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Innovation Incentives or Corrupt Conflicts of Interest? Moving Beyond Jekyll and Hyde in Regulating Biomedical Academic-Industry Relationships

Patrick L. Taylor

*Harvard Medical School*

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Innovation Incentives or Corrupt Conflicts of Interest? Moving Beyond Jekyll and Hyde in Regulating Biomedical Academic-Industry Relationships

Patrick L. Taylor

ABSTRACT:

The most contentious, unresolved issue in biomedicine in the last twenty-five years has been how to best address compensated partnerships between academic researchers and the pharmaceutical industry. Law and policy deliberately promote these partnerships through intellectual property law, research funding programs, and drug and device approval pathways while simultaneously condemning them through conflict-of-interest (COI) regulations. These regulations have not been subjected to the close scrutiny that is typically utilized in administrative law to evaluate and improve regulatory systems. This Article suggests that the solution to this standoff in biomedical law and policy lies in an informed, empirical approach. Such an approach must both recognize such partnerships’ legal and practical variations, as well as classify them based on their benefit to innovation and their harm to research biases. Ultimately, this approach must facilitate administrative reforms that would convert what is now an inherently arbitrary, yet widespread, regulatory regime into an epistemically rich mechanism for distinguishing between harmful and beneficial partnerships.

* Assistant Clinical Professor, Harvard Medical School; Director, Ethics Analysis and Applications, and Staff Scientist, Boston Children's Hospital Informatics Program; Former Deputy Counsel and Chief Counsel for Research Affairs, Boston Children’s Hospital. I gratefully acknowledge the influence and kindness of Professors Glenn Cohen and Benjamin Roin of Harvard Law School, Deans Gretchen Brodnicki and Margaret Dale of Harvard Medical School, Drs. Isaac Kohane and Ken Mandl of Harvard Medical School and Boston Children’s Hospital, and colleagues among the Fellows of the Petrie-Flom Center for Health Law Policy, Biotechnology, and Bioethics at Harvard Law School. I would also like to acknowledge the many scientists I have known closely over many years, as clients, friends, or occasionally antagonists, whose very diversity made manifest the central themes of this Article. This work was supported and made possible by a post-doctoral fellowship at the Petrie-Flom Center from 2010-2012.
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INTRODUCTION

For several decades there has been a close and productive working alliance between universities, research institutes, Government agencies, and private industry in the area of biomedical research. These relationships were enhanced significantly during the 1980's through new laws and regulations that improved the collaborative environment for research and innovation among Government and industry laboratories and the nation's research institutions. This partnership was strengthened by powerful incentives designed to encourage development and commercialization of innovative technologies initially discovered during Government-sponsored research. . . . These goals have largely been achieved. America leads the world in biomedical research and innovation through the transfer of technology spawned by these policies.  

[T]here is no conceivable social benefit in researchers’ having equity interest in companies whose products they are studying.2

The IOM committee is not familiar with any evaluations of the implementation or the consequences of different [conflict of interest] management strategies. This is a significant deficit.3

Medical innovation depends on academic discovery partnered with private sector corporate action, to translate novel science into practical applications. No longer may academic medical researchers simply labor in isolation for knowledge’s own sake, producing glowing abstractions from the Ivory Tower’s cocooned interior. Now, American society asks that researchers invent and that their inventions be available as cures. “Where are the cures?” is not just a headline,4 but an expression of a common expectation. The law reflects this

4 See, e.g., Sharon Begley, Where Are the Cures?, NEWSWEEK (Nov. 1, 2008), available at http://www.newsweek.com/2008/10/31/where-are-the-cures.html; Mary Carmichael & Sharon Begley, Desperately Seeking Cures—How the Road from Promising Scientific Breakthrough to Real-World Remedy Has Become All but a Dead-End, NEWSWEEK (May 15, 2010), available at
expectation by creating rewards for academic-industry collaboration and requiring compensation to be distributed accordingly. And this policy works; as incentivized collaboration streams inventions from academia to industry, this country’s biotechnological development booms.

Yet in the midst of this biotechnological wealth, critics abound. Professional leadership within organized medicine condemns industry affiliations across the board, implying that professional virtue can never be reconciled with innovation economics. Headlines involving research gone awry imply that nefarious financial incentives cause research trials to be unsafe. Medical journals dutifully aggregate author disclosures of industry payments, giving no attention to their potential variety and treating the cumulative number of these payments as irrefutable evidence of corrupted judgment. Such approaches treat all academic-industry partnerships as corrupt, without identifying those forms that genuinely contribute to innovation with reasonable terms calculated to avoid unmanageable research bias.

In short, society promotes collaboration, yet also despises it. The federal government requires institutions to regulate conflicts of interest through general standards of unresolved ambiguity, through an isolated mandate that is disconnected from procedures to address research integrity, protection of human and animal research participants, and professional obligations to patients. Yet these regulations give no weight to the need for innovation or what drives it. At the same time, in the distinct arena of technology transfer and tax credit, the law incentivizes biomedical researchers to engage with industry, but neither provides clear ethical constraints nor requires practical accountability to identify and address the potential harms to patients or science that could be produced by these conflicts of interest (COIs). The law promotes researchers’ active involvement in sharing knowledge with companies, but, in the name of transparency, or “sunshine,” the law requires disclosure of nominal payments, without explanation of the purpose or context, as if this fact alone would conclusively establish an improper relationship. It is apparent that the values of the academic scientific community—such as sharing data and discoveries—are at war with proprietary standards. Yet private and academic institutions continue to fuel these conflicts.

http://www.newsweek.com/2010/05/15/desperately-seeking-cures.html (observing that “judging by the only criterion that matters to patients and taxpayers—not how many interesting discoveries about cells or genes or synapses have been made, but how many treatments for diseases the money has bought—the return on investment to the American taxpayer has been approximately as satisfying as the AIG bailout”).

6 See generally Madey v. Duke Univ., 307 F.3d 1351 (Fed. Cir. 2002) (construing narrowly the common law research exception for academic and other research within the scope of patent rights and discussing the growing industrial role of universities given the title transfer and other provisions of the Bayh-Dole Act, 35 U.S.C. § 202(c)(4) (2000)). For an account of academic medicine’s reliance on Bayh-Dole to justify COIs, together with cogent arguments against its actual
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This fierce, internal battle in innovation and research policy calls for careful reconciliation of the competing goals at issue along with precise management. Instead, COIs arising from industry-academic relationships are subject to decentralized institutional management under federal standards so incomplete and vague that they are impossible to apply consistently. The federal standards require risk assessments, which adjudicators on COI committees can make only by relying on often idiosyncratic, personal assumptions about human behavior and incentives, which vary among institutions and committee members, and have not been evaluated for their generalizability. The resulting range of COI “management plans” has never been systematically evaluated for either its efficacy or its necessity. No mechanism exists to reconcile precisely the values and laws constituting the “innovation ecology,” whether in COI policymaking, in adjudicating and managing COIs, in licensing academic intellectual property to industry, or in creating academic-industry relationships. Currently, the regulatory system pays no heed to the benefit provided by innovation, fails to assess which compensated academic-industry relationships genuinely contribute to innovation, and lacks any factual basis to assess actual risk of bias. In this way, current regulations are unresponsive to the realities of both academia and the biotech industry. Current regulations also fail to establish basic requirements that would allow adjudications and policies to be consistently and soundly executed. Thousands of independent adjudicators, with no required qualifications, operate under an ambiguous standard. Their job is to identify collaborations that create bias risk; yet they have no empirical basis for doing so. Administrative law usually nests such tasks within a context of records, rights, and appeals, but this is not the case with these COI regulations. There is no mechanism for adjudicators to test their judgments with concrete evidence, correct themselves,
or contribute epistemically to the body of case law. So operationally incomplete are these regulations that it will be useful to compare them and the conduct they set in motion to jurisprudential accounts of which enactments really qualify as "law"—including such basic concepts as whether regulations provide sufficient notice or can even be obeyed. Those accounts set standards, which current regulations fail, for what a legal regulatory system concerning COIs would minimally entail. 8

Descriptively, this Article claims that current health policy fails to reconcile tensions that arise from its encouraging innovation through academic-industry collaborations, while simultaneously sanctioning these partnerships for their potential impact on research integrity. Policy mandates to work together do not distinguish those innovative collaborations, which could generate research bias, from beneficial ones. Furthermore, the administrative structure for COIs in this field demands guesswork about research harm and fails to distinguish between academic-industry partnerships on the basis of their innovation potential or the diverse nature of their contractual terms. These flaws render the regulatory structure inadequate, under general administrative law standards, and ineffective, in executing the specific task of distinguishing socially beneficial collaborations from destructive arrangements. Normatively, this Article claims that society may arrive at a better reconciliation of the competing imperatives of research integrity and biomedical innovations by precisely distinguishing among such collaborations—on the basis of their purpose, terms, and structure—and strengthening the form and factual basis for administrative regulation.

This reconciliation can occur by framing the choices facing these COIs in clear terms, rather than obscuring these challenges with an abstract demand for scientific independence that no longer comprehensively characterizes social expectations for research. With better data about which collaborations foster bias and which actually contribute unique scientific talent to the innovation process, regulation could be precise, predictable, factually founded, and reflect a conscious societal choice among potentially competing values. The key goals of this Article are thus: (1) to understand the basis for sound regulation and safe harbors, rather than grounding a system in ad hoc prohibitions relying on factual uncertainty; and (2) to establish default rules that lead us towards a greater understanding of what an optimal legal system would require to conservatively avoid human harms. The point is not to abandon virtue by permitting conflicts of interest. Rather, the goal is to reconcile our account of ethical research with social expectations by taking into consideration the likely effects of contractually

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distinct collaborations discerned from aggregate data. This factual account, however, requires adopting an evaluative stance less governed by the currently venerable, but incomplete, account of scientific virtue.

This Article proceeds in three parts. Part I focuses on COIs, their source in legal mandates for collaboration, their consequences, and their variety. While collaboration is inevitable, COIs are not. The standard inference from COI cases—that all collaboration must be avoided to prevent COIs—is therefore mistaken. Even when an improper collaboration incentive is identified, it is of little help in deciding whether other forms of collaboration should be suspect. Many variables pertaining to the context, purpose, and structure of collaboration arrangements can materially affect intuitive judgments about COI risk.

Part II focuses on regulations. It starts with a basic query: Are United States regulations well-equipped to address the nuanced differences among diverse collaboration arrangements? Since collaboration mandates and programs do not address COI risk, the focus of this query is the two main regulatory approaches to COIs advanced by the Food and Drug Administration (FDA) and the U.S. Public Health Service (PHS), a component of which is the National Institutes of Health (NIH), as well as the self-regulatory structure offered by the Association of American Medical Colleges (AAMC). To a student of administrative law, these regulatory structures will be like visiting the land that time forgot: so conspicuous is the absence of even rudimentary forms of administrative accountability and control. To highlight the point, Part II assesses the effectiveness of these systems through the perspectives of the jurisprudential categories proposed by Cass Sunstein and others. Ultimately, Part II shows that the regulatory proposals fail to attain their own goals, apart from the socially necessary goal of situating COIs in an innovation ecology that optimizes competing values.

Part III categorizes and discusses perspectives on COIs from the business and legal literature. Despite the merits of this literature, none of it recommends an empirical basis for COI management. Like the current regulations, the literature does not distinguish among collaborations on the basis of whether they make actual contributions to innovation or whether the arrangements find ways to minimize research bias while maximizing innovation value. The primary value of the existing literature is that it illustrates the limits of a nonempirical approach, with its energy spent on warring accounts of scientific virtue that yield no practical recommendation to reconcile collaborations’ innovation and COI

9 In Kwame Anthony Appiah, Experiments in Ethics (2008), Appiah argues that, henceforth, no account of human virtue should be ungrounded in the lessons of behavioral economics and other empirically demonstrable patterns of human thinking. Only then can virtue ethics—as an account of the ideal human life leading to happiness—fulfill its practical promise to make people both virtuous and happy.

10 See generally Sunstein, supra note 8 (contrasting perspectives on various forms of legal reasoning).
values.

Throughout the Article, I will build on the intuition that the very existence of a COI turns more on the terms, purpose, and context of academic-industry arrangements than on the simple fact of the industry-to-scientist payments to which most regulations attend.

I. ARE CONFLICTS OF INTEREST NECESSARY?

Financial conflicts of interest are not inherent to the research enterprise. They are entirely optional, unlike intellectual or personal conflicts of interest to which they are often compared. 11

Conflicts of interest are ubiquitous and inevitable in academic life, indeed, in all professional life. The challenge for academic medicine is not to eradicate them, which is fanciful and would be inimical to public policy goals, but to recognize and manage them sensibly and effectively. 12

A. Collaboration is Necessary and Unavoidable

Both industry and government are indispensable players in biomedical research and development. Collaboration is a necessity, for reasons that are economic, historic, and legal, and it is important to understand why this is the case.

Biomedical research is divided into stages, from basic inquiry to research directly involving human beings or their identifiable data. Approximately $30.9 billion was budgeted by the U.S. government for NIH funding for the fiscal year 2012. 13 Most of these dollars are allocated to basic scientific research (e.g., the stuff of petri dishes, signal transduction pathways, model organisms, novel chemical reactions, etc.); the remainder is for clinical (biobanking, biomarker diagnostics, novel surgical procedure development, etc.) and public health research (e.g., infectious disease preparedness, epidemiology of obesity, pervasiveness of self-destructive behaviors in the United States, etc.). 14 However,

12 David Korn, Conflicts of Interest in Biomedical Research, 284 JAMA 2234, 2234 (2000).
14 NIH funds are awarded through a highly competitive application process spelled out in a continuously updated, publicly available constellation of policies called collectively “grants policy and guidance,” together with refinements specific to a given program or funding opportunity publicized by the NIH. Applications can be found on the NIH website. NIH Office Of Extramural Research, http://grants.nih.gov/grants/oer.htm (last visited Dec. 2, 2012). For a
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it takes much more to turn basic science into diagnostics and therapies. Translating discoveries into products that are safe and effective for human use, and making those products available, necessarily involves private industry.

Reflecting the growing demand for drugs, industry sponsorship of biomedical research (including payments to academic researchers) has increased exponentially in the past two decades. One widely cited authority estimates that, between 1980 and 2003, such expenditures by U.S. pharmaceutical companies increased from $2 billion to $33 billion.\(^{15}\) Even if such figures are overstated,\(^{16}\) there is no question that industry funding for research, development, and influence over physicians and scientists, collectively, matches or exceeds government funding for biomedical research. Its rate of increase far surpasses the rate for government spending (calculable from the sources cited) in which inflation offsets, in real terms, the modest numerical increases over time. This industry spending helps sustain a pharmaceutical market that exceeds $200 billion per year in revenue in the United States alone.\(^{17}\)

formal, technically accurate, and binding set of official policies governing applications post-award management, see, NIH Grants Policy Statement, NAT' L INST. OF HEALTH (Oct. 1, 2012), available at http://www.grants.nih.gov/grants/policy/nihgps_2012/index.htm. The application requires a detailed discussion of the importance of the general research background and focus, hypotheses, research aims, methods to be employed, qualifications and competencies, and resources available. Importantly, the grant application need not identify for reviewers conflicts of interest or contractual commitments to third parties, which could affect the selection of the research problem, the design of the research, its conduct, data analysis, and reporting. If awarded, the money will come with certain conditions. As far as the scientist is concerned, there will be data-sharing mandates of varying force and specificity. There must also be a promise that, if there is an invention from the research, the institution will promptly disclose it to the NIH, elect whether to hold the title and seek to develop the invention through, for example, patenting it and then licensing it to companies. In return, at least 15% of the net revenue goes to researchers. Notably, for NIH-funded research, a scientist maintains modest discretion to stray from the project proposal during the discovery process. It is understood, and, indeed expected, that initial discoveries will lead to novel hypotheses and therefore novel experiments, using methods that cannot be specified in the application in advance. This also means, of course, that the researcher has discretion to reallocate, within reasonable limits, proposed expenditures that were used to justify an initial budget request. Thus, a scientist has professional discretion to deviate from the description of a proposed project that merited an award, in a system that itself promotes COIs through the revenue-to-inventor process. Furthermore, peer reviewers are not aware of any past, present, or future COIs arising from a scientist's economic stake in licensed patents from previous or concurrent federally funded research. There is no COI review at the application review stage.

