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SYMPOSIUM

**Institutional Corruption and the Pharmaceutical Industry**

Guest Edited by Marc A. Rodwin

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*Letter from the Editor*

*Cover image ©Corbis*

## Symposium Articles

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**INTRODUCTION:** Institutional Corruption and the Pharmaceutical Industry
*Marc A. Rodwin*

Today, the goals of pharmaceutical policy and medical practice are often undermined due to institutional corruption — that is, widespread or systemic practices, usually legal, that undermine an institution's objectives or integrity. In this symposium, 16 articles investigate the corruption of pharmaceutical policy, each taking a different look at the sources of corruption, how it occurs, and what is corrupted. We will see that the pharmaceutical industry's own purposes are often undermined. Furthermore, pharmaceutical industry funding of election campaigns and lobbying skews the legislative process that sets pharmaceutical policy. Moreover, certain practices have corrupted medical research, the production of medical knowledge, the practice of medicine, drug safety, the Food and Drug Administration's oversight of the pharmaceutical market, and the trustworthiness of patient advocacy organizations.

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**FOREWORD:** "Institutional Corruption" Defined
*Lawrence Lessig*

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**Parallel Problems:** Applying Institutional Corruption Analysis of Congress to Big Pharma
*Gregg Fields*

Dennis Thompson and Lawrence Lessig are leading thinkers in the realm of institutional corruption, the notion that inappropriate dependencies and conflicts of interest undercut the ethical foundations of institutions on which society relies. Both are particularly known for their work on institutional corruption as it affects government and politics. This essay examines the applicability of their writing to the private sector, particularly as it relates to vital and influential industries like pharmaceuticals.

### SYSTEMIC PROBLEMS

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**Pharmaceuticals, Political Money, and Public Policy:** A Theoretical and Empirical Agenda
*Paul D. Jorgensen*

Why, when confronted with policy alternatives that could improve patient care, public health, and the economy, does Congress neglect those goals and tailor legislation to suit the interests of pharmaceutical corporations? In brief, for generations, the pharmaceutical industry has convinced legislators to define policy problems in ways that protect its profit margin. It reinforces this framework by selectively providing information and by targeting campaign contributions to influential legislators and allies. In this way, the industry displaces the public's voice in developing pharmaceutical policy. Unless citizens mobilize to confront the political power of pharmaceutical firms, objectionable industry practices and public policy will not change. Yet we need to refine this analysis. I propose a research agenda to uncover pharmaceutical influence. It develops the theory of dependence corruption to explain how the pharmaceutical industry is able to deflect the broader interests of the general public. It includes empirical studies of lobbying and campaign finance to uncover the means drug firms use to: (1) shape the policy framework adopted and information used to analyze policy; (2) subsidize the work of political allies; and (3) influence congressional voting.

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**Corruption of Pharmaceutical Markets:** Addressing the Misalignment of Financial Incentives and Public Health
*Marc-André Gagnon*

This paper explains how the current architecture of the pharmaceutical markets has created a misalignment of financial incentives and public health that is a central cause of harmful practices. It explores three possible solutions to address that misalignment: taxes, increased financial penalties, and drug pricing based on value. Each proposal could help to partly realign financial incentives and public health. However, because of the limits of each proposal, there is no easy solution to fixing the problem of financial incentives.

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**Five Un-Easy Pieces of Pharmaceutical Policy Reform**
*Marc A. Rodwin*

Improper dependencies slant policy over a drug's life span, biasing the development of new drugs, the testing and marketing approval for new drugs, and the monitoring of patient safety after drugs are marketed. This article examines five ways in which the public improperly depends on pharmaceutical firms that compromise the integrity of pharmaceutical policy. Today the public relies on pharmaceutical firms: (1) to set priorities on drug research and development; (2) to conduct clinical trials to test whether drugs are safe and effective; (3) to decide what clinical trial data to disclose to the public; (4) to monitor post marketing drug safety; (5) to supply product information to physicians and to finance continuing medical education and other professional activities. The article suggests options to overcome each of these dependencies.

