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Some Principles Require Principals: Why Banning "Conflicts of Interest" Won't Solve Incentive Problems in Biomedical Research

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I. Introduction: Relational Duties And Regulatory Duties

Money seems to have supplanted state power as the principal concern of biomedical research ethics. Each year brings new illustrations of the tension between financial flows and the moral and legal duties of academic researchers[1]:

- A young man dies after university-based physicians with a commercial stake in a novel gene therapy ignore warning signs when enrolling research subjects to test the procedure.[2]
- A pharmaceutical company pressures a university to which it has promised a large gift to demote a researcher who had published research casting the company's products in a negative light.[3]

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1. This Article focuses on biomedical research using human subjects that is performed by or in collaboration with academic medical centers. Biomedical research has become a large-scale enterprise, implicating many organizational structures, incentives, and interests. Research susceptible to financial influence does not always make use of human subjects, but may involve animal studies, microbial studies, or in vitro bioassays. Some researchers work in universities, others in private industry, and still others in government. The missions and obligations associated with these settings differ, and in the case of academic medical centers, several missions occupy a single setting. A growing amount of human subjects research is also being conducted by "contract research organizations" (CROs), typically for-profit ventures that replicate in the community clinical research activities that traditionally were housed in academic institutions. *See, e.g.*, Ken Gatter, *Fixing Cracks: A Disclosure Norm to Repair the Crumbling Regulatory Structure Supporting Clinical Research and Protecting Human Subjects*, 73 UMKC L. REV. 581, 618 (2005) (describing CROs as organizations that exist separately from academic institutions that receive federal funding and noting that CROs can operate trials more efficiently and are better able to recruit study participants); Trudo Lemmens, *Leopards in the Temple: Restoring Scientific Integrity to the Commercialized Research Scene*, 32 J.L. MED. & ETHICS 641, 645 (2004) (explaining that CROs manage a significant number of clinical trials outside of academia at dedicated research centers). Some of this Article's insights apply beyond the clinical academic setting, but a detailed consideration of those environments is beyond this Article's scope. In particular, this Article does not address special issues that may arise in CROs.

2. Sheryl Gay Stolberg, *F.D.A. Officials Fault Penn Team in Gene Therapy Death*, N.Y. TIMES, Dec. 9, 1999, at A22.

3. Apotex pressured the University of Toronto, to which it had promised a multimillion dollar gift, to demote a hematologist who had published negative findings about its new iron-binding drug.

- A pharmaceutical company attempts to prevent a university researcher from reporting that, contrary to expectations, its proprietary formulation of a human hormone is not superior to cheaper generics.[4]
- Another pharmaceutical company pressures the university researchers with whom it has contracts not to publish findings that antidepressant drugs are ineffective and may increase the risk of suicide.[5]
- A prominent health care provider conducts clinical trials on a new use of a Food and Drug Administration (FDA)-approved radiofrequency ablation device in which the health care provider itself, its physician–CEO, and others had invested. The health care provider publishes its results in peer-reviewed journals, and treats over 1,000 patients with the device "off-label."[6]

These are serious situations that demand a response from the scientific establishment, the health care professions, and the government. Poorly conducted or managed research can harm research subjects, bias research outcomes, delay dissemination of useful research products, and threaten public trust in, and support of, science.

This Article challenges the legal and ethical language of the response that is occurring and the implications of that language—not the underlying need for current action or future vigilance. Criticism of financial relationships involving biomedical research has been widespread, with individuals, professional associations, and government entities universally labeling them "conflicts of interest." In 2004, the U.S. Department of Health

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Krista Foss, *Grievance Filed in Drug-Research Controversy at U of T: Doctor in Lengthy Battle with Company Over Freedom to Publish Her Negative Findings*, GLOBE & MAIL (Toronto), Dec. 18, 1998, at A11.

4. The maker of Synthroid, Boots Pharmaceutical, attempted to suppress the publication of research that it sponsored at the University of California, San Francisco, which failed to show its product to be advantageous. *See* Drummond Rennie, *Thyroid Storm*, 277 JAMA 1238, 1238–39 (1997); *see also In re Synthroid Mktg. Litig.*, 264 F.3d 712, 714 (7th Cir. 2001) (discussing the publication of a study concluding that Synthroid and generic levothyroxine are interchangeable).

5. Barry Meier, *Contracts Keep Drug Research Out of Reach*, N.Y. TIMES, Nov. 29, 2004, at A1.

6. David Armstrong, *Delicate Operation: How a Famed Hospital Invests in Device It Uses and Promotes*, WALL ST. J., Dec. 12, 2005, at A1. The Cleveland Clinic was criticized in 2005 for its relationship with AtriCure, the manufacturer of radiofrequency ablation equipment used to treat atrial fibrillation. A venture capital fund established by the Clinic had invested substantially in AtriCure, as had the Clinic's physician–CEO, who helped manage the fund, sat on AtriCure's board of directors, and developed and retained a royalty interest in a device AtriCure was marketing. Another Clinic physician, who treated patients with the device and reviewed it favorably in professional publications, was a paid consultant to the company, though his payments were disclosed to the journals involved. The Clinic's Institutional Review Board (IRB) learned of the financial relationships and brought them to the attention of the Clinic's conflicts of interest committee. The IRB required the Clinic to disclose the financial relationships to research subjects in the clinical trials. The conflicts committee recommended, but could not require, disclosure to patients receiving the device outside of the research protocols. *Id.*

and Human Services issued a detailed guidance document regarding financial conflicts of interest in medical research.[7] The guidance includes points for consideration by research institutions, institutional review boards (IRBs), and individual researchers in constituting themselves and with respect to the design and review of specific research protocols. Measures recommended to manage a financial interest include reducing or eliminating the interest, disclosing it to prospective subjects, separating financial from research decisions, independently monitoring research, and modifying the roles for particular individuals or the location of certain activities. In response to such mandates, or as a result of collective professional deliberation, academic research organizations have directed their IRBs to examine research proposals for conflicts of interest, and have chartered conflicts of interest committees to monitor individual and institutional behavior. In general, these bodies are expected to know a conflict of interest when they see one.

The current discussion of research conflicts builds on prior controversies over the commercialization of medicine, most recently involving managed care. In addition to reviewing the medical necessity of treatment, health insurers in the 1980s and 1990s began structuring financial incentives for physicians to promote cost-consciousness in the choice of treatment. Although health policy commentators generally accept the need for fairly allocating scarce resources among needy patients, vesting rationing authority in private insurance companies, which were often commercial enterprises, did not sit easily with the medical profession or the public. Many regarded capitated payment, even seen in its best light, as promoting a population-based medical ethic that was incompatible with the bond between individual physicians and patients that characterized traditional medical ethics.[8] The proliferation of intermediary organizations between physicians and patients in managed care systems—including employers as sponsors of health coverage and various contracting entities serving doctors and hospitals—also made it difficult to ensure that primary obligations of fidelity were honored.[9] This debate over financial incentives in managed care

7. Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection, 69 Fed. Reg. 26,393, 26,396 (May 12, 2004), *available at* http://www.hhs.gov/ohrp/humansubjects/finreltn/finalguid.pdf.

8. A capitated payment is a fixed monthly fee for each patient assigned to the care of an HMO physician, regardless of whether or how often the patient seeks treatment from that physician. *See* Jerome P. Kassirer, *Managing Care—Should We Adopt a New Ethic?*, 339 NEW ENG. J. MED. 397, 397 (1998) (arguing that a population-based ethic for the provision of health care—"intentionally providing minimally acceptable care to some for the benefit of others"—is wrong). *But see* Richard D. Lamm, *Rationing of Health Care: Inevitable and Desirable*, 140 U. PA. L. REV. 1511, 1513, 1515 (1992) (arguing that "[p]ublic spending on health care should attempt to maximize the nation's health," and asking what standard of care should be provided to individuals in order to achieve that maximization).

9. *See* Lawrence Casalino, *Managing Uncertainty: Intermediate Organizations as Triple Agents*, 26 J. HEALTH POL. POL'Y & L. 1055, 1055 (2001) (noting that entities such as HMOs are questionable in their service of patients' interests).

followed, by roughly a decade, a similar discussion of the ethical implications of converting Medicare reimbursement of hospitals to fixed, "prospective" payment.[10]

This Article argues that the term "conflict of interest" should not be employed so broadly. Some legal duties—which this Article calls "relational duties"—arise from identifiable private relationships. Others—"regulatory duties"—do not. Legal accountability (both duties and remedies) tends to differ depending on whether or not the actor's conduct is directed at an individual or group to whom the actor owes specific obligations. Contract represents a voluntary regime of private, relational duties. So-called "fiduciary" duties arise in private, pre-existing relational situations but are defined by both law and voluntary agreement. Tort liability can derive from pre-existing relationships or can involve strangers, with duties and damages traditionally set by law alone. Public accountability, typically removed from the circumstances of individual transactions, is secured through administrative and criminal enforcement, with different standards and sanctions for noncompliance than in private law settings.

Tensions between relational and regulatory duties in medicine reflect general societal concern about how money influences judgment and conduct. In business, politics, and other areas, revelations of cash changing hands in unexpected ways regularly provoke media coverage, public outrage, and legal scrutiny. These situations are particularly salient when they concern figures, such as physicians or public officials, whom average people feel occupy positions of power in everyday interactions. Most such debates are cast in relational terms. Corporate managers, for example, must avoid conflicts of interest because of their obligations to identifiable shareholders or securities purchasers.[11]

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10. *See, e.g.*, Alexander M. Capron, *Containing Health Care Costs: Ethical and Legal Implications of Changes in the Methods of Paying Physicians*, 36 CASE W. RES. L. REV. 708, 709, 748–50 (1986) (describing the unfamiliar ethical territory presented by a regime in which providing more care diminishes—rather than increases—health care providers' profits). DRGs converted a direct relationship between hospital and physician payment into an inverse one, in that a patient who required prolonged care continued to generate physician fees but eroded the fixed amount available to the hospital. Recognizing the danger to medical ethics, Congress enacted a law prohibiting hospitals (and the few HMOs then serving the elderly) from making incentive payments to physicians to induce them to limit services to Medicare or Medicaid beneficiaries. Omnibus Budget Reconciliation Act of 1986, Pub. L. No. 99-509, § 9313(c), 100 Stat. 1874, 2003 (codified as amended at 42 U.S.C. 1320a-7a (2000)). When Medicare and state Medicaid programs expanded their managed care contracting to serve a larger percentage of program beneficiaries, the prohibition on physician incentive plans in prepaid health plans was converted into a mix of substantive and disclosure-based regulation. Omnibus Budget Reconciliation Act of 1990, Pub. L. No. 101-508, §§ 4204(a), 4731, 104 Stat. 1388, 1388-108 to -109, 1388-195 (codified as amended in scattered sections of 42 U.S.C.); *see also* Final Rule, Requirements for Physician Incentive Plans in Prepaid Health Care Organizations, Requirements for Physician Incentive Plans, 42 C.F.R. § 417.479 (2007).

11. Principal–agent problems are a common concern in corporate law because of the separation of corporate ownership (by small shareholders and, to a degree, creditors) from corporate control (by large shareholders and executives). Henry Hansmann & Reinier Kraakman, *Agency Problems*

Because they literally share a common currency, financial scandals tend to build on one another, creating the appearance of a uniform problem when in fact the specific situations and surrounding contexts may vary widely. Moreover, an accusation of conflict of interest carries such moral weight with the press and public that it often forestalls full debate of the underlying issues and therefore prevents meaningful change. Laura Underkuffler argues that conflicts of interest that lead to bad outcomes are seen as "corrupt," a term that goes beyond specific legal violations to signify massive moral failings.[12]

This Article regards a conflict of interest as a fiduciary construct that only has clear meaning within a relational framework. From this perspective, one can define the term as follows: "A conflict of interest arises when a person (the agent) stands in a relationship of trust with another person (the principal) that requires the agent to exercise judgment on behalf of the principal, and where the agent's judgment is impaired because of another interest of the agent."[13] This approach is particularly suited to legal and ethical oversight of conflicts of interest involving professions. Professional duties have in common the existence of identifiable clients or other individuals to whom primary obligations extend. Accordingly, most entanglements that trouble scholars of conflicts of interest in the professional context are those that potentially compromise judgment and conduct in discrete relationships or transactions. The fact that professionals also make contributions to society as a whole does not negate the centrality of personal service.[14]

Some criticism of financial flows in biomedical research focuses on the relational rights and interests of specific parties, but most involves defending the overall purity of the medical–scientific community from corporate

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and Legal Strategies, *in* THE ANATOMY OF CORPORATE LAW: A COMPARATIVE AND FUNCTIONAL APPROACH 21, 21 (Reinier Kraakman ed., 2004). Professors Hansmann and Kraakman divide legal strategies to reduce agency problems into regulatory strategies and governance strategies, each of which can operate either before a breach of trust or afterwards. *Id.* at 23. Regulatory strategies include rule- or standard-based constraints on the agent, and requirements related to affiliation (e.g., disclosure before entry and opportunity for exit on fair terms). *Id.* at 23–24. Governance strategies include appointment rights (selection or removal of agents), decision rights (initiating or ratifying management decisions), and agent incentives (pay for performance or formal trusteeship obligations). *Id.* at 26–27.

12. Laura S. Underkuffler, *Captured by Evil: The Idea of Corruption in Law* (Duke Law Sch. Legal Studies Research Series, Research Paper No. 83, 2005), *available at* http://ssrn.com/abstract=820249.

13. W. Bradley Wendel, *The Deep Structure of Conflicts of Interest*, 16 GEO. J. LEGAL ETHICS 473, 477 (2003) (book review).

14. Steven Brint distinguishes "social trustee" professionals from "expert knowledge" professionals, and asserts a trend in favor of the latter, who tend to provide sophisticated services to paying clients. STEVEN BRINT, IN AN AGE OF EXPERTS: THE CHANGING ROLE OF PROFESSIONALS IN POLITICS AND PUBLIC LIFE 7–8 (1994).

influence, notably that of the pharmaceutical industry.[15] An "A-list" of physicians and ethicists recently called for stricter limits on financial relationships between pharmaceutical companies or medical device manufacturers and physicians affiliated with academic medical centers.[16] The recommendations were motivated by concern for "medical professionalism," with professionalism defined as "[p]hysicians' commitment to altruism, putting the interests of the patients first, scientific integrity, and an absence of bias in medical decision making."[17] These are unimpeachable goals, but they mix specific relational obligations to patients with general ideals that are challenged not only by commercialism but also by other human frailties. This vagueness is implicit in the definition of "conflict of interest" used in the article: "when physicians have motives or are in situations for which reasonable observers could conclude that the *moral* requirements of the physician's *roles* are or will be compromised."[18]

The distinguishing feature of biomedical research is that it benefits society as a whole rather than discrete, readily identifiable individuals. This rather amorphous, multi-body problem is much harder to solve than a two-body problem using the rights and remedies available to police conflicts of interest. If one severs professional duties from personal obligation, and rests them on a higher moral ground such as "justice" or "welfare," conflicts-of-interest discourse becomes particularly murky. This, the Article asserts, is the central problem of applying conflicts of interest to the modern biomedical enterprise. Mixed missions of real-world biomedical professionals and institutions cannot be advanced using blunt tools of relational accountability. Moreover, the illogical consequence of unbounded conflicts-of-interest discourse may be the further dehumanization of medicine and biomedical research when the opposite is desirable.

To what degree, for example, should commercial research sponsors control publication of research performed at academic medical centers?[19]

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15. Several muckraking exposés have been published recently detailing the pernicious influence of commercialism in the medical and scientific enterprises. *See, e.g.*, SHELDON KRIMSKY, SCIENCE IN THE PRIVATE INTEREST: HAS THE LURE OF PROFITS CORRUPTED BIOMEDICAL RESEARCH? 27–56 (2003) (criticizing university–business connections, particularly those involving patented technologies).

16. Troyen A. Brennan et al., *Health Industry Practices that Create Conflicts of Interest*, 295 JAMA 429, 429 (2006).

17. *Id.*

18. *Id.* at 430 (emphases added).

19. *See* David Blumenthal et al., *Withholding Research Results in Academic Life Science: Evidence from a National Survey of Faculty*, 277 JAMA 1224, 1224, 1226 (1997) (mentioning that 19.8% of academic researchers reported having delayed publication of findings for more than six months at the request of a sponsor). In a notorious example, Boots Pharmaceuticals blocked for several years findings of researchers at U.C. San Francisco that its branded synthetic thyroid hormone, Synthroid, was no more effective than much cheaper generic products. Rennie, *supra* note 4, at 1238–39; Lawrence K. Altman, *Drug Firm, Relenting, Allows Unflattering Study to Appear*, N.Y. TIMES, Apr. 16, 1997, at A1. To read the study, see Betty J. Dong et al.,

Balancing the public's interest in learning of negative research findings against its interest in promoting innovation by allowing companies to protect commercially valuable information is a legitimate and challenging regulatory problem to which both government and professional organizations have responded.[20] But relational harm in this situation is slight. A possible regulatory solution is required registration of clinical trials to ensure that the public and government regulators know which treatments and conditions have been studied, even if the results are not deemed desirable to publish by the researchers or research sponsors.[21] A similar but self-regulatory approach is for medical journals to refuse papers submitted by researchers or sponsors who do not participate in such registries.[22]

This Article seeks to bring greater discipline to the analysis of conflicts of interest in biomedical research, and by doing so to reveal trends and tensions in the research enterprise that require a more deliberate and longer term response. By comparing tensions in biomedical research to those affecting indisputably "relational" professionals such as lawyers, this Article concludes that "conflict of interest" is the wrong language to describe most of these situations, and leads to the wrong solutions. Conflict of interest analysis in law derives from an image of professional obligation running directly from expert agent to dependent principal. Because a dyadic researcher–subject relationship is no longer the essence of biomedical research, this Article asserts, attempting to insulate researchers from concerns other than the wellbeing of research participants using conflict of interest discourse will be ineffective or counterproductive.