\(^{17}\) Id. A company will wish to contractually commit a researcher to a definite course of research. The company then will claim for its own use the resulting intellectual property without necessarily sharing or developing it, and it will keep all data confidential, keep a researcher to a budget that is both justified and well defined, and focus on research aims that have a direct bearing on its business venture. If the sponsored research is clinical, then it is almost certain that the company is pursuing it in support of an application to the FDA to permit marketing of a diagnostic
Human testing is most often funded by industry, in connection with private companies exercising their rights and obligations under FDA regulations as “sponsors” of an application for approval to market a novel diagnostic or therapy.\textsuperscript{18} FDA approval depends on data supporting safety and effectiveness through favorable outcomes in clinical research studies that are often large-scale, expensive, and uncertain. Sponsors’ functions, such as establishing manufacturing facilities, independent trial monitoring, and sales networks, are far removed from typical academic functions. Thus, while the law does not prohibit academic investigators from being sponsors, and while novel therapies may start this way, in practice industry involvement is essential and almost universal. Yet the reliability and disinterestedness of clinical research is important in evaluating results from clinical trials. For this reason, those who conduct clinical research, termed “investigators,” are often academic researchers paid by industry for their research.

This simple fact is at the core of the COI problem. Academic researchers are key players in research and development. Universities and academic hospitals are the main progenitors of biomedical discovery, and they are necessary at every stage of knowledge and product development, up to and including studies to test products’ safety and efficacy on human beings. Eliminating all industry payments to academic researchers is neither practical nor desirable. The result would be industry assessing the safety and efficacy of its own products—hardly an increase in disinterestedness!

Other government policies also reflect public expectations that academic scientists involve themselves directly with industry and industry projects. First, under the “NIH Roadmap” or “translational research initiative,”\textsuperscript{19} an increasing amount of government funds will be spent on connecting the dots among basic research, the translational research that will lead to human applications, the clinical research on human participants to test safety and efficacy, and the resulting health care products. These products will, in turn, enable health care


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reforms in a process interwoven with industry partnership.

Second, the need to accelerate the development and distribution of therapies for AIDS led to special regulatory provisions for rapid approval and treatment access outside traditional clinical research protocols. However, decreased evidentiary review before human use means fewer opportunities to detect errors. Pressure to approve potential cures means, at the least, less incentive to question trial design or conduct, and perhaps even affirmative pressure to take a permissive approach (especially given the agency’s funding through user fees).

Third, a bundle of interrelated initiatives explicitly allows the FDA to approve drugs by relaxing standards that it might otherwise apply. For example, the FDA might permit a company to condense its clinical trial sequence into two phases (rather than the three or four phases normally required by regulation) or accept as sufficient data showing efficacy within shorter endpoints than it might otherwise demand. This policy is, and ought to be, controversial, for the practical impact might be the approval of a drug whose short-term or long-term effectiveness and safety is uncertain or whose effectiveness in one clinically defined sense might be rebutted by a narrower or broader description of the objectives of the trial. If a COI affects trial design decisions and approvals proposals, the potential consequences are significant.

Fourth, another incentive structure, designed to reward previous research and inventions, may also create COIs for future research. The 1980 Bayh-Dole Act, a cornerstone of innovation policy, revolutionized academic-to-industry knowledge transfers. Academic institutions may retain title to inventions


21 See generally Shulman & Kuettel, supra note 20.


23 Post-approval review does not resolve these COI-related concerns for three reasons. First, the FDA’s post-marketing surveillance and review is historically deficient and is still weak, as reported in the General Accountability Office’s most recent survey. See U.S. GOV’T ACCOUNTABILITY OFFICE, GAO-10-68, DRUG SAFETY: FDA HAS BEGUN EFFORTS TO ENHANCE POST-MARKET SURVEILLANCE BUT ADDITIONAL ACTIONS ARE NEEDED (2009), available at http://www.gao.gov/new.items/d1068.pdf. Second, in post-approval review, as in pre-market approval, the FDA is still dependent, in whole or in part, on researchers. If these researchers are non-industry academics, they are the very individuals whose COIs we are examining. Third, these two regulatory pathways are intended to address the needs of people who are gravely ill, or the safety characteristics of drugs whose accelerated approval ought to be uncontestable. Neither category would be well served by postponing evaluation of any effect of COIs until after patients and consumers have started consuming the drug to their detriment.

24 Bayh-Dole Act, 35 U.S.C. §§ 200-212 (2006); 37 C.F.R. § 401 (2012) (regulations associated with the Bayh-Dole Act). The Act (also called the Patent and Trademark Law Amendments Act) grants recipients of federally funded research grants and contracts, such as universities and research hospitals, the right to take title to intellectual property rights in any inventions that arise in the course of the federally funded research, provided that they are able to accomplish the following: (a) act diligently to protect the discovery, such as through patent filings
arising in the course of federally funded research, if, among other things, they actively seek to license the invention to the private sector for development, and if resulting net revenue is split between the academic inventors and the institution’s educational and research purposes. Thus, the Bayh-Dole Act mandates that an inventive scientist share in a discovery’s resultant revenue, if research and development confirm its potential value as a product. This would cause no COI if the inventing scientist then switched fields. But if, as is likely, the scientist continues to perform research in the same field, the potential profit stream from the discovery will readily create two forms of COIs. The first is in selecting research topics: a financial interest in confirming, perfecting and supplementing the licensed invention conflicts with exploring discoveries that would compete with it or break novel ground. The second reflects the scientist’s financial interest in producing results consistent with the prior discovery’s marketing.

Notably, none of these policy initiatives addresses the obvious potential they create for COIs. There are no requirements that collaborations be structured to avoid COIs, let alone parameters or safe harbors that might aid that purpose. In both regulation and academic discussion, two worlds emerge, instead of one. To create an integrated world, it is imperative to understand the source of potential conflict between legal imperatives for academic scientists to collaborate and other norms for academic scientists.

B. Collaborations Gone Bad: Individual Cases and Statistical Associations

Three influences have grounded COI policy to date, and it is important to distinguish among them. The first influence is a set of professional values, originating in an era before innovation policy started to demand or incentivize academic-industry collaboration. It is primarily leaders of organized biomedical science that articulate these professional norms, including independent judgment, fiduciary duties to patients, and exclusivity for physicians in making health care judgments; these are often portrayed as values under siege. These are the same values that led, in an earlier time, to legal doctrines rejecting the corporate practice of medicine, and, in modern times, to the medical profession’s steadfast opposition to managed care, corporate forms of quality assurance, and integrated care. After having notified the agency funder of that intention; (b) actively seek to license its use by the private sector in a reasonable way that will promote public benefit; (c) return some of the net proceeds to the inventor(s); and (d) devote the balance of net proceeds to education or research. Previously, the agency funders took title, and few transfers of discoveries to industry for development occurred. Bayh-Dole was designed to incentivize academic inventors to invent, institutions to license to industry, and for both academia and industry to form enduring collaborative relationships through which academic discoveries could flow through industry to the public.

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delivery systems. This value scheme teaches complete separation from industry, regards industry as quintessentially unable to make medically informed and disinterested research judgments, and prohibits all industry contact as inescapably threatening to the independence and integrity of physicians and scientists.

The separation must be even stricter for academic scientists and physicians because of their role as creators and guardians of knowledge. Physicians and scientists who work for corporations legitimately focus on advancing corporate goals, and physicians in private practice may practice for a profit. But academic scientists have superseding ethical obligations to research participants, present and future members of the academic community, research funders, and the public at large. Their work must reflect values essential to the credible advancement of knowledge — integrity, competence, objectivity, transparency, and reliability in the discovery process, as well as respect for human and animal research participants—that trump competing concerns, including economic ones. These values are reflected in sources as diverse as the Internal Revenue Code, policy manuals and regulations of the NIH, associational guidelines, and institutional


27 The medical literature by professional leaders is rich with debate in these terms. For leading examples of what I will call the “Virtue-Prohibitionist approach,” see JOHN ABRAMSON, OVERDO$ED AMERICA: THE BROKEN PROMISE OF AMERICAN MEDICINE 120–21 (2004); ANGELL, supra note 16, at 115–34; JERRY AVORN, POWERFUL MEDICINES: THE BENEFITS, RISKS, AND COSTS OF PRESCRIPTION DRUGS 292–94 (2004); and Jerome P. Kassirer & Marcia Angell, Financial Conflicts of Interest in Biomedical Research, 329 NEW ENG. J. MED. 570 (1993) (analyzing the effects of financial conflicts of interest on biomedical research and critiquing the policies used to handle disclosure of such conflicts); see also Troyen A. Brennan et al., Health Industry Practices that Create Conflicts of Interest: A Policy Proposal for Academic Medical Centers, 295 JAMA 429 (2006); Catherine D. DeAngelis, Editorial, Conflict of Interest and the Public Trust, 284 JAMA 2237 (2000) (introducing articles addressing the prevalence of conflicts of interest between physicians and companies that financially support teaching and research, along with the effects of this relationship on public trust of physicians). But for leading contrarians who argue that industry relationships should be cultivated as essential and beneficial, see William M. Sage, Some Principles Require Principals: Why Banning “Conflicts Of Interest” Won’t Solve Incentive Problems in Medical Research, 85 TEX. L. REV. 1413 (2007); Thomas P. Stossel, Regulating Academic-Industrial Research Relationships – Solving Problems or Stifling Progress?, 353 NEW ENG. J. MED. 1060 (2005).


29 See, e.g., Update on the Requirement for Instruction in the Responsible Conduct of Research, NAT’L INST. OF HEALTH (Nov. 24, 2009), http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-019.html (discussing mandate for training in research integrity and the responsible conduct of research, with links to other government resources detailing the required topics); Taylor, supra note 25, at 398–401 (noting that researchers’ legal data-sharing obligations are related to fundamental ethical norms of science, reinforced by ethical force of promises of social benefit made to research participants and research review boards).
charters and policies. Academic scientists are expected to be in a position to collaborate with private interests, but they must do so without putting personal profit before the values espoused by their profession. This common sense approach stands in stark contrast to the more extreme demands of some medical leaders, which require complete disengagement from financial ties.

The problem is that public expectations and government policies no longer permit a full account of professional virtue to exclude industry engagement. To the contrary, according to both public expectation and policy changes, a virtuous scientist is one who will engage with industry to bring a discovery to useful fruition, yet retain her scientific independence and good judgment. This is law’s ethical challenge to physicians and scientists.

If not overgeneralized, the other two forms of influence on COI policy provide some evidence that COIs can cause research lapses. First, there is a small set of publicly noted COI cases whose specific facts purportedly support broad conclusions about the negative effect of any industry relationship. Second, analyses and meta-analyses demonstrate correlations between scientist behaviors and industry relationships across populations, such as the statistical association between positive industry sponsorship of clinical trials and published positive trial results. Both forms of influence are contested, principally on the grounds that research mishaps in these publically noted cases are due to factors other than concurrent COIs and that population-based conclusions are best explained by other variables. To evaluate these conflicting claims, it is essential to understand the nature of biomedical research and the opportunities for bias it presents.

C. The Nuts and Bolts of Biomedical Research

Regulatory approval by the FDA is not based on a complete understanding of human biology or a universalized biochemistry. Instead, FDA approval depends on artfully designed experiments to demonstrate safety and effectiveness by showing that X is better than nothing for treating Y, with no other variables confounding the results, as measured at particular times and with specified measures.

From the framing of hypotheses to the analysis and publication of results,
the research process is filled with strategic and tactical judgments about how a scientific question is best answered. Such discretionary choices can be plausibly defended, even when they might also appear as necessarily intended to misrepresent, or inadvertently biased. In the notorious Vioxx debacle, for example, Merck researchers had knowingly deleted three heart attacks that occurred after a designated date end point. If those data had been included, the Vioxx safety and efficacy analyses would have changed dramatically. This deletion was discovered only because electronic editing traces remained. When revealed, the changes allegedly were justified by the general principle that one should not manipulate endpoints. Regardless of the legitimacy of Merck’s rationale, this case illustrates the power of even one study parameter (out of many) to affect the manner in which results and their implications are portrayed.

Biomedical research is ideally a combination of inquiry focused on a well-defined question, using methods precise enough to control confounding variables, and complemented by thoughtful, thorough analysis and sound inferences. Biases often are associated with incorrect inferences, but biases go much farther. Biases in a scientific study may be errors of selection (e.g., in defining comparative groups), differences of measurement (e.g., perception differences or instrument use), or intervention (e.g., systematic differential treatment signals). Some biases can be prevented easily, provided the study structure does not thereby become unethical. Thus, selection bias otherwise affecting participant selection in a clinical trial, or participant-researcher signaling, can be overcome by randomization and double-blinding. However, these are not always ethical choices for ill participants for whom one research arm is less than the standard of care. Some biases, such as those that affect the selection and formulation of a scientific question, or biases that permeate every stage of a study, may be very difficult to detect.

There are two kinds of evidence that COIs may create biases that affect outcomes. First, scholars have noted a number of notorious cases of research misconduct involving financially motivated investigators or institutions. David Blumenthal, for example, describes how a research fellow at the Massachusetts Eye and Ear Infirmary “benefited substantially from selling his holdings in a private company established to market a new drug he was testing in clinical


34 Consider a trial in which participants receive either a placebo or a test drug; it would be unethical to enroll seriously ill patients who would otherwise receive a moderately effective standard treatment.

35 See Hartman, supra note 33.
In these cases, proof of wrongdoing is perceived as proof of the influence of financial incentives.

A second kind of bias is subtler. Misconduct coexists with a financial interest, but the interest is not actually advanced through the misconduct, nor can one find unambiguous evidence that the financial interest was the sole, or even a "but for," cause of harm. In a widely publicized case, a young volunteer, Jesse Gelsinger, with an effectively treated congenital liver ailment, died in a phase I gene therapy trial following a massive immune response to the viral vector used. This clinical research trial was filled with mishaps, including a miscalculation of the risks, trial design errors, and flawed and untimely reporting of adverse events involving other participants. In addition, the decision to conduct the phase I trial using healthy volunteers became controversial, given the trial's substantial risks. A more accurate assessment of the risks might have led to a decision to restrict the trial to those for whom existing therapies had failed—unlike Jesse, whose condition had been stable prior to the research study.

Yet while these risk assessments were noted, it was not these factors that captured the attention of Jesse Gelsinger's father and the public. Rather, it was the fact that the investigator and the University of Pennsylvania had a substantial equity stake in the company owning the rights to the therapy being tested. Reporters focused on this collaboration, even though it is not clear that financial interests were pertinent to the clinical wrong that occurred. For example, there was no "smoking gun" evidence ever connecting dollars to improper shortcuts. Still, the financial relationship seemed to provide, in a single phrase, a simple explanation for how so much could have gone so wrong, through an imputation

37 Brian Deer, How the Vaccine Crisis Was Meant To Make Money, 342 BRIT. MED. J. 113 (2011).
39 See, e.g., Patricia C. Kuszler, Biotechnology Entrepreneurship and Ethics: Principles, Paradigms, and Products, 25 MED. & L. 491, 495 (2006) ("[L]apses in human subjects protection remains an ever-present hazard. This has been exemplified by a series of high profile research ethics scandals in the U.S.—the Jesse Gelsinger case in which a research subject in a gene-therapy experiment died and it was alleged that the researchers' financial interest in the vector influenced them to prematurely engage in the clinical trial that resulted in Mr. Gelsinger's death.").
of bad character and overwhelming profit motives. Unlike the first kind of misconduct case described above, the investigator and institution would have gained if the therapy had been effective, but instead gained nothing from the errors and flaws.

Some industry proponents of academic partnerships argue that financial relationships are seldom a material cause of misconduct and that in almost all cases financial associations are absent or accidental. On its face, this is an illogical argument, suggesting that from cases not involving financial interests one can learn something definitive about the causal role of financial interests in cases that do. Importantly, this contention also overlooks the first type of case mentioned, where the form and evidence of misconduct in fact demonstrates the salience of financial objectives. It is true that many cases of “bad science” or participant harm do not involve financial COIs. But this fact alone does not prove that the law and policy should not address financial COIs where they give rise to improper incentives. This argument suggests only that there are other sources of error beyond financial COIs.

