NOTES AND COMMENTS

An Argument Against Embedding Conflicts of Interest Disclosures in Informed Consent

Kathleen M. Boozang, Carl H. Coleman, and Kate Greenwood

ABSTRACT: This Comment advances three basic premises: (i) respect for patient autonomy requires disclosure of researchers' conflicts of interest; (ii) transparency is an inadequate tool for the management of serious conflicts of interest; and (iii) conflict of interest disclosures should not become part of the clinical trial informed consent process. Our primary focus is on this last point. The pre-trial informed consent process epitomizes information overload, a condition that diminishes transparency's benefits. Further, research participants do not have a contextual framework to analyze conflict of interest information and generally feel they lack alternatives to trial participation. Finally, disclosing conflicts of interest may increase the occurrence of research participants' therapeutic misconception and inculcate in physician-researchers unjustified confidence that they have fulfilled their duty to ameliorate the potential risks of their own conflicts of interest.

KEYWORDS: Clinical Trial, Conflict of Interest, Human Subject Research, Informed Consent

CITATION: Kathleen M. Boozang, Carl H. Coleman, and Kate Greenwood, *An Argument Against Embedding Conflicts of Interest Disclosures in Informed Consent*, J. Health & Life Sci. L., June 2011, at 230. An earlier version of this comment was originally published as *The Limits of Disclosure as a Response to Financial Conflicts of Interest in Clinical Research*, a White Paper by the Seton Hall Law Center for Health & Pharmaceutical Law & Policy, *available at* http://law.shu.edu/ProgramsCenters/HealthTechIP/HealthCenter/upload/health-center-whitepaper-dec2010.pdf.

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None of the authors has individual conflicts of interest related to this paper. Their employer, Seton Hall Law School, has received funding from life sciences entities. Detailed information is available at http://law.shu.edu/ProgramsCenters/HealthTechIP/HealthCenter/Disclosure-Statement.cfm.

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Introduction

Financial relationships between the pharmaceutical and medical device industries and health care professionals and institutions have led to concern about commercial influences on medical practice, research, publication, and education.[1] Congressional investigations, prosecutions, press reports, and published studies have generated public awareness of the pervasive nature of these relationships.[2] Along with other dimensions of professional activity, public inquiry has focused sharply on the implications of conflicts of interest in clinical research for the research participants' safety and welfare and the integrity of research results. In this Comment, we use the Institute of Medicine's (IOM) definition of conflict of interest as "a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest."[3]

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1 Ctr. for Health & Pharm. Law & Policy, Seton Hall Univ. Sch. of Law, Drug and Device Promotion: Charting a Course for Policy Reform 1 (2009), *available at* http://law.shu.edu/ProgramsCenters/HealthTechIP/upload/whitepaper_jan2009.pdf [hereinafter Promotion White Paper]; Bd. on Health Scis. Policy, Inst. of Med. of the Nat'l Acads., Conflict of Interest in Medical Research, Education, and Practice 23 (Bernard Lo & Marilyn J. Field eds., 2009) [hereinafter IOM Report]; Troyen A. Brennan et al., *Health Industry Practices That Create Conflicts of Interest: A Policy Proposal for Academic Medical Centers*, 295 JAMA 429, 429 (2006) [hereinafter *Health Industry Practices That Create Conflicts of Interest*]; Catherine DeAngelis & Phil Fontanarosa, *Impugning the Integrity of Medical Science: The Adverse Effects of Industry Influence*, 299 JAMA 1833, 1833–34 (2008) [hereinafter *Impugning the Integrity of Medical Science*].

2 *See, e.g., Paid to Prescribe? Exploring the Relationship Between Doctors and the Drug Industry: Hearing Before the S. Special Comm. on Aging*, 110th Cong. (2007), *available at* http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_senate_hearings&docid=f:39865.pdf; Natasha Singer, *Senator Moves to Block Medical Ghostwriting*, N.Y. Times, Aug. 18, 2009, *available at* www.nytimes.com/2009/08/19/health/research/19ethics.html?pagewanted=1; Press Release, Office of the N.J. Attorney Gen., Landmark Settlement Reached with Medical Device Maker Synthes (May 5, 2009), www.nj.gov/oag/newsreleases09/pr20090505a.html (last visited Feb. 15, 2011) [hereinafter *Landmark Settlement Reached with Medical Device Maker Synthes*]; Eric Campbell et al., *Institutional Academic-Industry Relationships*, 15 JAMA 1779, 1779–86 (2007).

3 We adopted this definition in our earlier White Paper. Ctr. for Health & Pharm. Law & Policy, Seton Hall Univ. Sch. of Law, Conflicts of Interest in Clinical Trial Recruitment & Enrollment: A Call for Increased Oversight 9 (2009), *available at* http://law.shu.edu/ProgramsCenters/HealthTechIP/upload/health_center_whitepaper_nov2009.pdf [hereinafter Oversight White Paper]. *See* IOM Report, at 46. As noted, the term "conflict of interest" does not equate to compromised judgment or action but to the risk of such compromise. *Id.*, at 26.

A common response to the conflicts of interest problem in clinical research has been to urge greater transparency about the relationships among industry, researchers, and academic medical institutions.[4] In response to significant calls from a variety of professional organizations and ethical codes, many academic medical centers and universities have revised their policies to include conflict information in the informed consent process for participation in clinical research.[5]

We argue that public policy should encourage researchers and institutions to make information about their financial relationships with industry available to the public, but—contrary to many other commentators' recommendations—we conclude that such disclosure should not be required as part of the informed consent process routinely. Although we recognize the importance of transparency as an ethical value, incorporating financial issues into the informed consent process would provide few, if any, benefits to research participants and could

4 *See, e.g.*, Sally J. Rockey & Francis S. Collins, *Managing Financial Conflict of Interest in Biomedical Research*, 303 JAMA 2400, 2402 (2010) (describing a "new era of transparency" in the management of financial conflicts of interest); 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 viii (AAMC 2008) [hereinafter AAMC-AAU 2008 COI Report] (recommending that disclosure of "managed conflicts of interest" be extended "both in scope and in audience, to assure full awareness of potential conflicts and institutional efforts to address them").

5 Although Yale's disclosure to research subjects policy does not appear to be absolute, U. Penn and Stanford's unequivocally require such disclosure. *Compare* Yale Univ. Human Research Protection Program, HRPP Policy 500: Disclosures and Management of Personal Interests in Human Research 2, *available at* www.yale.edu/hrpp/resources/docs/HRPPPolicy500COI_7-22-10_FINAL.pdf (discussion IRB obligations to "ensure that interests that have the potential to compromise the protection of human research participants or the integrity of the research are managed, reduced or eliminated…") *with* Univ. of Pa., Financial Disclosure Policy for Research and Sponsored Projects, www.upenn.edu/almanac/v47/n21/ORdisclosure.html (last viewed Feb. 15, 2011) (investigator "shall include a disclosure of his/her research-related conflict(s) of interest in the human subjects research informed consent form and such disclosure shall be approved by the Institutional Review Board…."); Stanford Sch. of Med., Faculty Disclosure Conflicts of Interest 2, *available at* http://med.stanford.edu/coi/documents/coi2006.pdf ("All faculty must disclose any personal financial interest related to human research to the subject in the consent form").

cause significant harms. In any case, we urge reliance on transparency as a primary tool to manage conflicts of interest only where the conflicts and their potential harms are insignificant.

Financial Relationships in Clinical Research

Industry's increased investment in biomedical research has concomitantly increased the existence and focus on conflicts of interest that may be detrimental to research participants. Before 1980, the National Institutes of Health (NIH) funded most clinical trials. Although NIH remains the single largest source of federal funding, between 2003 and 2007 NIH funding for biomedical research declined 8.6% when adjusted for inflation.[6] Total federal funding for biomedical research increased during that period, but by less than 1%.[7] By contrast, industry funding of medical research increased by 25% between 2003 and 2007.[8] Today, pharmaceutical and medical device companies fund nearly 80% more clinical trials than NIH.[9]

Various financial arrangements between industry and investigators or research institutions are possible. Often, pharmaceutical and medical device companies pay investigators or their employers a per capita fee for each participant enrolled in a study.[10] In academic medicine, payments for conducting clinical trials are made to the investiga-

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6 E. Ray Dorsey et al., *Funding of US Biomedical Research, 2003-2008*, 303 JAMA 137, 140 (2010) [hereinafter *Funding of US Biomedical Research*]. In 2008, the passage of the American Recovery and Reinvestment Act (ARRA) curbed this trend with a single $8.2 billion research stimulus. Robert Steinbrook, *The NIH Stimulus—The Recovery Act and Biomedical Research*, 360 New Eng. J. Med. 1479, 1479 (2009). However, the stimulus money runs dry in fiscal year 2011, and the NIH does not have another such funding windfall in the works. Jocelyn Kaiser, *Peering Over a Cliff at the Poststimulus World*, 328 Sci. 676, 676 (2010).