Therapeutic medicine is a matter of individual patient trust, to which conflicts of interest are meaningful. Research medicine is a matter of social trust, to which conflicts of interest, by and large, are not meaningful. Modern research ethics is predicated on a public commitment to sound research science, and aspires to parity rather than dependency between researcher and subject. In most controversial cases, incentives for sound

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Bioequivalence of Generic and Brand-Name Levothyroxine Products in the Treatment of Hypothyroidism, 277 JAMA 1205 (1997).

20. *See* Justin E. Bekelman et al., *Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review*, 289 JAMA 454, 464 (2003) (noting that as a first step in dealing with conflicts of interest, all researchers and sponsors should fully disclose the nature of their relationships and all results of clinical trials should be made readily available in a publicly accessible forum).

21. Currently, applicants conducting clinical trials under an investigational new drug (IND) application must submit certain information about the trial to the FDA, if the trial is for a drug to treat a serious or life-threatening disease or condition and it is a trial to test effectiveness. *See* Food and Drug Administration Modernization Act of 1997 § 113, 42 U.S.C. 282(j)(3)(A) (2000). The information is held in a data bank that can be accessed at http://www.clinicaltrials.gov.

22. *See, e.g.*, The Journal of the Am. Med. Ass'n Information for Authors and Reviewers, Clinical Trial Registration, http://jama.ama-assn.org/misc/authors.dtl#clinicaltrial.

research are at issue, and a regulatory rather than relational approach is needed. This is already occurring in some areas.[23]

Stepping away from conflicts-of-interest analysis allows one to recognize that the appropriate regulation of research incentives depends on the social goals being served, rather than on the existence of specific agency relationships. The key tasks are figuring out how to balance factors affecting the quality of research, such as expertise and financial incentives, and deciding how to prioritize the goals to be served by the balance, such as research productivity and the safety of human research subjects. In addition, limited, though important, relational duties will remain between researchers and subjects, and physicians who have fiduciary obligations to patients may have true conflicts of interest when serving in a research as well as clinical capacity. The challenge for regulation is to maintain traditional virtues associated with researchers feeling direct obligations to those on whom they experiment while maximizing objective benefits for society.[24]

II. Incoherent "Conflict-Of-Interest" Discourse In Biomedical Research

In contrast to the legal scholar's relational definition of conflicts of interest cited above, medical commentators posit a broader range of problematic behaviors. Consider the definition of conflict of interest that is the starting point for most bioethical commentary. In a 1993 article, Dennis Thompson defined conflict of interest as "a set of conditions in which professional judgment concerning a primary interest (such as a patient's

23. For example, the Food and Drug Administration regulates financial relationships between applicants seeking to market new drugs and medical devices and clinical investigators conducting studies of those drugs or devices. 21 C.F.R. § 54.1(a) (2005). Applicants must submit a list of clinical investigators, identify those who are employees of the study sponsor (funder), disclose financial relationships with non-employee investigators, or certify the absence of those relationships. *Id.* § 54.4. Relationships that must be disclosed include compensation affected by the outcome of clinical studies, significant equity interests in the study sponsor, proprietary interests in the tested product, or other payments exceeding $25,000. *Id.* §§ 54.3(f), 54.4(a)(3)(i)–(iv). Following such disclosure, the FDA may take various actions to ensure the reliability of the data being submitted by the applicant, such as data audits, requests for additional analysis, requests for additional independent studies, and disqualifying particular studies from consideration in connection with approval. *Id.* § 54.5(c)(1)–(4).

24. This discussion connects to a rich literature on the role of science in society that is beyond the scope of this Article. *See generally* GEORGE H. DANIELS, SCIENCE IN AMERICAN SOCIETY: A SOCIAL HISTORY (1971). A comprehensive regulatory approach to human subjects research would require greater social consensus than currently exists as to the relationship among democratic government, individual freedom of inquiry, and communal interests in the development and dissemination of knowledge. The ongoing controversy over government funding for stem cell research has surfaced a new generation of commentators on these topics. *See, e.g.*, DAVID H. GUSTON, BETWEEN POLITICS AND SCIENCE: ASSURING THE INTEGRITY AND PRODUCTIVITY OF RESEARCH (2000); CHRIS MOONEY, THE REPUBLICAN WAR ON SCIENCE: REFLECTIONS OF A SCIENCE JOURNALIST AT WORK (2005); Mark B. Brown & David H. Guston, A Democratic Theory of Science: The Right to Research 3 (June 24, 2005) (unpublished manuscript), *available at* http://www.cspo.org/ourlibrary/documents/right_to_research.pdf (arguing for a democracy- or society-based right of inquiry).

welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)."[25] Following this approach, most discussions of research conflicts fail to specify a principal party to whom the researcher's fidelity is owed, and do not distinguish relational obligations from generally desirable behavior among researchers. Yet the remedies these same commentators recommend, such as disclosure and segregation of functions, are based on an unacknowledged relational paradigm.[26]

Thompson's example of a patient's welfare is a relational obligation for that patient's treating physician. His other example, the validity of research, is not relational, at least vis-á-vis a research subject or patient. Conducting valid research may well be a relational obligation for a researcher who is employed by a university or pharmaceutical company, but it runs to the employer. Tensions between academic researchers' duties to their employers and their duties to the public are seldom recognized. In the last few years, research universities have adopted conflicts of interest policies in response to federal requirements. These policies, however, tend to mix concern over misappropriation of university property with concern over compromised objectivity on the part of individual researchers, with the two issues connected loosely (and tacitly) by the university's interest in preserving its reputation.[27]

Using the same term—conflicts of interest—to foster both an employee's loyalty to an employer and the employee's social consciousness is misleading. Suppression by a company researcher of internally generated findings, release of which would reduce the company's profitability, honors her obligation to her employer, yet may not be in the public interest. Is this a "conflict of interest" or something else, such as a violation of an independent legal obligation placed on the company to make results public or a lack of personal ethical commitment to "do the right thing" on the researcher's part?

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25. Dennis F. Thompson, *Understanding Financial Conflicts of Interest*, 329 NEW ENG. J. MED. 573, 573 (1993). There are other definitions available to the biomedical community that emphasize social over individual responsibility. *See, e.g.*, HOWARD BRODY, HOOKED: HOW MEDICINE'S DEPENDENCE ON THE PHARMACEUTICAL INDUSTRY UNDERMINES PROFESSIONAL ETHICS (2007) (arguing that influences that reduce public trust in the social role of physicians or researchers constitute conflicts of interest); *see also* Edmund L. Erde, *Conflicts of Interest in Medicine: A Philosophical and Ethical Morphology*, *in* CONFLICTS OF INTEREST IN CLINICAL PRACTICE AND RESEARCH 12, 12–41 (Roy G. Spece et al. eds., 1996) (arguing that trust in a social role is the trigger for conflicts of interest).

26. *See* Marcia Angell, *Is Academic Medicine for Sale?*, 342 NEW ENG. J. MED. 1516, 1518 (2000) (arguing for segregation of functions); John La Puma, *Physicians' Conflicts of Interest in Post-Marketing Research: What the Public Should Know, and Why Industry Should Tell Them*, *in* THE ETHICS OF RESEARCH INVOLVING HUMAN SUBJECTS: FACING THE 21ST CENTURY 203, 206 (Harold Y. Vanderpool ed., 1996) (arguing for greater disclosure requirements); Frances H. Miller, *Trusting Doctors: Tricky Business When It Comes to Clinical Research*, 81 B.U. L. REV. 423, 443 (2001) (arguing for greater disclosure requirements).

27. *See, e.g.*, VANDERBILT UNIV., CONFLICT OF INTEREST POLICY 1, 3–4, *available at* http://www.vanderbilt.edu/compliance/html/conflict_of_interest_policy.pdf (explaining that the conflict of interest policy must be followed to promote the "core values" and "best interests" of the university and including both misappropriation and research conflicts).

Confusion is greatest when the employer attempts to compromise the objectivity of non-employees who have primary allegiances to others. Pharmaceutical companies, for example, are often criticized for influencing physicians, who are independent businesspeople, to prescribe particular drugs for patients in situations where another product or service might be preferable.[28]

This source of incoherence became clear to me at the conclusion of an invitational conference on research conflicts of interest convened a few years ago by the Hastings Center, the oldest and most successful bioethics institute in the U.S.[29] Following two days of animated conversation, mainly focused on the need to reduce the financial influence of the pharmaceutical industry, the conference's host thanked the participants, and reminded them to send him their travel expenses to be reimbursed from grant funds provided by a charitable foundation.

One, and only one, participant immediately declined reimbursement: the director of ethics and compliance for a major pharmaceutical company. Accepting the Center's funds, she said, would violate her company's conflict of interest policy. The contradiction, which seemed lost on the other attendees, was that they had just finished criticizing the pharmaceutical industry for sending speakers to medical conferences at drug company expense, on the grounds that having speakers participate at no cost to the conference created a conflict of interest for the medical societies and hospitals that were typically the conference organizers. The pharmaceutical company employee was using the term "conflict of interest" to describe situations that might compromise her loyalty to her employer. The health care providers, researchers, and government officials at the conference were using the term to describe situations that might compromise the public interest.

According to the ethics director, the company had additional policies in place to address problems other than employees accepting payment from outside the company. One was a scientific misconduct policy for cases involving falsification of data or other behavior that violated internal standards, the company's contractual obligations, or legal requirements placed on the company. Another was a payment policy governing financial relationships between the company and outside consultants, particularly medical practitioners whose incentives might implicate federal fraud and

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28. *See, e.g.*, Eric G. Campbell et al., *A National Survey of Physician–Industry Relationships*, 356 NEW ENG. J. MED. 1742 (2007) (noting that 94% of physicians surveyed reported some relationship with the pharmaceutical industry, and 28% received payments for consulting, lecturing, or enrolling patients in research trials); Robert Pear, *Drug Makers Battle a U.S. Plan to Curb Rewards for Doctors*, N.Y. TIMES, Dec. 26, 2002, at A1, A28 (describing the pressure on doctors to shift Medicaid patients from generic to name-brand prescriptions, even though the name-brand medicines are often less effective).

29. *See* ETHICAL ISSUES IN THE MANAGEMENT OF FINANCIAL CONFLICTS OF INTEREST IN BIOMEDICAL RESEARCH (Thomas H. Murray & Josephine Johnston eds., forthcoming 2007).

abuse law. To me, this episode neatly captured the ambiguity of "conflict of interest" as used in biomedicine, mixing obligations to identifiable parties with general concepts of principled science.

A. Distinguishing Relational and Regulatory Obligations in Bioethics

An irony of current research regulation is that its founding documents were largely a moral reaction to government abuses: the Nuremberg Code to human experimentation by Nazi Germany, and the Belmont Report to the U.S. Public Health Service's Tuskegee Syphilis Study. Government, however, now plays the central role in protecting human subjects from the research professionals whom it funds. In other words, there has been a shift in concern away from the coercive power of the state to trump relational (humane) obligations of scientists to subjects, and toward assuring that scientists fulfill both relational obligations to subjects and, more importantly, nonrelational social responsibilities to the public that supports them.[30] Protecting the safety of research subjects has become part of the compact between scientists and society: instrumentally necessary to assure sufficient participation, reflective of sound research design, and consistent with public expectations.

The birth of American bioethics in the decades following World War II coincided with a fertile period of medical innovation. The authors of the Belmont Report and their immediate successors navigated a delicate transition from medical paternalism to a system that emphasized the right to self-determination of individuals who entrust themselves to medical professionals. This notion of autonomy was applied both to patients—persons seeking medical diagnosis or treatment—and to voluntary participants in medical research. Then, as now, there was significant overlap between these two groups because people with particular health conditions can help advance medical science with respect to those conditions, and those same people might reasonably believe that the physicians or hospitals conducting research on their problems would provide them with the best medical care.

The structure and funding of American medicine during this period compounded the overlap. The great majority of physicians were in solo

30. The Belmont Report emphasizes beneficence in research, which would prohibit "brutal or inhumane treatment" regardless of consent. THE NAT'L COMM'N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMED. & BEHAV. RES., U.S. DEP'T OF HEALTH, EDUC. & WELFARE, THE BELMONT REPORT: ETHICAL PRINCIPALS & GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH 17 (1978). This echoes the Nuremberg Code's prohibition on experimentation where there is an expectation of possible death or disabling injury. Nuremberg Code, *in* 2 TRIALS OF WAR CRIMINALS BEFORE THE NUREMBERG MILITARY TRIBUNALS UNDER CONTROL COUNCIL LAW, No. 10, at 182 (1949), *available at* http://www.ushmm.org/research/doctors/Nuremberg_Code.htm. The Nuremberg Code suggested that physicians themselves might ethically serve as subjects in particularly dangerous research, reflecting not only their superior knowledge of the risks but also their special duty to society. *Id.*

practice providing general medical care, with ready access to basic hospital resources but little advanced technology. Clinical research was the province of university-based physicians; they typically viewed their patients as objects of professional beneficence, and often outright charity, who were fortunate to be able to receive their services. Adding to role confusion was the fact that young physicians, who were increasingly interested in specialist credentials, were trained in research university settings before entering private practice.[31]

The early language of bioethics was a product of this environment. It is an open question, for example, whether "informed consent" was initially a research-based or a treatment-based construct. "Conflict of interest" arose in part in connection with vitiating informed consent, and inherited the underlying role ambiguity.[32] Conflicts-of-interest analysis in biomedical research therefore typically operates under the presumption that the principal party to whom loyalty runs is the patient–research subject, and makes no distinction between the two labels.[33]

Conflicts-of-interest analysis makes sense if ethics focuses on individual researchers' (especially combined clinician–researchers') professionalism in balancing research goals with patient care goals. Informed consent, for example, was described by early bioethicists as a personal, relational task—not a ministerial function in response to regulation. The Nuremberg Code emphasized that "ascertaining the quality of the consent . . . is a personal duty and responsibility which may not be delegated to another with impunity."[34] A partial explanation for the fact that the Nuremberg Code was not taken seriously by American researchers in the 1950s and 1960s may have been overconfidence in the strength of their relationships with research subjects. The emotional distance between the Nazi "doctor" and the victims of human experimentation, the Americans may (incorrectly) have reasoned, allowed abuses there that could not happen here.[35]

By contrast, modern mainstrcam research ethics takes a more regulatory approach to autonomy. Ethicists worry about "therapeutic misconceptions" that lead subjects to misperceive researchers as health care providers.[36] They also attempt to present risks comprehensively and objectively, and regard the

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31. *See generally* DANIELS, *supra* note 24 (generally discussing the role of science in society); Shannon Benbow, *Conflict + Interest: Financial Incentives and Informed Consent in Human Subject Research*, 17 NOTRE DAME J.L. ETHICS & PUB. POL'Y 181, 185–210 (2003) (documenting the evolution of the informed consent doctrine in the context of human subject research).

32. *See generally* Benbow, *supra* note 31.

33. *See, e.g.*, Gordon DuVal, *Institutional Conflicts of Interest: Protecting Human Subjects, Scientific Integrity, and Institutional Accountability*, 32 J.L. MED. & ETHICS 613, 614–15 (2004).

34. Nuremberg Code, *supra* note 30, at 181–82.

35. *See* George J. Annas, *Mengele's Birthmark: The Nuremberg Code in United States Courts*, 7 J. CONTEMP. HEALTH L. & POL'Y 17, 42–45 (1991) (noting that the Nuremberg Code was not taken seriously in the United States).

36. Paul S. Applebaum, *Clarifying the Ethics of Clinical Research: A Path Toward Avoiding the Therapeutic Misconception*, AM. J. BIOETHICS, Spring 2002, at 22, 23 (discussing the substantial prevalence of "therapeutic misconception").

dividends to science of well-conducted research rather than any personal health benefit as the proper motivator for participation.[37] Autonomy-based ethics attempts to disabuse research subjects of the notion that researchers (even ones trained as physicians) have their subjects' best interests at heart. This is principle-based, rather than principal-based, ethics. A principle-based approach to ethical research reduces the coherence of conflicts-of-interest discourse, and renders traditional devices for controlling conflicts of interest less compatible with research needs and goals.

As the limits of autonomy become apparent, not all bioethicists continue to think in this way. Attention is again being paid to professional beneficence in clinical medicine, despite the paternalistic risks.[38] Although the therapeutic misconception seems to be a real obstacle to understanding the risks of participation, strict role separation between clinicians and researchers remains unpopular as well as impractical. Oncology patients, for example, want their physicians to run their research protocols, not some stranger. Moreover, strong-form autonomy as manifested by voluntary transactions in a commercial marketplace is still distasteful to many bioethicists. As discussed below, however, conflicts-of-interest analysis may be a counterproductive approach to resurrecting relational research ethics, or to preserving humanity in medical relationships.

There are residual obligations running from researcher to research subject even in a principled rather than "principaled" system. There is a basic dignitary obligation of researcher to human research subject that encompasses respecting personhood and protecting physical safety. This obligation is not unique to the research context, though including it in formal research ethics is a useful reminder of the limits of scientific authority in society. It can be discharged in large part by complying with research regulation, but it also represents an application of care-based ethics. However, it is insufficient to support the strict fiduciary approach to research relationships that is required to make conflicts of interest meaningful.

