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PRIVATE-SECTOR RESEARCH ETHICS: MARKETING OR GOOD CONFLICTS MANAGEMENT? THE 2005 JOHN J. CONLEY LECTURE ON MEDICAL ETHICS

ABSTRACT. Pharmaceutical companies are major sponsors of biomedical research. Most scholars and policymakers focus their attention on government and academic oversight activities, however. In this article, I consider the role of pharmaceutical companies' internal ethics statements in guiding decisions about corporate research and development (R&D). I review materials from drug company websites and contributions from the business and medical ethics literature that address ethical responsibilities of businesses in general and pharmaceutical companies in particular. I discuss positive and negative uses of pharmaceutical companies' ethics materials and describe shortcomings in the companies' existing ethics programs. To guide employees and reassure outsiders, companies must add rigor, independence, and transparency to their R&D ethics programs.

KEY WORDS: business ethics, conflicts of interest, corporate responsibility, pharmaceutical companies, research ethics, scientific integrity

The private sector's role in biomedical research and development (R&D) is rapidly expanding. Today, industry supplies more funding for biomedical R&D than does the U.S. government, and pharmaceutical companies contribute about 70% of the funding for U.S. drug trials.[1]

Despite the private sector's growing dominance, scholarly and policy analysis of research ethics concentrates on government rules and conflicts of interest for academicians. Little attention is given to the internal ethical judgments influencing the choices industry scientists and other workers make about research. Yet, given the proportion of research that industry sponsors, drug companies' internal standards and policies could have at least as much ethical impact as those of the government.

Internal standards are overlooked as well in the debate over conflicts of interest in industry-sponsored research. Much of the

debate emphasizes the negative impact industry funding can have on academic values, such as the freedom to publish research results. Accordingly, in universities and academic health centers, concern centers on matters such as drug trial agreements between pharmaceutical companies and academic scientists and institutions.

It is not surprising that those in academic science focus on academic activities, but the general social goal should be to ensure that *all* decisions about biomedical research are consistent with standards for research integrity and public health protection. The worry that industry sponsorship could lead academic scientists to engage in unacceptable research practices, such as withholding study data unfavorable to an investigational drug, is a worry that should extend to scientists and other decision-makers within industry, too.

The wider social goal in industry-sponsored research is appropriate management of financial conflicts – appropriate management in *any* setting. Limiting the examination to conflicts in the academic sector is inadequate to achieve this wider goal. As of 2004, academic centers conducted only an estimated 26% of industry-sponsored clinical research in the U.S. The rest of the industry research was done in community settings by non-academic medical centers and for-profit contract research organizations.[2] Policies governing academic science alone have no impact on the majority of industry-sponsored trials.

In sum, it is not the threat to academic values that is the primary problem, it is the threat to public health interests that profit-driven research presents no matter where it is performed. Thus, the analysis of financial conflicts in industry-sponsored research must include an evaluation of how those conflicts are managed within industry. Internal ethical standards governing R&D activities are one indication of how pharmaceutical companies balance profits and public health protection.

In this article, I consider ethics in private-sector biomedical R&D.[3] I examine business, science, and medical ethics literature addressing this topic. I also describe pharmaceutical companies' statements about their ethical responsibilities. I discuss different functions that ethics programs can serve for companies and conclude with recommendations for strengthening those programs. The article focuses on the drug industry, but many points apply as well to other private-sector biomedical research sponsors, such as biotechnology and medical device companies.[4]

ETHICS AND PHARMACEUTICAL COMPANIES

The inquiry into pharmaceutical company ethics starts with the broader topic of corporate ethics. Scholars and professionals debate whether businesses have ethical responsibilities beyond those owed to shareholders. There is contemporary support for the view that they do, and that view is embraced – in public communications, at least – by the pharmaceutical industry itself.

Two views of corporate responsibility

Traditional economics holds that the corporation's only ethical responsibility is to shareholders. In a 1971 article, "The Social Responsibility of Business is to Increase Profits," Milton Friedman articulated this position.[5] He wrote, "Only people can have responsibilities" and because corporations are only "artificial persons," it is a mistake to assign them social responsibilities.[6] On this view, choices to promote the social good must be left to individual investors receiving profits from corporations devoted to their proper financial aims.[7]

For those holding Friedman's views, social and economic goals should be kept separate.[8] Businesses should seek "not the common good or moral purpose, ... but competitive advantage."[9] Any effort to inject moral judgment into corporate decision-making "is seen as inefficient and arrogant, and in the end both an illegitimate use of corporate power and an abuse of the manager's fiduciary role [to shareholders]."[10] Many of those objecting to corporate ethics see political action as the appropriate vehicle for applying moral considerations to business. If public interests warrant protection, they say, it is up to government officials to respond through law and regulation.[11]

But this view is less popular than it once was, among scholars and others. Today, many business academics and professionals think that corporations have responsibilities not simply to shareholders, but to *other* stakeholders, such as employees, customers, and the community.

