Conflicts of Interest, Institutional Corruption, and Pharma: An Agenda for Reform

Marc A. Rodwin

Why do physicians have financial conflicts of interest? They arise because society expects physicians to act in their patients' interest, while simultaneously, financial incentives encourage physicians to practice medicine in ways that promote their own interests or those of third parties. Because physicians' clinical choices, referrals, and prescriptions affect the fortune of third parties (providers, medical facilities, insurers, drug firms and suppliers of ancillary services), these third parties may offer physicians financial incentives to make income-driven clinical choices. In the past, physicians and scholars typically conceived of conflicts of interest as an ethical issue to be resolved according to individual judgment or professional and organizational norms. However, society can mitigate or eliminate conflicts of interest by changing financial and organizational arrangements in medicine. Conflicts of interest, therefore, are as much matters of public policy and management as individual choices or social norms.[1]

Society can use various strategies to cope with conflicts of interest. It can: (1) change the organization and finance of medical practice to eliminate or avoid conflicts of interest; (2) create structures and processes to manage the conduct of conflicted physicians; (3) create ethical standards to guide conduct; or (4) disclose conflicts of interest so that patients and third party payers can protect their interests.

Physician relations with pharmaceutical firms are a source of conflicts of interest that can bias their prescriptions and advice. Drug firms pay physicians for numerous activities including consulting, serving on advisory boards, lecturing, writing articles, and conducting clinical trials. They also make grants and gifts to physicians. Some physicians earn income by dispensing drugs. At the same time, physicians may participate in clinical trials that evaluate drugs, advise the Food and Drug Administration (FDA) regarding drug risks and benefits, write reports and articles on drug use, teach about drug use in medical schools or in continuing medical education forums, recommend that a hospital or insurer formulary include a drug, develop practice guidelines for drug use, and prescribe drugs for their patients.

Shifting the Focus from Physicians to Drug Firms and Institutional Corruption

Today when we evaluate financial ties between physicians and drug firms we typically focus on physician

Marc A. Rodwin, J.D., Ph.D., *is a Professor of Law at Suffolk University Law School and a Lab Fellow at the Edmond J. Safra Center for Ethics at Harvard University.*

conduct, but we can just as well focus on drug firms using either of two frameworks.

First, we can examine pharmaceutical firm conflicts of interests. The conflict-of-interest framework has less analytic power when applied to drug firms, however, than to physicians, which society has long considered as fiduciaries for patients.[2] Corporations are not typically considered patient fiduciaries or entities with conflicts of interest. True, corporate officers and directors have fiduciary duties to serve their shareholders, but that does not imply that the corporation has fiduciary duties.[3] On the other hand, Congress can eliminate that obstacle through legislation requiring drug firms to protect the interests of patients, and others. Just as the law has imposed requirements that regulate the self-serving conduct of banks, financial advisors, money managers, and other economic actors,[4] the law could restrict drug firms from engaging in certain self-serving conduct in order to protect the interests of patients. The greater the legal obligations of drug firms to act in the interest of patients, the more conflicts of interest can compromise those obligations.

Today when we evaluate financial ties between physicians and drug firms we typically focus on physician conduct, but we can just as well focus on drug firms using either of two frameworks.

Alternatively, we can use the lens of institutional corruption to analyze the pharmaceutical industry, an approach that I use in this article.[5] I use the term institutional corruption, following Lawrence Lessig, to mean widespread or systemic practices — usually legal — that undermine the institution's objectives or its integrity.[6] One source of institutional corruption is *improper dependence* by the institution or its key actors on the actions of third parties that have fundamentally different interests. For example, when legislators depend for their election on the financial support of special interests, they become less responsive to the voting public, which undermines representative democracy. Similarly, I argue that several types of inappropriate dependence on drug firms corrupt current medical practice, and compromise public health.