Institutions need not accept this all-or-nothing characterization of the potential for financial COIs to negatively impact research integrity, any more than they need accept an all-or-nothing answer to the question of whether industry payments to scientists contribute to innovation. Both questions have


42 The second kind of case has attracted particular attention because of the special delegated authority to manage COIs entrusted to both academic institutions and industry trial sponsors, to which we shall return in discussing the regulatory structure. Can institutional committees perform this function responsibly and fairly when, through its financial or intellectual property arms, the institution has invested in the success of the tested technology or its corporate licensee or sponsor? No one really knows the answer to this question or, more precisely, the variables on which an affirmative or negative answer may depend. While there are many scandalous cases of institutions acting on such interests to defeat academic values, there are also many cases in which institutions have exercised bad judgment without financial investments in a sponsor. Thus, there are cases like that of the Hospital for Sick Children in Canada, which hounded Dr. Nancy Olivieri for her release of negative trial data, which a financially close sponsor had sought to suppress. See David Nathan & David Weatherall, Academic Freedom in Clinical Research, 347 N. ENG. J. MED. 1368 (2002). On the other hand, there are cases like Oklahoma’s suppression of problems with a test melanoma vaccine, in which both the IRB chair and investigators, without such a financial interest, sought to avoid telling participants the truth about adverse effects and directly interfered in procedures. See Mark Barnes & Patrik S. Florencio, Financial Conflicts of Interest in Human Subjects Research: The Problem of Institutional Conflicts, 30 J.L. MED. & ETHICS 390 (2002). And surely, there are uncounted cases in which institutional investments are in effect walled off from review committees like IRBs, either through deliberate confidentiality or simply by the entropic force of administrative siloing within complex organizations, which is a daily feature of academic life.

43 For extensive, balanced discussion of cases of research misconduct disassociated from industry relationships, see Susan M. Kuzma, Criminal Liability for Misconduct in Scientific Research, 25 U. MICH. J.L. REFORM 357 (1992).
empirical dimensions that have not been explored. Isolated instances of harmful COIs are useful to raise public awareness, but they are neither numerous nor sufficiently diverse enough to ground all COI policy.

What makes the argument for some form of COI regulation compelling is not these isolated cases, but rather reported patterns of association between academic-industry collaboration and industry-favorable outcomes, such as above-average positive results for published industry-sponsored clinical trials compared to government- and non-profit-sponsored trials. In addition, the deeper insight that research is filled with discretionary judgments, which financial interests may conceivably influence, cannot reasonably be ignored. Finally, there is the interesting fact that, while the pharmaceutical industry has demonstrably succeeded in influencing researchers and physicians to some extent, the industry’s tools for achieving influence are few and selective. In short, the most interesting fundamental fact is that data indicate an incomplete association, suggesting that further analysis would reveal patterns worth exploring empirically for their differential assessment and remediation.

To address each of these points individually, first, research bias is often subtle. Compare this to discretionary prescribing of approved drugs for off-label uses, in which even small gifts can induce physicians to write these prescriptions, through the generation of good feeling and perhaps an unconscious desire on the part of the physician not to disappoint a pharmaceutical representative. This is not an outright quid pro quo exchange, as those affected are often completely unaware of this influence. Notably, no comparable study exists to assess the impact of COIs on research across a population.

Second, industry has been selective in how it pays for influence. Some of the most egregious examples of bias arise from the arrangements that are most lacking in academic contribution to innovation: speakers’ bureaus, in which a hired physician delivers an industry-prepared, pro-product talk for a significant stipend; ghostwritten manuscripts of industry-favorable clinical trial reports or articles in reputable journals to which physicians or scientists attach their name and reputation; studies that are so biased in design they would not pass independent scientific review; and reports of data that misrepresent clinical trial results to such an extent that the real conclusions oppose those that the company wishes to represent as truth. These examples confirm the reality that some such arrangements are negative, while at the same time highlighting the need to distinguish positive from negative collaboration arrangements.

Third, there is extensive literature concerning bias in reporting and publishing data, which demonstrates that industry sponsorship is correlated,
albeit incompletely, with positive reported findings and a systematically disproportionate number of proindustry publications. These biases are in part correlated with scientific journals’ own financial interests in reprints and advertising. Advocates for industry have argued that this is because industry wisely selects potential drugs and test compounds before commencing costly clinical trials. But studies demonstrate, in some cases, significant industry suppression of data relevant to safety-and-efficacy determinations. Indeed, some sponsors’ reports to mandated public trial result registries show, even across small samples, inconsistent data, and data deviations between published reports and registry information from the same sponsors. Finally, apart from industry relationships, overwhelming evidence links scientists’ personal stake in invention proceeds to delayed publication and reduced data sharing. But “links” is a soft term, denoting an incomplete association; thus instead of demonstrating that all academic-industry collaborations are venal, this evidence, too, invites us to discover the circumstances in which the association is strong and the circumstances where the association is weak or nonexistent.

The conclusion one ought to draw is not that all academic-industry collaborations should be avoided because all involve a conscious lapse from academic independence. It is, rather, that there are grounds to distinguish among collaborations. Some, like speakers’ bureaus and ghostwritten manuscripts, should be prohibited because of their obviously minimal contribution to innovation as weighed against their contribution to bias. Grounds for regulation of others exist to the extent that financial interests may, if improperly structured, operate on any medical researcher, consciously or unconsciously, to short-circuit ethical standards and technical quality, rather than reinforcing these values.

Addressing the moral hazards of these incentives is not an impossible task, but is merely one that is unfamiliar to biomedical researchers and doctors. Compare a familiar, time-tested and ubiquitous example: customers pay construction contractors a certain amount up front, but they make final payment contingent on satisfactory results. In medical research this is an incurable COI. In construction it is not; it is a desirable, routine incentive to drive high-quality results. Of course, research is not construction. But both share a reliance on


48 See, e.g., Fiona Godlee & Elizabeth Loder, Missing Clinical Trial Data: Setting the Record Straight, 341 BRIT. MED. J. c5641 (2010) (editorial introducing a British Medical Journal volume with a cross-section of pieces devoted to this subject); see also Benjamin Djulbegovic et al., The Uncertainty Principle in Industry-Sponsored Research, 356 LANCET 635 (2000).

49 Kerry Dwan et al., Comparison of Protocols and Registry Entries to Published Reports for Randomised Controlled Trials, 19 COCHRANE DATABASE SYST. REV. 1 (2011).

50 Eric G. Campbell et al., Data Withholding in Academic Genetics: Data from a National Survey, 287 JAMA 473 (2002); Taylor, supra note 25, at 398–401.
trusted expertise at every stage of an elaborate step-by-step process. They also share standards governing every stage whose primary focus is on how to make professional choices. It is primarily through the internalization of these standards by professionals in the field that they are given force. Violation of these standards can lead to misdeeds and abuse of trust in research, the death of research participants, and in construction, for example, a fire-resistant building that is consumed by flames in an instant. Institutions use externally codified standards and inspections to address the moral hazard of result-dependent payments, and they scrutinize payments that would induce corner cutting. The law provides homeowners with special rights in case a deal with a contractor goes wrong, and it strives to increase transparency in these relationships. This approach should inform our debate about industry-academic COIs in health care, as well.

As noted earlier, there are no data documenting management of COIs, an absence that ought to signal that academic and industry biomedical research has built a regulatory structure without a factual foundation. Yet, already datasets are available that, if correlated, could provide important insights into how the structure of incentives, compensation, and other terms affect whether a particular collaboration reinforces quality standards or undercut them. COI evidence should lead us to explore the variety of ways in which collaborations may be structured and the richness of terms that may be material—both to actual value in promoting innovation and negative influence on research integrity. Perhaps surprisingly, current literature on COIs fails to describe this existing array. The next Section suggests ways in which this gap may be filled.

D. Context, Terms and Structure: Collaboration Variables Material to COI Regulation

The argument thus far traces two unreconciled imperatives: that academic scientists and physicians must collaborate with industry and that they must avoid conflicts of interest. Also, I have maintained that value-based arguments condemning all collaboration misread the ethical challenge to collaborate well; moreover, these arguments over-read the COI evidence to proscribe any relationship. So far, indirect evidence adduced for material variation is present when statistical associations for the whole category are less than 100%; direct evidence is manifest in the list of clearly malignant collaborations, like speakers’ bureaus, ghostwriting arrangements, and payments for referrals and orders. But it is research agreements and consulting agreements that create the collaborations at the center of academic-industry relationships. This section is therefore devoted to demonstrating how the terms of these agreements affect the discretion that researchers retain and the existence and force of a COI. An overview of the categories of terms that might plausibly influence COIs leads to four hypothetical arrangements. These are designed to yield intuitive answers, but the fact-patterns
in these hypotheticals are composites of documented instances of COIs.

Industry relationships with academic researchers are common, but their details are little known. When the researcher is retained as an “investigator” under FDA regulations, the arrangement is called a “sponsored research agreement” and includes the researcher’s affiliated academic institution. But companies often seek advice from academic researchers through formal scientific advisory boards or in their capacity to serve as subject-matter experts. These arrangements are embodied in consulting agreements. While consulting agreements address many of the same issues as sponsored research agreements, they often do so differently. Sponsored research agreements must include precise descriptions of academic researchers’ responsibilities. However, consulting agreements may be more vague about what is expected of the researcher. Imprecision often raises questions about whether the payments are really for another purpose, such as influencing a physician researcher to prescribe the company’s product or encouraging a researcher involved in company research to report favorable outcomes. Some terms, such as intellectual property ownership and confidentiality, raise special problems where their scope seems to overlap with academic work. Applied literally, these terms may seize that academic work and assign it to industry or “gag” a researcher’s ability to publish results.51

It is important to understand at the outset the potential advantages and disadvantages of such arrangements. On the one hand, they are a vehicle both for disinterested expertise to influence corporate judgments and industry researchers to solicit a second opinion on matters with significant corporate financial implications. Indeed, through a payment structure independent of outcomes, consulting agreements may crucially insulate such research judgments from internal financial pressures faced by corporate scientists and executives. Industry and academia often have different perspectives on the significance of discoveries, and each may hold confidential data or rights to materials whose synergistic exchange would benefit knowledge and society. The translation from basic or medical science to industry clinical applications is often a complex one, where the scientific and clinical implications of alternative courses are unclear. The collaboration of researchers with industry is often useful to ensure that sufficient weight is given to noneconomic factors and to avoid costly mistakes, duplicated work, and misjudgments about who may benefit clinically from a discovery. Academic researchers may find that industry relationships help motivate their independent work in two ways: seeing a discovery benefit a patient may provide personal satisfaction, and consulting agreements may allow researchers, who

51 See Nathan & Weatherall, supra note 42, at 1368 (noting that a company’s effort to suppress and punish doctor’s “ethical” publication of negative trial data in violation of a confidentiality provision led to successful pressure on the doctor’s eminent academic hospital employer, the Hospital for Sick Children in Toronto, to terminate her employment and medical staff privileges).
would otherwise seek more profitable careers, to remain in academia.

On the other hand, if consulting income is contingent on researcher actions that otherwise ought to be performed at the discretion of the researcher, or if these payments motivate the researcher to please industry through favorable research outcomes, the researcher's independence might be jeopardized. This could have consequences ranging from bias in how research is conducted or reported, to harms to human participants, through understated risks or trial designs where shortcuts unconsciously skew data in favor of success.52

The next question, therefore, is what contractual terms could present challenges to researcher independence through the behavior they incentivize. Consulting agreements reflect many of the same concerns as industry-sponsored research agreements.53 In this case, however, the spine around which all limbs are arranged is not a research protocol and set of FDA regulations, but rather a contractual definition of “services” the researcher will provide to the company, which, once formally defined, will play out functionally in numerous contract sections. Usually, contracts note that “payment will be for services” and mutual indemnification by the researcher will be for claims “arising from services.” These agreements mandate confidentiality related to all information received or created by the researcher that “relates to” or “arises out of” services, and the intellectual property assigned to the company will include any legally protectable materials relating to, or arising from, the researcher's services, as well as all intellectual property that makes use of confidential information.

“Relates to” is a dangerously broad phrase that recurs in these contracts. It implies a topical subject-matter comparison, rather than a causal relation, frequently encompassing the very academic work that has made the researcher of

52 Under the model common to academic medicine, senior researchers are explicitly mentors for junior researchers. In addition, because of their roles as peer reviewers on NIH grant review committees and advisers on FDA advisory committees, their work and views influence many aspects of industry and academic research, including regulatory decisions by the FDA and EPA; the evaluation of biotech companies and their initiatives; the determination of who among their peers gets funded; and the public perception of science and medicine. If interaction with industry skews a researcher's judgment towards a particular company or approach, the ripple effects can magnify the impact of this influence.

53 Sponsored research agreements are complex, addressing many aspects of regulatory compliance, funding and oversight. See, e.g., INST. OF MED., FORUM ON DRUG DISCOVERY, DEVELOPMENT AND TRANSLATION: TEMPLATE FOR CLINICAL TRIAL AGREEMENTS (2009), available at http://www.iom.edu/~/media/Files/Activity%20Files/Research/DrugForum/April27-28/Template CTA%2042209.ashx. The set of provisions that will affect academic independence is varied but discrete, including, for example, limits on publication, privately held intellectual property rights in academic discoveries, preservation of a researcher's medical discretion to remove a participant from a study, and payment structure. Suspect payment structures might include incentive payments to recruit fast, special payments for rapid publication, and side payments to staff to foster a sense of priority for that sponsor's studies. Because sponsored research agreements always involve the researcher's academic institution, to which all payments are directed, it is easier for institutions to prevent obvious forms of purchasing influence or priority.

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interest to the company as a consultant. At the same time, the duties of assignment, confidentiality, and even indemnification are absolute, regardless of the degree of company contribution of information or ideas to the researcher's discoveries and inventions. Whether the contract involves a 1% contribution by the sponsoring company or a 99% contribution, by the company makes no difference. All discoveries belong to the company, and a little company information makes any discovery confidential and non-publishable, at the company's behest. This combines with the fact that industry services descriptions are nearly always vague and overbroad. If the principal investigator is interested in genetics, all of her NIH-funded research is in genetics, and the collaborating company is a start-up interested in genetics, then services will likely be described as "advising on genetics." A typical researcher is not likely to object to this description, assuming that it will allow him or her greater flexibility.

Consider the breadth of what is legally protectable—copyrights, patents, trade secrets, disclosures capable of being enjoined—and the result is the company proposal in almost all cases. The law prohibits the researcher from publishing academic manuscripts that overlap in topic. The researcher does not own the copyright, and the data may be confidential. The rights in discoveries have been exported from the academy, a world of communitarian scientific values and competing Bayh-Dole incentives, to a company with obligations primarily to its own profitability. This does not mean that companies abandon all discretion and enforce these rights regardless of their costs. To the company, continued academic work (funded by the NIH, not the company) and continued publications favorable to their cause will be useful. But when the stakes are high enough, companies use these rights, and in the short run they often "win." Unfortunately, a company's economic stakes are often directly proportional to the scientific and clinical importance of a discovery. For example, an iron-chelation compound used to mitigate thalassemia and a method for assessing the actual effectiveness of AIDS antiretroviral therapies each became embroiled in such company action.56

The exclusivity of an agreement for the researcher might also plausibly affect the existence and strength of a COI. The researcher's financial eggs will all be in one basket, and the negotiating leverage behind the company demands increases if the researcher is barred from comparable opportunities during and after the consulting arrangement. Exclusivity can be achieved indirectly through corporate ownership and control of a researcher's key inventions, or a founder's

54 See supra note 27 and accompanying text.
55 See supra note 26 and accompanying text.
56 See supra note 53 and accompanying text; see also Bd. of Tr. of Leland Stanford Junior Univ. v. Roche Molecular Sys., Inc., 131 S. Ct. 2188, 2192 (2011) (holding that Roche's ownership through a private assignment of an academic method to assess AIDS antiretroviral therapies trumps both the Bayh-Dole structure and a university agreement stating that researcher "will assign" any invention made thereafter).
role in a start-up based on the researcher’s invention with deferred and contingent vesting of optimally valuable stock options. A more direct method is through a “noncompete” clause. Noncompetes vary in duration, geography, and scope of the prohibition, but may go so far as to bar industry sponsorship of all of the researcher’s academic work except by the company. Conversely, multiple consulting relationships will decrease economic concentration, although their overall COI impact will still depend on other factors. Note the counterintuitive result: other things being equal, researchers with more consulting relationships may be more resistant to the blandishments or pressure of any one company.