Lynn Sharp Paine, a Harvard Business School Professor, is representative of the group. Paine describes a "value shift" in public perceptions of acceptable corporate behavior:

> Today's leading companies are expected not only to create wealth and produce superior goods and services, but also to conduct themselves as "moral actors"—as responsible agents that carry out their business within a moral framework. As such,

they are expected to adhere to basic ethical principles, exercise moral judgment in carrying out their affairs, accept responsibility for their deeds and misdeeds, be responsive to the needs and interests of others, and manage their own values and commitments. Contrary to theorists who for centuries have declared the corporation to be an entirely amoral creature and thus incapable of such behavior, society today has endowed the corporation with a moral personality.[12]

Paine further argues that companies themselves are accepting these ideas. She attributes this to their realization that good ethics can be good business. She presents case studies showing that ethics can enhance efficiency and research findings supporting that position. Her judgment that ethical conduct can advance business interests often involves assessing the company's long-term economic health and the overall effect of commitment to a certain set of values on its financial well-being. At a minimum, Paine argues, good ethics and financial self-interest are not necessarily in conflict. Though there are cases in which ignoring ethics is financially beneficial, she contends that in a large number of cases, ethical actions are consistent with financial benefit.[13]

Other ethics scholars take positions similar to Paine's. For example, Dennis Thompson, Director of the Harvard Center on Ethics and the Professions, discusses business ethics in the context of institutional ethics. He contends that it is a mistake to think that organizations and their officers should be ethically neutral. Instead, what is needed and what is emerging, he writes, is "a new view of business ethics" that sees corporate executives as responsible to "all stakeholders," including "employees, customers, suppliers, lenders, citizens of the local community, and even sometimes foreign nationals."[14] Thompson urges a "public dialogue" in which businesspersons and others discuss the principles and practices that should apply to business activities, with the aim of achieving an acceptable balance between profit and morality.[15]

Many contemporary writers considering corporate responsibility argue that companies today are and should be regarded as agents engaged in moral decision-making.[16] Although debate continues between this group and writers with positions like Friedman's, there is now respectable support for the view that businesses have ethical responsibilities other than to maximize profits for shareholders. And even those in Friedman's camp would support ethical conduct that is good for business.[17] Indeed, many businesses themselves acknowledge that they have ethical duties, and pharmaceutical companies are no exception.

Pharmaceutical Companies' Ethics Statements

In communicating with the public, pharmaceutical companies purport to reject the claims that ethical behavior is irrelevant to their corporate missions and that corporate duties are owed only to shareholders. Corporate websites offer evidence of the industry stance. Websites of the top ten pharmaceutical companies doing business in the U.S. (based on 2004 sales)[18] declare strong commitments to social responsibility, corporate responsibility, and ethical research and marketing. Nearly all of the companies have explicit materials under these headings and all invoke ethical and social responsibility concepts in general discussions of their commitments and R&D goals. Below are a few examples of these materials.

The top pharmaceutical company, Pfizer, Inc., recently changed its mission statement from "be number one" to "become the world's most valued company to our stakeholders."[19] In 2002, it became the first U.S.-based pharmaceutical firm to sign the United Nations Global Compact, which establishes principles for corporate responsibility. In announcing the decision, Pfizer's Chairman said,

> [s]ome companies may fear that if they sign the Global Compact, they'll be held to a higher standard of corporate citizenship. That's a challenge we frankly welcome, because being a good global citizen has long been at the core of how we do business. That's why after careful deliberation we determined that joining the Compact is in our business interest.[20]

The firm's website describes the rationale for signing the Global Compact as follows:

> The pharmaceutical industry itself was under attack for its focus on "Western diseases" and the price of its prescription medicines. ... [Pfizer's chairman] knew that, in order for Pfizer to fulfill its mission and sustain a productive business, it needed to engage these critics. The Global Compact was a network Pfizer could enter and immediately get to work learning from others, discussing issues and explaining how medicines are discovered and brought to market. The goal would be to find common ground and new solutions.[21]

Johnson & Johnson is another company recognizing ethical responsibilities to many stakeholders. The company's website highlights a Credo that the founder, Robert Wood Johnson, first drafted in 1943.[22] According to the Credo, the firm's "first responsibility is to the doctors, nurses and patients, to mothers and fathers and all others who use our products and services. In meeting their needs everything we do must be of high quality." The Credo next covers responsibilities to employees, then acknowledges duties to "the communities in

which we live and work and to the world community as well.'' Stockholders are last on the list. ''Our final responsibility is to our stockholders. Business must make a sound profit. We must experiment with new ideas. Research must be carried on, innovative programs developed and mistakes paid for....''[23]

The Merck Company website also emphasizes the company's commitment to public health over profits. The website highlights the following statement by the company founder, George Merck: ''We try never to forget that medicine is for the people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear.''[24] Merck's mission statement offers a similar outlook: ''In discharging our responsibilities, we do not take ethical or professional shortcuts. We expect profits, but only from work that satisfies customer needs and benefits humanity.''[25]

Other firms declare responsibilities to multiple stakeholders. According to AstraZeneca's *Corporate Responsibility Policy*, ''patient benefit and safety continue to be the core priority'' and workers ''maintain high ethical standards in our research and development of new medicines.'' The company also promises to ''be transparent in our communications about the work we are doing to meet these commitments ....''[26] Among Amgen's list of corporate values is the following: ''Be ethical: We are relentless in applying the highest ethical standards to our products, services and communications.'' Another is: ''Collaborate, Communicate and Be Accountable,'' which includes a pledge to ''involve key stakeholders in important decisions'' and ''clearly communicate decisions and rationales in a timely and open manner.''[27]

The websites include many similar statements from other top-ten companies. And the Pharmaceutical Researchers and Manufacturers Association (PhRMA), the trade association that represents pharmaceutical and biotech companies, also portrays its members as focused on the public good. According to the PhRMA website, the industry's goal is ''discovering, developing, and bringing to market medicines to improve human health, patient satisfaction, and the quality of life around the world, as well as to reduce the overall cost of health care.''[28]

In sum, both business ethics scholarship and corporate communications support the judgment that drug companies have ethical responsibilities to a wide array of stakeholders. In the next section, I consider whether the pharmaceutical business has features that support assigning drug companies distinct ethical responsibilities.