Public policy has spurred development of the pharmaceutical industry through subsidies and legal rules that promote investment. We expect drug firms to develop innovative therapies that improve patient care and public health, and to promote drug safety. But today the pharmaceutical industry neglects many of these goals, and sometimes even engages in activities that undermine them.[7]

Drug firms often develop products that have minor value, and neglect investing in significant innovative therapies. They often behave as if they have no responsibility for how physicians prescribe or patients use drugs. They sometimes promote drugs in ways that endanger the public's health. They market drugs for uses where risks outweigh the benefits. They fuel inappropriate prescribing while earning income from improper drug use. Worse, drug firms have slanted the information available to public officials who decide whether to authorize the sale of drugs and who monitor the risks of drugs on the market. They bias the information available to physicians, hospitals, policymakers, and insurers and thereby corrupt the practice of medicine.

It is a mistake to attribute these problems to the greed or immoral conduct of a few actors or even to conflicts of interest, because the root of the problem lies in the institutional corruption stemming from improper dependencies. I argue that the public, physicians, and patients inappropriately depend on drug firms to:

- set priorities on drug research and development;
- conduct clinical trials that the FDA uses to decide whether to allow sale of drug;
- monitor adverse drug reactions;
- evaluate drugs on the market;
- decide what clinical trial data to disclose;
- provide information about drug benefits and risks;
- finance continuing medical education through discretionary grants; and
- finance medical societies, conferences, journals, and other professional activities.

Dependence on Drug Firms to Set Drug Research and Development Priorities

The public today subsidizes pharmaceutical firms yet it relies on them to make wise choices about where to focus research and development. Drug firms, however, have an incentive to direct their efforts where it is most profitable, which often differs from research that yields major therapeutic advances or great public health benefits.

Most tax subsidies, patent law rules and other incentives for pharmaceutical firms share a common flaw: they apply equally to all research and development. They neglect to focus research on what the public most needs and wants, or to set any priorities. Consequently, rather than undertaking research directed toward producing major therapeutic advances, which requires substantial time and money, and where results are uncertain, firms often focus research where risks are low, potential profits are high, and products can be rapidly brought to market.

For example, once the FDA has approved a new drug, it is often relatively easy to create a minor modification, a so-called *me-too* drug. In fact, the FDA Center for Drug Evaluation and Research classifies new drugs by whether they are a new molecular entity, constitute a significant improvement over existing drugs, or offer only an incremental modification of existing therapy. It found that among the 1,284 new drugs approved from 1990 to 2004, only 22 percent offered a significant improvement over marketed products and just over 14 percent were new molecular entities.[8] True, me-too drugs have some value. Some offer slightly fewer risks or greater benefits than the original. And me-too drugs increase competition, but price reductions are small because usually the original and the me-too are patented.

The FDA grants higher priority to reviewing drugs that offer important therapeutic advances.[9] This alone, however, is not a strong incentive for investment in challenging and high-risk research. In a similar vein, drug firms also have weak incentives to evaluate potential new uses for the many drugs that were never patented, or have expired patents, or for new uses of existing drugs, even though they are a potential source of new beneficial therapies. The law allows patents for new uses of existing drugs. However, once a compound has been approved and marketed, the drug can already be purchased so new use patents often provide little incentive for investment.[10]

We need to develop more thoughtful incentives for research. We should revise patent law to vary the duration of drug patents based on the degree of innovation. Using the FDA's classification of drugs the law should grant patents of only a few years for drugs that offer only incremental therapeutic improvements, a longer patent duration for drugs that offer significant therapeutic innovation, and the longest patent duration for new molecular entities.

We also need to develop new means to fund research that the private sector does not undertake. We should have the public sponsor such research through the National Institutes of Health (NIH) research grants. Where would the government obtain the needed funds? Since the public already subsidizes drug firms through tax law, patent rules, and other means, it makes sense to assess drug firms a small percentage of their sales revenue to generate funds for the NIH to sponsor this research. Drug firms could absorb this cost, or pass it along in the price of its products.