7 *Funding of US Biomedical Research*, at 140.

8 *Id.*

9 Joseph Loscalzo, *The NIH Budget and the Future of Biomedical Research*, 354 New Eng. J. Med. 1665 (2006).

10 Oversight White Paper, at 9.

tor's department or institution. Although there is typically no direct relationship between the number of participants enrolled and an academic investigator's salary, physicians in academic medicine may find that, over time, their compensation reflects their overall success in obtaining clinical research funding for their institutions.[11] Academic physicians have other incentives to conduct externally-funded research, including the potential for future funding, as well as publication of the results in the medical literature, a requirement for tenure and promotion.[12]

In contrast to academic physicians, physicians in private practice generally are paid directly for conducting clinical research.[13] Compensation for clinical research can be a substantial part of a physician practice's income, prompting some physicians to attend seminars on how to make money in clinical research.[14]

In some cases, research sponsors may pay "finder's fees" to individuals other than the investigator—including other physicians, nurses, medical students, or persons previously enrolled in a trial—for identifying and referring potential study participants.[15] Although finder's fees

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11 Norman G. Levinsky, *Nonfinancial Conflicts of Interest in Research*, 347 New Eng. J. Med. 759, 759 (2002) [hereinafter *Nonfinancial Conflicts of Interest in Research*]; Alan R. Fleischman & Jason E. Klein, *Clinical Research in the Private Office Setting–Ethical Issues*, 113 Transactions Am. Clinical & Climatological Ass'n 126, 129 (2002) [hereinafter *Clinical Research in the Private Office Setting*] ("For years physician-investigators in academic settings have accrued substantial secondary gain to themselves or their departments from clinical trials, but as compared to the private practice setting, in academia direct personal financial gain has rarely been possible.").

12 *Nonfinancial Conflicts of Interest in Research*, at 759.

13 *Clinical Research in the Private Office Setting*, at 128.

14 *Id. See also* Jason Roberson, *Dallas Area Sees Significant Growth in Clinical Trials*, Dallas Morning News (Nov. 3, 2009) (reporting that "Synergyst Research, a San Antonio-based company . . . helps doctors land clinical trials for extra income," ranging from $50,000 for a trial with 10 research participants on the low end to in excess of $100,000 on the high end).

15 James Christiansen & James Orlowski, *Bounty-Hunting and Finder's Fees*, 27 IRB: Ethics & Human Res. 16 (2005); Stuart E. Lind, *Finder's Fees for Research Subjects*, 323 New Eng. J. Med. 192, 192–94 (1990).

have been called unethical,[16] and at least one company represents that it has stopped using them,[17] a 2006 survey of 300 clinical research coordinators revealed that nearly a third had worked in studies in which finder's fees were paid.[18] We believe that the Department of Health and Human Services (DHHS) should prohibit finder's fees because of the extraordinary risks they present to the integrity of the research subject recruitment process.[19]

Drug and device companies that sponsor research also may pay investigators bonuses for meeting certain benchmarks in recruiting or retaining research subjects in a trial.[20] Not unlike finder's fees, such bonus payments "could influence investigators' decisions about prospective participants' initial or continuing eligibility, thereby potentially placing enrollees at risk or undermining the scientific integrity of the study."[21]

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16 *See* Oversight White Paper, at 39 n.76.

17 Pfizer, Compensation to Investigators in Clinical Studies, www.pfizer.com/research/research_clinical_trials/compensation_investigators.jsp (last visited Feb. 15, 2011).

18 Joëlle Y. Friedman et al., *Perspectives of Clinical Research Coordinators on Disclosing Financial Conflicts of Interest to Potential Research Participants*, 4 Clinical Trials 272, 274–75 (2007).

19 *See* Oversight White Paper, at 28.

20 Kurt Eichenwald & Gina Kolata, *Drug Trials Hide Conflicts for Doctors*, N.Y. Times, May 16, 1999 ("Drug companies and their contractors offer large payments to doctors, nurses and other medical staff to encourage them to recruit patients quickly . . . Special cash bonuses for signing up specified numbers of people by a given date . . . are becoming part of the landscape."); *see also, e.g.*, Press Release, U.S. Attorney Michael J. Sullivan, Dist. of Mass., Dep't of Justice, New Jersey Company Agrees to Plead Guilty to Kickbacks and Conspiracy Charges and Pay More Than $22 Million Dollars in Criminal Fines (May 16, 2008) (physician-investigators paid $250 for enrolling between 1 and 5 patients, an additional $500 for enrolling between 6 and 10 patients, and an additional $750 for enrolling between 11 and 15 patients); Anna Wilde Mathews, *Fraud, Errors Taint Key Study of Widely Used Sanofi Drug*, Wall St. J., May 1, 2006, at A1 (physician-investigators paid $100 for each patient enrolled, $150 when they submitted results, and $150 when all questions were resolved).

21 *See* Oversight White Paper, at 11.

Equity interests in the sponsoring company, which give physicians and research institutions a direct stake in the outcome of the research, are a highly controversial form of payment. Recent prosecutions have brought to light several such compensation arrangements.[22] We recommended that the federal government prohibit compensation for research in the form of equity interests in the sponsor of a clinical trial.[23]

An increasingly common situation occurs when an investigator who owns the patent for the device or substance being tested, and/or the investigator's institutional employer, separately incorporates a for-profit subsidiary that owns and will develop the patent for commercial use, and in which the investigator and/or the institution holds significant equity interests. This for-profit subsidiary often brings in a large medical device or pharmaceutical company as an additional investor or joint venture partner when the invention comes closer to the clinical trial and market development stage, which may be another source of financial benefit to the investigator and institution. Once the product reaches Phase I trials, the subsidiary will seek relationships with one or more medical centers to host the trials, potentially including the institution with the equity stake. We believe this scenario is analytically comparable to compensation with an equity interest in the sponsor and should preclude the patent holder or investor from serving as an investigator, although it may be necessary and appropriate for the inventor to serve in a consultant status to the trial.[24]

In addition to payments directly related to research, physician-investigators may receive money for consulting, speakers bureau and advisory board participation, and other activities.[25] These payments may influence physicians' decisions about prescribing,[26] their opinions

22 *Landmark Settlement Reached with Medical Device Maker Synthes.*
23 *See* Oversight White Paper, at 28.
24 *Id.*, at 29.
25 *Health Industry Practices That Create Conflicts of Interest*, at 429, 430.
26 Ashley Wazana, *Physicians and the Pharmaceutical Industry: Is a Gift Ever Just a Gift?*, 283 JAMA 373, 375 (2000).

offered in the context of continuing medical education,[27] and their reported study results.[28]

Finally, as highlighted by prominent prosecutions, companies sometimes design "trials" for currently available products that are little more than guises for growing a new consumer base.[29] One such study enrolled 5,557 individuals in a head-to-head clinical trial of Vioxx and naproxen, with the stated purpose of evaluating Vioxx's gastrointestinal tolerability.[30] In fact, the trial was designed by the marketing department of Vioxx's manufacturer to familiarize primary care prescribers with the drug's benefits.[31] When companies misleadingly characterize efforts to promote a new product as scientific research, they deceive both physicians and the patients they recruit, thereby threatening to undermine the research enterprise as a whole. Although anecdotal evidence suggests this practice is now less common in the pharmaceutical sector, it is unclear if it has been eliminated entirely, particularly in the medical device context.

In sum, compensation arrangements between industry and physicians who oversee clinical trials raise conflict of interest issues that could expose participants to unacceptable risks, undermine the public's confidence in such trials, and affect the integrity of the research results. The shift of clinical trials from academic medical centers to the private practice setting, where trials are pursued as alternative revenue streams, exacerbates these dangers.

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27 Ronald Cervero & Jiang He, The Relationship between Commercial Support and Bias in Continuing Medical Education Activities: A Review of the Literature 9 (Accreditation Council for Continuing Med. Educ. 2008), *available at* www.arrs.org/uploadedFiles/ARRS/Life_Long_Learning_Center/Educators_ToolKit/ReviewOfLiteratureCommSupport%20Bias.pdf.

28 *Impugning the Integrity of Medical Science*, at 1833.

29 *See generally* Kevin P. Hill et al., *The ADVANTAGE Seeding Trial: A Review of Internal Documents*, 149 Annals Internal Med. 251, 251 (2008) (seeding trials are designed primarily to achieve marketing objectives).

30 *Id.* at 252.

