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The Current System Compromises Physician Integrity and Leads to Unethical Corporate Behavior

In chapter 7, I discussed how the pharmaceutical industry spends billions of dollars each year marketing its products to health care providers, particularly physicians. Beyond the tens of thousands of company salespersons deployed to directly market their products to physicians, pharmaceutical and medical device companies also pay a full two-thirds of the costs of continuing medical education in medical schools and teaching hospitals. Predictably, the content of the programming often reflects that influence. Drug company marketing also reaches into the level of direct care. One example of such controversial industry expenditures is paying providers to participate in “patient adherence programs,” which aim to encourage patients to take branded medicines.

There is no mystery to why pharmaceutical companies want to cultivate physicians and other care providers: these individuals write the prescriptions that dictate the company’s bottom line. As a Federal Trade Commission report said, in the current medical system, “the consumer who pays does not choose, and the physician who chooses does not pay.”
But there is another motivation as well. Surveys show that patients do not trust drug companies (in 2015, 74 percent believed pharmaceutical companies put profits before people) but that they do trust doctors (78 percent of Americans reported feeling positively about physicians). By winning over physicians to their products, pharmaceutical companies are purchasing some of that caregiver goodwill.

To many in the health care community, this is an alarming situation. The physician Ben Goldacre, in his book *Bad Pharma: How Drug Companies Mislead Doctors and Harm Patients*, explains to non-physicians why the drug industry’s central role in funding and shaping continuing medical education is so impactful:

Doctors spend forty years practicing medicine, with very little formal education after their initial training. Medicine changes completely in four decades, and as they try to keep up, doctors are bombarded with information: from ads that misrepresent the benefits and risks of new medicines; from sales reps who spy on patients’ confidential prescribing records; from colleagues who are quietly paid by drug companies; from “teaching” that is sponsored by the industry; from independent “academic” journal articles that are quietly written by drug company employees; and worse.

Citing the psychological research that has firmly established that even small gifts influence decision making, some leading voices in the medical field have called for the money to stop flowing from the drug corporations to physicians. A 2008 editorial in the *Journal of the American Medical Association* made the reasoning plain: “The profession of medicine, in every aspect—clinical, education, and research—has been inundated with profound influence from the pharmaceutical and medical device industries. This has occurred because physicians have allowed it to happen, and it is time to stop.” Similar concern among the public caused the U.S. Congress to pass in 2010 the Physician Payment Sunshine Act, which requires that drug and medical device companies report their financial relationships with physicians.

Beyond the influence of the pharmaceutical industry on the clinical practice of medicine, the corporate influence on medical research has caused just as much concern. A 2006 survey of department chairs in accredited medical schools and teaching hospitals revealed that almost two-thirds of
the chairs had financial relationships with the pharmaceutical and medical device industry. Industry roles for the department chairs included their serving as consultants, members of corporate scientific advisory boards, and paid speakers.\textsuperscript{10} According to Daniel Wikkler, Harvard ethics and health professor, these esteemed academic physicians are acting as “surrogate sales staff,” and entire academic departments have reputations of being “owned” by particular pharmaceutical companies.\textsuperscript{11}

A 2007 survey found that over half of academic life science researchers had a relationship with the pharmaceutical industry.\textsuperscript{12} That relationship sometimes comes with strings attached: many researchers who received pharmaceutical industry gifts reported that the corporation requested a prepublication review of articles or reports stemming from the use of the gift and sought promises that biomaterials provided would not be used for research that would compete with company products.\textsuperscript{13} As for the influential journals themselves, a former editor of the prestigious British medical journal the \textit{Lancet} has said, “Journals have devolved into information-laundering operations for the pharmaceutical industry.”\textsuperscript{14} Editors of several other prominent journals have agreed with him.\textsuperscript{15}

As with their marketing to clinical physicians, the motivation of the pharmaceutical industry for these marketing investments in the research field is clear: they help the corporate bottom line. Reviews of corporate-sponsored medical studies compared to non-sponsored studies show that the corporate-sponsored versions were significantly more likely to report that the drug studied was effective and beneficial, and less likely to find negative effects caused by the drug.\textsuperscript{16} On the level of the individual researchers, industry-sponsored physicians and scientists have been shown to report disproportionately industry-favorable results.\textsuperscript{17} As one former pharmaceutical industry executive plainly stated, this is exactly the desired outcome: “It is to industry’s advantage to selectively support particular researchers whose point of view supports marketing goals, and to encourage selective publication of articles.”\textsuperscript{18}