ETHICS AND THE NATURE OF MEDICAL PRODUCTS

Some people think that drug companies should make reasonable efforts to provide medications to people who cannot afford them. Note that there does not seem to be the same expectation for businesses manufacturing products that meet other human needs. We rarely hear calls for clothing companies to provide clothing or food companies to provide food to poor people. Why is this responsibility assigned to drug companies?

The judgment that drug companies have a duty to address access originates in beliefs about the nature of their business. To evaluate this and similar claims, we must consider a series of more general questions. Are there distinct features of the pharmaceutical industry that affect its ethical responsibilities? Should we assign to an industry that develops and markets products affecting human health ethical duties that are absent for industries making other products? Do the professional responsibilities of physicians and health researchers apply in some form to the businesses that design and manufacture the means to heal and prevent disease?

Some commentators argue that drugs are different from other products and that those differences support distinct ethical responsibilities for companies in the drug business. One is Marcia Angell, a former editor of *The New England Journal of Medicine*. In a book examining problems with the drug industry's R&D activities, she writes, "If prescription drugs were like ordinary consumer goods, all this might not matter very much. But drugs are different. People depend on them for their health and even their lives."[29] In a co-authored article, Arnold Relman, another former editor of the journal, joins Angell in asserting, "The misconception that drugs and their market are like other goods and markets explains most of the serious problems with the pharmaceutical industry today."[30]

Four health analysts considering pharmaceutical companies' financial conflicts also see these companies as different from others. Writing in the *Journal of the American Medical Association*, this group asserted that the public health importance of medical products confers on drug companies "the ethical and moral obligations that are normally associated with medicine and that are higher than the minimum standards of routine economic transactions."[31] Specific obligations include "a duty to disclose risks and inform patients and physicians of safety problems."[32]

Other analysts describe distinct duties for drug companies engaged in research activities. For example, one group of authors suggests that the terms of clinical trial agreements between sponsors and investigators should be more transparent than other business contracts. "Clinical research is special," they contend, "because of its implications for public health and safety."[33]

Ordinary people, too, seem to perceive the medical product business as different from other businesses. An illustration comes from a woman's letter to *The New York Times*:

> I was appalled to learn that manufacturers of medical devices do not always disclose information about flaws to doctors and patients. It is unconscionable that companies ... would withhold information that could prove fatal to high-risk patients because of fears about their reputation.
>
> Manufacturers of such devices must be held to higher standards than manufacturers of other products.[34]

Those describing special duties point as well to the benefits pharmaceutical companies gain from knowledge generated by government-funded basic research. According to these writers, the federal government's research support, together with the substantial R&D tax credit that companies receive for their own work, makes it fair to expect something in return. In exchange for the taxpayers' financial assistance, they say, pharmaceutical companies ought to assign considerable weight to the public good in decisions about drug development and access.[35]

Websites suggest that the drug companies themselves perceive distinct ethical expectations from outsiders. An example comes from a document on Pfizer's website: "Unlike any other industry in the world, the pharmaceutical industry sits at the crossroads where the global interests of business, science, government, religion and the general public can collide over issues of life and death."[36] This document also cites a 2003 survey by the International Institute for Management Development in Geneva, which found that "stakeholders expect more social responsibility from the pharmaceutical sector than from any other industry."[37]

More backing for the special responsibilities view comes from scholars discussing ethics in health care organizations, where financial considerations are balanced against patients' needs. In the health care business, they note, many of the workers are not like workers in other businesses. Physicians, nurses, and other clinicians are guided by ethical codes and professional responsibilities. Technical

complexity and the burdens of illness can also make patients more vulnerable than consumers in other markets.[38] For some scholars, these features justify assigning to health care organizations a mandate to make high-quality patient care the top priority. Echoing Lynn Paine's analysis, these scholars believe that health care organizations failing to recognize this distinct ethical obligation may do damage to the organization's financial position, as well.[39]

A similar set of considerations could apply to companies that are in the business of producing medical products. On this view, physicians, nurses, and scientists working for pharmaceutical companies must conform to the same ethical standards as their counterparts working in other settings. Health professionals may not put patients at risk to advance the company's financial interests. Scientists must design, conduct, and interpret research according to accepted scientific standards. And these professional duties carry over in some form to the managers and others working in the company.

At the same time, the above material only begins to examine the special responsibilities question. Responding to claims about pharmaceutical companies' ethical responsibilities, philosopher Dan Brock maintains that it is not enough simply to assert that medical needs create special corporate obligations. Instead, writers arguing for special duties must offer a developed account of why such duties exist and how they apply in specific situations. For example, Brock notes, governments, not businesses, are generally seen as responsible for ensuring that basic human needs for food and housing are met. And although "coverage of prescription drugs for the elderly is a major political issue in the U.S. today, ... no side in the controversy argues that it is the drug companies' social responsibilities of beneficence and justice to meet the need."[40] On Brock's view, people who believe that companies should play a role in providing drugs must explain why business has more than the usual responsibility in this case.

Brock's comments point to the need for more work on the "distinct responsibilities" question. Certain features of the drug business set it apart from other businesses. The special status of pharmaceutical consumers and the deep involvement of medical and research professionals in R&D activities may support some of the claims that drug companies have obligations beyond those of other business enterprises. For the pharmaceutical industry, corporate responsibility may require combining ordinary business ethics with elements of medical and research ethics. Determining whether and how these

applied ethics fields are relevant to drug company activities is a complicated task warranting more extensive analysis.

THE SPECIFICS OF ETHICAL CONDUCT IN PHARMACEUTICAL R&D

Besides creating a foundation for expectations regarding acceptable conduct, the nature of the pharmaceutical business shapes the specific ethical standards and practices that apply to R&D activities. To promote public health in these activities, corporate decision-makers must take into account many detailed ethical considerations.