Finally, to illustrate the imprecision of payment registries, it deserves emphasis that payment terms, not just payment amounts, vary. Compensation can take the form of a one-time transfer, a per diem dispersal, or a more periodic payment schedule. If compensation is in securities, it is likely to be in unregistered founder’s or common stock for companies that have not engaged in an initial public offering (IPO) or in options or warrants. The latter are most common if the researcher’s role allows participation in a stock ownership plan, but they may be offered either by publicly traded or privately held corporations.

Similarly, the vesting of rights in securities may be directly or indirectly contingent on results of the research. A vesting that depends on enrollment of the first patient in a phase III trial does not explicitly require that data be favorable, but a drug will not get to phase III unless safety and efficacy data from phases I and II are favorable. Contract options create a layered COI, in which the company must have reached a certain form of acknowledged public success, whether through registration and an IPO or through an increase in the publicly traded price above the option purchase price.

This does not mean that securities are all alike and that all security arrangements create greater COIs than cash transfers. If the payment is twice the scientist’s annual salary and is paid tomorrow, then the researcher might well prefer it to 30% of a 0.001 cent-per-share company that is ten years or more from an IPO. Or she might not. Even this comparison may be too coarse. If the cash deal comes with noncompetes, and the equity one does not, so that the researcher can consult for seven companies, diversify her risks, and multiply her benefits, which will she prefer? Or, to put the matter differently, which one creates the “greater” COI? To discuss the potential interplay of these terms in life-like transactions, the next section examines four COI cases in some contractual detail.

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CASE 1: Amount of Payment

Dr. Researcher is a department chair at a medical school and could easily command a $100,000 per year fee were he retained as a consultant by a
Case 1 undermines the concept that a payment registry accurately reflects problematic COIs. It shows that even a large compensation sum, like $15,000, does not mean that there is a COI that will harm research behavior. Instead, this case is an example of an academic leader significantly discounting his high rate in order to test whether a novel therapy is effective. He is optimizing the benefit of the therapy for the target patients because they are a population to whom he has a long, clear record of commitment. In addition, he properly seeks to mentor a junior clinician scientist. The fact that the compensation is advance-paid means that he will be compensated whether his advice is favorable or challenging to the company. While the possibility of a clinical trial, with attendant revenue, might suggest the presence of an incentive to distort the results in the company’s favor going forward, the incentive to engage in a clinical trial that would fail is small. Yet the incentive to engage in a sound clinical trial is probably substantial.

CASE 2: Scope of Discretion

Dr. Researcher is a Founder of Progressive Pharma, a pharmaceutical corporation. His $15,000 per year consulting agreement as chair of Progressive Pharma’s scientific advisory board (SAB) gives him a voice to object if Progressive seeks, based solely on business concerns, to terminate trials on several drugs he invented. Further, this money empowers the SAB to allocate 15% of company research funding among understudied diseases. Progressive Pharma, styling itself as “the ethical start-up,” made these concessions partly in return for Dr. Researcher’s waiver of start-up equity, partly because of the scientific and ethical profile he hopes Progressive Pharma will build, and partly because of the availability of FDA grants for understudied diseases.

Case 2 is an example of how consulting agreements in association with licenses of university-assigned inventions by the scientist might contain terms designed to protect the technology from business choices that, in the scientist’s view, would unethically interfere with the process by which an important new technology reaches patients. Companies are loath to give scientists any influence on commercial decisions. Here, the approach succeeded because a traditional scientific function, sitting on a scientific advisory board, became a quality-control function. The scientist’s commitment to this is evident in his sacrifice of his equity stake in a company developing a promising invention. Yet a payment
Dr. Researcher is a groundbreaking translational researcher, recruited at great expense by his academic institution, and fully funded by the government. Peer reviewers consider him among the most celebrated researchers in his field. He enters into a consulting agreement with a start-up pharmaceutical company, Mini-Progressive, for whom he agrees to consult exclusively. The agreement’s noncompete bar him from accepting other industry sponsorships for institutional research or collaborating with other companies in his institutional role. His compensation is a series of low dollar-options, which will vest in slowly increasing proportions over a five-year period, with a “bubble” at the end of 50% of the options vesting. Their current value, based on liquidation value of the company after debt repayment, is zero. However, in ten years if Mini-Progressive can keep its research costs low and foster its most promising developments, the options might eventually be worth millions of dollars.

Case 3 could be a truly pernicious example of an academic-industry COI. This scientist has foreclosed not only his own future consulting options, but also his collaborative options with the industry in the course of his academic appointment, for personal gain. Indeed, through not diversifying his own consulting risks, he is now highly and solely invested in the company’s success. The company wants to know which research projects to target, information he can likely share, given his expertise and the access the NIH will grant him as a reviewer of others’ confidential applications. The company wishes to lower its research costs, which he can do by ensuring that his NIH-funded research is focused on topics that will benefit the company—and perhaps even suggesting that he collaborate with the company in just the sort of translational manner that some current programs might celebrate. The compelling story around that collaboration, and perhaps a management plan of occasional peer review of his pre-submission manuscripts, could allow it to be misunderstood as a public model for the resolution of competing concerns. Worse, the agreement might completely evade registry disclosure based on the cash value of the securities.

Yet peer review of his manuscripts, apart from its own limits, given that reviewers are dependent on manuscript assertions for facts, will never penetrate what could be going on: direction of his NIH-funded research and private transfer of its most novel and interesting results to one company, for its and his own benefit. Peer reviewers cannot expose the researcher’s exclusive collaboration with one private partner, rather than more generally with industry for public benefit or the use of not-for-profit, tax-exempt resources for personal gain of a researcher and the for-profit enterprise in which he has investments. In this sense, peer reviewers do not act as a check on the supplanting of knowledge-seeking,
academic goals with profit-seeking applications. The latter are acceptable goals in the private sector, but they are mismatched for government-funded research operating under different rules and premises. Those scenarios are merely possibilities unless confirmed by investigation. Investigation is warranted not by some offensive pre-judgment of the researcher’s unvirtue but by a pattern of circumstances: the alignment of terms already contrary to the primacy of academic obligations with personal profit and company leverage, the arrangement’s exclusivity, the huge pay-off possible from violations the researcher can make almost impossible to detect, and the gap between modest academic salaries and industry’s greater payscales, bonuses and stock packages, despite a common professorial belief that academic qualifications, expertise, and contributions are more significant.

CASE 4: Launching a Start-up Company

Dr. Researcher’s suggestive papers that a newly identified “power molecule” could dramatically expedite wound healing have attracted the attention of several investors, who approach him about creating a start-up company around his discovery. His consulting agreement includes scientific supervision of the company’s validation experiments, as well as being the “scientific voice” to other potential investors concerning the merits of his discovery. Those investors will contribute the cash necessary for the first two years of development, projected to require a high “burn rate.” Discussions are amicable, and meetings with the investors go well. Soon, the company asks Dr. Researcher to leave academic work to become the company’s Chief Scientific Officer, at a salary three times that of his academic salary and supplemented by stock and options that will, if the company succeeds as projected, be valued at over $10 million. During these discussions, Dr. Researcher continues his research, which is partly funded by the NIH and partly by the company. From his expanded research funding, he is able to publish increasingly glowing accounts of the function of the “power molecule.” He cites the intellectual property and confidentiality provisions of his consulting agreement to justify his refusal to make his reagents available to other scientists interested in replicating his work.

Case 4 has many of the indicators of a successful handoff of an important discovery to industry. In fact, it is what some in industry would feel is their “dream case,” in which reagents, inventions, know-how, and personal credibility are all lent to the company. This arrangement is frequently the one that pharmaceutical companies strive to establish, yet it also has danger signals throughout. Marketing is no part of a scientist’s special expertise, and the company ought to be seeking independent validation of his claims, rather than putting him in a position where he is expected to invalidate them if required but has every financial reason not to. In short, his actual contributions to innovation
from such consulting (distinguished from the company’s interest in acquiring investors) are likely limited and undercut by competing concerns. The combination of interests and exclusivity bear investigation for their effect on research integrity.

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While new industry payment registries available to the public would treat all these cases in a categorical manner, by disclosing only the fact of a financial interest or relationship for whatever negative inference the public would draw, it is important to note that these are in fact very different cases. Equally important are the terms of the parties’ agreements and whether the academic research institution employing the researcher is included. The incentive effects that corporate support might create are subject to variable mitigation through both means. If the institution is a direct payee as employer of the scientist, a transfer to the scientist of risk-sharing dollars dependent on research outcomes would be much more toxic than a guaranteed institutional salary arrangement that research revenue simply helps offset. Contrast this to direct payment arrangements, with no institutional intermediation of dollars. But even without a financial arrangement, the institution may still be an important player in addressing COI risks if the researcher has a medical staff or research staff appointment at an academic hospital, a non-employment relationship unique to health law. The appointment implies some oversight and watchfulness by the hospital of the researchers’ qualifications and work, and it links the researcher to hospital-based systems for research approval. This could link research incidents and outcomes with a hospital’s ongoing, highly detail-observant, legally mandated systems to assess and improve patient safety.57

Later, this Article will recommend collection of data on the multiplicity of arrangements and their COI effects. For now, coupling the sources and text from the COI section with the discussion of collaboration arrangements yields the following variables to examine in a multivariate analysis:

1. the precise scope of a researcher’s industry services and their necessity in innovative progress;

2. the form, amount, and structure of compensation, including its independence from specific results;

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3. the degree to which the researcher may deviate from corporate interests (e.g., in publishing negative results or un-enrolling a participant for whom the burdens of participation are severe) without financial or other penalty;

4. the collaborative elements, or their absence, indicative of mutuality and public benefit, including mutual availability of reagents, data and rights;

5. the existence of other researcher motivations, such as the desire to shift employment from academia to industry, the desire to share in product profits, or a longstanding personal commitment to resolving specific diseases or aiding specified patients;

6. the areas of research judgment that the researcher has the discretion to influence, namely, their scope and impact;

7. corrective forces on the exercise of that discretion, such as guidance sufficiently clear to create standards, the role of collaborators without conflicts and their contributions, the strength, independence, and insight of oversight bodies, and the form of institutional involvement, if any;

8. the degree to which the academic scientist's services and inventions are nonexclusive and available to others; the degree to which the scientist herself, in her academic and non-company work, is affected by noncompetes and intellectual property provisions;

9. the degree to which the researcher's results will be confidential, affected by publication clauses, confidentiality provisions, exclusivity terms, and whether there are tacit agreements to funnel academic discoveries solely or first to the company, rather than to prompt publication;

10. the local social context and compliance environment in which the research will occur, and the clarity and force of its shared expectations.

Discerning the variety among collaborations is the key to identifying those that best reconcile genuine contributions to innovation with minimizing bias risk. The Article turns now to the COI regulatory structure, to assess its capacity to perform that task.

II. THE ADMINISTRATIVE MIRAGE AND THE MYTH OF REGULATION

Industry collaboration is necessary. But due to the varieties of collaboration terms, the likelihood of a COI will vary. This Article now discusses an important question: What is the capacity of administrators under current regulations to distinguish among collaborations, based on their value to innovation and their...
bias risk? The answer will sweep wider than the question, for the bases for incapacity will affect far more than the ability to distinguish: it will undercut the legitimacy of the regulations and the soundness of any of their principles.

The regulations do not reflect distinctions among industry arrangements, nor do they equip administrators to make sound judgments about bias risk and how to mitigate it. No comprehensive factual inquiry preceded these regulations, and, according to the Institute of Medicine (IOM),\textsuperscript{58} no factual inquiry has been undertaken to assess their effectiveness. Nonetheless, grants and personal property rights can be removed without any due process, under a standard dependent entirely on unavailable facts, with no check on the qualifications or biases of institutional adjudicators to whom the government decision is broadly delegated. There is no required record; no right to counsel; no right to confront witnesses or review adverse evidence; no possibility for any person affected, such as a research subject, to intervene; no whistleblower protection; no requirement for a written decision, let alone a reasoned one; and no right to an appeal, by either an investigator or anyone affected by an actual COI, whether a colleague or a research subject in a trial so affected. The regulations thus omit traditional methods for epistemic soundness (such as qualified and unbiased adjudicators) and self-correction (such as transparent written decisions and possible appeals) that might otherwise have helped make up for the absence of empirical inquiry that ought to precede any legal regulation.

There is no comprehensive regulatory system for addressing COIs in research or even across all federal agencies. For COIs, there are regulations promulgated in 1995 by the NIH, and very similar ones by the National Science Foundation, governing academic recipients of their funds for research. FDA regulations require industry (and other) funders of research, who will be applying for approval to market a drug or device, to collect certain COI information. In addition, while there is no law or regulation that requires Institutional Review Boards (IRBs) to address COIs arising in clinical research, the Office of Human Research Protections has issued guidance on what IRBs might consider, if they choose to look at COIs.\textsuperscript{59}

There are also five categories of self-regulation. First, the voluntary accrediting body for human research protection programs requires institutions to maintain COI management systems, with definitions that track the regulatory requirements. But this body does not assess the function or efficacy of such

\textsuperscript{58} See IOM REPORT, supra note 3, at 4.

\textsuperscript{59} The latter is well summarized in I. Glenn Cohen, Administrative Developments: New Human Subject Research Guidelines for IRBs, 28 J.L. MED. & ETHICS 305 (2000). The primary significance of that guidance is in recommending that IRBs review COIs, including for a set of factors encompassing the range of FDA definitions and a subset of the AAMC ones I shall discuss below. It is an influential, important document. However, for purposes of evaluating its strengths and defects, I will rely on the below discussion of those aspects within their other sources.
systems. Second, the PhRMA Code of 2009, a pharmaceutical industry association code, specifies that consulting should be for an appropriate purpose, compensated reasonably, and reflected in a written agreement that ensures it is for actual services. Third, various professional medical societies have put out specialty-specific suggested guidelines. One example is the investment-prohibitory rules that the American Society for Gene Therapy published in the wake of the death of Jesse Gelsinger. More commonly, rather than prohibiting whole categories of financial interest or relationship, guidelines recite both the importance of physician involvement with industry, and objectivity; exhort good judgment; and suggest that COIs always be disclosed to others such as colleagues, journals, and trainees, as if the issue were solely appearance, and later disclosure could address earlier unconscious bias effects. These guidelines parallel the requirements of journals mandating disclosure, but do not otherwise prohibit COIs or indicate that they have been disclosed to peer reviewers or that they have in any way affected the evaluation of a manuscript. Fourth, a special committee of the Institute of Medicine published a lengthy report in 2009, whose principal objectives were to establish and document the pervasiveness of industry’s interrelationship with medicine and medical education and make specific recommendations. The report ultimately articulated important principles for evaluating COI policies, including treating people fairly under transparent policies. Yet distinguishing based on evidence among unlike cases was not an achievement of this report. Fifth, the AAMC, which had elevated local control over other values, sought to bring order to the evident institutional chaos through three major reports and recommendations with respect to clinical research and a data symposium directed to establishing, for once and for all, that COIs can cause bias. However, there are inherent limitations on addressing COI issues without data. The resulting elegant policies were procedural not substantive, did not improve the epistemic competence of COI adjudications by rooting them in a body of established knowledge about differential bias risks, and

60 Human research protection programs are institutional or corporate systems for participant protection and ethical and scientific review, consisting, for example, of an IRB, investigator training, and scientific review committees. For more information about the accrediting body, the American Association of Human Research Protection Programs (AAHRPP), and its COI requirements, see AAHRPP, www.aahrpp.org (last visited Nov. 30, 2012).


63 As a reviewer for several scientific journals, I can attest that I have never been made aware of the COIs of manuscript authors. Some scientific journals require submission of a COI disclosure with the initial manuscript submission, unlike law reviews, which require none.

64 IOM REPORT, supra note 3.
translated the complexity of potential arrangements into a single presumption against, rebuttable by compelling necessity. The beneficial cases, Cases 1 and 2, above, would likely be disallowed under that standard, while Case 4, a problematic case, would likely pass through untouched since the researcher’s share of licensing revenue would not be considered conflicting, the uniqueness of his knowledge would justify his consulting relationship during the period he remained an academic and, for a simple reason applicable as well to problematic Case 3, the research involved is probably not clinical research.