FDA Dependence on Drug Firms to Conduct Clinical Trials Used to Decide Whether to Allow the Sale of a New Drug

Since regulations promulgated in 1970 to implement the Food, Drug and Cosmetic Act 1962 amendments, manufacturers can market a drug only after the FDA concludes that it is safe and effective for a specified use, based on evidence from clinical trials.[11] Congress and the FDA established these requirements after experience clearly showed that society could not reasonably rely on drug firms to impartially assess the risks and benefits of drugs, nor to market drugs in a manner that places the public's interest ahead of their own financial interest.[12] However, these reforms did not go far enough, because the FDA still relies on the company seeking to market the drug to conduct the clinical trials used to evaluate the drug's safety and effectiveness.

From 1962 to 1980, congressional hearings revealed the high risk of bias, fraud, and failures to disclose risks when drug firms conduct clinical trials as part of an application to market a new drug.[13] These risks were illustrated again in the 2005 congressional investigation into Merck's research on Vioxx.[14] Since 1980, scholarly literature has revealed that drug firms can design trials that bias the results, and interpret the data to assess the drug more favorably than warranted; they can also report data selectively to distort the evidence available to the FDA.[15]

When drug firm employees conduct research, they design the experimental protocol and choose the research methods. These choices can bias the results to enhance the apparent efficacy of the drug, or to diminish its apparent risks. Frequently, drug firms employ contract research organizations (CROs) or university-based researchers to test the drug. Still, the drug firm typically designs the clinical trial. Even when contract researchers design the study, the drug firm must approve their plan. And even if the drug firm delegates all responsibility to its contract researchers, CROs and university researchers know that the drug firm wants the study to convince the FDA to approve the drug. For post-marketing clinical trials, researchers know that the firm wants to use the study to help market their product. Drug firms displeased with their contract researchers can select different ones for their next project. Contract researchers have an incentive

to cater to the drug company's interests because they depend on drug firm contracts for their livelihood.

Since 1960, numerous medical researchers, consumer advocates and members of Congress have proposed having independent parties design and conduct clinical trials that the FDA uses to decide whether to grant approval to sell a drug, and if so, for what purposes and under what restrictions. Senator Gaylord Nelson (D-Wi) held hearings to examine this issue from 1967 through 1979, and introduced legislation to require independent testing of drugs. Senator Nelson and several individuals testifying at the hearings suggested that the federal government should either conduct the tests, or choose the researchers who would design and conduct the clinical trials. They proposed that firms seeking to market the drug must pay the costs of the drug testing, just as they do today.[16] Pharmaceutical industry opposition blocked enacting these reforms, and as a result, the FDA still depends on drug firms to generate data on the safety and benefits of their products. Congress should require independent testing in order to eliminate the compromising dependency that comes from public authorities' reliance on drug firms' need to seek marketing approval to evaluate the safety of their products.

We need to monitor drugs after the FDA authorizes firms to market them in order to identify the many risks that cannot be discovered during the initial clinical trials. Without post-marketing surveillance, the FDA will not be able to effectively warn physicians and the public about a drug's risks, or withdraw marketing authorization, or take other appropriate action.

Dependence on Drug Firms to Monitor Adverse Drug Reactions and Oversee Pharmacovigilance

We need to monitor drugs after the FDA authorizes firms to market them in order to identify the many risks that cannot be discovered during the initial clinical trials. Without post-marketing surveillance, the FDA will not be able to effectively warn physicians and the public about a drug's risks, or withdraw marketing authorization, or take other appropriate action.

Pre-market clinical trials use a sample that is too small to identify many of the adverse drug reactions that will occur in a much larger population. These trials fail to reveal risks faced by populations that differ from the test group. Typically, the population that uses a drug is more diverse than the small group of subjects on which the drug is tested. Drugs often are tested on middle-aged adults, but are later used by many individuals who are more susceptible to drug injuries, like children, the elderly, or pregnant women. Furthermore, pre-market trials cannot identify health problems that arise only after long-term use. Yet, many drugs are meant for long-term use; for example, drugs, for birth control, to stabilize blood sugar for diabetes, or to control high blood pressure, cholesterol, depression, or mood disorders. Also, physicians may prescribe drugs in ways that differ from how they were tested. The pre-market trial may test a pain reliever for short-term acute use, but some physicians may prescribe it for continuing use. Moreover, some injuries are caused by the interaction of two or more drugs, and are not discovered until they have been marketed and used by a larger population.