The design of industry-sponsored studies often benefits those marketing goals, too. Clinical trials are disproportionately industry-sponsored, and those trials routinely compare the company drug to only a placebo rather than to a similar medicine. That means the results of the study do not reveal whether the new medicine is actually better than existing products already available. The resulting “better than nothing” standard sets a
very low bar for the studied drug and does not yield the information that would be most valuable to physicians, who need to decide which medicine to prescribe.\textsuperscript{19}

There are other significant problems with industry-sponsored clinical trials. To Ben Goldacre, the most concerning is the widespread failure to share the results of trials that are not positive for the company. “For me, missing data is the key to this whole story,” Goldacre says. “It poisons the well for everybody. If proper trials are never done, if trials with negative results are withheld, then we can simply not know the true effects of the treatments we use. . . . With missing data, we are all in this together, and we are all misled.”\textsuperscript{20} In addition, some clinical trials sponsored by drug companies occur after the drug has already been approved. These trials are known as Phase IV trials. Although there can be legitimate research reasons to conduct these trials, the goals of these post-approval studies often appear less focused on actual research than on promoting the product through paying clinical doctors to use it on patients.\textsuperscript{21}

One particularly disturbing example of the impact of industry-sponsored research was the delayed reporting of the dangers of erythropoetin-stimulating agents (ESAs), used to treat anemia in cancer patients. Early industry-sponsored research in the 1990s showed ESAs had benefits, but later reports by independent researchers showed the drugs actually significantly increased the risk of patient death. While none of the industry-sponsored research reported these major problems, 90 percent of studies not funded by pharmaceutical corporations did.\textsuperscript{22}

Undoubtedly, some of the purchased industry influence on reported research results is working at the subconscious level. But some of the impact is not subtle at all. Two high-profile articles published together in the \textit{Journal of the American Medical Association} in 2008 outlined how Merck may have intentionally misrepresented the risks of its medicines in articles reporting research on its products. Those articles were apparently written by Merck employees but published under the names of academic researchers who had had little to do with the studies.\textsuperscript{23} Corporate-hired ghostwriters regularly author research articles that promote drugs manufactured by the company, yet the articles appear under the names of academic physicians. The ghostwriting tactic has also been used by Eli Lilly and GlaxoSmithKline, among others.\textsuperscript{24}
The deep and wide influence of the pharmaceutical industry on health care is no secret. Multiple books have been published decrying the situation, several written by esteemed authors who are faculty at Harvard Medical School or were once editors in chief of the *New England Journal of Medicine*.\(^{25}\) One of these authors is Marcia Angell, who was the editor of the *New England Journal of Medicine* in 2000 when the journal published an article studying an antidepressant. The author of the article, who was the chair of a university psychiatry department, had reportedly made over $500,000 in a single year consulting for corporations that manufactured antidepressants. A concerned Dr. Angell decided to write an editorial to accompany the article. The editorial was entitled, “Is Academic Medicine for Sale?”\(^{26}\) After the editorial was published, a physician from Detroit responded with a three-sentence letter to the editor. “Is academic medicine for sale?” repeated Thomas J. Ruane, MD. “No. The current owner is quite happy with it.”\(^{27}\)

Of course, it is not unusual for multinational corporations to engage in aggressive lobbying and marketing. But, as U.S. Senator Debbie Stabenow (D-MI) has said, “‘Medicine is different. It’s not like buying a car or tennis shoes or peanut butter.’”\(^{28}\) The World Health Organization has called this tension “an inherent conflict of interest between the legitimate business goals of (medicine) manufacturers and social, medical, and economic needs.”\(^{29}\) As we see in chapter 16, there is a long history of societies treating medicines as public goods, protected from the scarcity and profiteering that can affect access to less essential consumer goods.

In contrast, for the pharmaceutical industry the pursuit of profits has often transcended any reasonable definition of the “legitimate business goals” the WHO refers to. As the watchdog organization Transparency International wrote in 2016, “Within the health sector, pharmaceuticals stands out as sub-sector that is particularly prone to corruption. There are abundant examples globally that display how corruption in the pharmaceutical sector endangers positive health outcomes.”\(^{30}\)

Many examples of this were chronicled in a 2010 study by the U.S. nonprofit Public Citizen, which found that the pharmaceutical industry is far and away the largest defrauder of U.S. federal and state governments.\(^{31}\) Pharmaceutical corporations have been cited for dozens of major
violations of the U.S. False Claims Act, the Anti-Kickback Statute, the Foreign Corrupt Practices Act, and multiple state laws prohibiting Medicaid fraud. In the twenty-year period ending in 2010, pharmaceutical companies entered into 165 civil or criminal settlements with federal and state governments, and the number of citations showed steady annual increases at both the federal and state levels. The total settlements in that period added up to $19.81 billion.