A. The NIH Standard

Since their adoption in 1995, the COI regulations applicable to NIH-funded research as a component of the Public Health Service have been amended only once, on August 25, 2011. The amendments were focused and significant; where applicable, both former and new standards will be noted below. But the amendments did not address the most significant criticisms of the regulations that this Article will make.

The NIH standard for COIs always has been short and deceptively simple in appearance. Its purpose is to “promote[] objectivity in research by establishing standards to ensure there is no reasonable expectation that the design, conduct, or reporting of research funded under PHS [Public Health Service] grants or cooperative agreements will be biased by any conflicting financial interest of an Investigator.” It imposes no direct obligations on conflicted investigators, but institutions receiving such funds must have a system under which investigators are required to disclose to officials designated by the institution a listing of “the investigator’s significant financial interests (and those of the investigator’s spouse and dependent children).” The institutional official(s) will review those disclosures and determine whether any of the reported financial interests “could directly and significantly affect the design, conduct, or reporting” of the research. The recent amendments changed the definition of Significant Financial Interests from those that might reasonably appear affected by the research to those related to an investigator’s institutional roles—a much more objective standard, although one which goes far beyond research integrity matters.

If an official determines that a reported interest “could directly and

69 Id.
significantly affect” the research, the official must report this to the NIH, within sixty days or before funds are expended, and ensure that the institution has taken unspecified measures to manage, reduce, or eliminate the COI.\textsuperscript{70} Under the pre-amendment regulations the degree and manner of conflict reduction need not be disclosed, and potential management strategies noted in the regulation are neither mandatory nor exclusive. Through careful drafting, there is not even a conflict to report unless and until an institutional official determines there is one. Reporting is limited to cases of COIs as determined by the institution.\textsuperscript{71} From reporting alone, the NIH will not know if an institution is biased towards under-determinations.

Before the October 2011 amendments, the government did not receive notice of the relationship of the interest to the research and the management strategy adopted. There was no requirement that the institution itself assess the adequacy and appropriateness of any of its determinations; now, however, the revised regulations require the institution to perform a retrospective review of cases of noncompliance. The regulations give COI officials and committees significant power over researchers. For example, the regulation states that institutions may limit the investigator’s participation in the research, monitor the investigator, and direct the investigator to divest personal assets (including assets belonging to the spouse or dependent children). The institutional official may direct the institution and investigator to terminate their industry contracts.

Society expects administrative agencies with such power to be restrained and protected by a familiar set of adjudicatory requirements. But this is not the case. Institutional determinations need not be made based on data. Indeed, the word “data” does not appear anywhere in the regulatory mandate itself. No qualifications are specified for the “official(s)” who are institutionally designated to make determinations. Furthermore, there is no protection of the COI official or committee from external or institutional pressure; no protection for third parties, such as concerned employees, from investigator retaliation; and no protected or privileged investigation requirement that the institutional official have access to other data sources within the institution, such as institutional COI reports directed to other purposes, like abuse of management authority or position for personal gain, or databases of noncompliance with IRB human subject protection processes. There is no requirement that the official be unbiased or that the institution identifies and avoids any adjudicatory conflicts of interest it has, such as its interest in grant revenue. The indefinite NIH standard of potential significance need not be translated into any more concrete specifications, whether prospective, as rules restraining unbridled discretion and providing notice to investigators, or retrospective, as “case law,” to explain determinations to investigators and the public.

\textsuperscript{70} 42 C.F.R. § 50.605 (2011); 42 C.F.R. § 50.604 (2011) (sixty-day mandate).
\textsuperscript{71} 42 C.F.R. § 50.605 (2012).
Typically agencies also labor under requirements that ensure accountability, ranging from creation of a specified record, to an appellate review process. But not here. There is no requirement for a written decision; no requirement for any oral or written record of the proceedings; no investigator right to appeal (although the institution may appeal if the NIH sanctions it for not doing enough); no right to counsel; no required oversight or operational relationship to executive management, the board of trustees or directors or any operating component of the university or hospital; no required advisory board, let alone a board sufficiently inclusive to detect bias, promote legitimacy, give voice to ranging perspectives and approaches, audit the programs’ fairness and effectiveness, or require and oversee any aspect of quality improvement.

For this purpose, a “significant financial interest” before the 2011 amendments meant “anything of monetary value, including but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights).” Certain exempted categories include “salary, royalties and other remuneration from [an] institution”; outside payments to the investigator, spouse, and dependent children that are not “expected to” exceed $10,000 in the subsequent twelve months; and equity interests, similarly aggregated for spouse and dependent children, that are worth less than $10,000 by “reference to public prices or other fair market value.” Therefore, note the following: First, even where proposed research would definitely and dramatically affect the value of an investigator’s royalty interests from university licensed technology, the COI is ignored. Second, all equity interests are pooled as if identical in the risks they pose, except that unregistered securities are sui generis in not benefitting from the $10,000 threshold applicable to cash and publicly traded equity. And third, the purpose of the arrangement, and its contractual parameters, are irrelevant from beginning to end. The revised regulations made technical changes in some areas, such as reducing the threshold to $5,000, but the first and third points remain apt.

Finally, there were actually two different versions of the “Significant Financial Interest” standard to promote objectivity. While the investigator was obligated to disclose personal financial interests that “would reasonably appear to be affected” by the research, the official must tag those “interests that directly and significantly affect the... research.” One asks whether the interests could be affected; the other asks whether the research could be, and then the difference is spiced up with words like “reasonably,” “appear,” “significantly,” and “directly.” The difference between the two standards created worlds of complexity and uncertainty, singly and in their joint (or perhaps separate)

74 42 C.F.R. § 605(a) (2011).
application. For example, it was unclear which standard required a judgment personal to the investigator and whether “significance” should be judged with reference to the investigator as subject, the official as subject, or from the viewpoint of the “reasonable man.” No guidance clarified whether a judgment was to be made abstractly or in light of circumstances, such as the share-price history of a particular company or the relative wealth and wealth-seeking propensities of the investigator.

The regulations left unclear what weight should be given to a mistake of fact that produces a subjective, but ill-founded, COI. For example, an investigator might mistakenly think her research will have no impact and thus feel no incentive to distort her findings—or mistakenly think her work is of pivotal value to the company and thus subjectively feel a temptation to distort the results of her research. It was also unclear how certain the required probability judgments should be. These questions remain under the recent revisions. While the investigator’s standard for disclosure has broadened to a simpler one about the relationship between an interest and institutional roles, the institution’s standard remains inherently probabilistic, with no guidance about whether judgments should be based on generalities or specifics, with what degree of probability, and with what evidence to justify the assessment.

B. FDA Regulations

Since February 1998, the FDA has required anyone who submits a marketing application for a drug, biological, or other medical device to include a statement describing certain “disclosable financial arrangements” of any investigator involved in a clinical trial whose resulting data is submitted in support of a determination of efficacy. The agency has also required disclosure of any trial in which a single investigator makes a significant contribution to a determination of safety. 75 The applicant must have gathered that information before such a trial starts, and periodically thereafter until one year after a trial is complete. “Disclosable financial arrangements” means “compensation made to the investigator in which the value of compensation could be affected by study outcome” or “a proprietary interest in the tested product” (whether the interest is direct or indirect, including, unlike the NIH standard, through a university license). It includes any equity interest in a publicly held company that exceeds $50,000 in value or in the sponsor of a covered study regardless of value (with all forms of equity lumped together as the NIH regulation does).

While the FDA definitions are crisp and clear, this approach nonetheless has a number of defects. First, it not only fails to address COI issues for all of basic science research, it excludes many clinical trials, including, for example, phase I

75 See 21 C.F.R. § 54.2 (2011).
pharmacokinetic trials and any trial for which the sponsor chooses not to submit data. Indeed, it shares with the NIH approach a delegation of all responsibility to a highly interested judge (in this case, the industry sponsor). Unlike the NIH system, the sponsor must report in more detail both the nature of the COI and the measures taken to mitigate any negative effect on data. But like the NIH system, reported data will not reveal to the FDA whether the sponsor has failed to disclose completely these COIs, and the system conclusively presumes the sponsor, will act without bias. There are neither data nor guidance concerning what management strategies work or which of these situations is really problematic. The remedies of the FDA are also limited: monitoring, requesting further data analysis, soliciting additional studies, or declining to accept study data. The latter penalties certainly are financially consequential to a sponsor. The problem is that it is unknown whether they incent diligence or deceit. Indeed, this regulation, promulgated well before the COI incidents and evidence discussed above, was evidently insufficient to prevent them, and has continued unchanged to this day.

C. AAMC Self-Regulatory Efforts

Finally, I turn to the sequence of AAMC reports discussing COIs. The first of these reports suggested institutional procedures to address investigator COIs in clinical research through newly described COI committees. Rather than implementing the old regulatory standards, it replaced them with a rebuttable presumption against certain interests. The second AAMC report addressed institutional COIs through separation of intellectual property functions from administrative functions, management of the COIs of senior executives, and newly minted institutional COI committees. Finally, in the wake of a report suggesting that institutions had taken little action to create and implement COI policies, the AAMC attempted to address institutions’ evident uncertainty in how to apply the presumption with illustrative hypothetical examples. Throughout, the AAMC artfully attempted to couple preserving institutional local control under limited regulations, with an urgent message that institutions should voluntarily adopt uniform model policies. What made the policies “model policies” was less their empirical basis—the AAMC too was forced to act in the absence of data—than the blue ribbon membership and collective prestige of the commissions creating them, and the emphasis on maintaining public trust through stringent academic self-regulation. However, while procedures could point to competing values, they could not answer the very question they posed: Which arrangements are optimal?

D. Meaningful Law and Due Process Values

The NIH regulation is a standard, rather than a rule under Kaplow’s
understanding of these terms, meaning a decisional principle for case-specific judgments that are not outcome determined by a specific, less contingent rule. It shifts, from the issuers to those who interpret it and those who are subject to it, the obligation to give a concrete practical answer to the central question whether a particular form of collaboration, interest, or relationship would likely bias research. For interpreters of this standard to apply it meaningfully and consistently, they need sufficient facts to reach rational conclusions in applying its terms. They must understand the forms of collaboration and their effects, together with cultural factors affecting bias and contribution to innovation. Unfortunately, these interpreters do not have such pivotal facts at their disposal. The standard also fails to give them access to general or specific experience of others, and it does not include innovation-oriented values among factors to be weighed or reconciled. Interpreters are broadly empowered to dispose of assets and restrict personal freedom, but there is no appeal within or required by the regulations. And information about the wisdom of the choices that interpreters have made is inaccessible even to the interpreters themselves. No prescribed processes yield facts certain to be material, let alone reasoned conclusions to be tested or incorporated in a body of experience.

Imagine the following hypothetical, illustrating the excessive flexibility of the regulations before the October 2011 amendments: Dr. Researcher owns 10,000 shares of Merck common stock and is also doing NIH-funded research on next-generation Merck orphan drugs. The chairperson of the COI committee, distinguishing small companies from global giants, believes, with some factual basis, that the share price of large companies is affected by so many factors that outcomes of one small-market drug trial will not materially affect it. On this basis, the chairperson determines that the research could not affect the company’s value and thus that the value of Dr. Researcher’s Merck stock could not be affected by her research. Basing his view on that perspective, the chairperson finds that Dr. Researcher’s stock holdings do not create a COI requiring management. Dr. Researcher, however, believes that her ground-breaking work

78 See supra notes 25, 29 and accompanying text.
79 Of course, organizations have hierarchies and chief executive officers to whom one might or might not have recourse. Universities, academic hospitals, and research institutions may have academic or other procedures governing misconduct, and, perhaps informal processes that they may or may not choose to apply, without further guidance, to COI matters. Typically, these do not involve the array of due process rights—such as right to counsel, discovery, and cross-examination—required before permanent deprivation of property, because they are designed around withdrawal of what are generally academic privileges. Proceedings for research misconduct do require a record (though not counsel, discovery, or cross-examination), but they are limited to cases of fraud, plagiarism, and fabrication. The federal COI regulations, however, do not require such procedures. See 42 C.F.R. § 83 (2005). For ORI Policies and Regulations, see DEP’T OF HEALTH AND HUMAN SERVS., OFFICE OF RESEARCH INTEGRITY, http://ori.hhs.gov (last visited Dec. 8, 2012).
could affect stock price and has enough shares to find the potential profit interesting. Consciously or unconsciously, she distorts her results favorably to Merck. Yet, as far as the NIH COI regulations are concerned, both Dr. Researcher and the chairperson have complied with the regulations. Under the revised regulations, Dr. Researcher would have to disclose her interest as related to her institutional role. However, the same dichotomous results could occur: the chairperson determines that there is no COI, but the researcher, acting under different beliefs about how trial results affect share price, distorts her results.

With such an open standard, no uniform processes, and no data to appropriately shape discretion, there is no reason to believe that the many NIH-funded academic institutions will reach sound, consistent judgments. Instead, it is a reasonable hypothesis that they are reaching a diversely motivated set of judgments without any data concerning their actual necessity or effect.

That hypothesis has been tested, and it is true. A survey in 2000 of the ten top NIH-funded medical schools showed that "current conflict-of-interest policies at medical schools vary widely and have substantial shortcomings in the context of clinical trials." Only one medical school approached an ideal of comprehensiveness and avoided arbitrary exceptions. A contemporaneous survey of 304 major research institutions, including 127 medical schools, also found that "there was considerable variation among policies in all domains," "important terms were not adequately defined," and that "the only nearly universal feature was that management of conflicts and the penalties for nondisclosure were totally discretionary." Mandated disclosure to research participants, journals, funders, and colleagues was typically absent. On this basis the authors of this survey made several recommendations: that federal agencies should adopt a common and consistent rule; that institutions should report details of COIs and their management to funders; and that there ought to be complete disclosure to all journals, readers, and review committees such as IRBs. More than a decade has passed since the authors made these recommendations, but they have not yet been incorporated in laws or regulations, except as noted above.

In 2002, an NIH survey of grantee institutions found continuing variation with extraordinary lapses. The survey reported interesting statistics: 86% did not define "research," 52% did not reference the appropriate regulation, 74% did not commit to making COI information available to the NIH, 45% did not require a conflict to be reported to the NIH, and 68% did not require corrective action to be reported in the event a conflicted investigator had biased the research. A 2007

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80 Bernard Lo et al., Conflict-of-Interest Policies for Investigators in Clinical Trials, 343 NEW ENG. J. MED. 1616 (2000).

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Targeted Site Review of funded biomedical research institutions found continuing compliance problems, including defining “investigators” too narrowly, untimely and inadequate reporting, having inconsistent reporting processes, submitting grants before collecting required COI information, expending funds before or without notifying the NIH of COI resolution, and failing to monitor sub-recipients. These are all critical problems.

In 2008, the AAMC published another guide for COI procedures, in the hope of accelerating progress. That report did include model policies and some scenarios to guide consideration of cases. But it could not do what the federal government had not done: assemble or fund the assembly of the data necessary to determine whether a disclosed interest might actually affect research. This critical finding, required by the regulations, is impossible to make except through sheer guesswork or through generalizing one’s own biases in whatever context—whether anti-industry or pro-industry. There is no record except a disclosure, no factual basis for inferring its consequences as to the subject investigator, and both permissive exoneration and prohibitive disposition of the investigator’s assets or grant are equally arbitrary. With the key determinants of a judgment—the projections, experience, and intuitions of diverse members who require no qualifications—outside that limited record, what would or could an appeal even look like, and how could the process be subject to epistemic correction?

The FDA standards are more specific with respect to certain disclosures, but they too fall short. The regulations do not identify the standard by which the significance of disclosed arrangements shall be assessed. The FDA has made itself a black box, depriving investigators and industry of a means of ensuring that they have complied with applicable regulations.