The public has depended mainly on drug firms to monitor the safety of the drugs that they market. The law requires drug firms to forward to the FDA any reports they have received from doctors or patients of adverse drug reactions or suspected adverse drug reactions.[17] However, this system of spontaneous reporting identifies only a small percentage of adverse drug events. The FDA sometimes requires that manufacturers conduct studies of their marketed drugs in order to identify drug risks, but the FDA does not have a way to ensure compliance. Drug firms often postpone or do not conduct these studies, or they delay the reporting of serious risks revealed by the studies.[18]

It is not prudent to rely exclusively or even heavily on drug firms because performing excellent pharmacovigilance will never increase their revenue. In fact, pharmacovigilance might reduce manufacturers' profits. It could lead the FDA to withdraw marketing authorization, or to require the firm to warn of the risks, which then causes physicians to decrease prescriptions for the drug. When initially testing a new product, drug firms have an incentive to rush drugs to market, but when studying risks that may lead to their drug being withdrawn or prescribed less frequently, their incentive is to proceed with caution, to check the studies carefully before reporting them, and to conduct follow-up studies to make sure that the initial

study was not somehow flawed. When a firm sells a blockbuster drug that generates $1 billion to $2 billion a year, delaying for only six months any reports of risks that cause the FDA to withdraw the drug from the market will generate $500 million or $1 billion additional income for the firm. Firms have the same incentive for delaying reports of risks that will reduce the total number of prescriptions.

Legislation in 2007 set in place additional ways to monitor drug safety.[19] The reforms will supply the FDA with data from patient records that will make possible epidemiological studies of drug risks from a large population. These changes will reduce the public's reliance on drug firms for pharmacovigilance. However, public officials lack access to data on physician prescribing, which could increase the value of the epidemiological data and would also be another tool for pharmacovigilance. Drug firms, on the other hand, routinely collect or purchase data on physician prescribing for their marketing. If researchers tracking drug safety had information on patterns of physician prescribing, they could evaluate drug risks and track prescriptions for off-label uses. Public policy does not require drug firms to share this information with public authorities. We should require drug firms to report such data and other information on marketing that will help public authorities promote pharmacovigilance.

Physician and Patient Dependence on Drug Firms to Evaluate Drugs on the Market

By 2000, drug firms funded 70 percent of clinical drug trials, allowing them to influence the questions posed, research design, protocol, and methods.[20] Today, the medical profession and the public rely heavily on drug firms to conduct post-marketing evaluation of drugs, simply because we have not created another means to ensure that these studies are conducted.[21]

Drug firms routinely conduct clinical trials for new drugs because they must produce evidence of safety and effectiveness in order to receive authorization to market the drug. In contrast, conducting clinical trials after drugs are on the market is not generally required; additionally, drug firms' financial incentives to conduct studies post-approval are different from their financial incentives during the pre-approval stage. Moreover, pre- and post-marketing studies have different functions. Pre-marketing trials are designed to show whether a new drug meets minimum levels of safety and effectiveness for it to be sold, not how it compares to alternative drugs. Once a drug is on the market and there is more than one drug in a therapeutic class, physicians and the public want to know how a new drug compares to alternatives. Is it more or less effective? Does it have more or fewer undesirable effects and risks?

Drug firms design and conduct some post-marketing studies because the FDA requires that they do so as a condition for approving sale of the drug. However, it is dangerous to depend on drug firms for all evaluations of drugs on the market. Many firms refrain from funding comparative studies out of fear that they will reveal that another drug is comparable or superior. Moreover, firms that conduct comparative studies have an incentive to bias the trial design in ways that favor their product.