There are also direct relational obligations from physicians (or other clinical professionals) to their patients. These interact uncomfortably with research ethics in settings such as academic health centers where clinical and research functions routinely mix. Conflict of interest retains meaning under these conditions, but as discussed below, it cannot alone determine the professional responsibilities of the combined physician–researcher. Still, the more clinical the role of the individual receiving favors from a third party,

37. *See, e.g.*, Lainie Friedman Ross, *Payment in Pediatric Research*, 9 MICH. ST. J. MED. & LAW 1, 1–2 (2005) (presenting risks objectively and stating that, ideally, research subjects would "share in, support, and be motivated by the goals of the researchers"); Richard S. Saver, *Medical Research and Intangible Harm*, 74 U. CIN. L. REV. 941, 1009 (2006) (concluding that "ensuring that both negative and positive results are shared more openly may also help counter therapeutic misconception problems and the common overestimation about research's direct benefits").

38. *See, e.g.*, MARSHA GARRISON & CARL E. SCHNEIDER, THE LAW OF BIOETHICS: INDIVIDUAL AUTONOMY AND SOCIAL REGULATION (2003).

the more those favors plausibly constitute conflicts of interest. For example, payments by pharmaceutical companies to practicing physicians for enrolling existing patients in drug trials are more problematic than payments to dedicated academic researchers or contract research organizations that lack a treatment relationship to research subjects.

B. Confusing Conflicts of Interest with Incentives

A second source of confusion in the biomedical research context is the tendency to mix conflicts of interest with incentives. Conflicts of interest terminology is particularly strained when it attempts to divide acceptable from unacceptable motives and motivators for performance in the absence of specific relational obligations. The literature on "nonfinancial" conflicts of interest is virtually incoherent. Commentators such as Norman Levinsky correctly point out that a medical researcher, or anyone else for that matter, can be driven to achieve by the prospect of advancement, peer approval, public acclaim, family esteem, and many other things in addition to cash.[39] Because scientists and other smart people who work in government or non-commercial settings presumably care relatively more about these things than do similarly skilled people who work in business, Levinsky and others have labeled these motives "conflicts of interest."[40]

The difficulty is that these vague motives can just as easily align as misalign the incentives of researchers with those of parties whose relational interests they might arguably serve—whether patients, institutional employers, or funders.[41] Incentives matter, and they are challenging to get right in any principal–agent relationship, as even a cursory review of the executive compensation debate in corporate law or the pay-for-performance debate in health care will reveal.[42] Financial conflicts of interest are coherent

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

40. *See, e.g.*, Roger S. Foster, Jr., *Conflicts of Interest: Recognition, Disclosure, and Management*, 196 J. AM. C. SURGEONS 505, 509 (2003).

41. Professor DuVal sums it up reasonably as follows: "Neither financial nor non-financial interests are illegitimate in themselves and indeed the pursuit of such rewards may encourage greater production and discovery. However, all of these interests may also have the effect of skewing the proper exercise of judgment." DuVal, *supra* note 33, at 614–15. The unanswered questions are what constitutes "proper exercise of judgment" and what legal tools are appropriate to reinforce that judgment.

42. Performance-based compensation is routinely used in business to align managers' incentives behavior with the interests of shareholders—the corporation's owners, for whom management acts as agent. Experience has been mixed. Managers no longer can enrich themselves out of the public view for extended periods of time, but opportunities have arisen for them to exploit small swings in share price for personal gain in ways that do not benefit and may significantly harm the corporation's long-term interest. *See generally* LUCIAN BEBCHUK & JESSE FRIED, PAY WITHOUT PERFORMANCE (2004). The "pay-for-performance" movement emerging in U.S. health care as an alternative to both traditional fee-for-service payment and managed care capitation will eventually face similar tensions. *See generally* William M. Sage, *Pay-for-Performance: Will It Work in Theory?*, 3 IND. HEALTH L. REV. 305 (2006).

not merely because financial relationships are powerful motivators, but also because financial relationships are markers for relational obligations to which conflicts of interest analysis easily applies. Academics in general are usually motivated by rewards other than cash compensation, including hunger for results and desire for peer and public recognition. The fact that these incentives exist is generally a good thing, no matter to what principal party a researcher is thought to owe primary responsibility. The alternative, particularly for academics with tenure, is a generation of complacent, self-absorbed, unproductive scientists. For this reason, among others, unfocused science has largely given way to targeted support, regardless of whether the research sponsor is commercial, private nonprofit, or governmental.[43]

Why do critics not recognize this? One detectable undercurrent in the critical literature is moral judgment. Commentators seem to be looking for "pure-hearted" professionals—researchers whose raison d'etre is to pursue the ideals of science.[44] A practical consequence of this preference is to draw bright lines between corruptible and incorruptible scientists rather than assessing the degree of risk to judgment posed by specific arrangements. Another is to regard all commercial involvement by suspect sources as temptation to evil. Blanket prohibitions on contact between pharmaceutical companies and physicians, for example, fail to distinguish between interns who eat pizza paid for by drug detailers and department chairs who accept tens of thousands of dollars in cash.

A parallel problem is that real life seldom conforms to the expectations of moralists. No biomedical researcher is an island. Critics of conflicts of interest acknowledge that financial relationships are widespread in medicine and therefore cannot all be bad, but still freely condemn particular examples.[45] This has the effect of favoring the familiar for little reason beyond its familiarity. There is a strong urge to define conflicts of interest as "what you do that I don't." Medical journals, for example, were quick to condemn university scientists for accepting industry subsidies that could bias research,[46] and immediately imposed financial disclosure obligations on their

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43. *See* Leah Belsky & Ezekiel J. Emanuel, *Conflicts of Interest and Preserving the Objectivity of Scientific Research*, HEALTH AFF., Jan.–Feb. 2004, at 268, 270 (book review) ("[T]he distinterested nature of federal support for research seems to be becoming a historical relic. Increasingly, the government itself is acting much like industry, interested in having more influence over what is being researched and the preeise nature of the outcomes.").

44. *See generally* SHELDON KRIMSKY, SCIENCE IN THE PRIVATE INTEREST 230 (2003) ("By accepting the premise that conflicts of interest in universities must be subtly managed, rather than prohibited or prevented, nothing less than the public interest function of the American aeademic enterprise is at stake.").

45. *See, e.g.*, Mark Barnes & Patrik S. Florencio, *Investigator, IRB and Institutional Financial Conflicts of Interest in Human-Subjects Research: Past, Present, and Future*, 32 SETON HALL L. REV. 525, 526, 560–61 (2002).

46. *See, e.g.*, Jeffrey M. Drazen & Gregory D. Curfman, *Financial Association of Authors*, 346 NEW ENG. J. MED. 1901, 1901 (2002) ("'[T]he *Journal* expects that authors of such articles will not have any financial interest in a company (or its competitor) that makes a product discussed in the article.'").

contributing authors.[47] However, those journals have no qualms about their established practice of publishing articles without payment to the authors, making it inevitable that support for those articles will be provided by the authors' employers or third parties.[48]

Some of the criticism of novel business arrangements in biomedical research—positing sets of research norms and counternorms—may therefore represent misplaced nostalgia. Yearning for "good old days" is a common reaction to dislocation, particularly when professions with strong traditions of self-governance are challenged by social or economic change. Two generational effects can be hypothesized. One dynamic may reflect the homogeneous research profession of the 1950s and 1960s expressing discomfort with the much more diverse research profession of today. Scientists who accepted low salaries and limited public visibility but who were assured prestige within their peer groups may resent the collapse of those groups and the emergence of business and media entrepreneurs among their scientific successors. Another dynamic is suggested by the recent trend among medical schools to ban pharmaceutical companies entirely from their campuses.[49] The first wave of such policies came about twenty-five years ago as grassroots movements of medical students concerned about social issues such as care for the poor and prevention of nuclear war.[50] The current wave would seem to coincide with the same individuals having reached positions of authority on medical school faculties.

A less likely, though more sinister, explanation for criticizing payments to researchers is that anticompetitive conduct among universities is masquerading as concern over conflicts of interest. For example, Marcia Angell has suggested limiting universities' ability to share revenue derived from industry with individual faculty members, ostensibly because it might distort research agendas and behavior.[51] However, external revenue sources creating potential conflicts of interest exist largely because of the general need for cross-subsidization in academic medicine. As discussed below, universities often free ride on outside income available to their faculty.

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47. *E.g.*, The New England Journal of Medicine, Standard Disclosure Form, http://authors.nejm.org/Misc/disclosOA.pdf (requiring that potential authors disclose any past or pending receipt of consulting fees, paid advisory boards, equity ownership, commercial lecture fees, industry grant support, patents, royalties, or expert witness service in conneetion with their articles).

48. *See* Robert F. Weir, *The Process of Editorial Review*, *in* PUBLISHING WITHOUT PERISHING: A HANDBOOK FOR GRADUATE AND PROFESSIONAL STUDENTS ON PUBLISHING IN BIOETHICS AND THE MEDICAL HUMANITIES 7, 8 (Carolyn Ells & Tatjana Hugle eds., 1997), *available at* http://www.asbh.org/publications/pdfs/pubhandbk.pdf (indicating that, with a few exceptions, "most mainstream journals [do not] pay authors for their papers").

49. Chen Sampson, *More Medical Schools, Hospitals Ban Meals, Gifts from Pharmaceutical Companies*, Kaisernetwork.org (Jan. 22, 2007), http://www.kaisernetwork.org/Daily_reports/rep_index.cfm?DR_ID=42395.

50. Shortly before I entered Stanford Medical School in 1982, for example, the students had decided collectively not to accept free stethoscopes from pharmaceutical companies.

51. Angell, *supra* note 26, at 1517–18.

Tenure, academic freedom, and other noncompetitive norms in academia limit universities' bargaining leverage with respect to increasingly mobile faculty. Outside income offers a useful supplement for both parties.

Public policy has reinforced these practices by offering revenues from commercialization and academic–industry partnerships as an off-budget subsidy for universities.[52] The catalyst for today's environment was in many ways the Bayh–Dole Act of 1980, which allows universities to profit from patenting and licensing products derived initially from publicly funded scientific research.[53] These revenues, unfortunately, are highly variable—more a lottery ticket for participating universities than a diversified investment portfolio—and do not alleviate the pressure for predictable operating and supplemental funds.

In sum, biomedical research has undergone a major transformation in scale, scope, and funding. Ethicists, however, have tended to focus narrowly on the need for individual researchers to support the autonomy rights of research participants. The result has been to filter departures from an idealized notion of scientific integrity, particularly departures involving financial payments, through a relational lens and label them "conflicts of interest" without a clear sense of what is accomplished by that designation.

III. Mapping Relational Duties In Biomedical Research

How might one perform a systematic analysis of conflicts of interest in biomedical research? This Article argues that the best way to recognize in-

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52. University–industry relationships in the life sciences are common. Most involve short-term agreements in small dollar amounts. Some relationships, however, are substantial, such as the agreement between the Massachusetts General Hospital and Hoechst A.G. to fund a new department of genetics and build a research building. Eric G. Campbell et al., *Inside the Triple Helix: Technology Transfer and Commercialization in the Life Sciences*, 23 HEALTH AFF., Jan.–Feb. 2004, at 64, 66–67.

53. 35 U.S.C. §§ 200–12 (2000). The Bayh–Dole Act uses patenting by government-supported academic institutions and the grant of exclusive licenses to industry as its principal strategy to accomplish technology transfer and promote the development of practical applications. *See generally* Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 VA. L. REV. 1663, 1691–95 (1996) (tracing the history of the Bayh–Dole Act and its attempts to "facilitate [universities'] efforts to transfer technology to industry"). This strategy has critics. In addition to issues of potential research bias, concerns are sometimes raised about (1) government withdrawing public funding in reliance on industry support that is far smaller and less reliable, (2) high prices being charged for essential therapies originally developed with public funds, (3) innovation bottlenecks created by patents on research tools, and (4) lack of coordinated data collection to evaluate long-term effects. *See, e.g.*, Peter S. Arno & Michael H. Davis, *Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed upon Patents Deriving in Whole or in Part from Federally Funded Research*, 75 TUL. L. REV. 631, 684–91 (2001) (criticizing high prices of drugs initially developed with federal research dollars); Campbell et al., *supra* note 52, at 70–74 (questioning both Bayh–Dole's efficacy in providing universities sufficient revenue and the lack of data necessary to evaluate technology transfer); Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 698 (1998) (arguing that patenting of basic technologies retards innovation by ineffieiently segmenting ownership).

consistencies in current policy is to identify potential principals and agents in the research environment. If one can do so, then one can assert primary obligations of loyalty against which conflicts of interest can be measured. If one cannot do so, then it is a pretty good bet that, even if real tensions and risks exist in the modern research environment, conflicts of interest analysis is the wrong conceptual tool with which to approach those problems.

As will be shown, lawyers' ethics takes a disciplined approach to identifying and classifying conflicts of interest between the client as principal and other parties. If one approaches research conflicts of interest as a lawyer would, there are only three basic professional–client–payer permutations available to map the research landscape surrounding an individual scientist: research subject as client, university as client, and research sponsor as client. However, the facts do not clearly support any of these possibilities. Moreover, none of them leads to a successful governing structure for conflicts of interest in biomedical research.

A. Lawyers' Relational Ethics and Conflicts of Interest

The approach to conflicts of interest taken in the regulation and self-regulation of lawyers can serve a clarifying function for biomedical research. In the typical account of legal ethics as taught in professional responsibility classes and enforced by state courts and state bar associations, "role morality" for lawyers means the primacy of the single client's interest.[54] This duty of loyalty between lawyer and client includes as core values "zealous" advocacy,[55] confidentiality regarding both facts and communications,[56] and non-exploitation.[57]

Legal ethics addresses three types of conflicts of interest.[58] The first category encompasses "client–client" conflicts, involving competing positions and interests between current or former clients of the lawyer.[59] These are the most commonly discussed and the most routinely prevented or

54. For an explanation and discussion of the "role morality" of lawyers, see PAUL G. HASKELL, WHY LAWYERS BEHAVE AS THEY DO 35–38 (1998). *See also* MODEL RULES OF PROF'L CONDUCT R. 1.7 (2005) [hereinafter MODEL RULES] (forbidding representation of clients with "directly adverse" interests); *id.* at R. 1.9 (forbidding representation of clients with interests in conflict with a lawyer's past clients); *id.* at R. 1.8 (addressing other specific conflicts of interests).

55. MODEL RULES, *supra* note 54, at R. 1.3 cmt. 1 ("A lawyer must also act with commitment and dedication to the interests of the client and with zeal in advocacy upon the client's behalf."); MODEL CODE OF PROF'L RESPONSIBILITY Canon 7 (1980) [hereinafter MODEL CODE] ("A Lawyer Should Represent a Client Zealously Within the Bounds of the Law.").

56. MODEL RULES, *supra* note 54, at R. 1.6(a).

57. *Id.* at R. 1.8.

58. *See, e.g.*, JAMES E. MOLITERNO, ETHICS OF THE LAWYER'S WORK 206 (2d ed. 2003) ("Conflicts of interest come in at least three varieties: third party interference, lawyer interests that interfere with client interests, and interests of multiple clients that conflict with one another.").

59. *See* MODEL RULES, *supra* note 54, at R. 1.7 (current clients); *id.* at R. 1.9 (former clients).

addressed conflicts of interest in law,[60] but in other fields they are sometimes described as "conflicts of commitment."[61] The second category encompasses "client–lawyer" conflicts involving lawyer self-dealing or misappropriation.[62] The third category encompasses "client–payer" conflicts, in which someone other than the client pays for services to the client and seeks to control those services.[63] According to one law school casebook, "[a] single, central principle is implicated by every kind of conflict of interest problem: a lawyer must be able to exercise independent professional judgment on behalf of the client."[64] This statement also implies that lawyers' obligations to clients are not limited to following the clients' wishes and instructions, even though client autonomy remains a core professional value.

As with medicine, conflicts of interest analysis in law has become more complicated as legal practice has become more industrialized. The most lucrative legal practices serve corporations and other organizations, creating problems distinguishing the "client's" interest from the interests of individual constituents such as managers and employees.[65] Specialized lawyers are of-

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60. *See, e.g.*, John S. Dzienkowski & Robert J. Peroni, *The Decline in Lawyer Independence: Lawyer Equity Investments in Clients*, 81 TEXAS L. REV. 405, 497–545 (2002) (proposing new ways of thinking about equity investments in light of Model Rule 1.8(a)); Richard A. Epstein, *The Legal Regulation of Lawyers' Conflicts of Interest*, 60 FORDHAM L. REV. 579, 584–87 (1992) (discussing regulation of institutional conflicts of interest); Charles Silver & Lynn A. Baker, *Mass Lawsuits and the Aggregate Settlement Rule*, 32 WAKE FOREST L. REV. 733 (1997) (critiquing Model Rule 1.8(g), the so-ealled "aggregate settlement rule," whieh is designed to guard against the risks of common representation of multiple clients by a single lawyer).

61. *See, e.g.*, Patricia Werhane & Jeffrey Doering, *Conflicts of Interest and Conflicts of Commitment*, *in* RESEARCH ETHICS: A READER 165 (Deni Elliott & Judy E. Stern eds., 1997) (discussing eonflicts of commitment for scientific researchers); Ass'n of Am. Med. Cs., *Guidelines for Dealing with Faculty Conflicts of Commitment and Conflicts of Interest in Research*, 65 ACAD. MED. 487, 491–92 (1990) (same); *see also* Carol A. Needham, *The Professional Responsibilities of Law Professors*, 56 J. LEGAL ED. 106, 115–21 (2006) (discussing conflicts of commitment for academic researchers generally).

62. *See, e.g.*, MODEL RULES, *supra* note 54, at R. 1.8(a) (prohibiting lawyers from engaging in transactions with current clients in which the lawyer has an interest); MODEL CODE, *supra* note 55, at DR 5-101(A) (prohibiting self-dealing for monetary or personal gain); DOUGLAS E. ROSENTHAL, LAWYER AND CLIENT: WHO'S IN CHARGE? 96–112 (1974); William L.F. Felstiner & Austin Sarat, *Enactments of Power: Negotiating Reality and Responsibility in Lawyer–Client Interactions*, 77 CORNELL L. REV. 1447, 1459–72 (1992) (discussing techniques lawyers use to seize power in their relationships with clients).