As Professor Sunstein illuminates, there are good reasons that lawmakers sometimes prefer standards to rules, such as where facts sufficient to establish a specific rule are unavailable to issuers, but interpreters will have access to operative facts through the cases they adjudicate or otherwise. Pertinent here, and in defense of the regulatory approach described above, it can sometimes be important that local culture influences both interpretive processes, and, to a degree, specific outcomes. Here, there is no question that a university or research institution’s culture of oversight, the views of its scientific community on potentially private arrangements, the intellectual and financial resources these institutions have to devote to such efforts, as well the prevalence and variety of


84 See SUnSTEIN, supra note 8, at 149–51 (engaging in a pointed discussion of practical reasons to adopt a standard or case-based approach instead of a rule. The whole volume addresses the issue of rules, standards, and cases, as modes of lawmaking in a broader context, including their tolerance for political compromise as incompletely theorized agreements).
industry relationships, all might make a practical and cultural difference to how COIs are tolerated, ignored, or encouraged. Thus, a rule affecting diverse institutions might be under- or overinclusive and may be perceived as unfair, particularly if data are not used to formulate a sound rule. There might be multiple and diverse criteria affecting an outcome, and how to weigh such criteria might be uncertain a priori, as might the weight given to unpredictable nuances of specific cases. In addition, to the extent that fact-finding is more complete through the case-based observations and actions of many, rather than through the legislated policy generalizations of a few, it may be that the epistemic competence of the COI regulatory system as a whole would be maximized via committees acting rationally under a standard from a basic and evolving core of facts concerning collaboration variation, risks, and outcomes. But even worse than an unsound rule, which has at least consistency to recommend it, is floating a vague standard in a factual vacuum of only partial policy-scope to adjudicators without known epistemic competence. Even worse is to place institutional committees in a system that wholly lacks any method to gather and compare foundational factual assertions, contest its factual conclusions, and learn from its mistakes.

Practically, such a system will produce contested, inconsistent results over a prolonged period amidst mounting questions about its credibility, regardless of the best efforts or good faith of the adjudicators. Conceptually, the flaws of such a system are so fundamental that it is questionable whether it is even law under generally accepted standards of jurisprudence. The flaws of this regulatory system go beyond being “bad law” or “unconstitutional law,” both of which might be given effect until struck down or legislatively altered. It means this

85 Cf. ADRIAN VERMEULE, LAW AND THE LIMITS OF REASON (2009) (analyzing relative epistemic competence of judicial and legislative methods based on numerosity, diversity, timeliness, and potential for information aggregation, among other factors). Vermeule does not apply his analysis to a system where diverse adjudicatory committees, acting in effect like the arms of an administrative agency, operate under a standard. However, for purposes of his analysis, he groups the executive and the legislature together and distinguishes them from courts applying common law methods, leaving for the future how such an analysis might be applied to the regulatory agents of an executive agency. ld. This Article does not purport to lay out such an analysis. Among other things, that would make the practical question of how to address COIs in the innovation ecology depend on a branch-versus-branch debate among constitutional scholars, involving many distinct factors, that has no foreseeable definitive conclusion. However, the questions Vermeule asks of constitutional law ought to be asked of any law that purports to provide sound answers to important questions where facts are uncertain and proper policy is contested. Thus this article was conceived from asking about COIs within the innovation ecology these questions, to which existing law had no good answer: How will general and case-specific facts be ascertained and confirmed? How will general factual premises remain timely or evolve with system change? How will information aggregate and what are the epistemically relevant qualities of those who will gather and aggregate it? How will biases be avoided or corrected through the process leading to aggregation of information? Will the regulatory system address facts that support competing values?
regulation was never a successful act of lawmaking in the first place. A review of those jurisprudential standards, their defense, and the debate about their relative merits is outside the scope of this paper, but the standards are sufficiently well known that the discussion is warranted. To sidestep the debate about which is most “right,” I will investigate several that are leading candidates for defining “law.”

The most basic initial test, originating with H.L.A. Hart, is whether there is a “rule of recognition” that distinguishes what is a valid legal obligation, concerning how to structure academic-industry arrangements, from what is not. Ordinarily, promulgation through required administrative procedures would serve this purpose, but not here because each regulation involves an intermediary with incomplete legal authority. Thus, the NIH regulation provides a mandate for institutions to create a system affecting investigators. But from an investigator’s perspective it is unclear whether the institution will have done so in a valid manner. Compliance reports suggest that such institutions do not. In any event, since the regulations do not apply to investigators directly, whether the investigator has any legal obligations is an open question. Similarly, the FDA regulation imposes a rule on investigators to file certain disclosures with the sponsor and an obligation on sponsors to collect and file these disclosures, while imposing no obligation on institutions. The sponsor has no clear direction from the FDA about which arrangements to permit versus which to prohibit or manage. The sponsor has no authority to direct the investigator to do anything to alter arrangements, and neither does the FDA under its own regulations. For COI management and institutions more generally, there is no clear rule. To mandate that a researcher must disclose X—without knowing whether the state will or will not respond to this disclosure, and, if it were to take any action, would not reveal the criteria guiding that decision to act—is to create a rule that cannot be recognized as a law in the sense of “thou shall not X.”

Other less basic standards of jurisprudence would require more. They go beyond Hart’s “rule of recognition” test and demand realistic conformance to certain legal ideals to make a mandate “law.” Thus, they also look to whether there are either definitive rules, or less definitive standards coupled with the data and goal clarity sufficient to guide case law development; adequate, prospective notice of which conduct is permitted and which is proscribed; rational

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86 This analysis is not intended as a commentary on the constitutionality of the federal COI regulations or the constitutionality of any directives issued by universities or hospitals under their authority (such as a directive to investigators to divest personal assets even at a loss in order to participate in research necessary to provide them with required salary support). Apart from the interesting question of whether there is state action by those committees or officials not part of government institutions, an accurate answer would necessarily address the substantive and procedural effects, if any, of institutions’ supplementary academic procedures and policies’ unique wording.

87 HART, supra note 8, at 110–16.
promulgation of rules and standards, based on confirmable facts, case outcomes rationally explained by disinterested adjudicators applying a sufficiently clear standard to material facts adequately determined, and consistent predictable outcomes.\textsuperscript{88}

The COI regulations do not satisfy even one of these criteria. Of course, some of these are alternative considerations. Law need not simply be rules, and it need not be just cases. But it must at least provide for the sound creation and interpretation of one or the combination, based on factual predicates that not only ground its rationality at inception, but also ground its interpretation. Indeed, if the goal is public trust and legitimacy, and compliance by the regulated, then presumably the presence of the elements above must be visible both to regulated parties and to unregulated public observers. Not so here. In creating both standards without procedures, and omitting data that could ground or inform sound discretion, our existing regulatory systems are not law that manages COI problems—even apart from due process questions, and even apart from the competing framework of the innovation ecology in which scientists practically reside.

Interestingly, this critique of the existing regulations, like the due process observations, is wholly new. Although the regulations have been criticized, it is not on these grounds, but on grounds wholly captured by the virtue and non-virtue polarity. Before I set about discussing how better systems may be built, I will rapidly survey the minimal literature on COIs, both to demonstrate its limits and to see if it that literature can nonetheless help.

III. LITERATURE: VIRTUOUS ANSWERS TO HALF OF THE PROBLEM

If the real-world problem is to consider COIs and innovation together, the literature provides little direct assistance. Starting with the business literature, there are those who exhort corporations to be good citizens, obey the law, and avoid fraud, whether in general terms or through specified programs in corporate compliance with select mandates. There is also a separate literature on innovation. That innovators’ individual integrity or subconscious biases might be affected by incentive structures, and require mitigation through means other than corporate value statements and employee discipline for wrongdoing, does not enter into the business literature’s discussion of innovation.

But the business literature does speak, empirically, to a conception of innovation and its requirements that prove instructive for narrowing consulting agreements to where scientists’ unique contributions might actually lie and in what context. The business literature is most focused on promoting innovation

\textsuperscript{88} See sources cited supra note 8 and accompanying text. Lon Fuller has suggested additional, more stringent threshold criteria and harsher judgment. See Fuller, supra note 8. Fuller’s other criteria, however, remain disputed.
REGULATING BIOMEDICAL ACADEMIC-INDUSTRY RELATIONSHIPS

among corporate employees. Therefore, it naturally addresses how teams, organizational silos, and other commonplaces of the American corporate environment affect innovation. For example, it speaks to allowing innovators to be influential across organizational silos by focusing their contributions on their particular gifts, so that their credibility in different contexts is maintained, and what is particularly valuable in their approaches can be more widely disseminated. Reflecting a backdrop of American business bureaucracy, business literature discusses how one might systemize out-of-the-box thinking and foster teams with complementary expertise that will learn quickly, rather than demanding overbroad contributions from each individual. It recommends incentivizing scientists based on their discoveries rather than the degree to which nonscientific arms of corporations successfully exploit those discoveries. The literature further recommends using individual talent, within its bounds, for corporate goals without harming initiative by freezing it within a bureaucratic matrix more suitable for routine, high-volume tasks. 89

In contrast, current academic consulting agreements with industry frequently define services broadly, with scientists ostensibly being invited to give advice and perhaps advocate, with potential investors or regulators, for very generally described topics superficially resembling scientists’ specific expertise, but including matters outside their typical experience (e.g., such as marketing or patent strategies to avoid competition). Compensation is often contingent, linking payments or options to corporate revenue or new stock issuances supported by development or sales of a new drug or device. Such broad contingencies are outside a scientist’s knowledge or control, but generally suggest that the fate of the scientist and the company are intertwined. Each person’s financial interest becomes that financial milestone, each person’s job, if it is to be compensated, becomes doing what he can to support the same key financial goal. The goal is not just paramount: it is essential.

In fact, the major activity within such relationships may be entirely outside the scope or methods of underlying scientific insights, innovation, or intuition. The latter might well be confined to likely compounds to test and their likely behavior, the needs and vulnerabilities of various research participants given specific diseases or conditions, potential research methods or tools, or other ways scientists contribute unique expertise in interpreting and overcoming scientific roadblocks from knowledge of their field. This dichotomy between the goal of compensating scientists for their actual expertise and the structure of consulting


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arrangements should lead us to question whether broad-brush consulting arrangements are as critical to health care innovation as some opponents of COI regulation claim. Nonetheless, scientists can make a core of innovative contributions through engagement with industry, and the fairness of compensating them for those contributions is undeniable. Narrowing consulting services and payment arrangements to that core would help alleviate some COIs.

Probably because of a lack of familiarity with the subject matter, legal academic scholarship has proposed no integrative solution either. Indeed, the legal academic literature on COIs, measured by volume, is surprisingly small.

90 See, in particular, Stossel, supra note 29.

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Nearly all of the existing literature expresses outrage at some of the COI cases discussed in Part I, or others. This outrage is not misplaced, but it is partial, leading almost all authors to focus on COIs as a character problem not requiring situational, factual analysis, and separated from the industry collaboration and robust innovation ecology that legal colleagues in other disciplines simultaneously urge. It is as if COIs belong to criminal law, where bad acts lead inevitably to a search for the bad actor.

Finally, if COIs are an ethical problem, then one ought to look for solutions within biomedical ethics. But classic bioethics has had almost nothing to say about COIs, despite its general confidence that medical and scientific ethical problems can be addressed by considering beneficence, respect for persons, justice, and respect for community values. If ethical principles are invoked here, they are different ones: stewardship, transparency, and disinterestedness.92 A more balanced ethical approach would consider the virtues of industry collaboration, including both the altruistic and intellectual virtues associated with innovation. It would give due consideration to a practical orientation toward results, political collegiality, strategic thinking, credible candor, multidimensional thinking, conciliation, and devotion.93 These are the same collaborative and activist virtues that bioethicists credit political activism as potentially involving when bioethicists act beyond the Ivory Tower: One could add many other virtues, including courage, ability to articulate and act in accordance with principles when other group members disagree, and public mindedness. Yet bioethics has offered no such full account of industry collaborations involved in COIs or of the range of human responses—good and bad—to industry collaboration and its incentives. The virtuous avoid COIs, the pragmatic manage them without data or adequate regulatory basis, and the conceptual space between COIs and innovation ecology is vacant, involving separate perspectives that never meet except in the dueling expectations visited on scientists themselves.

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Concerning the COI regulations themselves, there are principally three critiques of the regulations from the legal literature: the virtue-prohibitionist critique, the counter-fiduciary critique, and the circumstance-based, “probabilist” critique.

A. The Virtue-Prohibitionist Critique

This critique, the primary response by leaders of organized medicine and most legal scholars who have written on biomedical COIs to COI cases, is that COIs are self-interested choices by scientists that reflect their weakening commitment to the traditional virtues of physicians and scientists, including independence, objectivity, and a single-minded fiduciary responsibility to patients. They argue that COIs are self-interested choices by scientists that reflect their weakening commitment to the traditional virtues of physicians and scientists, including independence, objectivity, and a single-minded fiduciary responsibility to patients. The consequences of COIs are, in their view, unmanageable, because of the primary harm, which is the corruption of academic independence; objectivity is accomplished the act of compensated collaboration. Moreover, secondary harms, like harm to participants, are certain to follow once those virtues are compromised. Their arguments are grounded in accounts of values and virtues and would prohibit all compensated collaboration. They claim that public trust requires a complete bar on academic-industry partnerships, because the public could not trust a scientist, physician, or research enterprise known to lack virtue.

There are three problems with this view. First, its account of virtue is historically false. Reimbursement, not just patient welfare, always has mattered with regard to defining such virtues, as does engaging patients in research despite researchers’ conflicting interest in gaining knowledge. Second, it ignores the potential variety of collaborations and the evolving role of scientists and physicians in applying knowledge. Third, it ignores the socially sanctioned competing values of innovation and the innovation ecology.

There are three principal variations on the virtue-prohibitionist approach.

94 See, e.g., Kassirer & Angell, supra note 27 (analyzing the effects of financial conflicts of interest on biomedical research and critiquing the policies used to handle disclosure of such conflicts); see also Brennan, supra note 27; DeAngelis, supra note 27 (introducing articles addressing the prevalence of conflicts of interest between physicians and companies that financially support teaching and research, along with the effects of this relationship on public trust of physicians); Liang & Mackey, supra note 90; cf. Greg Koski, Research, Regulations, and Responsibility: Confronting the Compliance Myth—A Reaction to Professor Gatter, 52 EMORY L.J. 403, 408-09 (2003) (arguing that COI regulations are flawed for emphasizing administrative approaches and a culture of compliance rather than promoting a culture of conscience, because good values, not regulations, will provide an answer to COIs and research ethics).

95 See, e.g., STARR, supra note 26, at 25–26 (illustrating the connection among professional autonomy, professional ethics, and control of competition and pricing); id. at 385–86 (discussing features of physician practice and pricing designed to increase health care costs and increase profit, including reducing the scope of surgeons’ actual service to patients while maintaining full reimbursement).

96 Taylor, supra note 57, at 290–91.
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The first variation is that responsibility for COI assessment and elimination should be transferred away from universities and hospitals, because their conflicting interests are unavoidable and surpassingly influential. Such assessment is factually outside the scope of the professional expertise and disinterested virtue required to justify the privilege of self-regulation.\(^97\) Ensuring the credibility, knowledge, and disinterest of data-educated interpreters is essential, of course. It is the data-independent, binary good/bad approach and innovation-apart resolution that place this within the virtue-prohibitionist camp.

The second variation is treating human subject regulations and institutional assurances of compliance as creating legal rights and obligations to be enforced civilly by participants or through criminal penalties.\(^98\) The apparent analogy is to antidiscrimination laws or the criminal law, except there are no defenses or affirmative defenses that might reflect some social weighing of competing concerns. (Consider the “No, I was innovating!” defense, for example.) This approach increases the size of the penalty and arguably has justice to commend it. However, it does nothing to address the fundamental question of what to hit, where, how hard, and whether perspicacious use of incentives would improve public policy.

The third version of the virtue approach starts from the same premises, but argues that if virtuous transparency is adopted through disclosure, COIs are adequately addressed.\(^99\) Empirical surveys of research participants and studies of global cultural variation rebuff this theoretical claim. Disclosure may produce confusion, and bargaining asymmetries or other factors may lead to embracing or acquiescing in problematic relationships.\(^100\)

B. The Counter-Fiduciary Critique

The Counter-Fiduciary critique, best articulated by William Sage, argues that a fiduciary conceptualization of COIs rests on mistake. Since fiduciaries are essentially agents, and researchers are not agents of participants, relational duties and language should be replaced by socially imposed duties reflecting a utilitarian calculus that accepts some participant harm as the cost of an appropriately balanced emphasis on promoting academic-industry collaboration.\(^101\) In Sage’s view, COI discussion based on professional fidelity to

\(^{97}\) See, e.g., Jordan, supra note 90.