Drug firms do not need to meet the FDA's standards of scientific rigor when they design their post-marketing studies because the firms rarely use these studies to seek FDA approval to market a drug for a new use. There is, therefore, a greater risk of bias in post-marketing trials than in studies designed to seek FDA marketing authorization. Moreover, no public authority scrutinizes post-approval studies, or what their sponsors claim the studies reveal. It is no surprise, then, that several reviews have found that when an interested party pays for a clinical trial, the trial tends to produce results that favor the interest of the funder.[22]

When drug firms have broad discretion, they often design and conduct post-marketing studies as a marketing tool.[23] For example, manufacturers sometimes conduct post-marketing studies to encourage physicians to prescribe drugs for uses that the FDA has not approved, so-called *off-label* uses. Although the FDA only authorizes the marketing of drugs for the uses that clinical trials have shown to be safe and effective, doctors can prescribe a drug for any use. Drug firms can conduct studies of off-label uses to take advantage of the gap between the uses for which the FDA allows them to market a drug, and how physicians chooses to prescribe it. If a study suggests the unapproved use has benefits, the drug firm or its researchers often publish the results in a medical journal. Physicians often refer to such publications to learn new information about drugs' therapeutic uses. Drug firms have a first amendment right to disseminate articles on off-label drug uses to doctors,[24] and can thereby encourage off-label prescribing without risking prosecution for illegal marketing.

We need a source of funding for conducting the types of clinical trials that drug firms are unlikely to voluntarily conduct, and to ensure that studies comparing drugs are unbiased. These measures will allow us to study the safety of marketed drugs, assess their comparative effectiveness, and evaluate the nature of their off-label drug uses. Congress should consider several options. It might assess drug firms a set percentage

of their sales revenue to be used to fund clinical trials overseen by a public agency. In addition, Congress could require firms to pay for independent third parties to conduct clinical trials to evaluate off-label drug use after sales of their drugs for off-label uses exceed a designated threshold. That would require us to track off-label prescribing, probably by requiring physicians to note the patient diagnosis, and the purpose for which they prescribe the drug on each prescription.

Physician and Patient Dependence on Drug Firms to Disclose Clinical Trial Data

Selective drug firm reporting of study results also distorts the information available to doctors and the public. Sometimes drug firms report the results of a single study with positive findings in multiple journals in ways that lead readers to believe that there were several different studies that found positive results.[25] Drug firms typically only publish studies when the results portray their product in a positive light and bury studies with negative findings.[26] Until recently, drug firms could easily suppress unfavorable results by hiding any mention of them. Outrage over this practice led to demands in the late 1990s for the creation of a clinical trials registry that could provide researchers and public officials with reliable information.[27] Medical journals then prompted drug firms to register clinical trials by stating that they would not publish results of any trial that had not been initially registered.[28]

In 2007, Congress required researchers to register their trials on ClinicalTrials.gov — a public database operated by the National Institutes of Health — for phase II and higher drug and biologic trials when either a trial site is in the United States, or the trial is part of an investigational new drug application.[29] Once a study is completed, researchers must then post key information on the site, including outcome measures, results, and adverse events. However, researchers can delay reporting until a year after collecting data, or a month after the FDA approves the drug. For studies of off-label drug uses, researchers have three years to post results.[30] Analysis of clinical trial registries show that firms often do not file on time and violate other requirements.[31] No authority checks whether the data posted on registries reflects the data of the clinical trial.[32]

Even more important, current law only requires the submission of partial data to clinical trial registries, which is often not only insufficient to interpret the study, but can also even be misleading. To evaluate a study, readers need information on the study design, methods, and full results. Surprisingly, clinical trial registries do not make available the most useful information: the clinical study report that summarizes the data and analyzes the results, and the drug firm report to governmental authorities to comply with international standards.[33] Nor do they make available the masked patient level data so that other researchers or government officials can analyze results themselves and draw their own conclusions. As a first step, Congress should require that drug firms disclose the clinical study reports for all other clinical trials they conduct for drugs that they market in the United States. Congress should also require that the FDA disclose all clinical study reports submitted by drug firms in seeking FDA approval to market a drug.[34] To enhance public understanding of these studies, and to promote FDA accountability, it also makes sense to require the FDA to disclose all of its reviews of applications for marketing new drugs, and to disclose all clinical trial data.[35]

Physician Dependence on Drug Detailers for Information about Drug Benefits and Risks

Physicians depend on pharmaceutical firms for much of the drug information they receive. Starting in the 1930s, drug firm sales representatives became the most important source of drug information for most physicians. Today, physicians continue to rely on pharmaceutical representatives to apprise them of developments in drug therapy, tell them the appropriate circumstances in which to prescribe their products, warn them about the risks of their products, and supply publications that evaluate drugs.