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**Institutional Corruption of Pharmaceuticals and the Myth of Safe and Effective Drugs**
*Donald W. Light, Joel Lexchin, and Jonathan J. Darrow*

Over the past 35 years, patients have suffered from a largely hidden epidemic of side effects from drugs that usually have few offsetting benefits. The pharmaceutical industry has corrupted the practice of medicine through its influence over what drugs are developed, how they are tested, and how medical knowledge is created. Since 1906, heavy commercial influence has compromised congressional legislation to protect the public from unsafe drugs. The authorization of user fees in 1992 has turned drug companies into the FDA's prime clients, deepening the regulatory and cultural capture of the agency. Industry has demanded shorter average review times and, with less time to thoroughly review evidence, increased hospitalizations and deaths have resulted. Meeting the needs of the drug companies has taken priority over meeting the needs of patients. Unless this corruption of regulatory intent is reversed, the situation will continue to deteriorate. We offer practical suggestions including: separating the funding of clinical trials from their conduct, analysis, and publication; independent FDA leadership; full public funding for all FDA activities; measures to discourage R&D on drugs with few, if any, new clinical benefits; and the creation of a National Drug Safety Board.

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**From Bad Pharma to Good Pharma:** Aligning Market Forces with Good and Trustworthy Practices through Accreditation, Certification, and Rating
*Jennifer E. Miller*

This article explores whether the bioethical performance and trustworthiness of pharmaceutical companies can be improved by harnessing market forces through the use of accreditation, certification, or rating. Other industries have used such systems to define best practices, set standards, and assess and signal the quality of services, processes, and products. These systems have also informed decisions in other industries about where to invest, what to buy, where to work, and when to regulate. Similarly, accreditation, certification, and rating programs can help drug companies address stakeholder concerns in four areas: clinical trial design and management, dissemination of clinical trial results, marketing practices, and the accessibility of medicines. To illuminate processes — such as conflicts of interests and revolving-door policies — that can jeopardize the integrity of accreditation, certification, and ratings systems, the article concludes with a consideration of recent failures of credit-rating agencies and a review of the regulatory capture literature.

## MEDICAL RESEARCH

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**Understanding Pharmaceutical Research Manipulation in the Context of Accounting Manipulation**
*Abigail Brown*

The problem of the manipulation of data that arises when there is both opportunity and incentive to mislead is better accepted and studied — though by no means solved — in financial accounting than in medicine. This article analyzes pharmaceutical company manipulation of medical research as part of a broader problem of corporate manipulation of data in the creation of accounting profits. The article explores how our understanding of accounting fraud and misinformation helps us understand the risk of similar information manipulation in the medical sciences. This understanding provides a framework for considering how best to improve the quality of medical research and analysis in light of the current system of medical information production. I offer three possible responses: (1) use of the Dodd-Frank whistleblower provisions to encourage reporting of medical research fraud; (2) a two-step academic journal review process for clinical trials; and (3) publicly subsidized trial-failure insurance. These would improve the release of negative information about drugs, thereby increasing the reliability of positive information.

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**Curbing Misconduct in the Pharmaceutical Industry:** Insights from Behavioral Ethics and the Behavioral Approach to Law
*Yuval Feldman, Rebecca Gauthier, and Troy Schuler*

Two insights of psychology on which we would like to draw are that people react to law in more complex ways than rational-choice models assume and that good people sometimes do bad things. With that starting point, this article provides a behavioral perspective on some of the factors that policymakers seeking to reduce the level of misconduct in the pharmaceutical industry should consider. Effective regulation and enforcement need to address the following questions: Who are the regulation's targeted actors — researchers or executives? Are the regulations directed toward research or marketing activities? Is the misconduct a product of explicit rational choice or implicit processes of which the actor is unaware? Is it reasonable to address all types of misconduct using the same approach? Certain misconduct — particularly by researchers — is due to automatic, intuitive, and unconscious decisions and needs to be addressed through different means than those used to address misconduct due to controlled, deliberate decisions. This article therefore recommends using

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different sorts of regulation depending on the context. It suggests more tailored enforcement mechanisms that will be sensitive to the pharmaceutical researchers' unique work motivations and to their awareness or lack of awareness of their own misconduct.