31 *Id.*

Disclosure of Financial Relationships: Existing Law and Guidance

A common response to the problem of conflicts of interest in clinical research has been to urge greater transparency about the relationships among industry, researchers, and research institutions. Calls for transparency have taken multiple forms, including mandated disclosure of the relationships to the government, to the researcher's academic home, to the public (often via company websites),[32] or to individual trial participants as part of the process of informed consent.[33] In this section, we summarize existing law and guidance on disclosure of financial interests in clinical research. Thereafter, we explain why we support public disclosure of conflicts of interest but oppose incorporating those discussions into the process of informed consent. Throughout, we continue to assert our belief that disclosure should not be seen as a panacea for conflicts of interest in clinical research. In itself, disclosure is likely to have only a minimal impact on the problems associated with conflicts of interest and must, therefore, be accompanied by direct regulation of the problematic financial relationships themselves.

Existing law

Clinical trials of drugs and medical devices are regulated by the Food and Drug Administration (FDA), which has adopted conflict of interest regulations to ensure that steps are "taken in the design, con-

32 AAMC-AAU 2008 COI Report, at 9; Press Release, The Pew Charitable Trusts, The Prescription Project Applauds Legislation Requiring Disclosure of Physician-Industry Relationships (Jan. 22, 2009), www.prescriptionproject.org/news/pressreleases?id=0022 (last visited Feb. 15, 2011); IOM Report, at 385.

33 *See, e.g.*, Kevin P. Weinfurt et al., *Disclosure of Financial Relationships to Participants in Clinical Research*, 361 New Eng. J. Med. 916, 916 (2009) [hereinafter *Disclosure of Financial Relationships to Participants in Clinical Research*]; Marion J. Finkel, *Should Informed Consent Include Information on How Research is Funded?*, 13 IRB: Ethics & Human Res. 1, 3 (1991) [hereinafter *Should Informed Consent Include Information on How Research is Funded?*].

duct, reporting, and analysis of [clinical trials] to minimize bias."[34] The FDA requires sponsors submitting marketing applications for drugs and devices to provide a list of the investigators who worked on "covered clinical studies," as well as their financial interests, as defined by the FDA.[35] Notably, payments to cover "the costs of conducting the clinical study or other clinical studies" are excluded from the definition of "significant payments of other sorts."[36] Sponsors provide this information subsequent to the conclusion of clinical trials as part of the market approval process. Further, the FDA's conflict of interest regulations do not require or suggest disclosure to prospective participants of investigators' financial relationships with industry.

In addition to disclosing information about financial ties, the FDA requires research sponsors to report steps taken to minimize the potential for bias.[37] If an investigator's disclosure raises data integrity questions, the FDA may audit the investigator's data, require further analyses or studies, or decline to credit the entire study's results.[38]

Sponsors' success in obtaining researcher compliance with necessary data gathering to ensure compliance, as well as sponsors' own compliance with these regulations, is deficient. In a 2009 report, the DHHS Office of the Inspector General (OIG) found that only 1 percent of clinical investigators identified on marketing applications had disclosed

34 Financial Disclosure by Clinical Investigators, 21 C.F.R. § 54.1(b). *See also* 21 C.F.R. §§ 54.2–.6.

35 21 C.F.R. § 54.4. The FDA regulations require sponsors to disclose to the FDA the following financial interests: (1) financial arrangements where the value of the compensation could be influenced by the outcome of the clinical trial; (2) "significant payments of other sorts," such as consulting or speaking fees, in excess of $25,000 from the sponsor to the investigator; (3) any proprietary interest, such as a patent or trademark, in the tested product; and (4) any "significant equity interest in the sponsor," defined to include equity in excess of $50,000 in a publicly-traded corporation or any equity in an entity that is not readily valued by reference to public prices. *Id.* §§ 54.4(a)(3), 54.2(b), (f).

36 21 C.F.R. § 54.2(f).

37 *Id.* § 54.4(a)(3)(v).

38 *Id.* § 54.5(c).

any financial interest, and that 42 percent of FDA-approved marketing applications were missing financial information.[39] Even when financial information was disclosed, the FDA frequently did not document any review of it.[40] The OIG recommended that the FDA require sponsors to submit financial information for clinical investigators *before* clinical trials commence and again at the time a marketing application is filed.[41]

DHHS has adopted additional regulations, designed to promote objectivity in research funded by the Public Health Service (PHS). These regulations require institutions to maintain and enforce a written policy that reduces or eliminates financial conflicts of interest.[42] Policies must include provisions for monitoring and reporting all significant financial interests of any investigator involved in PHS-funded research.[43] Investigators must report only significant financial interests, however, that "would reasonably appear to be affected by the research for which PHS funding is sought."[44] A 2009 report by the DHHS OIG found that 90 percent of grantee institutions "rely solely on researchers' discretion to determine which of their significant financial interests are related to their research and are therefore required to be reported."[45]

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39 Office of Inspector Gen., Dep't of Health & Human Serv., The Food and Drug Administration's Oversight of Clinical Investigators' Financial Information 14 (2009), *available at* http://oig.hhs.gov/oei/reports/oei-05-07-00730.pdf.

40 *Id.* at 16.

41 *Id.* at 23–25. The OIG also recommended that the FDA take steps to ensure that sponsors submit complete financial information for all clinical investigators and that its reviewers consistently review financial information and take action in response to disclosed financial interests.

42 42 C.F.R. § 50.604.

43 *Id*. Significant financial interests are defined to include, but are not limited to, salary, royalties, or other payments in excess of $10,000, equity interests in excess of $10,000 or that represent more than a 5% ownership interest in a single entity, and intellectual property rights such as patents and copyrights. *Id.* § 50.603.

44 42 C.F.R. § 50.604.

45 Office of Inspector Gen., Dep't of Health & Human Serv., How Grantees Manage Financial Conflicts of Interest in Research Funded by the National Institutes of Health 13 (2009), *available at* http://oig.hhs.gov/oei/reports/oei-03-07-00700.pdf.

Earlier this year, DHHS sought comments on proposed amendments to these regulations. The amendments would lower the threshold for a "significant financial interest" from $10,000 to $5,000[46] and would shift the onus of deciding whether a significant financial interest is related to PHS-funded research from the investigator to the institution itself.[47] Furthermore, in an effort to foster transparency, the proposed revisions would require institutions to post their compliance policies, as well as any known significant financial conflicts of interest of principal or key investigators, on a publicly available website.[48]

The recent health reform legislation, the Patient Protection and Affordable Care Act (PPACA), requires that every 90 days, beginning on March 31, 2013, pharmaceutical and medical device manufacturers notify the federal government of payments or "transfer[s] of value" made to physicians and teaching hospitals, including "stock, a stock option, or any other ownership interest, dividend, profit, or other return on investment," as well as "the name of the covered drug, device, biological, or medical supply" related to the payment. The law requires the government to establish a searchable public website with this information. However, publication of payments or transfers of value that relate to "a product research or development agreement for services furnished in connection with research on a potential new medical technology or a new application of an existing medical technology or the development of a new drug, device, biological, or medical supply," or in connection with a clinical trial, shall be suppressed until the manufacturer obtains FDA approval of the product or four years following the date of the compensation.[49]

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46 Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding is Sought and Responsible Prospective Contractors, 75 Fed. Reg. 28687, 28692 (proposed May 21, 2010).

47 *Id.* at 28695.

48 *Id.* at 28694, 28697.

49 Patient Protection and Affordable Care Act (PPACA), Pub. L. No. 111-148, 124 Stat. 119 § 6002(a)(1)(A) [hereinafter PPACA].

At least six states—California, Maine, Massachusetts, Minnesota, Vermont, and West Virginia—as well as the District of Columbia,[50] have passed laws requiring disclosure of financial relationships between drug and device companies and physicians to an appropriate state agency. Minnesota and, as of November 1, 2010, Vermont, require disclosure to the public as well. When the reporting requirements under PPACA take effect, however, they will preempt state laws that require redundant reporting.[51] Most of these states' reporting laws do not require disclosure to research participants of an investigator's or institution's compensation for research, financial interests in the outcome of clinical trials, or other financial relationships between the sponsor and the investigator or institution. One exception is California, where the informed consent law expressly requires disclosure "both verbally and within the written consent form, in nontechnical terms," of "[t]he material financial stake or interest, if any, that the investigator or research institution has in the outcome of the medical experiment."[52] However, these requirements do not apply to research subject to federal regulations governing the conduct of human subject research by virtue of federal funding. A more recent New Jersey statute covering medical research involving "persons with cognitive impairments, lack of capacity, or serious physical or behavioral conditions and life-threatening diseases" requires prospective research participants (or their guardians or authorized representatives) to be informed of "the material financial stake or interest, if any, that the investigator or research institution has in the research."[53]

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50 D.C. Code Ann. §48-833.03 (2010); Mass. Ann. Laws ch. 111 N § 6 (2010); Me. Rev. Stat. Ann. Tit. 22, § 2698-A (2009); Minn. Stat. § 151.47(f) (2009); W. Va. Code. R. § 16-29H-8 (2010); Vt. Stat. Ann. tit. 18 § 4632 (2010); Cal. health & Safety Code § 119402 (2010).