63. *See* MODEL RULES, *supra* note 54, at R. 1.8(f) (stating the general rule that "[a] lawyer shall not accept compensation for representing a client from one other than the client").

64. MOLITERNO, *supra* note 58, at 206.

65. *See* MODEL RULES, *supra* note 54, at R. 1.13(a) ("A lawyer employed or retained by an organization represents the organization acting through its duly authorized constituents."); *id.* at R. 1.13(f) ("In dealing with an organization's directors, officers, employees, members, shareholders or other constituents, a lawyer shall explain the identity of the client when the lawyer knows or reasonably should know that the organization's interests are adverse to those of the constituents with whom the lawyer is dealing."); Geoffrey C. Hazard, Jr., *Triangular Lawyer Relationships: An Exploratory Analysis*, 1 GEO. J. LEGAL ETHICS 15, 20 (1987) (describing conflicts of interest that arise if a law firm represents a corporation or organization charged to have been defrauded by an officer of the organization, where the law firm has previously represented that officer with respect

ten hired to structure very large transactions or to litigate multiparty cases, creating pressures to represent "deals" or client groups not easily analyzed under existing conflicts of interest rules. Corporatization affects the supply side of legal services as well as the demand side. Law firms may include hundreds of attorneys, with frequent turnover at both senior and junior levels, necessitating standards for imputing conflicts of interest to the firm itself that typically were analyzed at the individual professional level and managing those conflicts accordingly.

Recent years have seen pressures for "multidisciplinary" practice, combining lawyers with accountants, consultants, or other providers to offer comprehensive services to corporate clients, with attendant difficulties in conflicts analysis.[66] Defending insured parties against outside claims, a very common practice, implicates conflicts analysis for relatively routine desires of insurance companies to control administrative costs and have recourse in the event of malpractice, as well as in more controversial areas where the interests of the insurer and the insured might diverge.[67]

As should be clear from this summary, legal ethics has extensive experience with conflicts of interest. It is noteworthy that legal ethics does not automatically condemn conflicts unless they are unidentified and therefore unmanaged. Rather, conflicts are understood to be omnipresent risks of legal professionalism.

Depending on the type of conflict, management can take several forms.[68] One common approach is client consent after disclosure and

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those activities); Nancy J. Moore, *Expanding Duties of Attorneys to "Non-Clients": Reconceptualizing the Attorney-Client Relationship in Entity Representation and Other Inherently Ambiguous Situations*, 45 S.C. L. REV. 659, 663–64 (1994) (noting the conflicts of interest that arise because of difficulties in treating closely held corporations and small partnerships as entities distinct from their individual constituents); Ronald D. Rotunda, *Law, Lawyers and Managers*, *in* THE ETHICS OF CORPORATE CONDUCT 127 (Clarence C. Walton ed., 1977) (discussing the ethical obligations of inside and outside corporate counsel).

66. *See, e.g.*, John S. Dzienkowski & Robert J. Peroni, *Multidisciplinary Practice and the American Legal Profession: A Market Approach to Regulating the Delivery of Legal Services in the Twenty-First Century*, 69 FORDHAM L. REV. 83, 181–91 (2000) (highlighting the problems that multidisciplinary practices would encounter because of differing conflicts of interest rules between disciplines and conflicting professional obligations, and suggesting solutions to those problems).

67. *See* MODEL RULES, *supra* note 54, at R. 1.7 cmt. 13 (discussing the potential conflict of interest that arises when a lawyer is paid from a source other than the client); *see also* Thomas D. Morgan, *What Insurance Scholars Should Know About Professional Responsibility*, 4 CONN. INS. L.J. 1, 6–9 (1997) (examining the long-standing theoretical dispute over whether a lawyer representing an insured has one client or two).

68. The general rule is that conflicts are imputed to other members of the same firm. *See* MODEL RULES, *supra* note 54, at R. 1.8(k) ("While lawyers are associated in a firm, a [conflict of interest] prohibition . . . that applies to any one of them shall apply to all of them."); *id.* at R. 1.10 ("While lawyers are associated in a firm, none of them shall knowingly represent a client when any one of them practicing alone would be prohibited from doing so . . . ."); MODEL CODE, *supra* note 55, at DR 5-105(D) ("If a lawyer is required to decline employment or to withdraw from employment under a Disciplinary Rule, no partner, or associate, or any other lawyer affiliated with him or his firm, may accept or continue such employment."); *see also* Westinghouse Electric Corp.

sometimes required consultation with independent counsel.[69] This is typical for client–lawyer conflicts. Outright prohibition occurs in some cases, typically involving opposing parties in ongoing litigation.[70] The lawyer's duty of confidentiality can also render client–client conflicts unwaivable because the lawyer is not at liberty to make the disclosure required for informed waiver. A third approach, common within law firms, attempts to isolate lawyers serving one group of clients from other lawyers serving clients with conflicting interests.[71] This becomes more difficult as law firm management is itself professionalized, so that the firm becomes a unitary strategic actor rather than a loose confederation of individual professionals.[72]

Law has also evolved a range of remedies for conflicts violations. One straightforward, effective remedy that compensates a disadvantaged client while also punishing and deterring misconduct is disgorgement of legal fees collected during representations that fail to comply with rules of professional responsibility.[73] In more serious cases, counsel can be disqualified during representation, although this presents problems of prejudice when the client of the discharged lawyer or firm was blameless.[74] Because conflicts rules are explicit and essential components of mandatory professional codes for lawyers, formal disciplinary action up to and including disbarment is possible,[75] a remedy that emphasizes protecting future clients rather than aiding current clients. Tort claims alleging legal malpractice may be available also, but require proof that the violation of the conflicts rule caused measurable harm to the plaintiff.[76]

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v. Kerr–McGee Corp., 580 F.2d 1311, 1321–22 (7th Cir. 1978) (extending the rule to encompass the branch offices of a national law firm).

69. *See* MODEL RULES, *supra* note 54, at R. 1.10(c) (allowing a client to waive disqualification under the conditions set forth in R. 1.7).

70. *See id.* at R. 1.7 (precluding client waiver of a disqualification due to a conflict of interest where the representation "involve[s] the assertion of a claim by one client against another client represented by the lawyer in the same litigation or other proceeding before a tribunal").

71. This approach is usually called erecting a "Chinese wall," a term that has attracted criticism notwithstanding its purely geopolitical origins. *See, e.g.*, *Westinghouse*, 580 F.2d at 1321. "Berlin wall" would be more apt, considering that the purpose is to prevent mixing rather than to keep particular undesirables at a distance.

72. *See id.* (rejecting the "Chinese wall" as a way to avoid imputation).

73. *See, e.g.*, *In re* Granite Partners, L.P., 219 B.R. 22, 42–44 (Bankr. S.D.N.Y. 1998) (denying $3 million of a law firm's $5.2 million request for fees and expenses because of the firm's failure to disclose a conflict).

74. *See* Bd. of Educ. of New York v. Nyquist, 590 F.2d 1241, 1246 (2d Cir. 1979) (recognizing that, in some situations, disqualification of counsel may be necessary, but also that such disqualification has the immediate adverse effect on the client of separation from his or her counsel of choice).

75. *See* MODEL RULES, *supra* note 54, at R. 8.4(a) (defining a violation of the Rules as "miseonduct").

76. *See* RONALD E. MALLEN & VICTOR B. LEVIT, LEGAL MALPRACTICE § 71 (1977) (setting forth the elements of a legal malpractice claim as duty, breach of duty, proximate causation, and damages).

To facilitate comparison with biomedicine, it is also important to appreciate that substantial tensions in client representation are not addressed by the formal conflicts of interest rules that exist for lawyers. First, conflicts between lawyers' "role morality" in service of their clients and lawyers' personal beliefs and moral commitments are discussed in the codes of professional responsibility but resist clear rules beyond a permissive approach to withdrawing from representation.[77] Second, lawyers' public duties are not considered part of conflicts of interest analysis. Lawyers, particularly in litigation, are charged as "officers of the court" and have enforceable, though limited, responsibilities not to subvert the adversary system.[78] For example, lawyers must fully and accurately brief controlling law when arguing to a court.[79] Some "public" duties, such as responding truthfully, even benefit opposing parties in the adversary system, although they need to be detected in order to be enforced through court-ordered sanctions. Significantly, only narrow obligations associated with specific situations are part of the mandatory rules of professional conduct. General obligations such as to serve "justice," however laudable, are expressed in hortatory terms if at all.[80]

A final point that is essential to understanding the appropriate scope of biomedical conflicts of interests is that the *incentives* that induce a lawyer to undertake a particular representation and to expend effort on that representation are almost always distinct from conflicts of interest. These include practices such as accepting cases for litigation on contingency, with attorney fees payable as a percentage of a successful recovery, and taking

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77. *See* MODEL RULES, *supra* note 54, at R. 1.16(a), (b).

78. *See* MODEL RULES, *supra* note 54, at R. 3.3 cmt. 2 ("This Rule sets forth the special duties of lawyers as officers of the court to avoid conduct that undermines the integrity of the adjudicative process.").

79. *Id.* at R. 3.3(a)(2).

80. *See, e.g.*, *id.* pmbl. (2005) ("A lawyer, as a member of the legal profession, is a representative of clients, an officer of the legal system and a public citizen having special responsibility for the quality of justice."). A recent article notes a puzzle involving lawyers' obligations as "officers of the court." Legal commentators and bar associations have regarded the "officer of the court" designation in the *Model Rules of Professional Conduct* as hortatory, requiring only compliance with the stated ethical rules of the profession. Judges, on the other hand, routinely take advocates to task for failing in that role, reading independent obligations into the term. *See* Fred C. Zacharias & Bruce A. Green, *Reconceptualizing Advocacy Ethics* (San Diego Legal Studies Paper No. 07-15, Oct. 20, 2005), *available at* http://ssrn.com/abstract=829304. Zacharias and Green interpret this as evidencing an underlying reliance on "professional conscience" in lawyers' ethical codes. An alternative explanation is that, from the perspective of the overall profession, officer of the court responsibilities are regulatory in nature, and therefore inconsistent with the strong form of relational obligation between lawyers and clients that characterizes established legal ethics. From a judge's perspective, by contrast, a lawyer personally handling a case in the judge's courtroom has intense relational obligations to treat the judge properly. A judge also has a much more immediate set of penalties and rewards at her disposal to enforce those obligations than a professional disciplinary process, which lacks even a specific complainant (beyond opposing counsel) in such cases.

equity stakes in transactional clients in lieu of hourly fees or cash retainers.[81] No financial arrangements between lawyers and clients, or for that matter between any principal and any agent, perfectly align incentives.[82] Each attorney fee structure mixes effective with perverse incentives, and must be evaluated and refined periodically. Fee arrangements are discussed, and occasionally restricted, in lawyers' rules of professional conduct.[83] However, their regulation is separate from the regulation of client–client, lawyer–client, and payer–client conflicts of interest described above.[84]

B. Looking for "Clients" in Biomedical Research

Are there analogies in biomedical research to lawyers' conflicts of interest? For lawyers, the first step in defining an agency relationship amenable to conflict of interest analysis is to identify the client. Therefore, we need to ask whether one type of party involved in biomedical research has consistently "client-like" attributes. As we shall discover, many stakeholders in research behave like principal parties in certain respects, but no one of them clearly dominates.

Who has a contractual relationship with a researcher? Agency relationships can be formed by status, by contract, or by some combination of the two.[85] One way to identify agents in most economic sectors is to look for contracts they have entered into with principal parties to perform enumerated tasks. Contracts indeed govern large swaths of biomedical research.

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81. *See, e.g.*, MOLITERNO, *supra* note 58, at 259–61 (explaining the practice of contingency fees); MARC I. STEINBERG, LAWYERING AND ETHICS FOR THE BUSINESS ATTORNEY 105 (2002) (noting the basic concerns of lawyers accepting equity interests in their clients). Contingent fee payment (like its historical antecedents, barratry and champerty) is controversial in part because lawyers who stand to benefit hugely from the successful resolution of a claim may pursue the claim using methods that are unethical or dishonest. In these situations, however, the lawyer's incentives are aligned, though perhaps overly so, with those of the client to whom her professional obligation runs. Consequently, limitations or prohibitions on these incentives are articulated as problems of public interest, not conflict of interest. For example, lawyers may not accept contingent fee payment in family law cases, lest third parties such as minor children be harmed, or in criminal cases, lest the public safety be threatened when guilty parties go free. *See infra* note 83. In cases involving financial crimes, however, defendants assets are often forfeited if they lose, rendering the ability of lawyers to collect fees a de facto function of their success.

82. During the heyday of managed care, a major medical journal offered a system called "fee-for-time" as a supposedly neutral alternative to both fee for service and capitated payment of physicians. *See* Tom J. Wachtel & Michael D. Stein, *Fee-for-Time System: A Conceptual Framework for an Incentive-Neutral Method of Physician Payment*, 270 JAMA 1226 (1993). If the authors had asked any lawyer held hostage to billable hours, they quickly would have learned about the perverse incentives created by their proposal.

83. For example, the *Model Rules* and *Model Code* prohibit contingent fees in criminal cases and in some family law disputes. MODEL RULES, *supra* note 54, at R. 1.5(d)(2) (criminal cases); *id.* at R. 1.5(d)(1) (domestic relations cases); MODEL CODE, *supra* note 55, at DR 2-106(C) (criminal cases); *id.* at EC 2-20 (domestic relations cases).

84. *See supra* text accompanying notes 58–64.

85. A general economic definition of an agent is anyone who makes a decision on behalf of another. The law of agency defines its scope more narrowly, defining an agent as a fiduciary subject to the principal's right of control. RESTATEMENT (SECOND) OF AGENCY § 1 (1958)

Employment contracts of varying formality between individual researchers and either industrial or university employers create duties to the employer and extend to the individual researcher contractual commitments made by the employer to other parties. Academic–industry agreements establish terms for industry sponsorship of university research and for technology transfer of universities' patented innovations (most developed using public research funds) to industry for commercialization. Private grants from charitable foundations impose contractual obligations on university recipients. Research subjects are not directly represented in these agreements, however, making it difficult to see them as contractual principals.

In a quasi-contractual process, the federal government now routinely demands "assurances" from research institutions in connection with the National Institutes of Health, the National Science Foundation, or other grant programs that all human subjects research they conduct (not just research using federal funds or research to develop FDA-approved products) will comply with federal regulatory requirements.[86] Research subjects are plausible third-party beneficiaries of federal assurances because the federal regulatory framework is primarily an expression of concern over their autonomy and safety. But the government's principal goal in the assurance process is extending its regulatory jurisdiction, not directly empowering research participants.

Who reveals private information to researchers? In classic agency relationships, such as between lawyer and client or treating physician and patient, the security of the professional bond facilitates communication of private information by the principal to the agent. In biomedical research, individual subjects share intimate details regarding health and family with researchers both during the informed consent process for enrollment and in the course of participation. At the same time, however, commercial research sponsors may share a different sort of private detail with researchers—proprietary information regarding the business motive for the sponsorship and its profit potential.

Who receives information from researchers? Agents are typically obligated to inform principal parties of facts that affect their assignments, and in some cases of other information that might be material to the principals' interests.[87] Information conveyed to research subjects by researchers is narrowly focused on physical risks of participation and procedural rights and opportunities to withdraw from participation. Much of this information is provided in response to regulatory mandates.[88] Other

86. *See* 42 U.S.C. 289(a) (2000) (imposing guidelines for all human subjects research conducted at an entity that applies for a grant, contract, or cooperative agreement for government funds).

87. RESTATEMENT (SECOND) OF AGENCY § 381 (1958).

88. *See* 45 C.F.R. § 46.116(a) (2005) (setting forth disclosure requirements for obtaining informed consent of research subjects).

information of benefit to research subjects—both before participation, such as the availability of compensation for physical injury, and afterwards, such as the outcome of the study being conducted—is shared only sporadically. Industry sponsors and public and private grant-making organizations, not subjects, are the parties that receive the most detailed research reports and budget accountings from researchers. Contrary to relational traditions, most substantive output of university-based research is intended to be made broadly available through academic publication, with the controversial exception of potential intellectual property that has not yet been patented, and also information developed in certain joint ventures between private industry and the academy.

Who defines the goals of service? When a principal party engages an agent, the agent may exercise discretion based on his or her expertise, but the principal determines the purpose for which the agent is employed.[89] In biomedical research, sponsors establish terms for research when they award grants or enter into contracts with researchers for results. Even public funders, which used to be hands-off with respect to the goals of research, now often take a more active role.[90] Academic health centers and other research institutions may themselves set strategies for research departments, which in turn determine the direction taken by individual researchers. Most of all, researchers pursue the lines of inquiry that interest them personally, regardless of external demand. Research subjects and the communities from which they come exert little if any influence over research goals, although they remain free to participate or not as they see fit.

Who gains or loses from the research? Who benefits if biomedical research succeeds, and who suffers "injury" if it fails? In typical principal–agent relationships, the principal has the most at stake. In human subjects research, the subject may place herself at risk of physical injury from unproved treatment, and may forgo other therapeutic opportunities by electing to participate in a formal study. Research subjects therefore have principal-like attributes in this respect, but other parties also have claims to benefit or harm. For example, research sponsors put their current agendas and future prospects at risk, although they face economic or programmatic harm rather than physical harm if the research fails.