The four biggest offenders over this period—GlaxoSmithKline, Pfizer, Eli Lilly, and Schering-Plough—were all fined more than $1 billion each. In 2012, Pfizer settled charges that it had bribed health officials in multiple countries, and GlaxoSmithKline was fined for failing to report the adverse effects of one of its medicines. Several companies were cited for overcharging state Medicaid programs, sometimes collecting as much as twelve times the legal cost of their medicines. Some were punished for paying off potential generic competitors.

In addition, Purdue Pharma was criminally sanctioned for its role in falsely underplaying the addiction risks of its painkiller drug Oxycontin, and its aggressive and ethically suspect marketing of the drug has been cited as a chief trigger of an ongoing opioid and heroin epidemic in the United States. (Not coincidentally, the pharmaceutical industry was at the same time leading the opposition to the legalization of medical marijuana, as studies have shown that medical marijuana legalization leads to decreased prescribing of painkillers, anxiety medication, and other staples of corporate pharmaceutical product lines.) An ongoing case against Novartis, in which the company is accused of funneling kickbacks to prescribers through thousands of supposed “educational” meetings where doctors were wined and dined, may lead to a multibillion dollar fine. In 2016, pharma sales representatives were arrested and charged in New York with violating federal antikickback laws. The allegation is that the representatives from Insys used sham educational meetings as a cover for paying physicians to prescribe highly addictive opioids. Also in 2016, the South African drug maker Aspen Pharmacare was fined by Italian authorities for blocking supplies of several cancer drugs, a tactic the company employed to negotiate huge price increases.

For drug companies, the most commonly cited ethical offense involves a tactic called “off-label promotion.” Physicians are allowed to prescribe drugs off label, meaning prescribing them for a different disease or type of
patient than has been approved by regulatory agencies. But in the United States and other countries, pharmaceutical corporations are strictly prohibited from promoting these off-label uses of their products because those uses have not been analyzed for possibly dangerous effects. Nevertheless, they do just that. For example, Pfizer was charged in 2009 with illegally promoting off-label uses of the pain medicine Bextra, which was later pulled from the market for safety reasons.

Some of the many recent big-dollar fines levied for off-label promotions include the record-setting $12 billion settlement by GlaxoSmithKline regarding allegations it illegally promoted its antidepressant Paxil for use in adolescents, the $2.3 billion settlement by Pfizer regarding claims it illegally promoted drugs off-label, and the $1.4 billion payment by Eli Lilly after claims it illegally promoted its antipsychotic drug Zyprexa—even to the point of training its sales persons in how to avoid legal requirements.

“Marketing departments of many drug companies don’t respect any boundaries of professionalism or the law,” according to Jerry Avorn, a professor at Harvard Medical School. “The Pfizer and Lilly cases (for example) involved the illegal promotion of drugs that have been shown to cause substantial harm and death to patients.” One study analyzed the impact of corporate mismarketing alleged in five prominent cases (involving the drugs Vioxx, Avandia, Bextra, OxyContin, and Zyprexa), and estimated the annual costs to society caused by the resulting sickness and death. The resulting figure of $27 billion a year in cost is an amount roughly equal to the industry’s claimed research investments over the same period.

Government officials admit to frustration that the many fines do not deter off-label promotion. One physician complains that the punishments “are nothing more than parking tickets.” Even multibillion dollar penalties do not measure up to much more than a fraction of the annual profits of these companies. And much of that profit is being earned through the very practices that are being prosecuted; studies suggest that one out of every five prescriptions is written for off-label use.

Beyond off-label promotion, the pharmaceutical industry has aggressively engaged in a practice known as “disease mongering,” sometimes called the more polite term “condition branding.” The approach is to take unpleasant but common aspects of the human condition and label them as medical diseases that corporate drug products can address. Examples of this technique are numerous: shyness was rebranded as “social
anxiety disorder” to market the antidepressant Paxil, premenstrual syndrome became the ominous-sounding “premenstrual dysorphic disorder,” which Prozac was promoted to address, and heartburn was upgraded to gastro-esophageal reflux disease, which Zantac stood ready to remedy.\textsuperscript{53} The industry has come under heavy criticism for its role in what many believe to be a significant overdiagnosis of attention deficit–hyperactivity disorder in children and adults in the United States\textsuperscript{54}