51 PPACA § 6002(c)(1)(E)(i).

52 Cal. Health & Safety Code § 24173(c)(11).

53 P.L. 2007, Ch. 316, 237th Assem. § 3 (N.J. 2008), *available at* www.njleg.state.nj.us/2006/Bills/AL07/316_.PDF.

Other guidance

In 2001, the Association of American Medical Colleges (AAMC) proposed that financial conflicts of interest be disclosed in the informed consent forms signed by research participants, stating:

> The precise wording of disclosure in the consent form should be determined by the IRB [Institutional Review Board], but should include an explanation of the fact that the financial interest in question has been reviewed by the COI [conflict of interest] committee, approved subject to committee oversight, and determined by both the committee and the IRB not to pose any additional significant risk to the welfare of research subjects or to the integrity of the research.[54]

In 2008, the AAMC-Association of American Universities (AAU) Advisory Committee on Financial Conflicts of Interest in Human Subjects Research recommended that investigators report "all of their outside financial interests," no matter how small, as long as they were "directly or indirectly related to their professional responsibility to the institution."[55] This was a departure from the previous 2001 AAMC recommendations, pursuant to which investigators were instructed to report only financial interests that were "significant" and "would reasonably appear to be affected by [their] research."[56]

Various medical associations have opined on disclosure of financial incentives to research participants and patients. For example, the American Medical Association has stated that the "nature and source of funding and financial incentives offered to the investigators must

54 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 18 (2001), *available at* https://www.aamc.org/download/75302/data/firstreport.pdf [hereinafter AAMC 2001 COI Report].

55 AAMC-AAU 2008 COI Report, at 9.

56 AAMC 2001 COI Report, at 8.

be disclosed to a potential participant as part of the informed consent process."[57] Similarly, the American College of Physicians' *Ethics Manual* states that "[p]hysicians must disclose their financial interests in any medical facilities or office-based research to which they refer or recruit patients."[58]

In addition, the trade association for pharmaceutical companies, the Pharmaceutical Research and Manufacturers of America (PhRMA), has revised its *Principles on the Conduct of Clinical Trials* to recommend that "[c]linical investigators should disclose to potential research participants during the informed consent process that the investigator and/or the institution is receiving payment for the conduct of the clinical trial."[59] Like other codes that commend conflict disclosure, PhRMA's recommendations require only disclosure of the existence of compensation, with no requirement of quantification.

The IOM Committee on Conflict of Interest in Medical Research, Education, and Practice's 2009 report observes that public disclosures of conflicts of interest are beneficial if they lead physicians to avoid situations that potentially could compromise their professional independence, but that transparency can be harmful if researchers react by avoiding relationships "that promote important societal goals and that are accompanied by adequate measures to protect objective judgment."[60] The IOM report calls on researchers to report all information potentially giving rise to conflicts of interest to a variety of entities, including their academic homes, and supports a requirement for companies to disclose their relationships with physicians and

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57 AMA, Code of Medical Ethics, Opinion 8.0315 – Managing Conflicts of Interest in the Conduct of Clinical Trials, www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion80315.shtml (last visited Feb. 15, 2011).

58 Lois Snyder & Cathy Leffler, *Ethics Manual: Fifth Edition*, 142 Annals Internal Med. 560, 572 (2005).

59 Pharmaceutical Research & Manufacturers of Am. (PhRMA), Principles on Conduct of Clinical Trials: Communication of Clinical Trial Results 9 (2009), *available at* www.phrma.org/sites/default/files/105/042009_clinical_trial_principles_final.pdf.

60 IOM Report, at 67–68.

researchers on a public website (essentially the requirement adopted in PPACA). The IOM's recommendations emphasized that "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."[61]

At the international level, the Declaration of Helsinki, which was first adopted by the World Medical Association in 1964, requires that the "sources of funding, any possible conflicts of interest, [and] institutional affiliations of the researcher" be disclosed to all potential participants in human research.[62] The Council for International Organizations of Medical Sciences, an international, non-governmental, nonprofit organization representing the biomedical scientific community, recommends that "[b]efore requesting an individual's consent to participate in research, the investigator must provide [information regarding] . . . the sponsors of the research, the institutional affiliation of the investigators, and the nature and sources of funding for the research[.]"[63]

The Intended Goals of Disclosure

Scholars, professional organizations, and policy institutes have advanced various justifications and goals for requiring disclosure of financial interests by investigators and research institutions. These goals are discussed briefly in the following section.

Respecting participants' right to know. The "right to know" is premised on the idea that there are certain kinds of information to which a person is morally entitled, based on the individual's status as an

61 IOM Report, at 5 (emphasis added).

62 World Med. Ass'n Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects ¶ 24 (2008), *available at* www.wma.net/en/30publications/10policies/b3/17c.pdf.

63 Council for Int'l Orgs. of Med. Scis. (CIOMS), International Ethical Guidelines for Biomedical Research involving Human Subjects 37, 39 (2002), *available at* www.cioms.ch/publications/layout_guide2002.pdf.

autonomous moral agent. A core argument for requiring researchers to disclose their conflicts of interest is that, because research participants will be exposed to the risks of the research, they have a moral right to know how the investigator and research institution stand to benefit from the trial.[64] According to some recent survey respondents, participants "might feel morally wronged" if they learned "after the fact" of an investigator's financial relationships in a study.[65]

Establishing and maintaining trust in physicians[66] and clinical research.[67] A 2003 article on conflicts of interest in research observed that "there is virtual unanimity that the ultimate goal of reform is to promote public trust in the human research enterprise."[68] This notion of public trust is reflected in almost every statement addressing conflicts of interest in clinical research. For example, in their 2008 report, the AAMC and AAU stressed that a central goal of conflict management strategies is to promote public trust in research.[69] In a separate report, the

64 Kevin Weinfurt et al., *Disclosing Conflicts of Interest in Clinical Research: Views of Institutional Review Boards, Conflict of Interest Committees, and Investigators*, J. L. Med. & Ethics 581, 585 (2006) (more informed decision making is the most frequently discussed justification) [hereinafter *Disclosing Conflicts of Interest in Clinical Research*]; *see also* Ezekiel J. Emanuel & Dennis F. Thompson, *The Concept of Conflicts of Interest, in* The Oxford Textbook of Clinical Research Ethics 758, 764–65 (Ezekiel J. Emanuel et al. eds., 2008) ("Many people believe that research participants are entitled to information about the researcher's conflicts because they are bearing the risks of the interventions.") [hereinafter The Oxford Textbook of Clinical Research Ethics].

65 *Disclosure of Financial Relationships to Participants in Clinical Research*, at 918.

66 *See generally* Paul B. Miller & Charles Weijer, *Trust and Exploitation in Clinical Research, in* The Limits of Consent: A Socio-Ethical Approach to Human Subject Research in Medicine 25 (Oonagh Corrigan et al. eds., 2009); Eric G. Campbell, *Public Disclosure of Conflicts of Interest: Moving the Policy Debate Forward*, 170 Archives Internal Med. 667, 667 (2010).

67 *See generally* Nancy E. Kass et al., *Trust: The Fragile Foundation of Contemporary Biomedical Research*, 26 Hastings Center. Rep. 25 (1996); 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 (2006) [hereinafter *Views of Potential Research Participants on Financial Conflicts of Interest*].

68 Robert Gatter, *Walking the Talk of Trust in Human Subjects Research: The Challenge of Regulating Financial Conflicts of Interest*, 52 Emory L.J. 327, 355 (2003).

69 AAMC-AAU 2008 COI Report, at 32.

AAMC stated that its recommendations sought to maintain public trust to "retain the confidence of those who generously volunteer to participate in research."[70]

Protecting the integrity of clinical research results. A significant concern about conflicts of interest is their potential to undermine the reliability of research data. Many calls for disclosure reflect these concerns. For example, in recommending disclosure of researchers' financial interests, the AAMC emphasized that disclosures should be structured to avoid "any additional significant risk to . . . the integrity of the research."[71]

Deterring troubling financial relationships. In some contexts, the ultimate goal of mandating disclosure is to change the discloser's behavior.[72] It has been suggested that divulging investigators' financial relationships will create pressure on researchers to eliminate "unproductive" conflicts.[73] This expectation "assumes that investigators dislike having to disclose their financial interests in clinical trials and will avoid relationships that might suggest a conflict of interest."[74]

Dispelling the therapeutic misconception. The "therapeutic misconception" refers to the mistaken belief that decisions about the type of interventions given to research participants are based primarily on

70 AAMC Task Force on Fin. Conflicts of Interest in Clinical Research, *Protecting Subjects, Preserving Trust, Promoting Progress II: Principles and Recommendations for Oversight of an Institution's Financial Interests in Human Subjects Research*, 78 Acad. Med. 237 (2003).