Law and bioethics professor Gordon DuVal characterizes the business situation as follows:

> Pharmaceutical and biotechnology companies exist to maximize value to shareholders.... This is ... not to say that pharmaceutical and biotechnology companies are necessarily indifferent to the integrity of research or the protection of human subjects. It is simply to say that the profit motive often conflicts with these values and supplies an incentive to make decisions at odds with them.[41]

DuVal describes three kinds of threats in commercial research. First, industry's search for profitable products can produce research agendas that do not correspond with public health needs. Second, industry's eagerness to market investigational products can expose trial participants and patients to harm from a variety of practices, such as conducting questionably valuable studies, engaging in inappropriate study recruitment activities, paying insufficient attention to product risks, exaggerating potential benefits, and failing to report adverse events. Third, industry's marketing aims can encourage suppression of unfavorable results, bias in study design and data analysis, and manipulation of clinical trial outcomes.[42]

Pharmaceutical companies recognize the public and professional concern over specific corporate conflicts and respond to it in website communications. Several offer materials defending their research agendas. For example, Pfizer reports its decision to undertake research targeting malaria, SARS, and smallpox, even though drugs for these diseases would be unlikely to produce high profits. In announcing the decision, company officials promised that if the research produced positive results, they would work to deliver drugs to people in need. Pfizer's Chairman said, "We are getting into this battle because the human cost is so high and because we believe that

corporate citizenship and expanded access to basic healthcare are also central to Pfizer's importance."[43]

Another example comes from Amgen. One of the company's four guiding principles is the following: "(1) focus on grievous illness. Given that it is so hard to succeed at developing a new therapy, we focus our efforts on developing therapies that have a beneficial effect on patients suffering from the greatest unmet health needs."[44] In its Corporate Responsibility Principles, GlaxoSmithKline asserts, "We will continue to research and develop medicines to treat diseases of the developing world. We will find sustainable ways to improve access to medicines for disadvantaged people, and will seek partnerships to support this activity."[45]

Corporate websites also address research practices and disclosure of drug safety and effectiveness data. Johnson & Johnson's Ethical Code for the Conduct of Pharmaceutical Medicine supplements the company's Credo with more specific standards for its scientists, physicians, and other employees. According to the Code, "It is our responsibility to apply Credo-based values and judgment regarding the design, conduct, analysis and interpretation of clinical studies and results."[46] The Code accepts as well a "responsibility to ensure all Company-based, medically relevant product information is fair and balanced, accurate and comprehensive, to enable well-informed risk-benefit assessments about our products."[47]

AstraZeneca's Bioethics Policy on R&D activities contains many provisions on research methods and information disclosure. Among them are the following:

> Data analyses will be ... documented and logged in accordance with generally accepted principles for such activities.
>
> Safety data from development projects and marketed products will be periodically analysed to identify any significant new adverse reactions and possible safety signals from both clinical and non-clinical sources.
>
> As a general principle, all research results that may be of interest to the scientific community will be made available for publications.[48]

Finally, the trade association PhRMA has adopted Principles for Conduct of Clinical Trials and Communication of Clinical Trial Results. The principles assert that clinical trials will be designed and conducted "in an ethical and scientifically rigorous manner to determine the benefits, risks, and value of pharmaceutical products."[49] Companies subscribing to the principles also "commit to

timely communication of meaningful results of controlled clinical trials of marketed products or investigational products that are approved for marketing, regardless of outcome."[50]

These statements and others like them show that pharmaceutical companies are aware of how the quest for profits can threaten research integrity and public health interests. Through their websites, the companies are attempting to respond to public concern about their financial conflicts. But are the ethics statements genuine? Do they represent an honest commitment to the values and practices they recite? Below I discuss why it can be difficult to answer these questions.

EVALUATING CORPORATE COMMITMENTS

Public ethics statements may meet a variety of objectives for pharmaceutical companies, some more socially desirable than others. The statements may function as a form of advertising to promote trust among patients, health professionals, and other stakeholders. The statements may extend and supplement legal mandates, or they may be designed to discourage government officials from imposing new laws and regulations. The statements may articulate an authentic mission and may help researchers and other decision-makers resolve difficult ethical questions. Below I discuss each of these possibilities.

Ethics and marketing

It is entirely possible that pharmaceutical company codes and pledges are primarily public relations efforts. Companies could be declaring their allegiance to ethics because they think this is what the public and government officials want to hear. Corporate decision-makers could see elegant website materials about ethics as a form of advertising, designed to reassure outsiders about a company's good intentions and the safety and effectiveness of its pharmaceutical products.

If ethics statements are used as advertising, they should be scrutinized in the same way as other forms of drug advertising. In the U.S., government officials, the media, and interest groups evaluate promotional materials about drugs for accuracy and balance. The same criteria should apply to website materials on ethics. Companies should not offer public accounts of ethics standards and programs

that mislead readers about the actual influence that ethics has on corporate decision-making.

Pharmaceutical companies will undoubtedly protest the image of ethics as a marketing tool. But more than protests are needed to counter this image. To cultivate the trust they seek through ethics statements, companies should be willing to demonstrate their commitment to ethics. This would require companies to share more information about the application of ethics codes and policies than they do today.

Ethics and regulation

Laws and regulations often express ethical judgments, and this is true in research areas. Drug companies must comply with laws and regulations governing activities that are also covered in ethics statements. For U.S. companies, these include requirements for information disclosure to prospective trial subjects, requirements that trials undergo Institutional Review Board evaluation, and requirements to submit to the Food and Drug Administration studies demonstrating a drug's safety and effectiveness.