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**The Ethics of Pharmaceutical Research Funding:** A Social Organization Approach
*Garry C. Gray*

This paper advances a social organization approach to examining unethical behavior. While unethical behaviors may stem in part from failures in individual morality or psychological blind spots, they are both generated and performed through social interactions among individuals and groups. To illustrate the value of a social organization approach, a case study of a medical school professor's first experience with pharmaceutical-company-sponsored research is provided in order to examine how funding arrangements can constrain research integrity. The case illustrates three significant ways that institutional corruption can occur in the research process. First, *conflicts of norms* between pharmaceutical companies, universities, and affiliated teaching hospitals can result in compromises and self-censorship. Second, *normal behavior* is *shaped* through routine interactions. Unethical behaviors can be (or can become) normal behaviors when they are produced and reproduced through a network of social interactions. Third, funding arrangements can *create networks of dependency* that structurally distort the independence of the academic researcher in favor of the funder's interests. More broadly, the case study demonstrates how the social organization approach deepens our understanding of the practice of ethics.

MEDICAL KNOWLEDGE AND PRACTICE

635
**Key Opinion Leaders and the Corruption of Medical Knowledge:** What the Sunshine Act Will and Won't Cast Light On
*Sergio Sismondo*

The pharmaceutical industry, in its marketing efforts, often turns to "key opinion leaders" or "KOLs" to disseminate scientific information. Drawing on the author's fieldwork, this article documents and examines the use of KOLs in pharmaceutical companies' marketing efforts. Partly due to the use of KOLs, a small number of companies with well-defined and narrow interests have inordinate influence over how medical knowledge is produced, circulated, and consumed. The issue here, as in many other cases of institutional corruption, is that a few actors have accumulated the power to shape the information on which many others base their decisions. Efforts to address this corruption should focus on correcting large imbalances in the current political economy of medical knowledge. A sequestration of pharmaceutical research and development on one hand from pharmaceutical marketing on the other, though difficult to achieve, would address this and many other problems.

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**Drug Firms, the Codification of Diagnostic Categories, and Bias in Clinical Guidelines**
*Lisa Cosgrove and Emily E. Wheeler*

The possibility that industry is exerting an undue influence on the culture of medicine has profound implications for the profession's public health mission. Policy analysts, investigative journalists, researchers, and clinicians have questioned whether academic-industry relationships have had a corrupting effect on evidence-based medicine. Psychiatry has been at the heart of this epistemic and ethical crisis in medicine. This article examines how commercial entities, such as pharmaceutical companies, influence psychiatric taxonomy and treatment guidelines. Using the conceptual framework of institutional corruption, we show that organized psychiatry's dependence on drug firms has led to a distortion of science. We describe the current dependency corruption and argue that transparency alone is not a solution. We conclude by taking the position that the corruption of the evidence base in diagnostic and practice guidelines has compromised the informed consent process, and we suggest strategies to address this problem.

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**Rooting Out Institutional Corruption to Manage Inappropriate Off-Label Drug Use**
*Marc A. Rodwin*

Prescribing drugs for uses that the FDA has not approved — off-label drug use — can sometimes be justified but is typically not supported by substantial evidence of effectiveness. At the root of inappropriate off-label drug use lie perverse incentives for pharmaceutical firms and flawed oversight of prescribing physicians. Typical reform proposals such as increased sanctions for manufacturers might reduce the incidence of unjustified off-label use, but they do not remove the source of the problem. Public policy should address the cause and control the practice. To manage inappropriate off-label drug use, off-label prescriptions must be tracked in order to monitor the risks and benefits and the manufacturers' conduct. Even more important, reimbursement rules should be changed so that manufacturers cannot profit from off-label sales. When off-label sales pass a critical threshold, manufacturers should also be required to pay for independent testing of the safety and effectiveness of off-label drug uses and for the FDA to review the evidence. Manufacturers should also finance, under FDA supervision, programs designed to warn physicians and the public about the risks of off-label drug use.