71 AAMC 2001 COI Report, at 18.

72 Paula J. Dalley, *The Use and Misuse of Disclosure as a Regulatory System*, 34 Fla. St. U. L. Rev. 1089, 1105, 1096 (2007) [hereinafter *The Use and Misuse of Disclosure as a Regulatory System*]; *see also* Mark Hall & Robert A. Berenson, *Ethical Practice in Managed Care: A Dose of Realism*, 128 Annals Internal Med. 395–402 (1998) [hereinafter *Ethical Practice in Managed Care*].

73 The IOM's recommendations focus on the deterrence of questionable or inappropriate relationships. IOM Report, at 3–5; *id*. app. F at 387 ("Even if information on financial relationships or conflicts of interest were rarely used by patients, physicians, or others to make decisions, the fact of public reporting would probably motivate some researchers, physicians, and senior officials to eliminate unproductive conflicts.").

74 *Disclosure of Financial Relationships to Participants in Clinical Research*, at 919 (*citing Ethical Practice in Managed Care*).

an individualized assessment of each participant's therapeutic needs, just as treatment decisions would be made for patients receiving care outside of a study.[75] The therapeutic misconception is widespread among both research participants and even many physician-investigators.[76] Some proponents of disclosure argue that highlighting the financial relationship between investigators and sponsors will alert prospective subjects that the study's primary goal is to develop scientific knowledge, rather than to advance the medical best interests of the individual participants.[77]

Protecting research participants' welfare. It is possible that studies in which investigators or research institutions have financial conflicts of interest may pose greater risks of injury to participants than studies without such conflicts. If conflicts increase risks, requiring disclosure could protect individuals by making prospective participants more wary of enrolling, or by discouraging investigators and institutions from entering into the troubling arrangements.[78]

This was essentially the argument made in the lawsuit brought by the father of Jesse Gelsinger, an 18-year-old with ornithine transcarbamylase deficiency, who died as a result of his participation in a Phase I gene transfer study at the University of Pennsylvania. The lawsuit against the University and investigators alleged that the investigators committed fraud by not revealing that an investigator, the University, and other officials had financial relationships with Genovo, the bio-

75 Paul Appelbaum & Charles Lidz, *The Therapeutic Misconception*, in The Oxford Textbook of Clinical Research Ethics 737; *see also* Jonathan Kimmelman, *The Therapeutic Misconception at 25: Treatment, Research, and Confusion*, 37 Hastings Center Rep. 36 (2007); Christopher Daugherty et al., *Perceptions of Cancer Patients and Their Physicians Involved in Phase I Trials*, 13 J. Clinical Oncology 1062–72 (1995); Daniel Rayson, *Lisa's Stories*, 282 JAMA 1605–06 (1999); Matthew Miller, *Phase I Cancer Trials: A Collusion of Misunderstanding*, 30 Hastings Center Rep. 34 (2000).

76 Paul S. Appelbaum et al., *Therapeutic Misconception in Clinical Research: Frequency and Risk Factors*, 26 IRB: Ethics & Human Research 4–5 (2004); Dana J. Lawrence, *The Therapeutic Misconception: Not Just for Patients*, 52 J. Canadian Chiropractic Ass'n 139, 140 (2008).

77 IOM Report, at 51.

78 *Disclosure of Financial Relationships to Participants in Clinical Research*, at 919.

technology company that would take the gene vectors being studied to market in the event of a successful trial.[79] Jesse's father learned only after his son's death that the "principal investigator, James Wilson, owned stock in . . . [the] company [he had] founded, which contributed $4 million per year to human gene therapy research at the University . . . where the experiment took place."[80] The suit ended in a confidential settlement in 2000, six weeks after it was filed. In 2005, the University of Pennsylvania and Children's National Medical Center agreed to pay over $1 million in a False Claims Act settlement with the federal government to resolve allegations that the institutions failed to disclose necessary information and misled the government about the benefits of the treatment (the three physician-investigators—including Wilson—were also parties to the settlement).[81]

The Limits of Disclosure as a Conflict Management Tool

Conflicts of interest create significant risks to the integrity of the physician-patient relationship, medical education, and clinical research.[82] Although we believe in the importance of increased transparency in industry-physician relationships,[83] we are skeptical

79 Complaint, Gelsinger v. Trs. of the Univ. of Pa., No. 000901885 (Phila. County C.P. Trial Div. Sept. 18, 2000), *available at* www.sskrplaw.com/files/gelsinger_complaint.pdf. The Complaint also alleged that the investigators had failed to inform Jesse of the risks of the study, that they had failed to inform Jesse or the FDA of adverse events experienced by other participants in the same trial as well as the death of monkeys in an earlier animal study, and that the investigators had allowed Jesse to participate in the study despite not meeting the inclusion criteria due to the fact that his liver was not functioning within the study's 24-hour limit. *See also* Gerald R. Prettyman, Jr., *Ethical Reforms in Biotechnology Research Regulations*, 15 Va. J. Soc. Pol'y & L. 51, 69 (2007).

80 David Resnik, *Disclosing Conflicts of Interest to Research Subjects: An Ethical and Legal Analysis*, 11 Accountability Res. 141, 142 (2004).

81 *Settlement Is Reached in Fatal Experiment*, N.Y. Times, Feb. 10, 2005, at A18; *U.S. Settles Case of Gene Therapy Study That Ended With Teen's Death*, 51 Univ. of Pa. Almanac 4, 4–5 (2005), *available at* www.upenn.edu/almanac/volumes/v51/n21/pdf_n21/021505.pdf.

82 Promotion White Paper, at 21.

83 *See generally id.*

that disclosure is likely to provide significant protections to research participants or the integrity of research. Rather than burdening the already dysfunctional informed consent process with mandatory disclosures unlikely to achieve most of their sought-after benefits, we urge increased focus on the elimination, reduction, and management of conflicts of interest and propose that remaining conflicts be disclosed under a system modeled on transparency initiatives undertaken in other areas of health and consumer affairs.

In this section, we revisit the goals of disclosure previously discussed. We conclude that disclosure would promote participants' moral right to know, but that it is unlikely to achieve most of the other sought-after benefits. In the next section, we explain why disclosure of conflicts of interest should not be included routinely in the process of obtaining research participants' informed consent.

The right to know

Empirical evidence of research participants' desire for information about financial relationships demonstrates that financial incentives matter to some potential research subjects. One study, consisting of in-person interviews of 253 participants in cancer-research trials, revealed that a large minority—40%—wanted to be informed about the oversight system for investigator financial conflicts of interest, and nearly a third wanted to be told about investigators' financial interests, regardless of the monetary value.[84] Another study surveying 259 participants in 6 clinical trials for non-acute conditions conducted at Royal Melbourne Hospital in Australia found that 57% wanted to be informed about the sponsor of the clinical trial and 34% wanted to know how much funding was accrued at the study's completion.[85] A third study

84 Lindsay A. Hampson et al., *Patients' Views on Financial Conflicts of Interest in Cancer Research Trials*, 355 New Eng. J. Med. 2330, 2334 (2006) [hereinafter Patients' *Views on Financial Conflicts*].

85 Anastasia Hutchinson & Abe R. Rubinfeld, *Financial Disclosure and Clinical Research: What is Important to Participants?*, 189 Med. J. Aust. 207 (2008) [hereinafter *Financial Disclosure and Clinical Research*].

consisting of 16 focus groups conducted in 2004 and 2005 similarly found that many participants wanted to know about financial interests in research, even if they did not think it would make a difference in their decision to enroll in a study.[86]

> In a qualitative study of 33 individuals with serious, life-threatening, or chronic conditions who had participated in NIH studies for extensive periods of time, most respondents wanted to be informed about physician financial interests.[87] They thought prospective participants should be informed about investigators' financial interests, but only a few said that they would want the full details. Similarly, a survey of over 5,000 individuals with chronic conditions who had indicated a willingness to participate in clinical trials revealed that most respondents wanted to be informed about potential conflicts of interest, even though only a minority (ranging from a low of 2 percent to a high of 32 percent depending on the nature of the hypothetical financial tie) actually would decline to participate due to a perceived conflict.[88] In both of these studies, the individuals who wanted information about financial relationships tended to be more highly educated.[89]

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86 *Views of Potential Research Participants on Financial Conflicts of Interest*, at 904.

87 Christine Grady et al., *The Limits of Disclosure: What Research Subjects Want to Know about Investigator Financial Interests*, 34 J. L. Med. & Ethics 592, 596 (2006) [hereinafter *The Limits of Disclosure*].

88 Scott Y. Kim et al., *Potential Research Participants' Views Regarding Researcher and Institutional Financial Conflicts of Interest*, 30 J. L. Med. & Ethics 73, 73, 75, 77 (2004) [hereinafter *Potential Research Participants' Views*].