Pharmaceutical companies may see ethics materials as regulatory enhancements, or they may see them as regulatory alternatives. In the first situation, corporate decision-makers create ethics codes and principles to promote compliance with regulations. Regulations incorporate normative judgments about appropriate conduct and companies may develop ethics statements to serve as guides and supplements to regulatory requirements.

Corporate websites often portray ethics materials in this light. For example, several of GlaxoSmithKline's Corporate Responsibility Principles present ethical standards in conjunction with a pledge to comply with or go beyond regulatory and other legal requirements.[51] AstraZeneca characterizes its R&D Bioethics Policy as setting independent ethical standards that operate in tandem with the relevant laws and regulations.[52]

In the second situation, pharmaceutical companies offer ethics statements to deter regulation, which can be more rigorous and restrictive than general ethical commitments. For example, in response to legislative proposals requiring pharmaceutical companies to release more clinical trial data, PhRMA developed a voluntary information disclosure plan for its members. When congressional bills mandating data release were introduced in 2005, a PhRMA

spokesman urged Congress to postpone action to give the voluntary program a chance to work.[53]

From a public policy perspective, relying on regulation alone is problematic. There are clear rights and wrongs that can be addressed through legal rules, and there are situations in which regulation is the only effective method for producing desired conduct. Thus, regulation plays an essential oversight role. At the same time, regulation usually demands substantial interpretation and resolving ethical questions about drug R&D often requires detailed factual analysis. In short, regulation is a blunt instrument that leaves much room for ethical judgments to handle different situations that arise.[54] An authentic commitment from the pharmaceutical industry to promote ethical decision-making could enrich and extend regulatory efforts to promote research integrity and public health protection.

Ethics and genuine commitment

Society would be best served if corporate ethics materials were part of a real effort to prevent financial considerations from compromising research integrity and public health interests. It would be best if pharmaceutical company officers and managers operated ethics programs that met the standards of a good organizational ethics program. Such programs would seek "to develop and evaluate the organizational mission, to create a positive ethical climate within the organization that perpetuates the mission, to develop decision models for insuring this perpetuation as reflected in organizational activities, and to serve as a cheerleader, evaluator, and critic of organizational, professional, and managerial behavior."[55] The question is whether the pharmaceutical company programs are designed to achieve these aims.

Pharmaceutical company websites seek to assure readers that their ethics commitments are both genuine and influential in research decision-making. The website pledges are hard to reconcile with critics' accounts of drug company conduct, however. And in the current circumstances, outsiders often have a difficult time evaluating the companies' actions.

Inadequate access to the facts is a major impediment to assessing whether drug companies actually apply their ethical codes and principles. Corporate representatives, consumer activists, and the media tend to present different and often conflicting versions of events surrounding particular drug R&D decisions. And pharma-

ceutical companies are typically reluctant to release documents about their internal ethical decision-making.

When drug companies make claims about their ethical standards, but are unwilling to demonstrate that those standards are truly considered, they invite charges of hypocrisy. Secrecy about information relevant to research integrity and the health of trial subjects and patients triggers suspicion that the companies' ethical claims are insincere.

And even with adequate information, evaluating private-sector conduct can be challenging. Sometimes drug companies engage in R&D conduct that clearly violates regulatory standards, or widely accepted ethics standards, or both. Other times, however, things are not so simple. Some situations raise issues about which reasonable people might disagree (for reasons other than financial considerations). Other situations require decision-makers to examine extensive, often incomplete, empirical data and to make predictions about a future that is uncertain.

Take the example of research agendas. How should companies assess public health needs and determine the areas in which R&D are most justified? The proper research priorities are debated in the public sector, too, and the topic provokes heated discussion. Should priority go to conditions that cause death or serious disability to a relatively small number of people, or to less severe conditions that affect many more individuals? Should priority go to causes of premature death rather than to chronic diseases of aging? And what priority should wealthy countries like the U.S. give to research aimed at reducing the burden of disease in poor nations? Do government and private research sponsors have obligations to invest resources in studying conditions that pose little threat to U.S. residents?[56]

A general lack of agreement on how to answer these questions complicates the effort to evaluate pharmaceutical companies' research agendas. In a recent article, policy analysts Thomas Croghan and Patricia Pittman described two preconditions to revising the pharmaceutical industry's research agendas: "consensus on the definition of medical need and a priority-setting process."[57] They suggested that more work to develop consensus in these areas would furnish a stronger basis for aligning corporate priorities with health needs.

There can be disagreement as well about the appropriate responses to drug safety questions. This sort of disagreement is evident in a recent series of articles examining Bayer Corporation's actions

regarding Cerivastatin (Baycol), a statin drug presenting a relatively high risk of rhabdomyolysis, a serious and sometimes lethal condition. The drug was eventually withdrawn and the ongoing controversy and litigation address whether Bayer's response to adverse event reports was adequate. The articles take very different positions on this issue.

In one article, health researchers acting as plaintiffs' experts in tort litigation make the case that the company possessed data supporting drug withdrawal nearly 2 years before it acted.[58] But an expert retained by the defense points out that before its decision to withdraw the drug, Bayer made labeling changes, notified physicians, and commenced a formal study to generate rigorous risk data about the product. "Although hindsight always raises questions about whether a problem could have been detected earlier," he writes, "the events surrounding cerivastatin serve as a clear example of how the system should work."[59]

Despite their disagreement over whether Bayer acted responsibly in this case, the experts concur on one point: there is an element of judgment involved in monitoring drug safety. These judgments can be affected by financial interests, but there are other potential sources of bias. For example, experts lacking industry ties often disagree on whether to issue a drug warning or withdrawal because they have different opinions about the importance of the benefit a drug confers or the harm it can impose.[60] And investigators whose support comes from the government or a nonprofit organization may expose trial subjects to unwarranted risk in the quest to advance knowledge or their professional careers.[61] Although commercial interests may taint the judgments of corporate physicians and scientists, other factors can also make drug safety and effectiveness contested matters. As in the academic setting, there will often be a range of views regarding the ethical action for drug company officials in specific cases.