MARKETING

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**Physicians under the Influence:** Social Psychology and Industry Marketing Strategies
*Sunita Sah and Adriane Fugh-Berman*

Pharmaceutical and medical device companies apply social psychology to influence physicians' prescribing behavior and decision making. Physicians fail to recognize their vulnerability to commercial influences due to self-serving bias, rationalization, and cognitive dissonance. Professionalism offers little

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protection; even the most conscious and genuine commitment to ethical behavior cannot eliminate unintentional, subconscious bias. Six principles of influence — reciprocation, commitment, social proof, liking, authority, and scarcity — are key to the industry's routine marketing strategies, which rely on the illusion that the industry is a generous avuncular partner to physicians. In order to resist industry influence, physicians must accept that they are vulnerable to subconscious bias and have both the motivation and means to resist industry influence. A culture in which accepting industry gifts engenders shame rather than gratitude will reduce conflicts of interest. If greater academic prestige accrues to distant rather than close relationships with industry, then a new social norm may emerge that promotes patient care and scientific integrity. In addition to educating faculty and students about the social psychology underlying sophisticated but potentially manipulative marketing and about how to resist it, academic medical institutions should develop strong organizational policies to counteract the medical profession's improper dependence on industry.

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**From Community to Commodity:** The Ethics of Pharma-Funded Social Networking Sites for Physicians
*Amy Snow Landa and Carl Elliott*

A growing number of doctors in the United States are joining online professional networks that cater exclusively to licensed physicians. The most popular are Sermo, with more than 135,000 members, and Doximity, with more than 100,000. Both companies claim to offer a valuable service by enabling doctors to "connect" in a secure online environment. But their business models raise ethical concerns. The sites generate revenue by selling access to their large networks of physician-users to clients that include global pharmaceutical companies, market research and consulting firms, and hedge funds and other investors. In exchange for a fee, these clients are offered a variety of tools to monitor, analyze, and solicit physicians' opinions. In Sermo's case, clients are also offered opportunities to conduct "awareness campaigns" on the site that are aimed at influencing physician sentiment about specific drugs and medical devices. In effect, these online networks have created an even more efficient means for the pharmaceutical industry to track physician sentiment, disseminate messages, and cultivate key opinion leaders. This paper argues that the dual nature of these sites (a) undermines their integrity and transparency as forums for the exchange of medical opinion and (b) presents an ethical conflict for the doctors who use them.

PATIENT ADVOCATES

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**Patient Advocacy Organizations:** Institutional Conflicts of Interest, Trust, and Trustworthiness
*Susannah L. Rose*

Patient advocacy organizations (PAOs) advocate for increased research funding and policy changes and provide services to patients and their families. Given their credibility and political clout, PAOs are often successful in changing policies, increasing research funding, and increasing public awareness of medical conditions and the problems of their constituents. In order to advance their missions, PAOs accept funding, frequently from pharmaceutical firms. Industry funding can help PAOs advance their goals but can also create conflicts of interest (COI). Research indicates that bias may occur, even among well-meaning professionals, when people and organizations have financial COI. Industry funding may therefore influence PAOs to act in ways that favor the interests of their donors, which may increase the risk of harm to patients. This article extends the analysis developed in the Institute of Medicine report, Conflicts of Interest in Medical Research, Education, and Practice, and applies the analysis to understand PAOs and their relationships with industry. It argues that the preferred goal of institutional COI policies should not be to promote trust, but to promote trustworthiness and appropriately placed trust.

## Independent Articles

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**Approval and Withdrawal of New Antibiotics in the U.S., 1980-2009**
*Kevin Outterson, John H. Powers, Enrique Seoane-Vazquez, Rosa Rodriguez-Monguio, and Aaron S. Kesselheim*

Numerous reports have noted decreasing numbers of antibiotic approvals. To determine the context for this decline, we examined all new molecule entities (NMEs) and new biologic licenses (NBLs) approved by the FDA from 1980-2009, and compared approval rates of the 61 approved antibiotics to trends in other drug classes. We also tracked withdrawals of approved drugs and found more withdrawals for antibiotics than other drug classes. After adjusting for drugs subsequently withdrawn, the record for antibiotic innovation is less dire than previously reported. We also report problems with the quality of the approved antibiotics studied. Future policies providing incentives for new antibiotic development should not be based on simple numerical targets and key provisions should ensure appropriate quality as well as quantity of antibiotic drug innovation.