Who pays? Although payment of a professional agent such as a physician or lawyer does not conclusively demonstrate that the payer merits primary loyalty, principal parties are often the ones who finance the services of agents. Researchers receive money from their academic employers, who

89. RESTATEMENT (SECOND) OF AGENCY §§ 14, 18 cmt. a (1958).

90. *See, e.g.*, Belsky & Emanuel, *supra* note 43; Brian G. Schuster, *VA Continues to Play Key Role in PTSD Research*, VA RES. CURRENTS (Dep't of Veterans Affairs, Baltimore, MD), Feb. 2005, at 1, 3, *available at* http://www.research.va.gov/resources/pubs/docs/va_research_currents_february_05.pdf (explaining that VA research and funding has "played a major role in the expansion of our understanding of [posttraumatic stress disorder]").

in turn are paid by public and private research sponsors. Except for industry sponsors, these parties tend to be either government or nonprofit organizations whose financial investments derive from funds impressed with a public trust to serve particular charitable objectives. Research subjects do not pay for research, and in fact are often paid by the researchers for subjecting themselves to the inconvenience and risk of participation.[91]

Who forms a personal relationship with researchers? Especially where physical wellbeing is concerned, principal parties and their agents tend to form a personal bond, whether labeled "friendship" or described in domain-specific terms associated with the service being offered. As discussed below, deterring friendships from forming is a common strategy being taken by medical schools concerned about the influence of pharmaceutical companies over their trainees.[92] Who becomes "close" to a biomedical researcher? Sometimes the research subjects matter as individuals to the researchers, but other times they do not. Researchers' friendships are primarily with other researchers, whether at the same or different institutions, and occasionally with representatives of research sponsors, particularly industry partners who work directly with researchers rather than grant sponsors who evaluate them at arm's length in relatively anonymous applications for grant funding.

C. *Why Research Subjects Aren't "Clients"*

One plausible permutation of agency relationships in biomedical research is to position the research subject as the researcher's "client." Translating from research terms into lawyers' terms, the public or private research sponsor would be cast as the payer for services to the client, other subjects and patients would be either joint or competing clients, and the academic health center would be analogous to a law firm.

The logical problem with considering the research subject the principal party in a supposed principal–agent relationship is that, in biomedical research, the putative beneficiary of relational activity by definition would not be able to benefit from that activity. As discussed above, recent conceptions of research ethics hold that the only benefit that accrues to a research subject is altruistic gain from contributing to a socially useful enterprise.[93] Bioethicists have largely discarded the argument that research subjects are medically aided by participation.[94] This is obviously the case for "normal

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91. *See* Neal Dickert et al., *Paying Research Subjects: An Analysis of Current Policies*, ANNALS INTERNAL MED. 368, 368 (2002) (noting that paying research subjects is a "common and long-standing practice").

92. *See infra* notes 144–46 and accompanying text.

93. *See supra* notes 36–37 and accompanying text.

94. Franklin Miller criticizes bioethicists and policymakers for conflating the ethics of clinical research with the ethics of clinical medicine. Franklin G. Miller, *Research Ethics and Misguided Moral Intuition*, 32 J.L. MED. & ETHICS 111 (2004). He notes the curiosity that foundational documents in research ethics such as the Declaration of Helskinki assume that researchers must act with "therapeutic beneficence" toward human subjects. *Id.* at 111. Miller points out that recent

healthy subjects" who volunteer for what is sometimes called "nontherapeutic" research, such as safety testing of investigational new drugs in Phase 1 clinical trials. But it also applies to patients, including those with serious diseases, who may become healthier if an experimental treatment turns out during the course of the research to be beneficial, but who equally may not improve or may worsen if the experimental treatment turns out to be less effective than existing therapy. This category of investigation is sometimes called "therapeutic" research, but that designation has been harshly criticized as misleading the subject into believing that his or her best medical interests, not the acquisition of new knowledge, is the objective of participation.[95]

Labeling the research subject a principal party under these background conditions creates a paradox. Equating the subject's physical wellbeing with his or her interests leads to the conclusion that any goal of research contrary to the interests of the subject in avoiding physical harm is a conflict of interest, which is clearly unworkable. Equating the subject's altruism with his or her interests leads to the conclusion that no conflict of interest arises if the questionable conduct furthers "sound science." The latter inference obviates the need to consider fiduciary obligations as running to research subjects in the first place by assigning to research subjects an idealized degree of social awareness that they seldom if ever possess. In effect, this approach ignores a generation of medical ethics by substituting "best interests" for autonomy—disregarding actual motivation in favor of what a medical or ethical professional deeides that motivation "should be." This is not to say that researchers owe no duties to subjects (discussed below), just that subjects cannot logically occupy the role of principal in the sort of agency relationship that is amenable to conflicts analysis.[96]

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conccptions of research ethics minimize direct benefit to the subject as the basis for participation, stressing instead altruistic desire to hclp future suffercrs among the general public, or within susceptible subgroups in whose wellbeing the participant has at most an indirect interest. *Id.* at 114. Participants may accept the risk of harm to further these nonpersonal goals, and researchers may ethically subject them to such risk in most circumstances. *Id.* Accordingly, Miller does not consider research practices such as performing sham surgery on a control group or using a psychotropic agent to provoke symptoms for the purpose of testing a new treatment inherently unethical, even though they depart from therapeutic norms. Instead, he concentrates his ethical analysis on whether the practices "are necessary to answer valuable scientific questions and whether the knowledge gained by the research can justify the risks." *Id.* at 113.

95. Peter A. Clark, *Placebo Surgery for Parkinson's Disease: Do the Benefits Outweigh the Risks?*, 30 J.L. MED. & ETHICS 58, 61–62 (2002) (explaining the potential "therapeutic misconception" that research "promises beneficial treatment," which "could be viewed as a form of undue influence").

96. Miller puts the point well: "to argue that investigators do not have the same therapeutic obligations to patients in the context of clinical research as in medical care does not imply that they have no obligation to protect research participants from harm and exploitation." Miller, *supra* note 94, at 114. This is a regulatory and self-regulatory matter, but not one suited to conflicts of interest analysis.

Commercialization of medical research also raises issues regarding the rights, if any, that patients and families who participate in studies, contribute tissue samples, or otherwise devote time

If individual "representation" of research subjects by researchers is impractical, might researchers represent subjects in the aggregate? Legal ethics disfavors group representation unless the client is an organized entity with a separate legal identity such as a corporation. However, class action and mass tort lawyers represent groups of plaintiffs in litigation, and with proper consent corporate lawyers may occasionally represent several parties to a transaction without violating rules of professional conduct. Similarly, group representation by medical professionals is possible but problematic, as demonstrated in the 1990s by the attempt to reorient physicians' ethical obligations from individual patients to "population-based care" in order to permit rationing of scarce economic resources.[97] However, research subjects cannot form a "corporate client" and do not naturally share interests. Even in a specific study, subjects may participate for different reasons and hold different preferences regarding risks and procedures. Ultimately, the idea of representing research subjects as a group converges with serving the public interest in sound but safe science, which this Article argues is not amenable to governance in relational terms.

D. Could Anyone Else Be a Research "Client"?

In the abstract, other principal–agent combinations could be structured into the legal governance of biomedical research. One option is that individual researchers serve the objectives of the nonprofit universities that are typically their employers. In this conception of research agency, research sponsors pay for researchers to serve academic objectives but do not themselves control the conduct of funded research. A second option portrays research sponsors (whether public, private charitable, or industrial) as the clients, with the university playing the part of the professional firm that assembles the talents of individual researchers.

What if one conceives of the academic center as the client of individual researchers and therefore the party to whom they are loyal and by whom they are paid?[98] Considering the ubiquity of employment relationships in

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and resources retain in patentable products that result. The trend appears to be to uphold private contractual arrangements but not otherwise to consider researchers to be financial agents of research subjects. *See* Moore v. Regents of the Univ. of Cal., 793 P.2d 479, 483, 493–97 (Cal. 1990) (requiring informed consent but refusing to grant property rights in tissue donated by a leukemia patient); Mary R. Anderlik & Mark A. Rothstein, *Currents in Contemporary Ethics*, 31 J.S. MED. & ETHICS 450, 451–52 (2003) (describing an order in litigation denying fiduciary and informed consent claims relating to patenting by researcher of genetic test for Canavan disease).

97. *See* Kassirer, *supra* note 8 (summarizing and commenting on debate in the medical community about whether it would be ethical and otherwise desirable to move toward a system of population-based care).

98. Regulated industries in which firms employ licensed professionals are difficult to analyze in relational terms, especially if the organizations themselves lack institutional principal–agent duties to individual customers. In the Martha Stewart case, for example, the Merrill Lynch broker who passed along information about another client's trading may have been acting in the best interests of his employer by keeping a famous and important customer happy. Donald C. Langevoort, *Reflections on Scienter (and the Securities Fraud Case Against Martha Stewart that Never*

biomedical research, academic health centers and other nonprofit health care organizations might construct conflicts of interest policies that, like the pharmaceutical firm's in the anecdote related above, concentrate on assuring that their employed clinicians and researchers remain loyal to them. One constraint is that research universities historically have had decentralized governance, which both derives from and reinforces notions of academic freedom. Revenue streams tend to be decentralized also—both clinical payments and research grants typically attach to individuals or their departments, not the institution as a whole. It is hard to demand loyalty to the institution when there is a power vacuum at the top of the organizational chart.

Another problem is the mixed missions of biomedical institutions, including research, education, and clinical care.[99] Although generally acceptable within the broad constraints of state nonprofit corporation law or federal law governing tax-exempt organizations, this amalgam of objectives is problematic from a relational perspective if the academic center is playing the role of professional firm serving research sponsors as clients. Even if biomedical institutions demanded loyalty from their employees, the institutions themselves would still face the temptations of self-dealing or have conflicting obligations to constituents. The interests of two private charitable foundations supporting research may not conflict, but using the same clinical infrastructure for research, teaching, and clinical care may subject the academic setting to irreconcilable conflicts similar to those raised in the recent debate over "multidisciplinary practice" among law firms.

Unlike the rich literature on individual conflicts of interest, institutional conflicts have received scant attention until very recently.[100] Critics who posit a destructive effect when outside sponsors pay researchers directly, or offer them travel to conferences in nice locations, often make little fuss when the outside sponsor pays the institutional employer, which in turn pays its employees.[101] In fact, "unrestricted grants" from pharmaceutical companies to academic health centers have become a preferred vehicle for (supposedly) reducing conflicts of interest that might tempt individual physicians in those

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Happened) 18 (Georgetown Law and Econ. Research Paper No. 808104, Dec. 2, 2005), *available at* http://ssrn.com/abstract=808104. Recent efforts to regulate securities analysts, who are employees of large brokerage firms, highlight relational–regulatory ehallenges. One recent article considers analysts both actual agents of their corporate employers and "quasi-agents" of the public, and therefore assigns them an independent duty of "reliability." Jill E. Fisch & Hillary A. Sale, *The Securities Analyst as Agent: Rethinking the Regulation of Analysts*, 88 IOWA L. REV. 1035, 1039–40 (2003).

99. *See* David Korn, *Reengineering Academic Medical Centers: Reengineering Academic Values?*, 71 ACAD. MED. 1033 (1996) (discussing the impact of the different goals and functions of academic medical centers on the centers themselves and the industry as a whole).

100. For a comprchensive, balanced discussion of institutional conflicts of interest, see DuVal, *supra* note 33. As the title—*Institutional Conflicts of Interest: Protecting Human Subjects, Scientific Integrity, and Institutional Accountability*—conveys, DuVal considers a rangc of primary obligations, with both relational and regulatory connotations.

101. *See, e.g.*, Brennan et al., *supra* note 16, at 431–32.

institutions to favor the interests of the donor company over the best medical interests of patients.

According to an Association of American Medical Colleges task force report, "[a]n institution may have a conflict of interest in human subjects research whenever the financial interests of the institution, or of an institutional official acting within his or her authority . . . might affect—or reasonably appear to affect—institutional processes for the conduct, review, or oversight of human subjects research."[102] Like most recent statements on the topic, this commentary subsumes within "conflict of interest" several institutional roles, and does not distinguish among them. An academic health center has various compliance obligations, both to government directly and to self-regulatory organizations such as accrediting bodies to which government has delegated authority. These obligations must be performed properly, and policing them (including through prescriptive rules regarding procedures) is an important responsibility of the regulator or self-regulator. But it is not particularly helpful to describe them as vulnerable to conflicts of interest because institutional interest is presumed to be in tension with them, or else they would not exist.

On the other hand, academic health centers routinely perform functions to which law attaches specific relational duties, such as caring for patients, and assume other relational obligations by voluntary agreement, such as accepting research grants. One set of such activities may indeed constitute a conflict of interest with another set, and all may be vulnerable to conflicts with other institutional interests, such as the financial concerns of the general university that often controls an academic health center. Traditional conflict management tools and safeguards such as internal governance procedures, disclosure policies, limits, and prohibitions may be appropriate for these situations.[103]

Centralized management in academic health centers, as in large law firms, is a recent phenomenon resulting from the much larger financial revenues now available to both sets of organizations and the intensification of competition for those revenues. As centralization progresses, research institutions will find it easier to demand loyalty from employees but harder to accommodate their mixed missions within a relational framework. In particular, "corporate" decisioumaking reduces the effectiveness of isolating particular individuals or departments from one another where conflicting interests are present.[104] Nor is a civil service approach to preventing conflicts of interest among employees practicable in modern university settings.

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102. TASK FORCE ON FIN. CONFLICTS OF INTEREST IN CLINICAL RESEARCH, ASS'N OF AM. MED. COLLS., PROTECTING SUBJECTS, PRESERVING TRUST, PROMOTING PROGRESS II 2–3 (2002).

103. *See* DuVal, *supra* note 33, at 621–23.

104. *See, e.g.*, Sarbanes–Oxley Act of 2002 § 201, 15 U.S.C. § 78j-1(g) (Supp. II 2003) (prohibiting public auditors from offering other services to audit clients rather than allowing internal "walls").

Interns and residents may work long hours for very low pay with outside payments prohibited because they know they will earn substantial returns in practice after their training is completed—a version of the "revolving door" that challenges the ethics of senior civil servants. Faculty and permanent academic staff, however, no longer act like career employees satisfied with job security and local prestige, but routinely seek more lucrative employment elsewhere.

A third obstacle to demanding that researchers be loyal to their university employers is that nonprofit enterprises seldom pay full freight to their faculty from institutional funds as salaries and benefits. As a result, they tolerate and even endorse the pursuit of outside remuneration that has the effect of supporting the academic mission. At the University of Texas, for example, general staff are cautioned not to accept payments from external sources, but the university's official policy for faculty states that "faculty are *encouraged* to seek remunerative outside employment" that does not compromise their teaching duties or use university resources.[105]

A conflict of interest policy emphasizing institutional loyalty is incompatible with this pattern of cross-subsidies. If a pledge of institutional loyalty is desired, it may be necessary to channel more of these financial rewards through employer institutions, as is the case for most patent revenues. This would include honoraria, royalties, and consulting fees of various sorts. Of course, this approach would create internal political challenges regarding the distribution of funds. In addition, centralizing the receipt of funds could raise legal issues for both public and private tax-exempt institutions if faculty members receive side payments for services that the institution itself cannot lawfully provide, such as lobbying.

What does this analysis tell us? That there is no single principal party to whom researchers can demonstrate loyalty, and therefore no logical foundation for constructing policies based on conflicts of interest. In particular, research subjects, however deserving of protection and respect, cannot occupy the principal's position. A more effective governance mechanism for research incentives must shed the relational pretense.

IV. Recasting "Conflicts" As Regulated Incentives

The preceding Parts of this Article make the case that conflicts of interest discourse is historically understandable but logically incoherent as applied to biomedical research in academic settings. This Part argues that the relational implications of conflict of interest discourse may be harmful to public policy, and that a regulatory approach is superior in several ways.

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105. According to the required employee compliance training materials at the University of Texas at Austin, "Faculty are *encouraged* to aecept paid outside consulting and professional opportunitics." The University of Texas at Austin, General Compliance Training Program, http://www.utexas.edu/administration/oic/cts/cw126e/alt/page4.htm.

One can respect research participants' personhood, rights, and interests without using principal–agent language. Modern research ethics takes a much more legalistic, regulatory approach than its relational, largely self-regulatory predecessor, a trend that an obsession with "conflict of interest" threatens to reverse. The basic goal of research regulation is to maximize the output of ethical research for a given level of funding. The Bayh–Dole Act, for example, was at root an exercise in off-budget, incentive-based regulation intended to facilitate technology transfer and therefore research productivity.

Placing public regulatory duties on biomedical researchers, including physicians, does not ereate irreconcilable "role conflict" but simply subjects their traditional role-governed ethics to additional rules of conduct. Physicians have always had public-interested as well as patient-interested duties. Recognizing this, medical ethics gives physicians greater freedom to limit relational duties to patients than legal ethics gives lawyers to limit relational duties to clients. Few parallels exist in clinical medicine to the client–client conflicts of interest that play a large role in lawyers' ethics; payers are allowed a more directive function in medicine than in law; and confidentiality rules are more often waived to allow physicians to benefit third parties or further broad social objectives.

Specialization in research makes a regulatory approach easier because there is less likelihood of interfering with the relational obligations of treating physicians to their patients. Industrialization has similar effects: research institutions are an efficient focus for regulatory efforts, whereas it is hard to enforce detailed regulations against a large number of individual professionals. As mentioned above, however, combining clinical obligations with research obligations creates problems for both individuals and institutions. The privacy requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA), for example, permit disclosure of confidential medical information for treatment, payment, and health care operations without patient consent, but require specific authorization for research uses.[106] This concern about the propriety of subsuming research within the relational framework of medical treatment constitutes public acknowledgment that research objectives differ categorically from the objectives of clinical medicine.