Drug companies face complicated ethical issues in R&D activities, issues that are difficult for scientists, clinicians, and managers in any research setting. In the current circumstances, however, it is too hard for outsiders to discern when companies make reasonable choices reflecting defensible ethical judgments, and when they make choices primarily based on financial considerations. If companies want the public to regard them as trustworthy managers of financial conflicts, they ought to reveal more about their ethical deliberations.

RECOMMENDATIONS

Scholars and policymakers should adopt an expansive perspective on conflicts of interest in biomedical research. Because the majority of drug trials are conducted without the participation of academic scientists, it is shortsighted to consider academic standards alone. And it is unwise to rely heavily on academic scientists as a brake against improper behavior, because they may not be involved at all, or because their financial interests put them in a position similar to that of an industry scientist.

Analysts and officials should consider all situations in which financial interests pose threats to research integrity and public health protection. This means going beyond examining how to protect research integrity and public health in industry-sponsored academic research to examining how to protect research integrity and public health in all industry-sponsored research.

From this vantage point, the sensible approach is to target corporate scientists, physicians, and managers, who are the ones influencing conduct both inside and outside the academy. If the aim is to ensure ethical conduct by industry decision-makers, developing appropriate standards and implementation strategies becomes the major challenge.

A reasonable and fair message to the pharmaceutical industry would be, "It is not enough to say you observe ethical standards, you must also demonstrate a good faith effort to do so." Without such a showing, many people will see the companies' ethics materials as mere tokens, simply another form of marketing. Progress could come if pharmaceutical companies add rigor, independence, and transparency to their ethics programs.

Pharmaceutical companies should have robust ethics programs with adequate substantive standards. While some companies' websites contain reasonable and relatively detailed policies addressing R&D ethics, the ethics materials on other websites are too general to offer sufficient guidance to employees or reassurance to outsiders.

Website materials reveal similar disparities in the drug companies' procedural approaches to resolving ethical issues. Some companies disclose specific information about internal procedures, others say little or nothing about this topic.[62] As Lynn Sharp Paine notes, "principles and codes are nothing until brought to life in the context of human activity," and "codes and principles are neither self-applying nor self-interpreting."[63] A central challenge in drug com-

pany R&D is to reconcile the company's financial interests with ethical standards protecting public health and research integrity. Because the proper choice in specific cases is not always obvious, the process by which decisions are made can be crucial to defensible outcomes.

Pharmaceutical companies must also go beyond public recitations of ethics standards and procedures. Companies interested in establishing effective ethics programs must be open and candid about specific applications of their ethics standards. To operate internal programs that are both useful to employees and reassuring to outsiders, companies must accept independent review of, and transparency in, ethics decision-making.

By incorporating independent review into their ethics programs, pharmaceutical companies can guard against the risks of isolation. Individuals within an organization are at times unaware of ethical problems that would be obvious to outsiders. By exposing important decisions to independent review, companies can avoid conduct that unaffiliated clinicians, scientists, or the general community would question. Moreover, companies willing to share decisions with a group of outsiders signal to the public a commitment to resolve conflicts in a responsible fashion.[64]

Corporate officers should also aim for more transparency in their ethics decision-making. This approach is consistent with Dennis Thompson's appeal for corporate executives to "account to the public in public for their actions, and give moral reasons that appeal to principles shared with their fellow citizens."[65] To earn public confidence, he notes, "corporations will have to be more open about what they do within their own walls."[66]

To achieve greater transparency about ethics, companies will probably have to reveal some information traditionally treated as proprietary, including relatively detailed descriptions of product studies and more extensive records of post-marketing surveillance. Greater transparency will require companies to examine the extent and limits of their legitimate proprietary interests, to consider what should and should not be kept secret to protect those interests. In the current climate, however, overbroad notions of secrecy are neither good ethics nor good business for pharmaceutical companies.

Adding rigor, independence, and transparency will require companies to act, not merely to assure. Companies today have many opportunities to show outsiders that they see ethics as more than a marketing tool. Clinical trials registries offer one such opportunity.

Industry research sponsors participating in registries submit information about every clinical trial they initiate. When a trial is finished, its sponsor reports the findings. Because there is a record of all trials, it is difficult for sponsors to conceal data unfavorable to their financial interests.[67]

Trial registries hold pharmaceutical companies accountable for following through with their ethical commitments to, for example, disclose "all research results that may be of interest to the scientific community."[68] In fact, analysts have criticized three of the top U.S. drug companies for failing to disclose adequate information to an existing trial registry. In 2005, the registry director commented, "There are a lot of public statements from drug companies saying that they support the registration of clinical trials or the dissemination of trial results, but the devil is in the details."[69]

Without more affirmative efforts, pharmaceutical companies will face skepticism about their ethics commitments. To gain credibility, companies must deliver on their ethics pledges. They can do this by inviting independent experts and members of the public to review their decisions and by releasing more information about their reasoning in particular ethics cases. Besides voluntary actions by drug company officials, regulatory action may be needed to strengthen internal ethics programs.[70]

That familiar quotation about government: "Every nation has the government it deserves,"[71] could apply to pharmaceutical companies, too. Public and professional expectations strongly influence the way businesses manage ethics. Scholars, researchers, clinicians, and patients who think that the "corporations have no ethical responsibilities to society" approach is wrong, and that the "ethics on paper but not in demonstrable action" approach is inadequate, must express their dissatisfaction. Pharmaceutical companies must be persuaded to go beyond website assurances to create active and effective programs for reconciling financial interests with R&D ethics.