89 *The Limits of Disclosure*, at 594; *Potential Research Participants' Views*, at 77; *see also* Judith Hibbard et al., Identifying Medicare Beneficiaries with Poor Health Literacy Skills: Is a Short Screening Index Feasible? 1 (2005), *available at* http://assets.aarp.org/rgcenter/health/2005_01_literacy.pdf ("[i]nadequate health literacy skills prevent people from being involved and active participants in their care."); *Financial Disclosure and Clinical Research*, at 208.

Although a subset of research participants is interested in receiving information about financial incentives, it does not appear that the information is likely to affect many individuals' ultimate decision to participate.[90] In one study, for example, the authors surveyed a random sample of 470 adults diagnosed with coronary artery disease.[91] All respondents were presented with an informed consent document for a hypothetical clinical trial evaluating a new medication to treat their disease. For one group, the informed consent document provided no information about investigator financial ties. For a second group, the document stated that the investigator received a per capita payment that covered the costs of research, including the investigator's salary. For the third group, the document stated that the investigator was an investor in the company sponsoring the research. The informed consent documents shown to the second and third groups stated that an IRB and another committee had reviewed the financial interest and did not believe it would affect the safety or scientific quality of the trial, and that more information was available on request. The authors found that per capita payments had no effect on participants' willingness to enroll, although an equity holding by the investigator significantly decreased willingness.

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90 *See* Adam Licurse et al., *The Impact of Disclosing Financial Ties in Research and Clinical Care: A Systematic Review*, 170 Archives Internal Med. 675, 680 (2010) [hereinafter *The Impact of Disclosing Financial Ties in Research and Clinical Care*]. Some empirical evidence shows that, for a minority, information about an investigator's financial relationships would affect the decision to enroll in research. For example, a study consisting of in-person interviews of 253 patients in cancer-research trials revealed that approximately 15% of survey respondents reported that knowledge of any investigator financial tie would have prompted them not to participate in the cancer trial in which they were currently enrolled. *Patients' Views on Financial Conflicts*, at 2336. Another study of 102 patients enrolled in cancer trials found that, although the majority would be willing to participate despite knowledge of a conflict of interest, 37% would be either unwilling or uncertain about participating. Stacy W. Gray et al., *Attitudes Toward Research Participation and Investigator Conflicts of Interest Among Advanced Cancer Patients Participating in Early Phase Clinical Trials*, 25 J. Clinical Oncology 3488, 3492 (2007).

91 Kevin P. Weinfurt et al., *Effects of Disclosing Financial Interests on Participation in Medical Research: A Randomized Vignette Trial*, 156 Am. Heart J. 689, 689–91 (2008) [hereinafter *Effects of Disclosing Financial Interests on Participation in Medical Research*].

Similarly, a 2006 survey study of 297 undergraduates found that various investigator conflicts of interest did not have a statistically significant effect on the students' willingness to participate in a hypothetical clinical trial.[92] The survey respondents were asked the importance of the following three conflicts of interest:

1. an investigator employed by the sponsor;
2. an investigator employed by the sponsor and paid a fee for each participant who completed the study; and
3. an investigator who developed the product under investigation and would receive royalty payments from all potential sales.[93]

None of the three affected the students' willingness to participate.[94]

Whether disclosure of information is likely to affect an individual's decision may depend on whether the individual believes he or she has options or alternatives.[95] The importance of genuine choice cannot be understated:

> [T]he value of information nearly always depends on the potential for someone to act on it. Although creating a naked "right to know" can be seductive in the heat of politics, lasting benefit from disclosure generally requires the availability of choice through entry and exit, ongoing control, political voice, or other forms of self-help through legal or extralegal mechanisms.[96]

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92 Jeffrey N. Gibbs & Gregory A. Guagnano, *Investigator Financial Disclosures and Its Effect on Research Subjects*, 62 Food & Drug L. J. 727, 733 (2007).
93 *Id.* at 732.
94 *Id.* at 733.
95 *Views of Potential Research Participants on Financial Conflicts of Interest*, at 903 (noting that some potential research participants "felt that if they were extremely ill and desperate for a cure, they would not care about financial interests" although others, in particular parents of children with leukemia or brain tumors, believed that disclosure was of paramount importance because "[w]e've got little folks with lives on the line").
96 William M. Sage, *Regulating Through Information: Disclosure Laws and American Health Care*, 99 Colum. L. Rev. 1701, 1827–28 (1999).

In the financial context, for example, would-be investors, once provided with information about an advisor's relationship with a company whose stock he or she is recommending, are likely to understand that they can choose not to invest at all or invest in something else.[97] Prospective participants in clinical trials, by contrast, often do not believe they have realistic alternatives outside the study. For some prospective participants, clinical trials offer the last hope when all treatments have failed. Although it may be possible for these individuals to obtain investigational treatment outside of a study, either by obtaining an off-label prescription (if the drug is approved for another indication)[98] or by seeking a compassionate use exemption for an unapproved drug,[99] many individuals do not have the knowledge, access, or resources to pursue these alternatives. Even if alternative treatments theoretically are available outside the trial, patients who are uninsured or underinsured may not realistically have access to them. When the patient believes that enrolling in a clinical trial is the only viable option, mandated transparency does not improve choice.

Establishing and maintaining trust in physicians and clinical research

The argument that disclosure will enhance trust is dubious on both empirical and ethical levels. As an empirical matter, it is not clear what impact disclosure of financial relationships will have on trust in physicians or research institutions. One study showed no statistically significant difference in investigator trust between potential research participants told of per capita payments made to the investigator and those told nothing at all.[100] Participants told that the investigator had

97 Bryan K. Church & Xi Kuang, *Conflicts of Interest, Disclosure, and (Costly) Sanctions: Experimental Evidence*, 38 J. Legal Stud. 505, 507 (2009) [hereinafter *Experimental Evidence*].

98 Jerry Menikoff, *The Hidden Alternative: Getting Investigational Treatments Off-Study*, 361 Lancet 63, 66 (2003).

99 In August 2009, the FDA published new rules to clarify the methods by which patients can access investigational drugs. *See* 21 C.F.R. §§ 312.300 –.320, 316.40.

100 *Effects of Disclosing Financial Interests on Participation in Medical Research*, at 691.

an equity interest, on the other hand, were less trusting than those told of per capita payments and those told nothing.[101] Interestingly, disclosure did not affect trust in the sponsor and institution at all.[102] Other studies have found that disclosure of financial incentives could undermine trust in the physician[103] or could have no effect.[104] One study found that when enrollees in a capitated managed care plan were told how the plan compensated participating physicians, their trust in their doctors increased.[105]

As an ethical matter, it is not clear why promoting trust in researchers or research institutions is desirable. It is possible that, to the extent that disclosure enhances trust, potential participants will not exercise enough caution in weighing the studies' risks and benefits.[106] Unalloyed trust might exacerbate the problem of the therapeutic misconception. For example, in one study, "[m]any volunteered that they trusted their

101 *Id.*
102 *Id.*
103 *The Impact of Disclosing Financial Ties in Research and Clinical Care*, at 679; *see also* Tracy E. Miller & Carol R. Horowitz, *Disclosing Doctors' Incentives: Will Consumers Understand and Value the Information?*, 19 Health Aff. 149, 150 (2000) (for comment on a similar decrease in trust seen in the managed care setting).
104 Studies have found that, although "[p]erceived trust of the investigator was significantly related to willingness to participate, [t]he perception of trust . . . was not correlated with the level of financial stake . . . It is not clear whether subjects were more willing to participate because—on whatever basis—they had concluded that the investigator was trustworthy, or they first decided that they wished to participate and that influenced the way they responded to the question regarding trustworthiness, or due to some other mechanism. The basis for the means by which they formed trustworthiness evaluations is an area meriting further research." Jeffrey N. Gibbs & Gregory A. Guagnano, *Investigator Financial Disclosures and Its Effect on Research Subjects*, 62 Food & Drug L. J. 727, 736 (2007). *See also* Steven D. Pearson et al., *A Trial of Disclosing Physicians' Financial Incentives to Patients*, 166 Archives Internal Med. 623 (2006) (finding that disclosure either increased trust or did not affect it).
105 Mark A. Hall et al., *How Disclosing HMO Physician Incentives Affects Trust*, 21 Health Aff. 197 (2002). Enrollees in a second plan, which paid its physicians in a different way, experienced no change in trust levels after being told how their physicians were compensated. *Id.*
106 *See* Daylian M. Cain et al., *The Dirt on Coming Clean: Perverse Effects of Disclosing Conflicts of Interest*, 34 J. Legal Stud. 1, 5 (2005) ("[T]here is at least suggestive evidence that people tend to be naturally trusting and credulous toward their own advisors.") [hereinafter *The Dirt on Coming Clean*].

physician and that he or she would not ask them to participate unless they were regarded as an appropriate candidate."[107] For these individuals, a healthy dose of skepticism might be more beneficial than measures to promote greater trust. One of informed consent's main goals is, after all, to encourage individuals to behave as active decision-makers about treatment or research opportunities.