Other expert economic sectors, including law and accounting, have also been forced to navigate a transition from self-governing profession to regulated industry. For lawyers, regulation now supplements rules of professional responsibility in several specific areas, placing direct public duties on lawyers even though they may be in tension with the traditional primacy of client interests. The Sarbanes–Oxley Act, for example, imposes regulatory duties on auditors, by banning corporate consulting income in

106. Health Insurance Portability and Accountability Act of 1996, Pub. L. No. 104-191, §§ 1173, 1179, 110 Stat. 1936, 2024–26, 2030–32 (codified as amended in scattered sections of 26, 29, and 42 U.S.C.).

order to further their obligation to report objectively to the public, and on lawyers, by relaxing strict standards of client confidentiality when financial fraud is at issue.[107] Specialization and industrialization of these professions has facilitated regulation. Not every lawyer is a securities lawyer; not every accountant audits public companies. Those performing such functions, however, subject themselves to regulatory as well as relational monitoring. For those within regulated specialties, moreover, the rules apply to law firms and accounting firms as institutions as well as to individual lawyers and auditors.

A. Calibrating Incentives for Research Productivity

Shifting from conflicts of interest discourse and other relational constructs to explicit public regulation of biomedical researchers has several potential benefits. Without the rhetorical distraction of parsing "conflicts of interest," public regulation can examine the complete picture of medical research and can calibrate incentives to stimulate desirable behavior. A public regulator can establish benchmarks for research quality and productivity, and can assess empirically the extent of financial relationships involving biomedical researchers and the measurable harm arising from those relationships.[108] By contrast, there is no general "efficiency defense" to a conflict of interest violation cast in relational terms. Under traditional statements of fiduciary law and ethics, principal parties are entitled to

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107. 15 U.S.C. § 78j-1 (Supp. II 2003); *see also* Thomas G. Bost, *Corporate Lawyers After the Big Quake: The Conceptual Fault Line in the Professional Duty of Confidentiality*, 19 GEO. J. LEG. ETHICS 1089, 1090 (2006) (detailing disclosure requirements for attorneys under Sarbanes–Oxley); Stephen J. Choi, *A Framework for the Regulation of Securities Market Intermediaries*, 1 BERKELEY BUS. L.J. 45, 63 (2004) (discussing prohibitions on auditors from receiving consulting income).

108. The fact that government health agencies use expert advisors from the private sector to inform their decisions raises a legitimate issue of conflicts of interest with respect to individuals who serve on advisory committees to government. Current law allows government latitude to balance its need for expert advice against potential conflict of interest, and to grant general or specific waivers with varying degrees of public disclosure. *See* 18 U.S.C. § 208(b)(1), (b)(3) (2000); 21 U.S.C. § 355(n)(4) (2000); 5 C.F.R. 2640.301-.302 (2006); *see also, e.g.*, U.S. FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH & HUMAN SERVS., FDA GUIDANCE ON CONFLICT OF INTEREST FOR ADVISORY COMMITTEE MEMBERS, CONSULTANTS AND EXPERTS (2000), http://www.fda.gov/oc/advisory/conflictofinterest/guidance.html. In February 2005, FDA issued a general waiver of conflict of interest rules to a joint meeting of its Arthritis Advisory Committee and Drug Safety and Risk Management Advisory Committee, which voted narrowly to allow highly profitable cyclooxygenase-2 inhibitors to remain on the market. Ctr. for Drug Evaluation & Research, U.S. Dep't of Health & Human Servs., Transcript of Joint Meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee, http://www.fda.gov/ohrms/dockets/AC/05/transcripts/2005-4090T1.htm. It was eventually disclosed that ten of the committee's thirty members had financial ties to the drugs' manufacturers, and that their votes changed the outcome of the deliberations. Robert Steinbrook, *Financial Conflicts of Interest and the Food and Drug Administration's Advisory Committees*, 353 NEW ENG. J. MED. 116, 116 (2005). The law was subsequently amended to prohibit advisory committee participation under similar circumstances. Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act of 2006, Pub. L. No. 109-97, § 795, 119 Stat. 2120, 2164.

categorically undivided loyalty.[109] A similar transition from relational to regulatory focus is already occurring with respect to the ethical analysis of payments to people participating in human subjects research. Rather than condemning payment in relational terms as "undue influence," ethicists increasingly focus on the need to adequately incentivize participation in research—including by vulnerable populations that historically have had less access to medical innovations—and rely instead on substantive regulation to ensure that the risks imposed on paid subjects are reasonable in light of the potential benefits to society of having the research take place.[110]

Building on baseline measurements, a regulator can model the effects on research outcomes of alternative policies altering the balance of competitive and cooperative incentives affecting researchers and research institutions. How, for example, do direct cash payments from industry sponsors to individual researchers compare with deferred compensation through equity interests and patent royalties, focused grant support of research departments, and general support of academic institutions in terms of quantity of research produced, reliability of results, and ethical treatment of human subjects? If owner–innovators are permitted to test their inventions using human subjects, do the products turn out better or worse? Are the research subjects safer or less safe?[111] How much will it cost to partition research from treatment functions to prevent divided loyalties? Regulatory approaches, unlike many relational ones, allow empirics to matter.

B. Reputational Intermediaries and Self-Regulation

Even in a regulated environment, self-governance remains necessary and desirable to reinforce norms of proper conduct, adjust to changing

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109. *See* Pegram v. Herdrich, 530 U.S. 211, 235 (2000) (confirming that a fiduciary must act with "an eye single" in the interests of beneficiaries).

110. Initial concern among bioethicists about the generally corrupting influence of commercialization in research resulted in payments to patients being treated on a par with payments to their treating physicians. The federal "Common Rule," for example, states that investigators shall seek informed consent under circumstances "that minimize the possibility of coercion or undue inducement." 45 C.F.R. § 46.116 (2005). Although both constitute recruitment incentives, only payments to physicians create a conflict of interest. Recent commentary uses improved risk disclosure and direct risk regulation to protect research subjects, and does not assign independent significance to whether they receive money for participating. *See, e.g.*, WILLIAM M. SAGE, PAYING RESEARCH SUBJECTS: THE U.S. EXAMPLE (forthcoming 2007); Ezekiel J. Emanuel, *Ending Concerns About Undue Inducement*, 32 J.L. MED. & ETHICS 100 (2004).

111. An analogy in the medical treatment context is legal restrictions on "self-referral" of patients for services in which the referring physician has a financial interest. Laws prohibiting self-referral are primarily intended to reduce government health insurance payments and avoid social waste, rather than to keep doctors loyal to patients in a strict relational sense. Among the important empirical questions are whether patients get better or worse quality care in physician-owned facilities, whether costs are higher, and whether physician ownership of referral facilities improves patient access to services in particular communities.

conditions, and leverage public enforcement resources.[112] Analyzing financial relationships in relational terms makes self-regulation susceptible to oversimplification of remedies and generational in-fighting, as discussed above. With incentives monitored by public processes directed at achieving explicit public objectives, self-regulation can work in more constructive ways.

One possibility is the deliberate use of reputational intermediaries in the biomedical research environment.[113] Organizations that endorse research results for public use are well positioned to monitor incentive structures and ensure that individual research scientists are responding in the desired ways. Universities and scientific journals are peer-governed institutions that put their own reputations on the line when they hire or promote researchers or publish research results. Indeed, both sets of intermediaries have stepped forward in recent years to scrutinize research for counterproductive financial incentives, as well as for data fabrication, plagiarism, and other scientific misconduct.[114] However, there has been no direct government review of these activities except in connection with financial or safety audits of individual institutions.

Self-regulation is often invoked by critics of research commercialization. Brennan and colleagues, for example, call for "more stringent regulation," envisioning most restrictions being imposed through self-regulatory processes rather than direct governmental intervention.[115] They propose a leadership role for academic medical centers, though they do not clearly distinguish among contract-based relational claims that such institutions have on physicians and researchers they employ, contractual and fiduciary relational claims that patients have on academic medical centers, and the institutions' legal and ethical obligations to the public at large.[116] Similarly, former Office of Human Research Protections Director Greg Koski believes that self-regulation, backed by the threat of severe government sanctions in "the most egregious cases," will increase acceptance

112. *See generally* Richard H. McAdams & Eric B. Rasmusen, *Norms in Law and Economics* 26–37 (Mar. 29, 2005) (unpublished manuscript), *available at* http://www.rasmusen.org/papers/norms.pdf (surveying the role and shortcomings of norms as guides to behavior).

113. *See* John C. Coffee, Jr., *Gatekeeper Failure and Reform: The Challenge of Fashioning Relevant Reforms*, 84 B.U. L. REV. 301 (2004) (discussing auditors, securities analysts, and others as regulated gatekeepers in corporate and securities law); Ronald J. Gilson & Reinier H. Kraakman, *The Mechanisms of Market Efficiency*, 70 VA. L. REV. 549, 618–21 (1984) (proposing investment bankers as reputational "gatekeepers" for securities offerings).

114. *See, e.g.*, Nichols Wade, *University Panel Faults Cloning Co-Author*, N.Y. TIMES, Feb. 11, 2006 (discussing the efforts of a panel formed by the University of Pittsburgh to investigate a researcher's failure to verify data—which his co-author falsified—as well as improper commingling of interests between the researchers).

115. Brennan et. al., *supra* note 16, at 431–32.

116. *Id.* at 430.

of the underlying principles and focus scientists on preventing ethical lapses.[117]

Universities could be effective reputational intermediaries for biomedical researchers.[118] Institutional compliance has the advantage of allowing clear relational obligations of employee to employer (rather than abstract duties to society or science) to define conflicts of interest, while centering public regulatory compliance at the institutional level where enforcement tends to be more straightforward.[119] Government's primary role in this framework would be to regulate the universities to further public goals regarding research ethics and productivity.[120] For example, government could determine the allowable extent of university–industry affiliation considering the service, research, and educational missions of nonprofit biomedical institutions. This is not an easy task. Industry represents a useful source of financial subsidy that supplements government funding of research, allows academic centers to offer salaries to clinical faculty that are competitive with private practice, and provides resources for education that

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117. Greg Koski, *Research, Regulations, and Responsibility: Confronting the Compliance Myth—A Reaction to Professor Gatter*, 52 EMORY L.J. 403, 411 (2003). Accordingly, Koski views the prompt issuance of guidelines on conflicts of interest by the Association of American Medical Colleges, the Association of American Universities, and a host of other professional organizations following the threat of direct regulation of conflicts of interest by HHS as a positive sign. *Id.* at 413–15.

118. As Brennan and colleagues observe, "AMC faculty have a central role in the training of new physicians and represent their own institution, [and therefore] should not function as paid marketers or spokespersons for medicine-related industries." Brennan et al., *supra* note 16, at 432. In several instances, the authors support mechanisms to substitute centralized funding of specific academic medical centers by industry for decentralized funding of individual faculty. *Id.* at 431 (continuing education); *id.* at 432 (physician travel and general research grants without deliverables).

119. Another issue in shifting from personal to institutional obligations is persuading individual professionals that imposing such duties at the institutional level will not strip them of professionalism and subject them to micromanagement. A variant of this phenomenon occurred in 1993, when the Clinton administration proposed shifting malpractice liability from physicians to managed care organizations as part of national health reform. Physicians reacted violently in opposition, notwithstanding their longstanding antipathy toward malpractice law. They viewed the proposal as confirmation that managed care would play the central role in clinical decisionmaking, and that physicians would be reduced to a secondary one. One medical leader claimed that the government was trying to take away his "constitutional right to be sued." *See* William M. Sage, *Enterprise Liability and the Emerging Managed Health Care System*, 60 LAW & CONTEMP. PROBS. 159, 170 (1997) (noting that physicians' groups feared that, under the Clinton proposal, if exposed to increasing liability, managed care providers would "terminate high-risk physicians and micromanage clinical practice"); William M. Sage et al., *Enterprise Liability for Medical Malpractice and Health Care Quality Improvement*, 20 AM. J.L. & MED. 1, 27 (1994) (remarking on physicians' concern about the possible constraints risk-averse health plan operators could place on doctors' autonomy, but concluding that holding health plans liable for medical malpractice would offer the positive result of making the plans responsible for the clinical effects of their cost-management decisions).

120. The authors observe that their approach arguably "transfers the pressure surrounding financial conflicts to the institution" but assert that "public access [i.e., disclosure] and peer pressure will more effectively operate at the institutional level and such a policy is preferable to banning all contact between manufacturers and academic centers." Brennan et al., *supra* note 16, at 432.

relieve pressure on medical student tuition and graduate trainee stipends and working conditions.

Peer-reviewed medical journals could be effective self-regulatory organizations to monitor financial flows in research because they publish nearly all research findings, and can make or break academic careers. The top journals, such as the *New England Journal of Medicine* and the *Journal of the American Medical Association*, wield enormous influence over public and professional opinion, and generate huge windfalls in revenue and reputation for the professional associations that own them. As with academic health centers, government could explicitly define the regulatory responsibilities of medical journals, which tend to be owned by nonprofit entities.

The editors of major medical journals have become exquisitely sensitive to issues of this type, such as the hazards of accepting paid advertising from pharmaceutical companies and publishing "editorials" authored by company consultants.[121] Most journals require disclosure to the editors of authors'

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121. *See, e.g.*, Margaret A. Winker et al., *Guidelines for Medical and Health Information Sites on the Internet: Principles Governing AMA Websites*, 283 JAMA 1600, 1603 (2000) ("To maintain the integrity of the AMA Web sites, advertising . . . cannot influence editorial decisions or editorial content . . . . Decisions to sell advertising space are made independently of and without information pertinent to specific editorial content."); New England Journal of Medicine Online Advertising Policy, http://www.nejm.org/aboutnejm/adpol.asp ("Advertising is separate from content. Advertisers and sponsors have no advance knowledge of our editorial content, nor do the editors shape content to accommodate advertising. . . . Advertisers do not influence any of our editorial decisions or advertising policies. Publisher's advertising sales representatives have neither control over, nor prior knowledge of, specific editorial content before it is published."). The *Medical Letter on Drugs and Therapeutics*, which publishes expert evaluations of new drugs, refuses all advertising. The Medical Letter on Drugs and Therapeutics, http://www.medicalletter.org/html/who.htm (asserting that "[t]he Medical Letter, Inc., is completely independent. It is supported solely by subscription fees and accepts no advertising, grants or donations"). This debate has been extended to financial relationships between drug companies and authors of practical review articles that potentially influence the clinical decisions of large numbers of physician readers. The *New England Journal of Medicine* briefly banned physicians who receive drug company funding from writing review articles, but retreated to a mandatory disclosure policy when it realized that virtually all true experts would be precluded from contributing. Jeffrey M. Drazen & Gregory D. Curfman, *Financial Associations of Authors*, 346 NEW. ENG. J. MED. 1901, 1901 (2002) (changing a policy requiring that review authors have *no* financial interest in a company (or its competitors) whose product is being reviewed to a policy requiring no "*substantial* financial interest," after concluding that the former policy was constraining the Journal's "ability to provide comprehensive, up-to-date information." (emphasis added)); Scott Gottlieb, New England Journal *Loosens Its Rules on Conflicts of Interest*, 324 BMJ 1474 (2002) ("The *New England Journal of Medicine* is relaxing its longstanding rules on conflict of interest so that it can publish evaluations of new drugs by researchers with financial ties to the manufacturers because it cannot find enough experts without financial ties to drug companies.").

There is no easy fix to problems of publication bias. For example, open-access journals are a growing alternative to traditional medical publishing, mainly as a result of increasing subscription costs. Instead of signing away copyright to a journal that receives revenues from subscribers, researchers or their sponsors pay a fee to publish in peer-reviewed, online journals that are free to readers. This broadens access to the results of research, but increases the journals' reliance on research funding to support their operations. Catherine Zandonella, *Open Access: Will it Spell the End of the Medical Library?*, 9 MED. ON THE NET 1, 1–7 (2003), http://www.hcpro.com/pub-

funding and financial relationships for all articles, including the scientific submissions that are the journals' bread and butter, and in many cases the journals publish that information if and when the article appears in print. In addition to supporting these efforts, government could monitor journals for collusion masquerading as protection of research integrity, such as joint policies mandating transfer of copyright ownership, nonpayment of authors, restrictions on prior publication, and prohibitions on multiple article submissions.[122]

An explicitly regulatory orientation could also help improve the operation of Institutional Review Boards (IRBs), the principal self-regulatory bodies charged with protecting human subjects within research institutions. IRBs are permanently embedded in the regulatory fabric of federal research, but have come under criticism for being arbitrary and ineffectual.[123] One problem with IRBs is that their mission has been defined largely in relational terms—"representing" the interests of human subjects—when their energies would be better directed at ensuring the scientific soundness of research and protecting subjects from excessive risks of harm.[124]

3476.html. Ultimately, a combination of journals' reputational capital, disclosure of research support, and click-through access to underlying data are likely to prove most effective.

122. Unlike the typical media outlet with paid staff or freelance contributors, medical journals never pay for the artieles (or even the editorials) they solicit or accept from outside authors, although they all require accepted authors to convey copyright to them, and most strictly enforce prepublication bans and single-submission rules—practiccs that often were collcctively adopted and that in combination reduce competition among journals and provide substantial benefits to the journals that attract high-profile studies. *See, e.g.*, New England Journal of Medicine Author Center, Instructions for Submitting a New Manuscript, *available at* http://authors.nejm.org/Misc/NewMS.asp (detailing rules on transfer of copyright and prohibitions against prepublication); Canadian Medical Association Journal, CMAJ Editorial Policies, *available at* http://www.cmaj.ca/authors/policies.shtml (discussing copyright and submission rules for the CMAJ). The employers of the published authors—typically academic medical centers, hospitals, and large medical groups—subsidize this return to the journals, but this subsidy is so pervasive and so entrenched that journals never bother to consider whether it is a conflict of interest for them to "free ride." Compared to pharmaceuticals and medical devices, moreover, it is hard to charactcrize the service side of the American health eare system as "industry," although the revenues it generates are immense.