However, drug firms employ sales representatives to promote sales.[36] They typically pay drug detailers bonuses as high as 25 percent of their fixed salary if they meet targets for increasing sales.[37] As physicians write more prescriptions for a firm's drug, the sales representatives earn higher bonuses. Consequently, drug detailers are rewarded for increasing physician prescribing, not for providing accurate information. These incentives prompt drug representatives to suggest that doctors use a drug for a wide variety of symptoms, rather than warn doctors about the drug's risks, or advise doctors to limit prescriptions to narrowly defined uses or patient groups.

To evaluate the accuracy of information provided by sale representatives in the United States, a group of pharmacists audio-taped presentations made at 13 conferences by 12 pharmaceutical representatives from 9 drug companies at hospital lunch-time presentations in the first half of 1993. A pharmacist sat in the front row, and placed the tape recorder in plain sight with a red light on to indicate that it was recording. The tapes were transcribed and the representative's comments were compared with readily available

information. The researchers classified statements as inaccurate only if they were unsupported by information available in medical literature, or if the comments were contradicted by a source quoted by the representative or by official prescribing information for the drug or a competing drug. The drug detailers made 106 statements about the promoted drugs that could be supported or contradicted by readily available information. Among these, 11 percent or 12 statements were inaccurate. All of the inaccurate statements cast the drug in a favorable light. Seven of the 9 representatives made statements that were contradicted by available information.[38] Two similar studies of drug detailer information in Australia and Finland yielded similar findings.[39]

In a similar vein, a study by the journal *Prescrire,* based on reports after visits from pharmaceutical detailers to individual French physicians between 1991 and 2005, also found that detailers supplied biased information. They continued to supply incorrect or poor quality information despite efforts to reduce biased information sharing, including a European Community directive on drug marketing in 1992, French legislation in 1994 and 1996 that tried to reform marketing, and the French pharmaceutical manufacturers association's (*Les Entreprises de Médicament,* or LEEM) revision of its marketing code of conduct.[40] In 2004, an accord between LEEM, physician unions, the High Authority on Health, and the Committee on the Economics of Health Products created a Charter for Pharmaceutical Representatives that purported to ensure accurate information.[41] Nevertheless, in 2005, over a third of physicians reported that medical representatives indicated drug uses that differed from what the official résumé of drug characteristics stated. Most medical representatives failed to provide crucial information: only 16 percent reported drug contra-indications; 13 percent discussed drug interactions; 14 percent discussed precautions on use; 15 percent reported undesirable side effects.[42]

Commercial firms have a right to market their product, and the tax code typically allows them to deduct their expenses for marketing and advertising. However, the public does not need to subsidize drug marketing, particularly since evidence reveals that it produces misinformation and biased evaluations of drugs that undermines good medical practice. Courts have generally allowed Congress to tax industries in different ways and at different rates. The Supreme Court has held that the 14th Amendment Equal Protection Clause does not prohibit taxes that favor certain industries or taxpayers.[43] Therefore, Congress could eliminate the tax deduction for pharmaceutical firm advertising, detailing and other promotions, or even tax spending on these activities. It should do so and use the new revenue to fund independent sources of information on drug risks and benefits for physicians and patients.

In principle, Continuing Medical Education (CME) can help counter the problem of biased information and false statements made by drug detailers and other promotions. However, in recent years drug firms pay for much of the cost of accredited CME, which undermines the possibility of CME representing a source of unbiased information.