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NOTES

[1] Michelle Mello, Brian Clarridge, and David Studdert, "Academic Medical Centers' Standards for Clinical-Trial Agreements with Industry," *New England Journal of Medicine* 352 (2005): 2202–2210.

[2] Robert Steinbrook, "Gag Clauses in Clinical-Trial Agreements," *New England Journal of Medicine* 352 (2005): 2160–2162.

[3] Discussions of private-sector ethics, corporate good citizenship, and social responsibility often consider a wide range of activities. For example, according to a Pfizer Corporation document: "Citizenship defines our role in local and global communities and how we strive to conduct business responsibly in a changing world. Being a good corporate citizen includes listening to, understanding, and responding to our stakeholders about their needs regarding Pfizer's policies and operations. Stakeholders are people or groups who affect, or are affected by, Pfizer's business activities." Pfizer, "What Is Corporate Citizenship?" available at http://www.pfizer.com, accessed July 8, 2005.

[4] Two recent books apply business ethics to companies involved in biomedical research, with a particular emphasis on biotechnology companies. They are Margaret Eaton, *Ethics and the Business of Bioscience* (Palo Alto: Stanford Business Books, 2004) and Rahul Dhanda, *Guiding Icarus: Merging Bioethics with Corporate Interests* (New York: John Wiley & Sons, 2002).

[5] Milton Friedman, "The Social Responsibility of Business Is To Increase Its Profits," *New York Times Magazine*, September 13, 1970, pp. 32–33, 122–126.

[6] Ibid., p. 33.

[7] Margaret Eaton notes that Friedman did favor ethical behavior that would benefit shareholders through avoiding legal penalties or adverse public reaction. See *Bioscience*, cited in note 4, above, at pp. 27–28.

[8] Michael Porter and Mark Kramer, "The Competitive Advantage of Corporate Philanthropy," *Harvard Business Review on Corporate Responsibility* (Boston: Harvard Business School Press, 2003), pp. 27–64.

[9] Kenneth Goodpasture and John Mathews, "Can a Corporation Have a Conscience?" in *Corporate Responsibility*, cited in n. 8, above, at p. 141.

[10] Ibid., p. 142.

[11] Ibid., pp. 142–143.

[12] Lynn Sharp Paine, *Value Shift: Why Companies Must Merge Social and Financial Imperatives to Achieve Superior Performance* (New York: McGraw-Hill, 2003), p. x.

[13] Ibid., pp. 27–79.

[14] Dennis Thompson, "The Privatization of Business Ethics," *Restoring Responsibility: Ethics in Government, Business, and Healthcare* (Cambridge: Cambridge University Press, 2005), pp. 300–317, p. 313.

[15] Ibid., p. 314.

[16] For examples, see Goodpasture and Mathews, cited in note 9, above, and Porter and Kramer, cited in n. 8, above.

[17] Eaton, cited in note 4, above, pp. 27–28.

[18] See NDCHealth, "Excerpts from 2005 Pharma Insight," available at http://www.ndchealth.com/press_center/uspharmaindustrydata.asp, accessed July 8, 2005.

[19] Pfizer Corporate Citizenship: "How We're Changing," available at http://www.pfizer.com/subsites/corporate_citizenship/how_were_changing.html, accessed May 23, 2005.
[20] Quoted in Nancy Nielson, "Pfizer: A New Mission in Action," pp. 242–243, available at http://www.pfizer.com/subsites/corporate_citizenship/how_were_changing. html, accessed May 23, 2005.
[21] Ibid., p. 250.
[22] Johnson & Johnson, "Our Credo," available at http://www.jnj.com/our_company/policies/index.htm, accessed May 19, 2005.
[23] The Credo influenced Johnson & Johnson's response to the 1982 Tylenol crisis. At that time, the company voluntarily removed this over-the-counter medication from stores after seven unexplained deaths were associated with the product. Later, it was discovered that individual criminals were responsible for contaminating the product. Nevertheless, the company spent $100 million to switch to tamper-proof packaging and the case is often used to illustrate good corporate ethics. See Paine, cited in n. 12, pp. 30–31, 143–144.
[24] Merck, "Corporate Responsibility: Chairman's Message," available at http://www.merck.com/about/cr, accessed August 26, 2004.
[25] Merck, "Corporate Philosophy: Mission Statement," available at http://www.merck.com/about/mission.html, accessed August 26, 2004.
[26] AstraZeneca, "Corporate Responsibility Policy," available at http://www.astrazeneca.com/Article/11106.aspx, accessed May 19, 2005.
[27] Amgen, "Our Mission and Values," available at http://www.amgen.com/about/mission_values.html, accessed May 19, 2005.
[28] Mission, PhRMA Annual Report, 2002–2003, available at http://www.phrma.org/actions/printFriendlyPage.cfm?t = 46&r = 829, accessed June 29, 2005.
[29] Marcia Angell, *The Truth about the Drug Companies: How They Deceive Us, and What to Do about It* (New York: Random House, 2004), p. xix.
[30] Arnold Relman and Marcia Angell, "America's Other Drug Problem," *The New Republic*, December 16, 2002, pp. 27–41.
[31] Bruce Psaty, Curt Furberg, Wayne Ray, and Noel Weiss, "Potential for Conflict of Interest in the Evaluation of Suspected Adverse Drug Reactions: Use of Cerivastatin and Risk of Rhabdomyolysis," *Journal of the American Medical Association* 292 (2004): p. 2629.
[32] Ibid.
[33] Mello, Clarridge, and Studdert, cited in n. 1, above, p. 2209.
[34] Hannah Hahn, "The Flaws in a Heart Device," *New York Times*, May 31, 2005, at p. A18.
[35] Jerry Avorn, *Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs* (New York: Knopf, 2004), pp. 198–216. See also Angell and Relman, cited in n. 30, above.
[36] See Nielsen, cited in n. 20, above, p. 243.
[37] Ibid., p. 254.
[38] Edward Spencer, Ann Mills, Mary Rorty, and Patricia Werhane, *Organizational Ethics in Health* Care (New York: Oxford University Press, 2000), pp. 9–10.
[39] Ibid., p. 12.