123. *See* David A. Hyman, *Institutional Review Boards: Is This the Least Worst We Can Do?* 10–18 (U. Ill. Law & Econ. Research Paper No. LE06-024, 2006), *available at* http://ssrn.com/abstraet=942862 (stating that "[t]here is no empirical evidence that IRBs have any benefit whatsoever," and lamenting the high costs resulting from the variability and inefficiency of the approval process); *see also* Philip Hamburger, *The New Censorship: Institutional Review Boards*, 2004 SUP. CT. REV. 271 (arguing that federal mandates for IRB approval of rescarch unconstitutionally subject speech to licensing requirements).

124. Other legal scholars with bioethics expertise have made similar pleas for more substantive oversight of research by IRBs. *See* Carl H. Coleman, *Rationalizing Risk Assessment in Human Subject Research*, 46 ARIZ. L. REV. 1 (2004) (arguing for more stringent risk assessment by IRBs); Lars Noah, *Informed Consent and the Elusive Dichotomy Between Standard and Experimental Therapy*, 28 AM. J.L. & MED. 361, 384 (2002) ("IRBs may become preoccupied with reviewing the niceties of the consent form and perhaps less concerned about their separate obligation to make independent risk-benefit assessments about the research protocol . . . ."). Although recurring patterns of bureaucracy no doubt explain much of the misguided formalism of IRBs, it does not help that IRBs sce themselves as enforcing relational obligations of researchers to subjects. *See* Todd J.

C. *Information Flow*

Information disclosure is a mainstay of relational governance.[125] Short of outright prohibition, conflicts of interest are typically addressed by requiring agents to disclose competing demands to principal parties. The idea is that a principal with full information can decide whether or not to engage the agent, on what terms, and with what additional monitoring of performance. Disclosure requirements are often the first resort of policymakers concerned about conflicts of interest; a number of states, for example, are considering publishing lists of doctors who accept gifts from drug companies.[126]

However, disclosure under fiduciary constraints can be difficult. First, relational disclosure of conflicts of interest is effective only if it is understood by the principal. Framing researchers' financial incentives "objectively" for approval or rejection by research subjects is challenging given subjects' varying degrees of education, cultural familiarity, and cognitive bias when presented with risks. Disclosing financial flows to overcome conflicts of interest also commits the legal system to honoring the principal party's subjective beliefs and preferences regarding the disclosed information. To some research subjects, financial incentives for researchers will seem corrupting, while others may believe that researchers with a financial stake in success will do a better job. Finally, disclosure is an imperfect solution to conflicts of interest if the agent making the disclosure already occupies a position of control and influence over the principal party.[127] In the research context, a healthy volunteer subject with no prior relationship to the researcher may be able to accept or decline participation based on a conflict of interest disclosure, but a research subject who is already a patient, or who is ill and emotionally vulnerable, may have little real choice.[128]

Information policy based on public concerns is easier to design. Freed from the need to identify and cater to an identified principal party, regulation

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Zywicki, *Institutional Review Boards as Academic Bureaucracies: An Economic and Experiential Analysis*, NW. U. L. REV. (forthcoming 2007).

125. *See* Paul G. Mahoney, *Mandatory Disclosure as a Solution to Agency Problems*, 62 U. CHI. L. REV. 1047, 1048 (1995) (proposing "the reduction of agency costs as an efficiency justification for mandatory disclosure" in federal securities law); William M. Sage, *Regulating Through Information: Disclosure Laws and American Health Care*, 99 COLUM. L. REV. 1701, 1746–52 (1999) (discussing the "agency rationale" for mandatory disclosure).

126. *See* Kevin B. O'Reilly, *More States Considering Gift-Disclosure Legislation*, AM. MED. NEWS, Mar. 20, 2006, at 8–9 (describing bills in 15 states). Interestingly, these laws typically exclude compensation to physicians for participating in clinical research from the amounts that must be disclosed.

127. *See* Sage, *supra* note 125, at 1760 (describing disclosure by existing fiduciaries as presenting the peculiar question of "I know you need to rely on me, but is it OK with you that I may be unreliable?").

128. Moreover, having disclosed a conflict of interest, an agent may feel justified in engaging in self-serving behavior that is still a violation of trust. *See* Daylian M. Cain et al., *The Dirt on Coming Clean: Perverse Effects of Disclosing Conflicts of Interest*, 34 J. LEGAL STUD. 1, 7 (2005).

of research information can channel disclosure to audiences that can use it effectively, even if those are not the research subjects themselves. Peer reviewers for journals, for example, may be a useful audience for required disclosure in connection with the review process (a practice that many journals have adopted).[129] Furthermore, a regulatory approach to transparency can emphasize the form and content of disclosed information that helps promote sound research, and convey its findings to health care providers and the public, rather than focusing narrowly on financial incentives and how risks are communicated to subjects.[130] In terms of "performance benefits" to researchers of having to examine their own practices with a view to disclosing them, it is probably easier and more effective to educate researchers and research institutions about regulatory criteria for proper conduct than force them to display a moral purity and lack of concern with financial matters that is in daily conflict with their real-world experience.

De-emphasizing conflicts of interest as the justification for disclosure also may make information intended for research subjects more useful to them. Specifically, methods and content of communications that convey respect for personhood and concern for subjects' physical safety arguably help research subjects more than extensive disclosure of financial flows.[131] It may even be possible to evolve an intermediate form of disclosure that captures information of interest to research subjects in a consistent, cost-effective form that can also be used by regulators. Mandatory disclosure by corporations issuing shares to the public, for example, is directed toward an identifiable group of likely investors but is also designed for use by government itself during pre-offering review of marketing materials.

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129. *See, e.g.*, Annette Flanagin et al., *Update on JAMA's Conflict of Interest Policy*, 296 JAMA 220 (2006) (requiring complete disclosure of financial relationships and other sources of author bias at time of article submission in order to make that information transparent to peer reviewers, among others).

130. For example, federal law now requires public disclosure via the Internet of conflicts of interest involving scientists and physicians who serve on FDA advisory panels, replacing a prior policy of routine waiver of those conflicts. Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act of 2006, Pub. L. No. 109-97, § 795, 119 Stat. 2120, 2164–65 (2005).

131. An analogy in securities law is the regulation of mutual funds, which have replaced individual stock picking as the principal vehicle for securities investment by individuals. The Securities Act of 1933 emphasizes disclosure by corporate management of firm-specific risks, including self-dealing, that might affect the value of purchased shares, an approach that was largely carried over to mutual fund regulation in the Investment Company Act of 1940. Securities Act of 1933, 15 U.S.C. §§ 77a–77aa (2000); Investment Company Act of 1940, 15 U.S.C. §§ 80a-1–80a-64 (2000). As Henry Hu persuasively argues, however, today's mutual fund investors need more information about principles of portfolio construction and the overall risks of investing in certain classes of assets. He urges the SEC to emphasize general investor education in its regulation of mutual fund disclosure rather than continuing to focus only on firm-specific relational matters. Henry T.C. Hu, *The New Portfolio Society, SEC Mutual Fund Disclosure, and the Public Corporation Model*, 60 BUS. LAW. 1303, 1338–53 (2005).

Clinical trials registries, if properly structured, may also serve this dual function.[132]

D. Remedies for Injuries to Research Subjects

A contradiction in the current federal approach to human subjects protection is that seemingly strong statements of concern for the welfare of research participants are not matched by individual recourse under federal law for injuries suffered in the course of research. Violations of the Common Rule, for example, subject the violator to federal administrative remedies up to and including exclusion from federal programs, but do not trigger a private right of action if harm to subjects results.[133] Furthermore, unlike other countries, the United States does not require research institutions to have clinical trials insurance, and compensation policies for research injuries are erratic and incomplete.[134]

A pragmatic explanation for the paucity of individual recourse under federal law is that lawsuits for harm from biomedical research historically were brought, if at all, in state court as medical malpractice claims.[135] Litigation is somewhat more common today. The large amounts of money flowing through the biomedical research system, the more obvious involvement of for-profit corporate interests, and greater public expectations regarding the quality and safety of cutting-edge medical care are among the factors that may open the floodgates to research-related lawsuits.[136]

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132. *See supra* note 21.

133. 45 C.F.R. § 46.123 (2005). *But see* Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807 (Md. 2001) (denying summary judgment under state tort law to defendants in case involving alleged violations of federal research regulations).

134. In a recent study of 129 voluntary policies (consent forms) from 102 U.S. academic medical centers, compensation for research injury was uncommon, and inconsistent even when available. Robert Steinbrook, *Compensation for Injured Research Subjects*, 354 NEW ENG. J. MED. 1871, 1872 (2006). In 51.2% of the policies reviewed, free medical care was not provided by the researchers or their institutions in the event of injury arising from research. *Id.* Free medical care was provided according to the terms of 16.3% of policies, and in another 10.1% of policies free care was provided if the research subject did not have health insurance. *Id.* Case-by-case decisions were offered regarding compensation in the event of research injury in 3.9% of the policies reviewed, and in the remaining 18.6% of policies, no statement on compensation for research injury was publicly available. *Id.*

135. "If at all" refers to the charitable immunity that for decades protected academic medical centers from suit in most states before eroding as health insurance became prevalent in the 1950s and 1960s. *See* Tunkl v. Regents of Univ. of Cal., 383 P.2d 441, 448 (1963) (rejecting UCLA's argument that patients willingly submitting themselves for treatment in a research-oriented teaching hospital waived their right to sue for injury).

136. Carl Coleman identifies recent litigation against clinical researchers as a pressing reason to define clearly the obligations owed by researchers to subjects, particularly because the template for such litigation is the obligation of physician to patient under established laws of medical malpractice and informed consent. Carl H. Coleman, *Duties to Subjects in Clinical Research*, 58 VAND. L. REV. 387, 388–91 (2005); *see also* Michelle M. Mello et al., *The Rise of Litigation in Human Subjects Research*, 139 ANNALS INTERNAL MED. 40, 43 (2003) (describing relevant legal theories, including conflicts of interest). Coleman identifies but rejects polar visions of clinical researchers as physicians who owe subjects a full obligation of therapeutic beneficence

Adhering to relational standards for judging conflicts of interest involving research compounds the risk of excessive litigation, forcing the debate over individual recourse into an all-or-nothing choice rather than a reasonable middle ground. Building on public concern over tensions between patient welfare and financial advantage that arose during the backlash against managed care in the 1990s, some legal scholars have argued for a general right to sue health care providers for disloyalty as opposed to substandard care.[137] In *Grimes v. Kennedy Krieger Inst., Inc.*, the Maryland Court of Appeals essentially took that approach, blasting the defendant's research study on lead paint exposure as unethical and holding that research subjects and their families could sue in state court for harm suffered.[138] In addition to the violation of federal regulations, the court cited the defendant's special relationship to the study participants and its alleged financial interest in the research.[139]

Regulating financial flows as incentives serving public objectives would allow limited but meaningful individual remedies in the event of research injury. False or incomplete disclosure to human subjects of material facts about research risks—not about arguable sources of disloyalty—would give rise to claims for lack of informed consent or, in extreme cases, fraud. In medical product cases, disclosure would be evaluated by applying established theories of failure to warn. However, abandoning a relational, fiduciary standard would prevent litigation where the causal link between the communications failure and the injury was attenuated. A useful analogy is whether liability for failing to obtain informed consent to treatment arises from nondisclosure of financial incentives by physicians. Allowing claims for any injury received during medical care because some fact about the financial structure of care was not discussed with the patient substitutes open-ended liability for liability that arose under established informed consent law only if an undisclosed physical risk of treatment manifested itself and caused harm. If noncompliance with research standards became widespread despite these limited remedies, Congress could add an express private right of action to its regulatory statutes.

E. Humanity and Compassion

One of the biggest public policy challenges in health care is preserving the "personal touch" in an increasingly specialized, industrialized, expensive,

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notwithstanding their consent to serve as subjects, and as pure scientists who have no responsibility to promote subjects' wellbeing once consent is received. Coleman, *supra*, at 396–404. Instead, he favors a fiduciary analysis that combines disclosure with objective fairness. *Id.* at 448–49. Interestingly, Coleman draws fiduciary analogies from trustees, corporate directors, and business partners, but not from lawyers. *Id.* at 390.

137. *See, e.g.*, Maxwell D. Mehlman, *Dishonest Medical Mistakes*, 59 VAND. L. REV. 1137 (2006).

138. 782 A.2d 807 (Md. 2001).

139. *Id.* at 843–47 & n.36.

and bureaucratic system. The public, and often the law, still conceives of medicine as a dyadic enterprise involving one physician and one patient. For that reason, many efforts to improve the overall cost-effectiveness of care have been halted by heart-tugging anecdotes and the suggestion that every change in system design directly threatens identified lives.[140]

Somewhat paradoxically, Anglo-American bioethics as translated into law has undercut the humanity of medical relationships.[141] The connection between law and ethics has always been uncertain, particularly in areas such as human subjects research that have developed an extensive regulatory infrastructure. Having achieved legal change, the bioethics community may substitute compliance with the law for adherence to the ethical principles that they believe motivated the law, no matter how incompletely or ineffectively those principles are expressed in the law and no matter what other ethical issues have surfaced in the political or legislative process.

As discussed above, the most recent generation of bioethicists has emphasized patient autonomy over professional beneficence.[142] Some physicians, reacting to the complexity of medical practice today, have interpreted this position as a license to abdicate primary responsibility for their patients' welfare in favor of giving patients information and freedom of choice. Relational analysis of conflicts of interest carries this trend further by interrogating for improper purpose or effect, and attaching legal consequences to, any personal commitment by the agent other than to the identified principal party.

The current wave of attempts to ban contact between pharmaceutical company representatives and physicians, particularly trainees in academic medical centers, demonstrates the risks of this approach. Unlike previous conflicts of interest policies, which emphasized the risks to professional judgment created by lavish gifts of cash or luxury goods from drug

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140. *See* David A. Hyman, *Do Good Stories Make for Good Policy?*, 25 J. HEALTH POL. POL'Y & L. 1149 (2000) (arguing that when atypical or incomplete stories motivate health care "reform," unsound policies may result); William M. Sage et al., *Bridging the Relational-Regulatory Gap: A Pragmatic Information Policy for Patient Safety and Medical Malpractice*, 59 VAND. L. REV. 1263, 1301–05 (2006) (discussing the relationship between health policy and the characterization of lives as "identified" or "statistical").

141. *See* David A. Hyman, *How Law Killed Ethics*, 34 PERSP. BIO. MED. 134 (1990); William M. Sage, *The Lawyerization of Medicine*, 26 J. HEALTH POL. POL'Y & L. 1179, 1184–87 (2001) (describing bioethics today as having "reoriented itself" under the influence of law away from its traditional focus on physician beneficence and toward a focus on patient autonomy).

142. Greg Koski argues that the Belmont Report, which gave rise to the current system of federal regulation based on external oversight by IRBs, was at odds with scientific norms that favored researchers' personal responsibility for protecting "their" subjects. Koski, *supra* note 117, at 408. To Koski, this denial of medical scientists' humane duties both reduced acceptance of the IRB-based system and provided an easy, acceptable way for many scientists to escape that personal responsibility. *Id.* Koski therefore argues for a "culture of conscience" rather than a "culture of compliance" in human subjects research. *Id.* at 410. Koski does not specify the relational obligations that modern medical scientists should assume, or how they could be reconciled in a legal framework with the public goals of biomedical research.

companies, the most recent prohibitions apply equally to token gestures that previously would have been considered harmless. Brennan and colleagues, for example, argue that even small gifts will compromise physician decisionmaking by invoking social norms of reciprocity associated with the receipt of gifts, regardless of monetary value, and they hope that banning those gifts and other opportunities for sales representatives to form friendships with physicians, such as industry-sponsored continuing medical education seminars, will make physicians dispassionate prescribers.[143] In other words, industry critics seek to sever the human bond between physician and pharmaceutical representative in the name of strengthening the bond between physician and patient.

Can one channel "caring" so narrowly? Or does reducing human connection in one area reduce it in others? Physicians are not otherwise cloistered, nor should they be. For them and other health professionals—including, one would hope, biomedical researchers engaged in human subjects research—human impulses such as compassion and beneficence are indispensable. Moreover, a sense of personal solidarity with one's colleagues is considered to be at the heart of many professions.[144]

Would critics of the pharmaceutical industry reach consensus so easily if the question were whether physicians should recommend minimal-benefit, high-cost treatments because their personal relationship with a patient or family biased them to action rather than inaction?[145] Or whether physicians should socialize with other physicians and health professionals to whom they might refer patients? It is true that drug detailers, like all accomplished salespeople, are trained to feign friendship in order to promote their products.[146] American health care, the world's most expensive cottage industry, is frighteningly susceptible not only to these blandishments, but also to habitual practices and norms of behavior that have little scientific basis and enormous cost implications. Still, walling off physicians from personal relationships with pharmaceutical representatives and other

143. Brennan et al., *supra* note 16, at 430–32.

144. *See, e.g.*, ROSCOE POUND, THE LAWYER FROM ANTIQUITY TO MODERN TIMES 5 (1953) (defining a profession as a "learned art, practiced as a common calling, in the nature of a public service").

145. *See* Donald A. Redelmeier & Amos Tversky, *Discrepancy Between Medical Decisions for Individual Patients and for Groups*, 322 NEW ENG. J. MED. 1162 (1990) (showing that physicians have a stronger impulse to treat despite risks when decisions are presented as applicd to individual patients rather than patient groups).