Medical Profession Dependence on Drug Firms to Finance Continuing Medical Education through Discretionary Grants

In principle, Continuing Medical Education (CME) can help counter the problem of biased information and false statements made by drug detailers and other promotions. However, in recent years drug firms pay for much of the cost of accredited CME, which undermines the possibility of CME representing a source of unbiased information.[44] Furthermore, although most states require physicians to earn CME points to maintain their license, they do not establish a curriculum. As a result, what drug firms decide to fund determines the choice of topics offered. Not surprisingly, drug firms fund courses related to the products they sell. This practice biases CME toward drug therapy instead of providing information about other therapies, or teaching diagnostic and practice skills. It also favors courses related to drugs that are patented rather than those that are unpatented or with expired patents. We would never consider allowing medical school curricula to be based on what courses commercial interests chose to fund, especially if they could boost their profits by selecting the courses, yet this is precisely what we do for CME.

We know from multiple sources — scholarly studies, congressional investigations, reports of investigative

journalists, and documents made public through lawsuits against drug firms — that from 1980 through the early 21st century, drug firms often exerted significant influence over the content of many presentations in accredited CME. Drug firms have made many CME programs a tool for marketing their products.[45] They helped develop the curricula, chose the individuals who spoke, and sometimes even edited the text that speakers presented. They produced slides and materials distributed. As a result, CME presentations downplayed the risk of their products, exaggerated their benefits, encouraged prescribing drugs for uses that the FDA had not approved, and encouraged the use of branded products rather than generics. Regulatory oversight by the Medicare Office of Inspector General and Senate Finance Committee in the early 21st century appears to have reduced the prevalence of the worst abuses,[46] but we do not know with any certainty the extent of the improvements because it is difficult to monitor the content of CME, and the relationships between drug firms and the organizations that they fund to create CME. In any event, dependence on discretionary pharmaceutical industry funding creates conditions prone to abuse, and biases the offering of CME topics.[47]

We need a need a new system to fund CME. Commercial interests should not be allowed to sponsor or to donate funds, even indirectly, for accredited CME. Congress should impose a tax on drug firms to finance independent CME. A federal authority should allocate these funds to government-certified, not-for-profit institutions that would distribute the funds to independent entities for the development of CME. Pharmaceutical firms would either absorb the tax from their surplus and lower their profits, or pass the cost on in the price of their drugs. American drug firms could easily absorb this cost and in fact commercial interests already fund about half of accredited CME. If firms currently pass on these costs in the price of their products, then insurers and the public are already picking up the tab. In that case, it makes sense to have the public pay to ensure unbiased CME.

Dependence on Drug Firms to Finance Medical Societies, Conferences, Journals, and Important Medical Activities

Professional medical societies, medical journals and many important medical activities depend on discretionary grants from the pharmaceutical industry. Drug firms, however, make grants to advance their most pressing financial goal — increasing drug sales — rather than out of charitable impulse. Firms' profit-oriented incentives affect their selection of which professional medical activities to fund. Firms favor activities that help promote drug sales.[48]

Dependence on discretionary pharmaceutical company funding also enables drug firms to use their support as leverage to influence the behavior of grant recipients. Drug firms often make grants to physicians who serve on a health plan or hospital formulary committees as a means to get their drug added to the formulary.[49] Other times, firms fund physician and medical society activities to influence their clinical practice guidelines, which influences physician prescribing.[50] They also use their funding to influence the practices of physician opinion leaders whom other clinicians often follow.

Occasionally, drug firms use their grants as an explicit quid pro quo, in return for physicians prescribing drugs or making other decisions that boost drug sales. Such payments are often illegal. Firms also make grants without receiving express promises of favorable action by the grantee; what the grantor wants is only implied and understood. Frequently, firms make grants to physicians who are key opinion leaders in order to develop a relationship that generates a sense of obligation and goodwill. This encourages reciprocity.[51]

Drug firms can also use their purchase of advertising as a means of leverage over medical journals and professional medical societies. This practice has a long history. Until the early 20th century, the AMA Journal relied on advertisements from patent medicines, which prevented the AMA from taking effective stands against the advertisers' products. Newspapers also were reluctant to expose patent drug abuse because they too depended on drug advertising. Drug firms often insisted on advertising contracts with newspapers that prohibited the newspaper from disparaging their product in news articles.[52]