Protecting the integrity of clinical research

To the extent that financial relationships between industry and researchers or institutions create a risk to data integrity, disclosure of those relationships is unlikely to eliminate that risk. Despite disclosure, conflicted investigators would remain in a position to influence study design, recruitment of subjects, conduct of trials, or reporting results in a manner favorable to the investigators' financial interests. The AAMC and IOM both outline a variety of appropriate responses when financial relationships create risks to research or data integrity, including eliminating the conflicts or managing them through techniques such as independent data monitoring,[108] asking the investigator to reduce the interest creating the conflict, changing the project design, or substituting a principal investigator without a conflict of interest.[109]

Deterring troubling financial relationships

There is little-to-no evidence that disclosure will influence physician-investigators to modify problematic behavior by avoiding questionable relationships or deciding not to participate in research. Indeed, it is possible that physicians will be more willing to enter into these relationships if they think that disclosure "sanitizes" them, thereby giving them a perceived "free pass."[110] As some commentators have suggested, "by

107 *Should Informed Consent Include Information on How Research is Funded?*, at 2.
108 AAMC-AAU 2008 COI Report, at 29.
109 IOM Report, at 81.
110 *The Dirt on Coming Clean*, at 18 ("Disclosure . . . benefited the providers of information but not its recipients").

laying their cards on the table, investigators might adopt an attitude of caveat emptor and become less vigilant in policing their own judgmental biases with regard to enrolling patients, collecting data, interpreting results, and other research activities."[111] It has been argued that individuals may look at "compliance with disclosure as a moral license to follow their self-interest."[112] One study demonstrated that:

> [A]dvisers are more biased when conflicts of interest are disclosed as opposed to suppressed. . . . [D]isclosure gives advisers moral license to exploit their informational advantage. . . . [A]dvisees . . . are worse off when conflicts of interest are disclosed. Although disclosure affords a forewarning of biased advice, advisees do not adequately adjust for the bias—in fact, adjustment is woefully inadequate. . . . [D]isclosure is not always beneficial and is potentially harmful.[113]

Disclosure that financial relationships have been approved by a conflicts of interest process may lead both investigators and participants to believe that the disclosed arrangements do not pose any risk precisely because the arrangements have undergone an approval process.

Dispelling the therapeutic misconception

Although it has been posited that disclosure of financial relationships to potential research participants might reduce the therapeutic misconception by shedding light on the relationship between the investigator and the sponsor, we doubt that the therapeutic misconception can be so easily dispelled, particularly where physicians refer their own patients to participate in research. For example, in one study, 24 percent of participants who were a part of other ongoing clinical research

111 *Disclosure of Financial Relationships to Participants in Clinical Research*, at 919.
112 *Id.* at 919; *see also*, Jason Dana & George Lowenstein, *A Social Science Perspective on Gifts to Physicians from Industry*, 290 JAMA 252 (2003).
113 *Experimental Evidence*, at 507.

trials reported no risks or disadvantages of their treatment, even though they had previously been explicitly told about such risks.[114] Some commentators note that disclosure might "paradoxically" reinforce the therapeutic misconception, explaining that "[d]ata suggest that some people place more faith in an experimental intervention when the investigator has a financial stake in the product being tested, believing that the investigator's investments signal his or her confidence in the product."[115] Other evidence suggests that participants might believe that a greater financial interest would make the investigator do a better job, due to his or her investment in the outcome of research and the product or drug being tested.[116]

Protecting research participants' welfare

The danger that financial relationships between companies that sponsor research and investigators or institutions will lead to riskier studies is a serious concern. However, the proper remedy for this problem is the elimination or management of problematic conflicts. Relying on disclosure to prospective participants on the theory that these individuals can then protect themselves by asking the right questions is unrealistic and may lead institutions to become lax in their oversight responsibilities. It is also unlikely to help those who need it most. As social scientists have observed, disclosure of financial incentives is most likely to have a beneficial impact on the "sophisticated estimator," even though "unsophisticated estimators are exactly the ones who are most likely to need protection from exploitation."[117]

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114 Charles Lidz et al., *Therapeutic Misconception and the Appreciation of Risks in Clinical Trials*, 58 Soc. Sci. Med. 1689, 1693-94 (2004).

115 *Disclosure of Financial Relationships to Participants in Clinical Research*, at 917.

116 *Views of Potential Research Participants on Financial Conflicts of Interest*, at 903. *See also* Jesse A. Goldner, *Childress Lecture: Regulating Conflicts of Interest in Research: The Paper Tiger Needs Real Teeth*, 53 St. Louis L.J. 1211, 1225-26 (2009) (summarizing the "evidence that disclosure of conflicts of interest may actually encourage potential subjects to agree to participate in a study").

117 *The Dirt on Coming Clean*, at 20. "For disclosure to be effective, the recipient of advice must understand how the conflict of interest has influenced the advisor and must be able to correct for that biasing influence. In many important situations, however, this understanding and ability may be woefully lacking." *Id.* at 4.

Conflicts Disclosure Should Not Be Incorporated into the Consent Process

The previous section explained why disclosure of financial conflicts of interest is unlikely to achieve most of the goals espoused by advocates of disclosure. In itself, that is not an argument against incorporating a discussion of conflicts of interest into the informed consent process; even if the potential benefits are small, disclosure might be appropriate if the costs are equally low. However, adding discussions about conflicts of interest to the informed consent process would impose significant burdens that outweigh the limited expected benefits. For this reason, requiring routine disclosures of conflicts of interest to potential research participants would be unwise public policy.

First, informed consent documents are becoming increasingly long and complex, thereby confusing and overwhelming potential research participants.[118] Evidence indicates that participants often are unable to sift through the morass of information to tease out the salient or material content.[119] Adding to the lengthy document by including information that participants may be unable to process or absorb—

118 James Henry et al., *Reformed Consent: Adapting to New Media and Research Participant Preferences*, 31 IRB: Ethics & Human Res. 1 (2009) [hereinafter *Reformed Consent*]; Ezekiel Emanuel, *Is Longer Always Better*, 38 Hastings Center Rep. 10, 11 (2008) ("[I]nformed consent documents have become longer, more complex, exhaustive, and exhausting without clearly promoting subjects' understanding.").

119 *See Reformed Consent*, at 1 ("longstanding evidence that increased document length hinders participant comprehension of key information"); Nancy N. Dubler, *Remaining Faithful to the Promises Given: Maintaining Standards in Changing Times*, 32 Seton Hall L. Rev. 561, 568–69 (2002) (describing "'informed consent' documents, which neither inform nor empower, but rather dump all of the possibly foreseeable—however remote—risks on the patient. How is a patient to distinguish the most important of these risks, those of serious impact and frequent occurrence, from the less significant? With the exception of possibly teratogenic drugs, which usually come with warnings in bold and capital letters—again for risk management reasons—the rest of the form disappears into the tombstone gray of endless, invariable discourse."); Omri Ben-Shahar & Carl E. Schneider, *The Failure of Mandated Disclosure* 58 (Univ. of Chi. Law & Econ., Olin Working Paper No. 516, 2010) ("[M]andated disclosure can crowd out useful information.") [hereinafter *The Failure of Mandated Disclosure*].

and which is of less utility than information related to the risks, potential benefits, and alternatives to research—will simply exacerbate the problem. Indeed, evidence shows that information overload, particularly when it includes irrelevant or insignificant information, can cause decisionmaking that is worse than if the user had been provided less information or no information at all.[120] For example, disclosing financial relationships may cause participants to overemphasize the importance of the information, increasing the salience beyond its intended significance.[121]

In recognition of the danger of information overload, one might suggest that the solution is to include brief statements regarding investor/industry financial relationships in the informed consent process. Yet, in one qualitative study, Kevin Weinfurt and colleagues found that brief, concise statements about financial interest within informed consent documents rarely were understood, and sometimes only confused potential participants.[122] Other commentators have noted that "the cure for the mandated disclosure failure is not as simple as merely *make-them-simple*. Sometimes even a simple mandate to disclose simple information has undesirable consequences."[123]

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120 *The Use and Misuse of Disclosure as a Regulatory System*, at 1115. *See also* Ronald M. Epstein, *Withholding Information from Patients – When Less is More*, 362 New Eng. J. Med. 380, 380 (2010) (noting that cognitive overload may be compounded by the emotional nature of medical decisions).