[40] Dan Brock, "Some Questions About the Moral Responsibilities of Drug Companies in Developing Countries," *Developing World Bioethics* 1 (2001), p. 35.
[41] Gordon DuVal, "Institutional Conflicts of Interest: Protecting Human Subjects, Scientific Integrity, and Institutional Accountability," *Journal of Law, Medicine & Ethics* 32 (2004): 613–625, p. 616.
[42] Ibid., pp. 617–621.
[43] Nielsen, cited in n. 20, above, p. 252.
[44] Amgen, "R&D Vision," available at http://www.amgen.com/medpro/research_vision.html, accessed May 19, 2005.
[45] GlaxoSmithKline, "Corporate Responsibility – CR Principles," available at http://www.gsk.com/about/responsibility/management/principles.htm., accessed August 26, 2004.
[46] Johnson & Johnson, "Our Ethical Code for the Conduct of Pharmaceutical Medicine," available at http://www.jnj.com/community/policies/index.htm, accessed May 19, 2005.
[47] Ibid.
[48] AstraZeneca "Bioethics Policy," available at http://www.astrazeneca.com/Article/11106.aspx, accessed May 19, 2005.
[49] PhRMA "Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results," available at http://www.phrma.org, accessed November 17, 2004, p. 19.
[50] Ibid.
[51] GlaxoSmithKline "CR Principles," cited in n. 45, above.
[52] AstraZeneca "Introduction, Bioethics Policy," cited in note 48, above.
[53] Jennifer Couzin, "Facing Criticism, Industry Offers to Share Data," *Science* 307 (2005): 89.
[54] For more detailed discussion of the different roles that legal requirements and ethics materials can have in business activities, see Eaton, cited in n. 4, above, pp. 59–64.
[55] Spencer, Mills, Rorty, Werhane, cited in n. 38, above, pp. 3–4.
[56] See Rebecca Dresser, *When Science Offers Salvation: Patient Advocacy and Research Ethics* (New York: Oxford University Press, 2001), pp. 73–108.
[57] Thomas Croghan and Patricia Pittman, "The Medicine Cabinet: What's in It, Why, and Can We Change the Contents?: A Framework for Aligning Business Objectives with Medical Need," *Health Affairs* 23 (2004): 23–33.
[58] Psaty et al., cited in n. 31, pp. 2622–2631.
[59] Brian Strom, "Potential for Conflict of Interest in the Evaluation of Suspected Adverse Drug Reactions: A Counterpoint," *Journal of the American Medical Association* 292 (2004): 2643–2646.
[60] E.g., Nancy Olsen, "Tailoring Arthritis Therapy in the Wake of the NSAID Crisis," *New England Journal of Medicine* 352 (2005): 2578–2580.
[61] Norman Levinsky, "Nonfinancial Conflicts of Interest in Research," *New England Journal of Medicine* 347 (2002): 759–761.
[62] Two companies that offer information on procedures are AstraZeneca and GlaxoSmithKline. AstraZeneca describes internal mechanisms for reviewing safety data and resolving controversies related to R&D ethics. AstraZeneca Bioethics Policy, cited in n. 48, above. GlaxoSmithKline describes internal management procedures for corporate responsibility issues, including R&D ethics. GlaxoSmithKline "Manage-

ment of Corporate Responsibility,'' available at http://www.gsk.com/about/responsibility/management/index.htm, accessed August 26, 2004.

[63] Paine, cited in n. 12, p. 202.

[64] These ideas were influential in developing the review committees that consider human subjects research in the U.S. and other nations. See Dresser, cited in n. 56, pp. 109–128. One pharmaceutical company, Roche, has established a Science and Ethics Advisory Group composed of external experts and lay community members. The group's role is limited to participation in decisions about genetics and human tissue research, however. See Roche ''Ethics Advisory Group,'' available at http://www.roche.com/home/science/sci_eth_seag.htm, accessed May 23, 2005.

[65] Thompson, cited in n. 14, above, pp. 314–315.

[66] Ibid., p. 315.

[67] The International Committee of Medical Journal Editors made registration a requirement for publication in member journals beginning July, 2005. Catherine De Angelis, Jeffrey Drazen, Frank Frizelle, et al., ''Clinical Trial Registration: A Statement from the International Committee of Medical Journal Editors,'' *New England Journal of Medicine* 351 (2004): 1250–1251.

[68] AstraZeneca Bioethics Policy, cited in n. 48, above.

[69] Alex Berenson, ''Despite Vow, Drug Makers Still Withhold Data,'' *New York Times*, May 31, 2005, at A1.

[70] For example, the U.S. Congress is considering whether to require companies to participate in a federal clinical trials registry. See Rebecca Dresser, ''A New Era in Drug Regulation?'' *Hastings Center Report* 35, no. 3 (2005): 10–11.

[71] Joseph de Maistre, ''Letter to X,'' in *Bartlett's Familiar Quotations* 16th ed., ed. J. Kaplan (Boston: Little, Brown, 1992), p. 353.

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