After the AMA Journal secured independence by generating enough revenue from members in 1905, it ended patent medicine advertising and began a system of private regulation of drugs. However, the AMA became dependent on advertising revenue from ethical drug firms, those that produced drugs considered legitimate. Starting in the late 1930s, there were more medical publications directed toward doctors in which drug firms could advertise. They reduced their advertising in the AMA Journal in favor of advertising in other journals. By the early 1950s, the AMA faced a financial crisis and sought to increase advertising revenue. It then stopped its program of certifying drugs and reviewing the content of advertising, and took other actions to help drug firms increase their drug sales. Drug advertising then increased in AMA journals again. The AMA reversed its longstanding

policy in favor of regulation of drug firms and opposed the 1962 Food and Drug Law amendments. As Henry Dowling, former Chair of the Council on Drugs, noted, "Facts force the neutral observer to conclude that the AMA has swung around 180 degrees from being the champion of consumers of drugs to being the champion of the drug industry."[53]

There have been reports of drug firms that reduced advertising in medical journals after the journal published studies that showed risks related to their products. There have also been reports of journals not publishing critical articles out of fear that they would lose advertising. In 1992, drug firms reduced advertising for several months in the *Annals of Internal Medicine* after it published a study exposing misleading drug advertisements. The editor of *Dialysis Transplantation* cut a planned editorial that questioned a drug's efficacy in 2004 because he was "overruled" by the marketing department.[54] These reports are probably tips of the iceberg, and likely do not reveal the true extent of journals' self-censorship due to their dependence on revenue from drug firm advertising.

Government officials tolerate industry funding that compromises professional medical activities in part to avoid both battling pharma and organized medicine to stop the practice and in part to avoid publicly funding these activities. They hope to limit the negative effects of industry funding. However, banning kickbacks while allowing industry funding does not end physician dependence that compromises their practice; it merely shifts the mechanisms used to influence physicians. It solidifies a form of institutional corruption that resists reform.

We need to create an alternative to the pharmaceutical industry having financial control over professional activities. Public policy should tax commercial interests and insurers to support professional activities. A government agency should distribute these funds either directly, or through a government-sponsored independent entity. Legislation should prohibit all industry gifts and financial support — including funds donated indirectly through an intermediary — to physicians, physician organizations, and organizations that develop professional medical activities.

Countering Institutional Corruption

Often dependency arises from necessity. But in the situations described in this article the public is not helpless. The pharmaceutical industry is shaped by public policy to a much greater degree than most industries. Indeed, the industry's profitability depends on public financing, legal protection and regulation. Laws that create patents, marketing exclusivity, and other policies nurture the industry. The government pays much of the cost of purchasing drugs through public insurance programs, and it subsidizes drug purchasing through private insurance. Favorable tax treatment also subsidizes drug development and other drug firm expenses. Federal and state governments also fund a large share of biomedical research upon which the industry relies to develop products.

Because public policy plays such an important role in the pharmaceutical industry, the public has leverage to end our corrupting dependence on pharmaceutical companies and reform the pharmaceutical industry. Since public funds pay to purchase drugs and subsidize industry expenses, public policy can require that the industry designate some of its revenue to promote drug safety and other specified purposes.

Because public policy plays such an important role in the pharmaceutical industry, the public has leverage to end our corrupting dependence on pharmaceutical companies and reform the pharmaceutical industry. Since public funds pay to purchase drugs and subsidize industry expenses, public policy can require that the industry designate some of its revenue to promote drug safety and other specified purposes. Public policy thus has the tools to reform the pharmaceutical industry and pharmaceutical policy. Marshaling those resources, of course, presents a major political challenge.

The details of the reforms suggested in this article need to be worked out, the proposals have limitations, and there certainly are alternative ways to reduce improper dependency on pharmaceutical firms. My aim has been to outline an agenda to eliminate institutional corruption in pharmaceutical policy and the pharmaceutical industry and to stimulate thinking about strategies for reform.

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