121 *The Use and Misuse of Disclosure as a Regulatory System*, at 1114 ("The availability bias, for example, leads people to respond to information based on the 'ease with which instances or associations could be brought to mind.' Thus, people will overestimate the risk of an accident after seeing or hearing about such an accident.") (*citing* Amos Tversky & Daniel Kahneman, *Availability: A Heuristic for Judging Frequency and Probability, in* Judgment Under Uncertainty: Heuristics and Biases 163–64 (Daniel Kahneman et al. eds., 1982); Robert Prentice, *Whither Securities Regulation? Some Behavioral Observations Regarding Proposals for Its Future*, 51 Duke L. J. 1397, 1469–70 (2002) (noting that "while making decisions, people tend to concentrate on facts that are 'available' in their memories"); Cass R. Sunstein, Behavioral Law and Economics 1, 3–5 (2000) (describing various kinds of biases, including the availability bias).

122 Kevin P. Weinfurt et al., *Developing Model Language for Disclosing Financial Interests to Potential Clinical Research Participants*, 29 IRB Ethics & Human Res. 2 (2007) [hereinafter *Developing Model Language for Disclosing Financial Interests to Potential Clinical Research Participants*].

123 *The Failure of Mandated Disclosure*, at 62 (emphasis in original).

These findings are unsurprising. Given the level of trust that pervades relationships between participants and investigators, one would imagine that only highly sophisticated or skeptical individuals would intuit that disclosures of conflicts of interest are designed to alert participants that the researcher may be acting in a self-interested manner. Further, even if prospective participants understand why the information is being provided, they would have no context within which to evaluate the information. For example, most people would have no way of knowing whether a particular conflict is significant, or whether it has influenced the study design.

> Theoretically, one response to this concern would be to provide longer descriptions, explanations, and context to disclosures of financial information in informed consent documents. However, Weinfurt and colleagues found that, even after longer descriptions about financial interests were provided, many participants required discussion with the group to understand the meaning of the descriptions. They explained, "[e]ven when participants did understand the definitions, they did not always understand why the information was relevant to them."[124]

Further, because an individual's level of education correlates with the level of concern about investigator financial interests,[125] commentators have cautioned that an unintended harm of mandated disclosure is that it can lead to inequity. Disclosure could very well help "most those who need help least and help[ing] least those who need help most," thereby increasing the disparity between educated and uneducated, or rich and poor.[126]

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124 *Developing Model Language for Disclosing Financial Interests to Potential Clinical Research Participants*, at 2.
125 *Potential Research Participants' Views*, at 76.
126 *The Failure of Mandated Disclosure*, at 60, 61 (pointing to healthcare as the principal example of the inequity of mandated disclosure).

Our conclusion that financial conflicts of interest should not be disclosed routinely as part of the informed consent process is not inconsistent with the California Supreme Court's decision in *Moore v. Regents of the University of California*.[127] In that case, a physician removed the plaintiff's spleen as part of the plaintiff's treatment for hairy-cell leukemia. He encouraged the plaintiff to return for several follow-up visits during which additional tissue was removed. Throughout this time, the physician was using the plaintiff's biological material in experiments with considerable commercial potential, but never disclosed this fact to the plaintiff.[128] The research ultimately resulted in a valuable commercial product, and the plaintiff sued for a share of the profits. Although the court concluded that the plaintiff did not have a property interest in the product developed from his biological material, it found he had stated a valid claim for breach of fiduciary duty or, in the alternative, failure to obtain informed consent. The court reasoned that a reasonable person in the plaintiff's position would have wanted to know about the physician's research activities, because those activities created "a possibility that an interest extraneous to the patient's health has affected the physician's judgment."[129]

Although *Moore* creates the possibility that, in the right set of circumstances, a physician's failure to disclose research-related financial interests could give rise to liability, it does not mean that any and all financial relationships with industry necessarily must be disclosed. Rather, as in any informed consent claim, liability would depend on the plaintiff's ability to establish the element of causation—i.e., that, if the omitted information had been disclosed, a reasonable person in the plaintiff's position would not have consented to the procedure.[130]

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127 Moore v. Regents of the Univ. of Cal., 793 P.2d 479 (Cal. 1990).

128 *Id.* at 481-482. The physician actively misled Moore by telling him that the research team was "engaged in strictly academic and purely scientific medical research" and "there was no commercial or financial value to his Blood and Bodily Substances." *Id.* at 486.

129 *Moore*, 793 P.2d at 484.

130 *Id.* at 520.

Such proof would be possible only in situations involving truly serious conflicts, which we believe should not be permitted to proceed anyway.[131] In other words, our proposed approach to informed consent presumes that any conflict serious enough to affect a reasonable person's decision about enrollment has already been eliminated, and that the remaining conflicts are relatively minor. For the reasons set forth above, we believe that requiring disclosure of these residual conflicts would not be good public policy; we also believe that the failure to disclose them would not be grounds for liability under *Moore*.[132]

Financial Interest Information Should Be Available Elsewhere

Although we oppose the disclosure of financial conflicts of interest as part of the informed consent process, we recognize that some potential participants will want this information.[133] To accommodate these individuals and to promote the inherent ethical value of transparency, we encourage dissemination of information about financial relationships in research through other mechanisms, such as pamphlets in doctors' offices and physician and hospital websites. Some academic medical centers publish online databases to disclose the financial ties of their physicians to industry.[134] Consumer guides such as those

131 Oversight White Paper, at 13.

132 We note, however, that if a serious conflict—i.e., one significant enough that, if disclosed, would lead a reasonable person to refuse to participate in a study—slips through the IRB or Conflicts of Interest Committee and a participant is injured, the participant may well have a valid cause of action based on the failure to disclose. However, even if such a conflict had been disclosed, it is far from clear that the disclosure would be sufficient to insulate the investigator and/or institution from liability for the injuries.

133 *See, e.g., Patients' Views on Financial Conflicts,* at 2334; *Views of Potential Research Participants on Financial Conflicts of Interest*, at 904; *Potential Research Participants' Views*, at 77.

134 *See, e.g.*, Duke Clinical Research Institute, Conflict of Interest, https://dcri.org/about-us/conflict-of-interest (last visited Feb. 17, 2011); Cleveland Clinic, Find a Doctor, http://my.clevelandclinic.org/staff_directory/default.aspx (last visited Feb. 17, 2011) (listing each staff physician's "industry relationships," including consulting fees, on his or her individual biographical page).

released by the American Health Lawyers Association can aid potential enrollees in understanding the rights and responsibilities of research participants and suggest questions that participants can ask their physicians to put the information in context.[135]

We should not, however, place too much faith in these methods as a means of changing behavior, as experience in other areas of health and consumer affairs has shown that the benefits of mandated disclosure often are quite limited. For example, laws mandating quality report cards for hospitals have not been as effective as originally hoped, due to the limitations in the art of quality measurement, ambiguity as to what information patients actually need, and an inadequate understanding of how consumers process the information.[136] Research has shown low cooperation by healthcare workers and a failure to report or integrate information into communications with patients. Additionally, quality report cards have led to unintended harmful consequences. For example, report cards on bypass surgery reportedly caused some hospitals to "game" the system by rejecting sicker patients.[137]

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135 Reesa Benkoff et al., Medical Research: A Consumer's Guide for Participation (AHLA 2009), *available at* www.healthlawyers.org/Resources/PI/InfoSeries/Documents/MedicalResearch09.pdf.

136 *See* Jason Ross Penzer, Note, *Grading the Report Card: Lessons from Cognitive Psychology, Marketing, and the Law of Information Disclosure for Quality Assessment in Health Care Reform*, 12 Yale J. Reg. 207, 254–56 (1995); Eric C. Schneider & Arnold M. Epstein, *Use of Public Performance Reports: A Survey of Patients Undergoing Cardiac Surgery*, 279 JAMA 1638, 1642 (1998) ("Without a tailored and intensive program for dissemination and patient education, efforts to aid patient decision making with performance reports are unlikely to succeed."); *The Failure of Mandated Disclosure*, at 26 ("[D]espite decades of research, scholars have not found reliable indicia of medical quality, principally because it has proved impossible to factor out all the influences on medical success. And since exceptional doctors attract risky cases, success may not reflect skill."); *see also* Twerski & Cohen, *The Second Revolution in Informed Consent: Comparing Physicians to Each Other*, 94 Nw. U. L. Rev. 1 (1999) (describing the application of the informed consent cause of action to disclosure of the relative risks associated with the providers who would perform medical procedures).

137 David Wessel, *Eatery Report Cards: A Model for Schools?*, Wall St. J., May 29, 2003, at A2; *see generally* David Dranove et al., *Is More Information Better? The Effects of "Report Cards" on Health Care Providers*, 11 J. Pol. Econ. 555 (2003).

Conclusion

Transparency is an important ethical value. Financial relationships between commercial sponsors of clinical research and investigators or research institutions should not be kept secret. It does not follow from this that information about such relationships should be incorporated into the informed consent process, however. Available empirical evidence suggests that doing so would provide few, if any, benefits to research participants and could cause significant harms. To the extent that financial relationships between sponsors and investigators are problematic, they must be directly regulated. Research participants cannot be expected to protect themselves against the risks that financial relationships pose to researchers' judgment.