Storm*, 277 JAMA 1238, 1238-43 (1997).

There are no uniformly adopted policies among medical schools protecting principal investigators and universities from sponsor control of the published research findings. A commentary by an editor of JAMA alerted schools to the dangers of accepting contracts that restricted the autonomy of researchers to publish their findings whether or not a study favors the financial interests of the sponsoring organization. In cases where medical schools fail to take leadership in preventing sponsor control over data and research findings, journal editors have stepped in. For example, a group of thirty-seven editors of heart journals signed consensus documents on the responsibility of scientific authors, which state: "Authors must give final approval of the version to be submitted and any revised version to be published."<sup>86</sup>

As a greater percentage of clinical trials is being carried out by medical investigators operating through private organizations known as Contract Research Organizations (CROs), rather than by teams of scientists contracted through medical schools accountable to academic deans, ethics committees, and university administrators, the contracts between drug company sponsors and CROs are more likely to be responsive to sponsor-oriented covenants.

Withholding data from publication has been one of the outcomes of sponsor-controlled contracts. As an example, the German pharmaceutical company Bayer A.G. hired a CRO to test its drug Trasylol, which was given to patients before surgery to reduce the risks of blood loss. Bayer did not release the results of a trial that was not in their financial interests. The Food and Drug Administration learned of the trial and issued a public health advisory stating that "[the] use of Trasylol may increase the chance for death, serious kidney damage, congestive heart failure and strokes."<sup>87</sup> Medical schools that accept contracts that permit sponsor control of data, interpretation of results, or publication status compromise the scientific autonomy and independence of their scientists. Moreover, such covenants are almost always secret.

#### CONCLUSION

Public concerns over conflicts of interest in biomedical science and medical practice have spawned support for increasing transparency by scientists and physicians who hold competing interests. Universal disclosure of COIs will not address several core ethical issues including the systemic bias in commercially-funded research and the public's loss of confidence in biomedical scientists and physicians who balance their Hippocratic Oath and commitment to scientific standards with commercial interests. There are many types of bias resulting from COIs that are too subtle for referees to pick up in

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86. Hugo Ector et al., *A Statement on Ethics from the HEART Group*, 51 J. CARDIOVASCULAR PHARMACOLOGY 521, 521 (2008).

87. Gardiner Harris, *F.D.A. Says Bayer Failed to Reveal Drug Risk Study*, N.Y. TIMES, Sept. 30, 2006, at A1.

their reviews. When a field has been dominated by a few funding sources, the scientists funded by these sources may not even be aware that their framing of issues and interpretation of results has been influenced by the financial interests of their commercial patrons. The autonomy afforded to academic scientists and independent physicians makes this a challenging issue for government and university oversight. The 1995 guidelines of COI management issued by the National Institutes of Health and the National Science Foundation were designed for local management of conflicts of interest by and within institutions. Recently, investigations by Senate staff members show that transparency rules have not fully succeeded in keeping scientists honest about their conflicts of interest. The current debates among journals, medical schools, government agencies, and professional organizations are about the extent to which certain COIs should be proscribed in order to protect the integrity of scientific and medical institutions and the knowledge they produce. While increased transparency may not reduce the bias inherent in certain conflicts, it has allowed social scientists to document the bias associated with the “funding effect.” As a consequence, some scientific groups and institutions are beginning to see the moral rationale for banning conflicted activities for which there is little public tolerance.