\(^{98}\) See, e.g., Clamon, supra note 90.

\(^{99}\) See, e.g., Kuzma, supra note 43; Sharp & Yarborough, supra note 90.

\(^{100}\) See Timothy Caulfield, Globalization, Conflicts of Interest and Clinical Research: An Overview of Trends and Issues, 8 WIDENER L. SYMP. J. 31 (2001); Kuszler, supra note 39; see also Christine Grady et al., The Limits of Disclosure: What Research Subjects Want to Know about Investigator Financial Interests, 34 J.L. MED. & ETHICS 592 (2006); Mark G. Kuczewski, Conflict of Interests in Biomedical Research: Beyond Disclosure, 19 ANNALS HEALTH L. 103 (2010).

\(^{101}\) See Sage, supra note 27.
patients misses the reality of the researcher-participant relationship. Sage’s position is the most powerful independent critique of the Virtue-Prohibitionist approach. Its difficulty is that, from the perspective of an opposing combatant, it is only as strong as the premise that fiduciary obligations are no more than agency obligations with a fancy name, which is contested both historically and jurisprudentially. In addition, absent data, it may well be premature to assume that supporting innovation will come only at the expense of increased and unmanaged bias in related research.

Far less sophisticated versions of the Counter-Fiduciary critique (typically advanced by researchers with consulting agreements) abound in the biomedical literature. However, they simply repeat in different forms the beneficence of collaboration in generalized terms, without grappling with competing views, articulating the basis for modified discussion, or formalizing an ethical defense.

C. The Circumstance-Based, “Probabilist” Critique

The Circumstance-Based, “Probabilist” critique is a response to, and analysis of, demands that the regulations be interpreted to take into account individual researchers’ propensities and scientific reputations in COI management. The leading example, the IOM 2009 report, defines a COI as “a set of circumstances that creates a risk that professional judgments or actions regarding a primary interest will be unduly influenced by a secondary interest . . . . A COI describes a situation, and is not per se a judgment about the character or actions of an individual.”

A variation on this approach, deemphasizing a psychological focus on the researcher, looks to the probable effect on others. COIs are not wrong, only their bad effects are problematic where they occur. The probabilist critique claims to avoid individual character determinations by turning to circumstances. It seems to promise objectivity, but it actually does not. The passive voice may conceal it, but one is still left with “risk for whom, me or you or some unknown reasonable man” and “as assessed by whom” and under what standards? Indeed, since the circumstantial categories may end up reflecting on character, the escape from personal character judgments is more apparent than real, unless the categories are gross enough that they only vaguely reflect differential risks. In addition, like virtue criticisms, it looks only at one side of the New Scientist equation, offering no assessment or model for integrating, adapting or optimizing the parameters for collaboration and innovation.

Since coherence with the innovation ecology is not a goal of the COI literature, and debating competing principles rather than investigating convergent facts is its main method, that literature provides neither data nor insight into how to foster both research integrity and innovative translation of discoveries through

102 See IOM REPORT, supra note 3, at 46.
103 See, e.g., Kubiak, supra note 90; Ossorio, supra note 90.
precise adjustments in academic-industry relationships.

Understanding COIs requires richer knowledge of the context of collaborations and contract terms that guide those agreements. First, regardless of enforceability, these terms may represent understandings that have a psychological or behavioral impact. Second, they may be the basis of study, looking towards a fuller understanding of their influence in COI creation and mitigation and their utility or necessity in understanding optimal researcher participation with industry. In this light, the claim that consulting agreements of unspecified services are necessary for drug innovation is clearly overbroad. Conversely, implicit claims in “sunshine-oriented” databases – indicating only dollar amounts paid to researchers by private funders, not the payment purpose or terms of use – are insufficient, misleading and unjust to both researchers and industry. Consulting should neither be demonized nor canonized, but understood and represented in context. Third, if their links to behaviors and their social context are both understood, contract terms may be tools–other than divestment or limitations on research participation–for defining permissible and impermissible situations, particularly if they are considered within understanding the parties’ overall relationships. Indeed, if a scientist’s services are narrowed to providing advice on matters where their advice could support innovation development, with contractual terms eliminating distorting incentive structures and protecting academic values, then institutions will have a mechanism to connect COI analysis to the innovation ecology.

IV. RECOMMENDATIONS

The critiques of existing COI regulations are a fundamental starting point for reform. There is no reason to believe that a completely deregulated system will address these critiques, in part because of COIs’ potentially covert nature, and in part because of their extraordinary variability and the extraordinary variability in sophistication and insight among actors. Indeed, the federal government experimented with deregulation before 1995, when pressures to collaborate were fewer, and it did not work. Lack of regulation created the circumstances leading to the current regulations.

Thus, despite their fundamental invalidity as a matter of jurisprudence, and their wide-ranging departure from the established norms of administrative law, current regulations should be improved, not simply abolished. The process to do so should include (1) rectifying procedural defects, using lawyerly values and procedural devices for increasing accountability, case-specific accuracy and systematic epistemic competence; (2) empirical investigation, sufficient for regulation of COIs within the innovation ecology, and informed choices about forms of collaboration that create both significant benefit and significant risk; (3) interim use of default rules that create useful incentives until optimal ones can be created; and (4) creating “how-to” models for collaboration among institutions,
researchers, and industry, so that the efficiency, justice, consistency and rational basis of prospective, published, testable, factually-grounded regulatory guidance would replace unpredictable retrospective adjudications. I will take up each of these topics in turn below.

A. Fix the COI Regulations Procedurally

The procedural infirmities identified in Part III should be rectified, in order to respect due process values and to improve the epistemic competence of the system, through qualified interpreters ascertaining facts according to empirically defensible inferences concerning both behavioral responses to incentives and effective management strategies. There are three additional steps the NIH could take:

1. Ensure that regulatory interpreters, functioning as “judges” with extraordinary power, are qualified. Ensure also that COI committees themselves are sufficiently diverse, and organizationally situated, to be recognized as legitimate, knowledgeable, and independent. The regulations permit COI decisions to be made by individuals as diverse as a mid-level research administrator, the university provost personally, or a research hospital’s general counsel. It is obvious that each is likely to approach this open-ended inquiry with different dispositions, understanding, and authority. Specifically, committees should include the following personnel: senior scientists experienced in working with industry and with demonstrated ability to remain independent; legal counsel not involved in industry transactions being evaluated; community membership not limited to business representatives; the IRB chair; the chief academic officer or other officer in a position to regularly compare research endeavors and publications with collaborations; and, as staff to answer questions, but not participate in deliberation, advocacy, or decision making, a senior research administrator; and the head of the office responsible for technology transfer and industry relationships. In a training institution, the committee should include students and fellows.

2. Protect the COI process from institutional COIs. Regulations prohibit an IRB determination that research is unethical from being overturned by administrative decisions from above. Should the same be true for a COI committee, to be committed to its independence? If some institutions are reluctant to accept this, it may be because, internally, arbitrary and unpredictable results may flow from the lack of any regulatory guidance on committee member qualifications, procedures, inferences, management

104 45 C.F.R. § 46.112 (2011).
strategies, and data. The wise course would be to design a system sufficiently inclusive and rational in its thinking that it both deserves and receives that special, independent authority. The committee and its authority should be sanctioned by a directive of the Board of Directors, and the committee should report to the Board directly, in executive session. The board directive should clarify that the committee will consider requests for reconsideration, but that there is no appeal from its adverse decisions except based on error; and then the appeal is to a committee of the board.

3. Assuring the legitimacy of COI management may require changes in the obligations and goals of institutional technology transfer offices. Various recommendations exist that could be the basis of regulations, including a recently published, comprehensive National Academies Report that deserves careful attention, and a recent Consensus Statement by The Hinxton Group on data and materials sharing in stem cell science. The AAMC and others have urged the separation of intellectual property structures from integrity-related ones, in order to safeguard integrity. This is idealistic but imperfect, for it fails to address the institutional corollary of the innovative virtue of the new scientist. Moreover, the price in practice is technology transfer run amok, unless one thinks that the role of the university is to reduce access to medical care as long as doing so makes money, threaten academic stem cell researchers who might compete, and deceive donors of tissues and funds as long as the price is right. Academic management of intellectual property and its licensing should not be divorced from the obligations of a university to the public, or of a research hospital to present and future patients. One of the great challenges of our time is to get this right, training the vine of idealism on the trellis of reality and practical fact. The issue for the institution is the issue of the profession spelled large: to reconcile competing concerns within a coherent framework.

**B. Collect Data**

An empirical basis for regulation requires data and the systemic competence to use and revise it. The preceding Section provided a taste of how fine-grained data collection should be, collecting information about contractual variables from


result-dependent compensation structures to noncompetes. My goal in this Section is to move the discussion forward one more step, both by (1) describing the parameters of a system that would effectively generate inquiry and employ its answers and by (2) giving some examples of how data might help guide policy choices through verifying or falsifying their assumptions or premises. The following Sections will then (3) suggest interim default rules to use until data justify better ones and (4) outline steps towards the creation of constructive “how to” models to replace, at least in part, the retrospective and necessarily arbitrary structure that is in place now.

Before setting out what may appear as an ambitious agenda, it is useful to demonstrate that data are readily within reach. As the IOM observed, there are no data on effective management of COIs. As this Article has reiterated, there are no public data supporting the judgments that COI committees are routinely asked to make, or analyzing the COI effects or innovation contributions of quite various collaboration arrangements. But what the government and academic institutions do have are datasets that, if correlated, could provide important answers to whether, as in other areas of law, the way incentives, compensation, and other terms are structured affects whether they reinforce quality standards or undercut them. What is missing is the effort and infrastructure to correlate these variables. Academic IRBs have isolated adverse event data from clinical trials, not presently evaluable against financial interest information. The federal government has data on research misconduct, arising from the Office of Research Integrity’s oversight of academic proceedings for scientific fraud and plagiarism, but these data are not publicly cross-linked or searchable for whether financial interests or financial relationships of various forms are differentially associated with misconduct. State and federal health departments, hospitals, and health-product consumers all have access to safety information, though this is also not cross-linked or searchable against research participation or financial interests. Yet all of these sources, and others outlined in the recommendations of this Article, provide a basis for optimism. Problems with financial interests and relationships could be linked in more interesting ways, if data sets are parsed. If not all relationships cause problems, but some do, and if only some really promote innovation, regulations could be promulgated accordingly. The data to determine this are already partly created. COI management could be reserved for those that are socially useful and regulations could prohibit those that are not as socially useful, or at least require institutions to internalize to scientists their management costs.

1. Creating a Networked System for Collection and Use of Data

Situating COIs in the innovation ecology will require a networked system of

108 See IOM REPORT, supra note 3.
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data collection. This data collection should occur longitudinally through time, yet should be comparable and searchable across cases for correlations among key variables relating to incentives, behaviors, misconduct, and management. If decisions are to be made locally, then data must be collected locally, shared, aggregated, and analyzed nationally. It also must be made available, with analytic results, both locally and nationally, publicly and academically.

Data must be maintained in a manner that permits new premises and hypotheses to be tested, trends to be noted, and conclusions to be shared and examined. Data should encompass and link outcomes such as harms to participants, misconduct allegations and determinations, protocol deviations, results that cannot be replicated, and withdrawn publications. Those and other harms should be assessed for their degree of correlation with key variables, such as incentives and their structures; industries, since industries seem to vary in their COI and misconduct susceptibility; and the others used in current population studies referred to above. Studies that would examine the linkages described above are currently impossible, not because informatics tools are lacking, but rather because there is no recorded data. Or if these data exist, they are not linked or shared. Yet this sort of study, involving other variables, is now very possible in most other areas of medicine and biotechnology. The informatics tools exist and are in widespread use.

In collecting data, creating standards, formulating rules, and evaluating impact, it would be beneficial to examine contract terms in determining whether an academic-industry relationship is positive or negative and whether its consequences are probable or improbable. So-called sunshine public databases that purport to justify an inference of wrongdoing based only on dollar values should become more sophisticated, rather than more unjust. A $3.00 “payment” of unregistered securities can be far worse than a $20,000 payment for consulting. Registries should be improved through additional data fields, so that the public and regulators alike can distinguish toxic and dangerous relationships from praiseworthy and innovation-producing ones.

In this regard, relevant and correct data categories must be assessed and separated from those policy-driving factual categories that are not demonstrably consequential. Above, for example, I rejected the principle that COIs from securities are always worse than COIs from cash because contracts and context make a pivotal difference. Yet that overbroad principle is widespread, and the NIH’s zero-dollar threshold for unregistered securities reflects precisely this. Presumably it is based on the view that securities can inflate in value (while cash cannot) and an identifiable cognitive transposition error: since lawyers call options, warrants, privately held stocks, and publicly traded stocks all “securities,” this term should be defined in precisely the same way in COI policy. But in this context, the definition should optimally depend on clusters of like behavioral effects.
It is necessary to examine the effect of the network of obligations that surround a scientist. The current regulations, which do not do this, presume that the significance and effect of interests can be assessed in isolation. To the contrary, the network of obligations both shapes the actual impact of agreements and provides a tool to mitigate their effect. A sponsored research agreement that prohibits sidebar agreements or requires that consulting revenues be assigned to a general departmental research fund immediately mitigates or prevents COIs. A sponsor’s per-participant research payments can create a COI if paid to a principal investigator, but not if pooled with other studies’ payments, and distributions are made, regardless of the incentives, for charitable purposes. NIH, IOM, and AAMC recommendations miss these important tools.

Continuing our network concept, COI management should be linked to the network of other existing systems that could support the identification and management of COIs, to improve participant protection and to correct our current reliance on self-reporting of adverse events by financially interested researchers—the very matter criticized in the Gelsinger case, which still, ten years later, remains uncorrected by mandated system improvements. Legally mandated systems devoted to patient safety, which can be as fine grained as reporting on the EKG and CO2 levels of a patient every few seconds, should be enlisted to support the safety of research participants. This would be more beneficial than, for example, insulating from the clinical team all knowledge of their patient’s participation in a research study that would allow them to distinguish clinical trial expected side effects from unexpected and troubling morbidities requiring naive exploration at the expense of patients’ time, energy, and suffering.

2. Using These Data

Science and data cannot dictate directly which conflicts of interest to tolerate and what balance of innovation and bias to tolerate. This involves inescapably normative decisions that ought to be publicly transparent and publicly influenced. As Robin Feldman has argued, legal importation of scientific standards, under the false assumption that data themselves will establish decisional norms, inevitably oversimplifies complex factual questions and conceals complex normative ones. It is as mistaken as using virtue narratives, without empirical roots, to make COI policy.

109 See supra note 41 and accompanying text.
110 ROBIN FELDMAN, THE ROLE OF SCIENCE IN LAW 49–78 (2009) (providing examples where the transfer of scientific results or principles to justify reasoning or create rules misstated the scientific evidence or founded normative rules on fragile empirical foundations); id. at 200 (“[R]elying on science creates the illusion of reasonable resolution [and] masks our failure to resolve the issues at hand or to take responsibility for the decisions we have made. We gain authority through obscurity rather than the careful unfolding of legal analysis.”).
Data can and should be used to confirm or falsify the assumptions used in policy-making. As examples, I shall start with the easy (and unlikely) outliers. If every form of consulting arrangement and every Bayh-Dole payment always produces substantial uncontrollable bias or corruption, Bayh-Dole should be altered, and consulting, barred. It will have been demonstrated that they uncontrollably harm research, and it will be equally evident—since development depends on accurate research results—that biased results do a disservice to innovation development. In that event, the aims and preconditions for research integrity and robust innovation would be one and the same, so current conflicting imperatives would be replaced by a more consistent one: protect the innovation ecology, research objectivity, and human research participants by eliminating all forms of compensated academic-industry advising. The link would also be established by the contrary, equally unlikely finding that no consulting arrangements or Bayh-Dole licenses harmed research objectivity or participants and that in all cases, regardless of the nature and scope of services, they benefitted innovation development.