The iconic example of disease mongering is the transformation by the pharmaceutical industry of impotence into “erectile dysfunction,” accomplished by saturation ad campaigns and testimonies from paid researchers and physicians. The drugs promoted to treat what the industry labeled “E.D.” have become blockbuster sellers.\textsuperscript{55} That success soon inspired an effort to create a parallel “hypoaffective sexual desire disorder” for women. Despite the lack of any scientifically established norm for sexual desire or any evidence that low libido is an actual medical condition, pharmaceutical corporations pushed for approval to market testosterone patches and gels to address the situation.\textsuperscript{56}

Beginning in the mid-2000s, hypoaffective sexual desire disorder was exhaustively promoted in industry-funded continuing medical education (CME) courses. Those courses drove home some commercially favorable messages: the disorder was common and underdiagnosed, women may not even be aware they have the condition, and clinicians should initiate conversations on the topic with their female patients.\textsuperscript{57} One CME module even said that women who were highly interested in sex, just not with their current partner, may still be appropriately diagnosed as having a “situational” form of the disorder.\textsuperscript{58} Not surprisingly, a \textit{Journal of Medical Ethics} review of the campaign around hypoaffective sexual desire disorder called it “inventing a disease” and “a typical example of the medicalization of a normal state.”\textsuperscript{59}

The pharmaceutical industry has also been accused of unethical behavior for its use of what seems at first glance to be a positive practice: medicine donation programs, sometimes known as patient-assistance programs. “The glorified term, ‘patient assistance program’ is nothing but a marketing strategy,” an Indian medical ethicists told the \textit{New York Times}.\textsuperscript{60} There are multiple examples to back up that statement. Novartis has been sharply criticized for giving away far less of its cancer drug Gleevec than it had promised and for then threatening to stop donations in countries

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where generic versions were permitted. Novartis also pushed the recipients of its donations to lobby their governments to buy the drug at high prices and to oppose generic competition, a common request made to individual patients and patient groups who receive drug company donations. Many desperate patients and families are willing to comply with company requests, but are disappointed to learn that these programs are much less extensive than industry rhetoric suggests, especially since Medicare, Medicaid, and veterans’ program enrollees are not eligible and many programs require private insurance coverage.

Insurers and industry observers say the leveraging of drug donations for brand promotion and to discourage generics has the effect of driving up the cost of medicines—and the profits of the companies. In 2016, Bloomberg News conducted an investigation into such programs, concluding that they are a public relations-focused “billion-dollar system in which charitable giving is, in effect, a very profitable form of investing for drug companies.” Later that year, a whistleblower lawsuit filed by a former Celgene employee claimed that the company was using its donations to patient charities as a mechanism to ensure that Medicare covered its drugs, thus directing billions of dollars in payments to the company.

This dispiritingly long list of ethical problems in the pharmaceutical industry cannot conclude without a mention of the financial machinations that huge pharma corporations use to avoid paying taxes, particularly in the United States. In 2015, the U.S. pharmaceutical giant Pfizer announced it would pursue the largest ever “tax inversion,” a strategy in which a corporation merges with a foreign competitor to relocate its legally defined headquarters to a country with lower taxes. In 2014, U.S. President Barack Obama called inversion companies “corporate deserters.” The Pfizer plan to merge with Dublin-based Allergan and shift its headquarters to low-tax Ireland drew sharp criticisms. “The Pfizer-Allergan deal will be the biggest inversion yet, and it is nothing short of a disgrace,” wrote John Cassidy in the New Yorker in late 2015. “Drug companies like Pfizer have long benefitted from taxpayer-funded research carried out under the auspices of organizations like the NIH and the National Science Foundation. Now, Pfizer is seeking to avoid paying the taxes that are due on its profits.”

The Pfizer-Allergan merger was eventually abandoned. But the philosophy it represented is alive and well. Even as U.S.-based pharmaceutical corporations rely on taxpayer-supported research and high-price
high-volume government drug purchases (see chapters 16 and 17), they still relentlessly pursue methods to avoid paying U.S. taxes. Pfizer has stashed $74 billion in profits overseas to avoid U.S. taxes, and Merck has $60 billion similarly tucked away. Gilead, the U.S. company whose blockbuster hepatitis C medicine was created using U.S.-funded research and is purchased primarily by U.S. government agencies, has transferred the patent for the medicine to an Irish subsidiary. As Frank Clemente, executive director of Americans for Tax Fairness, said, “Gilead is making a fortune selling essential drugs to the very government and taxpayers that helped pay to develop them, and then dodging taxes on the resulting profits.”