146. *See* Adriane Fugh-Berman & Shahram Ahari, *Following the Script: How Drug Reps Make Friends and Influence Doctors*, 4 PLOS MED. E150 (2007), *available at* http://medicine.plosjournals.org/archive/1549-1676/4/4/pdf/10.1371_journal.pmed.0040150-L.pdf (explaining pharmaceutical sales tactics and stating that "[r]eps may be genuinely friendly, but they are not genuine friends"); Michael J. Oldani, *Thick Prescriptions: Toward an Interpretation of Pharmaceutical Sales Practices*, 18 MED. ANTHROPOLOGY Q. 325 (2004) (observations from a former drug representative turned medical anthropologist).

businesspeople while hoping they deal humanely with patients, colleagues, and the needs of society may prove impossible.

F. Explicit Relational Strictures for Research by Community Physicians

Finally, draining financial relationships of knee-jerk moral opprobrium in debates over the public duties of researchers creates opportunities for reinforcing fiduciary constructs in specific circumstances where they seem indicated. One such area is the mixed missions of academic health centers, which are supposed to balance patient care, research, and education, and which survive on a combination of revenue sources including health insurance reimbursement, charitable contributions, public research grants, and industry contracts. As discussed above, academic centers as agents serve many principals with different interests, a fact that deserves greater public attention than it now receives.[147]

Institutional conflicts of interest policies for academic health centers need to provide not only transparency but also explanation to the public and private constituencies who rely on them. Deliberately neutral bodies within academic centers, such as IRBs, may require stricter safeguards against institutional bias in their composition and operation. If IRBs enforcing regulatory standards no longer need consider themselves primarily agents for research subjects, it may be advisable in riskier studies to appoint formal "research advocates" to represent individual participants, as Dresser has proposed.[148] Another possibility is to create external testing bodies for some new drugs and medical devices that are formally chartered as "public research auditors." Unlike academic health centers, these entities can be regulated in terms analogous to those applied to financial auditors, such as prohibitions on receiving payment in stock and on allowing inventors to direct the testing of their own products.

There is also need to revisit the loyalty obligations of treating physicians to patients in the research context. Physicians have never been "pure advocates" for patients, despite political desire at the height of managed care to charge them with this duty. Nonetheless, the law generally holds physicians to relational standards for representing their patients' interests. Coleman observes that the research physician's obligations to the subject as patient are in tension with good research practice at several points: randomization, standardized rather than customized treatment, data gathering

147. The University of Texas at Austin, for example, recently adopted a policy on institutional conflicts of interest. However, it defines conflicts narrowly as equity ownership, patent rights, and other explicitly commercial transactions with industry, and does not consider the "mixed mission" question from an institutional perspective. *See* THE UNIV. OF TEX. AT AUSTIN, REVISED HANDBOOK OF OPERATING PROCEDURES, INSTITUTIONAL CONFLICT OF INTEREST IN HUMAN SUBJECTS RESEARCH No. 11.B.2 (2006).

148. Rebecca Dresser, *Patient Advocates in Research: New Possibilities, New Problems*, 11 WASH. U. J.L. & POL'Y 237, 245–46 (2003) (discussing the responsibilities of patient advocates in research).

that offers no clinical benefit, and blinded design, which can make it difficult to evaluate and respond to unexpected events.[149] It is particularly hard to address conflicts of interest for physicians in solo or small-group clinical practice, whose main job is to help patients and for whom a few thousand dollars in supplemental research payments can be a significant motivator.

Finder's fees paid to physicians by clinical trials sites, mainly hospitals, in exchange for referring patients therefore raise conflicts of interest in relational terms.[150] Payment by a third party that is contingent on patients participating in a specific research study will almost certainly influence the course of treatment the physician recommends. In its barest form, a finder's fee for research recruitment is simply a kickback, no different than a side payment for prescribing a drug or admitting a patient to a hospital.[151]

However, medical ethics has been more concerned with "free money" than with money paid by outside sources for actual work that physicians perform. It has taken medicine relatively long to recognize and respond to the conflict of interest inherent in research payments to ordinary physicians.[152] The American Medical Association's first opinion on conflicts of interest in research emphasized that "remuneration received by the researcher . . . be commensurate with the efforts of the researcher on behalf of the company."[153] This rule had the unintended consequence of favoring

149. Coleman, *supra* note 136, at 396–403.

150. The Office of the Inspector General of the U.S. Department of Health and Human Services has documented "disturbing recruitment practices" linked to physicians, hospitals, and nursing homes that receive substantial payments from pharmaceutical companies. JUNE GIBBS BROWN, OFFICE OF INSPECTOR GENERAL, DEP'T OF HEALTH AND HUMAN SERVICES, RECRUITING HUMAN SUBJECTS: PRESSURES IN INDUSTRY-SPONSORED CLINICAL RESEARCH 2 (2000). Commentators report that payments of $2,000–$5,000 per subject are common, and some physicians who hold themselves out as clinicians probably earn more from recruitment than from clinical care. *See* Jesse A. Goldner, *Dealing with Conflicts of Interest in Biomedical Research: IRB Oversight as the Next Best Solution to the Abolition Approach*, 28 J.L. MED. & ETHICS 379, 382 (2000); Trudo Lemmons & Paul B. Miller, *The Human Subjects Trade: Ethical and Legal Issues Surrounding Recruitment Incentives*, 31 J.L. MED. & ETHICS 398, 398 (2003). Lemmons and Miller offer a sophisticated analysis of the legal and ethical issues, but concern themselves with what they consider the generally corrupting influence of research commercialization rather than the specific risk of divided loyalty.

151. The equivalent in law might be money returned to a lawyer by an expert consultant who has performed services that were billed at full cost to the client. These payments situations are different than referral fees associated with the initial formation of a professional relationship and fee-splitting for wholly transferring professional services from one practitioner to another—ethical concerns in both medicine and law—which raise issues of professional competence, wasteful services, and lay interference with professional practice, but not divided loyalty. Am. Med. Ass'n, *Code of Medical Ethics: Current Opinions with Annotations*, COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS OPINION 6.02, at 164 (2006–2007 ed.).

152. Unlike law, where the rules of the adversarial system (at least in litigation) circumscribe the attorney as zealous advocate, physicians are accustomed to exercising broad discretion in their professional roles. *See generally* William M. Sage, *Physicians As Advocates*, 35 HOUS. L. REV. 1529 (1999).

153. Am. Med. Ass'n, *supra* note 151, 8.031, at 185–86. The Canadian Medical Association's policy is that "[i]t is acceptable for physicians to receive remuneration for enrolling patients or participating in approved research studies only if such activity exceeds their normal practice

payments to physicians who work really hard to get their patients to participate in studies—with a much higher attendant risk that the patient's original course of care will be altered as a result—over payments made to physicians who maintain a passive but perhaps less harmful attitude. Sensing this danger, the AMA clarified its position in a subsequent opinion, stating bluntly that "offering or accepting payment for referring patients to research studies (finder's fees) is unethical."[154]

There is as yet no effective legal model for policing conflicts of interest for self-employed physicians who receive payment for assisting community-based research. At a minimum, informed consent requires that treating physicians disclose the uncertainties associated with care they recommend if it includes a research component. Disclosure of any specific financial interests physicians have in potential advances is probably warranted as well.[155]

More is needed. The community setting is remote from most existing legal enforcement mechanisms. Physicians are for-profit businesspeople not subject to the state and federal nonprofit corporation and tax exemption rules that apply to universities and their medical centers. Federal fraud and abuse enforcers are more likely to pursue large institutions that bill Medicare for research expenses than physicians in private practice who receive payments from pharmaceutical companies for referring patients.[156] IRBs, which play the most important oversight role in the research regulatory system as currently constituted, are also primarily concerned with activities within academic medical centers (leaving aside CROs). Moreover, IRBs deal

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pattern." CANADIAN MEDICAL ASSOCIATION, CMA POLICY: PHYSICIANS AND THE PHARMACEUTICAL INDUSTRY 2 (2001); *see also* Lemmons & Miller, *supra* note 150, at 406–08 (discussing and comparing the policies of both the Canadian and American Medical Associations regarding the ethical and legal responsibilities of physicians involved in research).

154. Am. Med. Ass'n, *supra* note 151, 6.03, at 166. However, the AMA may have put too fine a legal point on what is a fundamental ethical issue. The opinion's principal goal was to codify as medical ethics recently enacted federal prohibitions (called the "Stark laws"), the primary purpose of which was to protect the financial integrity of Medicare and Medicaid, not to reinforce physicians' obligations to patients. *See* 5 BARRY R. FURROW ET AL., HEALTH LAW CASES, MATERIALS AND PROBLEMS 1033–35 (2004) (noting that the "principal problem identified by academic studies that led to the enactment of Stark I was excessive and perhaps inappropriate referrals by physicians to entities in which they had an ownership interest," which in turn resulted in additional costs to the Medicare program); William M. Sage, *Fraud and Abuse Law*, 282 JAMA 1179, 1180 (1999) (arguing that the anti-kickback law and self-referral prohibitions theoretically apply whether or not the conduct at issue increases Medicare spending, and that this tends to bring enforcement into conflict with sound health policy).

155. *See* CODE OF MEDICAL ETHICS, CURRENT OPINIONS WITH ANNOTATIONS, § 8.032:181 (2004–2005 ed.).

156. For a discussion of how the False Claims Act, the anti-kickback law, and the Stark laws might apply to research payments, see Paul E. Kalb & Kristin G. Koehler, *Legal Issues in Scientific Research*, 287 JAMA 85 (2002). However, payments to faculty members of academic medical centers for assisting institutional research fall within an exception to the fraud and abuse laws for bona fide employment relationships, even if the payments influence the physicians' recommendations regarding patient care. State fraud and abuse laws may offer greater protection for patients in these situations.

routinely with physicians who divide their time between clinical and research activities, and IRBs themselves are subject to pressures from their home institutions. Consequently, IRBs can help avert flagrant community-based abuses of patient welfare, but probably cannot articulate a vision of conflict management that has widespread application.

This gap in public policy will only prove more challenging in the future because NIH's new clinical and translational research programs emphasize building networks of community physicians who can recruit current patients as human subjects.[157] The AMA's ethics opinions on research payments have yet to permeate professional norms, and finder's fees and other recruitment incentives for physicians remain common. Even if enforcement were possible, it is doubtful that the AMA's revisionist bright-line prohibition will survive the emergence of broad networks of electronically linked community physicians participating in government sponsored research, as opposed to pharmaceutical company consultancies that were intended more to build prescribing goodwill than to generate actual scientific research. A possible compromise is some combination of nonrelational federal regulation, relational state legislation making certain payments unlawful, and individual litigation in state court alleging violation of fiduciary duty.

V. Conclusion

As the biomedical research enterprise expands and restructures, many critics have been quick to condemn money changing hands between researchers and other parties as "conflicts of interest." Criticism has extended as well to nonfinancial incentives that, in the critics' opinion, might compromise what they consider fundamental values of biomedical research.

In response to real instances of dishonest or sloppy research, some causing serious harm to patients or research subjects, public and professional bodies have employed these "conflict of interest" arguments to require disclosure of many financial relationships and to suggest banning others. However, there is as yet no evidence that these reforms will be beneficial, and little if any indication of how society might actually measure their effects.

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157. Elias A. Zerhouni & Barbara Alving, *Clinical and Translational Science Award: A Framework for a National Research Agenda*, 148 TRANSLATIONAL RESEARCH 4, 4–5 (2006). Modern science policy recognizes a role for "innovative clinical practice," meaning the incorporation of an ongoing commitment to research into ordinary physicians' everyday activities. David G. Nathan et al., *Opportunities for Medical Research in the 21st Century*, 285 JAMA 533, 534 (2001), *available at* http://www.laskerfoundation.org/reports/jama_lasker/v285n5/fpdf/jcd10001.pdf; *see also* Nancy M.P. King, *The Line Between Clinical Innovation and Human Experimentation*, 32 SETON HALL L. REV. 573, 576 (2002) (discussing the tension between legal oversight and clinical innovation). Physicians have always viewed experimentation that improves clinical care as part of their professional mission, such as surgeons tinkering with existing operative procedures or equipment, or physicians administering FDA-approved drugs "off-label" for new indications. CODE OF MEDICAL ETHICS, *supra* note 155, at xiv.

This Article asserts that approaching the financing of research in this fashion is likely to fail because it confuses researchers' obligations to specific parties such as research subjects ("relational duties") with their obligations to society as a whole ("regulatory duties"). The Article argues that the relational–regulatory balance in American medicine is unstable, and that the size of the U.S. health care system and the biomedical research enterprise it supports makes addressing that instability a priority for public policy.

Like many regulatory issues involving professions, conflict of interest policy in biomedical research is largely about change and resistance to change. Industrial and social change certainly complicate professional relationships, but change also breeds self-interested resistance that can be rationalized and justified as public-regarding "ethics." Alleging conflict of interest is a common strategy in these situations. The superior alternative for biomedical research is to deal with financial flows as an overall question of research integrity and productivity.

The transition from relational to regulatory governance in biomedical research, as in health care generally, will be a very difficult one. A regulatory approach may be jarring to old school researchers, particularly physicians, who prefer being a "profession" to being a "regulated industry" in terms of control over their work and satisfaction of their material and psychic needs. Consider the following passage entitled "Government in Medicine": "It is not that physicians do not want oversight and open discussion of delicate matters but, rather, that we want these discussions to occur among informed and knowledgeable people who are acting in the best interests of a specific patient. Government regulation has no place in this process."[158] Although it reads as if written decades ago, it appeared in an declaration by the Editor-in-Chief of the *New England Journal of Medicine* on May 24, 2007 categorically opposing both legislative and judicial activity that regulates medical practice.

Problems of relational–regulatory balance are not limited to biomedical research, nor even to health care. They arise frequently in rapidly industrializing sectors of the economy where private legal disputes governed by courts have been liberally supplemented, if not fully superseded, by public legislation and administrative law. Experience with conflicts of interest and incentives in these areas, however, demonstrates the limits of using relational duties to serve broader social interests, as well as the need for substantive regulation.

In the corporate context, for example, the courts have struggled to define a theory of "fraud on the market"—liability for harm to the investing public generally—using simple fraud between one seller and one buyer as a

158. Jeffrey M. Drazen, *Government in Medicine*, 356 NEW ENG. J. MED. 2195, 2195 (2007) (reacting to a U.S. Supreme Court decision upholding a congressional ban on "partial-birth abortion").

starting point.[159] Fraud on the market differs from traditional securities fraud because the damages are suffered in the secondary trading market, with aggregate market losses typically dwarfing any direct transactional gains to the actual perpetrator of the fraud (the corporate issuer). The losers in these situations are purchasers of shares at inflated market prices, while the winners are those who sold to them at those prices, with both parties equally innocent of the fraud and typically unaware of the specific information that was misstated. A successful lawsuit for fraud on the market results in payment to the original losers mainly by the company's current shareholders, who are innocent of the fraud as well. Thus little corrective justice results from the imposition of liability and the requirement of compensation. The only clear benefit is a regulatory one—deterrence of corporate misrepresentation—which improves efficiency of share prices and maintains public confidence in the capital markets. Other corporate law controversies that implicate the relationship between fiduciary harm and social harm include the Sarbanes–Oxley Act[160] and insider trading.

By exploring relational and regulatory duties in the context of biomedical research, this Article intends to flag the larger question of building a system of public accountability on a foundation of relational accountability as well as to shed light on a specific problem in health care. Whether American society relies primarily on a system of relational research ethics (including conflicts of interest) or a system of regulated research ethics

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159. *See, e.g.*, John C. Coffee, Jr., *Causation by Presumption? Why the Supreme Court Should Reject Phantom Losses and Reverse* Broudo, 60 BUS. LAW. 533 (2005); Merritt B. Fox, *Demystifying Causation in Fraud-on-the-Market Actions*, 60 BUS. LAW. 507 (2005). The Supreme Court recently clarified, in a securities fraud class action suit, the relationship between failure to fulfill regulatory duties to the investing public and rights to specific financial recovery by identifiable investors. Dura Pharm., Inc. v. Broudo, 544 U.S. 336 (2005). Fraud on the market liability requires a material misrepresentation, scienter by the misrepresenter, a connection with the purchase or sale of a security, transaction causation (reliance), economic loss, and loss causation. *Id.* at 341–42. In *Dura*, the Court brought the legal theory of recovery, which had become increasingly regulatory, back to its common law relational roots by rejecting an "inflated purchase price" as sufficient proof of economic loss and loss causation, and requiring that a plaintiff allege and prove proximate cause in terms of a connection between the misrepresentation and an eventual fall in value of the plaintiff's shares. *Id.* at 345–46. At the same time, however, the Court accepted the notion that purchase of a widely traded security at market price constituted reliance on public representations of which the plaintiff was not specifically aware. *Id.* at 341–42.

160. Stocks and bonds are conveyed by identifiable buyers to identifiable sellers, with attendant obligations of fair dealing, but these transactions constitute in the aggregate a major determinant of national prosperity and public confidence in government. Donald Langevoort suggests that Sarbanes–Oxley's

> most important effects on business may be less about investor protection per se and more about renegotiating the boundary between the public and private spaces in big corporations, a much deeper ideological issue. The legislation may reflect a political instinct that the incentive structure in the modern public corporation generates risks that require public (not just investor) accountability to be legitimate.

Donald C. Langevoort, *The Social Construction of Sarbanes-Oxley* (Georgetown Law and Economics Research Paper No. 930642, Sept. 18, 2006), *available at* http://ssrn.com/abstract=930642.

(with fewer conflicts of interest) is a matter of substance, not merely semantics. The public duties incumbent upon ethical research have societal rather than individual benefits, and therefore are not amenable to the usual control mechanisms for conflicts of interest. In other words, conflict of interest analysis cannot create the correct incentives to serve "principles" when those goals are not embodied in discrete, identifiable "principals."

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