More realistically, in order to demonstrate how powerful and worthwhile data collection could be, let us consider the following example in which hypothetical data concerning the differential positive effects of contractual noncompetes and unregistered equity might support a currently counterintuitive policy outcome:

A scientist’s area of expertise is in a certain biological factor, found in human blood, believed to play multiple roles in red blood cell metabolism. Through continuing NIH-funded research, he discovers that a particular enzyme enhances the metabolic effect of the factor and hypothesizes that the enzyme could be used to alleviate certain anemias. The university files a method patent claiming use of this enzyme as a therapy for this purpose and licenses it to a start-up. Consulting by the scientist is limited to addressing side effects given the factor’s other multiple roles, and, non-exclusively, other enzymes that might also increase the factor activity. Noncompetes are barred, but company confidential information will be strictly protected. The company has no claims to his future inventions, except the nonexclusive one noted. In this case, his research is intimately related to the company’s application — in fact there is no possible separation. But his independent academic research goal, finding other enzymes that enhance this one, is consistent with both societal therapeutic goals and company goals. The danger that he will siphon off novel information to the company, which may suppress competition, is plausible, but given the bar on noncompetes, and the potential to engage with another company...
around other factors, so is the opposite. He is allowed to hold unregistered equity in the company, with no further options or deferred vesting, provided processes can ensure that his novel information is really nonexclusively provided and is generally published through the scientific media. So put, with the burden of doing so on him, he has an incentive to help design and maintain a sufficiently transparent system. Failing that, his privilege to hold equity will be revoked. Data show that holding unregistered equity without further result-dependent options or vesting is actually harmless, because its ultimate sale will occur only after a long process of multiple independent valuations of the technology. Scientists know this and the remoteness and hypothetical nature of the benefit produce negligible bias incentives compared to their academic and personal incentives to do innovative, replicable, sound science.

To Virtue-Prohibitionists, and even to COI-moderates, the example above is provocative, given their belief that equity is always evil.111 This example challenges a reflex to deny equity and involvement by the scientist in a project squarely within his academic research, as well as an opposing reflex in industry to turn him into a jack-of-all-trades scientific salesman with potential investors. The scientist’s role is really quite precise: do your academic work, continue to publish it nonexclusively, and, if in the development of this there are insights that would protect patients from side-effects, or boost the therapeutic value, tell the company. The scientist takes a part, as Bayh-Dole demands, of the value of the original invention, and remains aligned to see that it works in practice. At the same time, no commitment is made to this company that it will be the only one, and if he generates more discoveries, other companies will be interested in competing for his attentions. He is in a position of having to maintain confidentiality among companies, something that lawyers have become accustomed to without difficulty, as have doctors with patients.

For our second example, let us suppose that data show that institutionally managed service arrangements can effectively mitigate bias influences that would otherwise arise under certain consulting arrangements:

A scientist, who is an expert in genomic informatics analysis, is approached by a large company that wants her to adapt her already powerful analytic software tools to a “new generation” of DNA sequencers that look beyond single nucleotide polymorphisms (SNPs) and exomes. The key challenge in DNA

111 See, e.g., Angell, supra note 2.
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sequencing is determining which elements and associations are meaningful, how meaningful they are, and which are recurring, but accidental. Hybridizing the company’s premier sequencing capabilities with the next stage in her informatics platform is exciting to her, and, if it works, worthwhile, given the new window into understanding genes in operation. The company wants to engage her exclusively to consult and to own her output, which would be funded in part by NIH grants already awarded for the same work. They would offer her $150,000 per year.

Given what data show and the normative appreciation for the social importance of the work, the agreement is converted into a service agreement between the university and the company. Improvements to the platform that are not unique to the company’s technology will be owned by the university and made available open source. Unique improvements that co-depend on company technology and would therefore reveal trade secrets are co-owned, but the university’s uses are limited to internal research. And the collaboration is mutual, not unilateral, in that the company agrees to make its advanced sequencing services available at discount for a well-publicized effort to address certain pediatric orphan diseases. Publication is joint with respect to materials that are not trade secrets. She receives $150,000 per year: half personally as salary support with an increment, and half, by her choice, paid directly to a research fund for her at the university. She intends to use these funds in the event that her NIH funding dries up.

This example is also deliberately provocative. Yet, I submit it is possible that it may be eminently sensible in promoting industry innovation at the same time it co-funds NIH-funded scientific advances for the public good that are made available in an open-source format. Based on a combination of real examples negotiated by the author, it takes seriously the idea that even where originally misaligned, company and academic goals can become realigned in a way faithful to academic values and the purposes of federal funding. This case is better than the first one, because the company is playing an active reciprocal role. The scientist’s contribution to innovation is real and direct. The company’s contribution to co-funding, with the federal government, improvements to technology that will become publicly available also is tangible and direct. The generation of applications for the private sector, sought by Bayh-Dole, is direct. The benefit to the public from open source improvements is direct. And yet, if
one had posed the question of whether the doctor can take $150,000 per year from a company to do consulting work in the area of her funded research, the conventional COI answer would have been "absolutely not."

C. Default Rules

A comprehensive regulatory framework cannot be adopted until more data collection occurs. In the interim, however, some basic default rules can guide policy implementation and practice:

1. Prohibit deferred vesting, noncompetes, result-dependent transfers of unrestricted publicly traded equity, publication restrictions except for trade secrets, terminations without cause, company sole ownership of academically overlapping IP, and service definitions not tied to the original innovation or that aspect of development within contributory expertise.

2. Require collaborative improvement licenses or co-ownership by academic institutions for internal research, and ensure, at the least, nonexclusive availability of academic improvements subject to company trade secrets and distinct company patent rights.

3. Convert direct payments into institutionally managed payments provided that no institutional COIs are created in the process. This would require taking action to assure the independence of institutional review processes.

Our default rules should incentivize issuers, interpreters, and subjects of contractual agreements to act appropriately. Interpreters, for example, might be incentivized to develop pertinent databases and quality improvement program-based approaches by inflicting the severer sort of prohibition. In effect, this takes the AAMC presumption and kicks it up one notch, from the individual to the organization interpreter, and up two notches in the case of the funder or regulator as issuer. Harsher rules are likely to incentivize the faculty to participate in such efforts in data collection to support some other, perhaps local, rule, although, given what is at stake, the biases inherent in their impulse would also have to be controlled for. A funder’s default rule could be prohibitory, or it could possibly be disclosure oriented, to require scientists to self-identify to peer reviewers their form and degree of industry involvement (including purpose, role, and contract commitments). The goal would be for NIH to develop and fund research programs and databases devoted to resolving the fundamental issues.

Our default rules should also internalize to researchers and companies the costs of assessing and managing self-serving and socially ambiguous COIs by imposing a financial assessment on researchers engaged in such COI-generating activities. In its ideal state, this would distinguish between researchers based on a
behaviorally validated function, differentially cost-shifting arrangements that deviate from a socially ideal mixture of functions that optimize ethical and efficient development of safe and effective diagnostics while minimizing bias. It seems unlikely that there is a single point at which all values are maximized, while biases are minimized. Yet the thought that utility maximization, with or without de-consequentialist parameters, may be more complex than X, Y, and an asymptote, or a straight inclined line within a region of zero risk, has not defeated utilitarianism yet. Indeed, competing functions may disparately weigh many variables. But whether the justification is as theoretical as internalizing costs, as pragmatic as disincentivizing COI complexities, or as practical as funding the management process so it can actually occur, there seems little to be said in favor of allowing the present COI management system to continue—allowing scientists to free-ride on other systems to pursue private benefit, if it is socially undesirable and solely self-serving.

D. Move from Retrospective COI Determinations to “How To” Models

COI management currently involves retrospective, nontransparent administration under a vague standard. Voluntary compliance is difficult. The value of data-informed transactional safe harbors, or “here is how to do it right” models, is obvious. Describing such models means rethinking the boundaries of researchers’ and doctors’ professional virtues. This is an exercise long overdue. Some fear that doing so will require abandoning professional virtue. Let us address this important concern through an example from health care professionalism itself.

Fifteen years ago, in the heights of managed care, the great conflict-of-interest issue was the antagonism perceived between cost containment and a fiduciary obligation to individual patients to provide optimum care. It was in such terms that the issue came to the Supreme Court. A patient’s appendix ruptured, due to a belated referral to an in-network provider incentivized by a physician payment structure in a physician-owned HMO.112 The Court was asked whether, in the ERISA context in which the case arose, the physician had a fiduciary duty to the patient. The Supreme Court answered in the negative, issuing a binary decision in a complex area. This was a pyrrhic victory for managed care, because it spelled the beginning of a series of legislative reversals in almost every state around the country that ultimately destroyed managed care.

Drawing the connection between the death of managed care and professional self-definition, Einer Elhauge predicted that, for care cost to be addressed, physicians would have to redefine their fiduciary focus from the individual to the group—an idea that no doubt seemed wholly demonic from the perspective of

physician leaders. Yet, I would submit that this is exactly what has occurred, and in a manner that has enhanced, not undermined, the virtue of the profession.

The route was through the concurrent development of evidence-based medicine and safety systems, linked with concerns about undertreatment, overtreatment, and mistreatment. It is only a small step to move from those concerns to defining overtreatment as treatment with diminishing marginal benefits and increasing individual patient harms across a population. It is another small step to create treatment protocols, based on the population, that will typify proper treatment in similar terms. It is only one more small step to broaden the concept of marginal benefit and marginal cost to take into account the allocation and optimal investment, from a care perspective, of limited physician, nursing, and other professional resources in a context of diminishing benefit. Given that labor costs drive the bulk of hospital and physician bills, such a concept implies a virtuous “group” model. The virtue of physicians is no longer measured just by an intention towards an individual patient. It is measured by the physician’s devotion, judgment, and skill in relationship to a clinical treatment ideal, the ability to weigh competing concerns, and the ability to make exceptions when clinically appropriate in relationship to outcomes: in short, the ability to act justly – to treat like cases as like and different cases differently, where there is a special justification. Justice and treatment based on knowledge sound like virtues. Fulfilling Elhauge’s prediction did not require abandoning virtue. It required an interlinked maturation of how the profession conceived itself and the systems that would allow it to act consistently with that definition. With that maturation it became possible to design incentives and care structures that promoted appropriate utilization as an aspect of patient care.

Here, data are needed to establish when collaborations are useful, and what collaboration structures should be avoided or followed. There are plausible candidates already. Institutional collection, pooling, and redistribution of consulting revenue in connection with technical advisory services, all mediate incentives and focus contributions. The default rules, if vindicated empirically, suggest others.

V. CONCLUSION

Industry and academic biomedical research draw continuously closer, as inevitable partners in creating the practical fruits of scientific discovery. If industry relies on academia for new insights, academia relies on industry to

113 See Einer R. Elhauge, Can Health Law Become a Coherent Field of Law?, 41 WAKE FOREST L. REV. 365, 387 (2006). Professor Elhauge’s prediction was made in the context of two important observations: that the law supports systems of payment and care that not only compete but mutually detract; and that professional and public morality have had an extraordinary influence on the chosen paradigms. Id. at 379–84. His views on the causes of mutual incoherence, as well as the professional challenges they create, are applicable in this context as well.
demonstrate the practical value of basic science to a public that requires more than knowledge for knowledge’s sake. Fear of research bias, or its appearance from industry contact, has been a preoccupation of academic medicine, its funding agencies, and its political arms. Reputable journals decry highly paid relationships with industry as “typical,” implying that all public advice and academic research have become untrustworthy. Yet such conflict has been addressed without collecting data as to whether, how, and when it occurs or assessing the actual benefit of different forms of industry collaboration, or offering precise guidance reflecting those facts.

The regulatory structures created in consequence are loose and weak. Agencies are divided among several government entities and hundreds of research universities and research hospitals—all operating under unarticulated or inconsistent standards, created with limited or no data concerning their necessity or effect, and many without processes to control the institutional conflicts of interests that could demonstrably affect their reliability and bias. So piecemeal and inconsistent is the legal structure, so diversely rationalized, and so premature compared to datasets, that a student of law might well ask whether the structure is law and what makes it so. It is law in only the barest of senses. There is a basic mandate to do X. And if X is not done, the issuer will do something predictably bad. Except that not even that has happened; the NIH did not enforce these regulations, even when the system repeatedly failed over the course of many years.

This aerial sense of law rightly has been replaced by a more sophisticated

\[114\] See, e.g., Charles Seife, How Drug Company Money is Undermining Science, SCI. AM. (Nov. 21, 2012), available at http://www.scientificamerican.com/article.cfm?id=how-drug-company-money-undermining-science. Although he observed that “such relationships are not all bad,” Seife does not identify or establish that any are actually beneficial. Instead he describes as “typical” (1) known cases in which senior government advisors on drug or device approval have simultaneously maintained highly compensated advisory relationships with industry; (2) extreme practices, such as companies “ghost writing” publications describing research results that are signed by academic researchers who had little involvement, but accepted both fees and attribution; and (3) critics’ claims that the NIH is doing little to police such situations. Seife asserts that only a change in research culture can restore trustworthiness to science. This Article, however, disputes the assertion that such arrangements are typical of all scientists and collaboration arrangements, and the conclusion that cultural segregation is the only (or even a complete) solution. As I have shown, collaboration arrangements are far more varied, and the arrangements to which Seife refers are neither representative nor ubiquitous. The small number of senior advisers to both pharma and government, who have met the substantive and political selection criteria each imposes, are hardly representative of the thousands of relatively unknown academic scientists whose primary work is in laboratories in research universities. The disgraceful practice of ghost writing is limited to some companies and faculty. Institutional and professional culture are important, but Seife fails to mention the ways in which they have been fostered by the NIH and the HHS Office of Research Integrity (ORI), nor does he reconcile it with our innovative ecology. See, e.g., Brian C. Martinson et al., Scientists behaving badly, 435 NATURE 737 (2005); Brian C. Martinson et al., Scientists’ Perceptions of Organizational Justice and Self-Reported Misbehaviors, 1 J. EMPIR. RES. ON HUM. RES. ETHICS 51 (2006); 42 C.F.R. § 93.300(c); and 45 C.F.R. §§ 689.1-.10 (2002).
one that seeks (1) an interplay of law and facts—a connection between the issuer’s objectives and the interpreter’s methods based on facts reasonably known to be material, both to predictable resolution of foreseen problems and to wise resolution of unforeseen ones; and (2) an assessment of the rationality against multiple perspectives, including the perspectives not just of issuer and interpreter, but those subject to regulation, and those observing, and sees how a law is understood and thus made real, not once, but over time, again and again and again, as it travels through society. The COI problem therefore teaches a general lesson about the dangers in the law-making domain of even the highest virtue when it is separated from the interrelationship of law and fact. Those who ride under the banners of virtue and public trust and seek to make law their mount must bend to the demands that lawmakers places on all of us, including the truthfulness of their empirical premises, the rationality and empirical testability of their solutions, the values that law translates into paradigm and practice, and the transparency and acceptability—and therefore authority—of a proposed resolution.

The solution proposed by this Article is simple yet radical: to recognize our mistake and to correct it with an epistemically competent system operating from ascertained and pertinent facts. This will require critical novel features: a set of common and clear norms rationally derived from data and evidence, representative of both innovation and research integrity; competent and qualified agencies that will consistently teach and enforce them; and mechanisms for sharing and aggregating information, self-assessment, accountability, and evolution.

The point is not that morals should be abandoned. Rather, it is that the temptations of a facile hypocrisy incentivizing collaboration with one hand, while punishing with another, should be relinquished. What is at stake is more than whether researchers are forced into the discomfort of eternal cognitive dissonance. It is whether the social compact that underlies the sanctioned pursuit of knowledge will hold. The Virtue-Prohibitionists have this right: to the extent that scientists are perceived as trading integrity for personal wealth, the lay society will respond accordingly. Our current scheme for biomedical research is a powerful recipe for destroying public trust, since internal conflicts make failure inevitable. Neither knowledge nor democratic influence over scientific direction will benefit from one-sided, incomplete renditions of COIs in the innovation ecology.

A fuller discussion of the variety of collaboration arrangements—both the net of contracting parties in a research-related relationship and the diversity of contractual terms—is beyond the scope of this article. But such detail is not necessary to understand the basic frame of the argument or recommendations. Resolving these tensions ethically, practically, and effectively is one of the major challenges of our time. It will take a practical, fair, data-grounded, but still
principled, approach. This will not arise through disintegrated policy that dispenses with precision about the drivers and checks on human fallibility, and the true contributions of academic knowledge.