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**"Something of an Adventure":** Postwar NIH Research Ethos and the Guatemala STD Experiments
*Kayte Spector-Bagdady and Paul A. Lombardo*

The STD experiments in Guatemala from 1946-1948 have earned a place of infamy in the history of medical ethics. But if the Guatemala STD experiments were so "ethically impossible," how did the U.S. government approve their funding? Although much of the literature has targeted the failings of Dr. John Cutler, we focus on the institutional context and research ethos that shaped the outcome of the research. After the end of WWII, Dr. Cassius Van Slyke reconstructed the federal research contracts process into a grant program. The inaugural NIH study section recommended approval of the Guatemala STD experiments at its first meeting. The funding

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and oversight process of the Guatemala research was marked with serious conflicts of interest and a lack of oversight, and it was this structure, as opposed to merely a maleficent individual, that allowed the Guatemala STD experiments to proceed. We conclude that while current research regulations are designed to prevent the abuses perpetrated on the subjects of the Guatemala STD experiments, it takes a comprehensive understanding of research ethics through professional education to achieve the longstanding ideal of the responsible investigator, and ensure ethical research under any regulatory scheme.

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**Ethical Quandaries in Gamete-Embryo Cryopreservation Related to Oncofertility**
*Leslie Ayensu-Coker, Ellen Essig, Lesley L. Breech, and Steven Lindheim*

While cancer rates continue to increase, therapy has dramatically decreased the mortality rates. The increased efficacy of current therapies may unfortunately have profound toxic effects on gamete function in both adolescent and reproductive age groups, with infertility as an expected consequence of cancer therapy. Significant progress in the advancement of fertility preservation therapies provides realistic options for future fertility in cancer survivors. However, a number of challenging issues need to be considered when presenting fertility preservation options. This overview highlights some of these considerations including religious-cultural-ethical values, access to care and cost of services, developmental capacity and consent, and posthumous reproduction.

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**Producing Knowledge about Racial Differences: Tracing Scientists' Use of "Race" and "Ethnicity" from Grants to Articles**
*Asia Friedman and Catherine Lee*

The research and publication practices by which scientists produce biomedical knowledge about race and ethnicity remain largely unexamined, and most of the existing research looks at the knowledge production process at a single point in time. In light of this, we specifically focus on the questions of whether and in what ways researchers' discussions of race and ethnicity change over the course of the research process by comparing grant proposals to published articles. Using content analysis, we investigated the use of race and ethnicity in 72 grants funded by the National Cancer Institute of the National Institutes of Health between 1990 and 1999 and 144 matched articles published between 1996 and 2010, tracing the production of biomedical knowledge from study design to published findings. This is also the first study to look at whether the NIH Inclusion Mandate, which went into effect in June of 1994, changed the way investigators research and write about racial and ethnic differences. In following this knowledge production process, we explore how scientists "deliver" on their research proposal goals. In addition, we provide insight into whether and how state policies directed at guiding research practices can shape output.

## Columns

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**Currents in Contemporary Bioethics**
Epigenetic Exceptionalism
*Mark A. Rothstein*

This article considers the distinctive features of epigenetics and discusses whether, as a matter of ethics and law, epigenetics should be considered separate from genetics.

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**Public Health Law**
Major Trends in Public Health Law and Practice: A Network National Report
*James G. Hodge, Jr., Leila Barraza, Jennifer Bernstein, Courtney Chu, Veda Collmer, Corey Davis, Megan M. Griest, Monica S. Hammer, Jill Krueger, Kerri McGowan Lowrey, and Daniel G. Orenstein*

Since its inception in September 2010, the Network for Public Health Law has responded to hundreds of public health legal technical assistance claims from around the country. Based on a review of these data, a series of major trends in public health practice and the law are analyzed, including issues concerning: the Affordable Care Act, tobacco control, emergency legal preparedness, health information privacy, food policy, vaccination, drug overdose prevention, sports injury law, public health accreditation, and maternal breastfeeding. These and other emerging themes in public health law demonstrate the essential role of law and practice in advancing the public's health.

**Symposium articles** *are solicited by the guest editor for the purposes of creating a comprehensive and definitive collection of articles on a topic relevant to the study of law, medicine and ethics. Each article is peer reviewed.*

**Independent articles** *are essays unrelated to the symposium topic, and can cover a wide variety of subjects within the larger medical and legal ethics fields. These articles are peer reviewed.*

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*Next Issue:*

**Human Rights and Disability**

A Symposium Guest Edited by John-Stewart Gordon and Jerome Bickenbach