When a great profession and the forces of capitalism interact, drama is likely to result. This has certainly been the case where the profession of medicine and the pharmaceutical industry are concerned. On display in the relationship between doctors and drug companies are the grandeur and weaknesses of the medical profession — its noble aspirations and its continuing inability to fulfill them. Also on display are the power, social contributions, and occasional venality of a very profitable industry whose products contribute in important ways to the health and longevity of the American people but that at times employs methods that are deeply troubling and even criminal. Government also plays a part as it tries with limited success to help the profession stay true to its own tenets and to deter the industry’s most egregious excesses. The spectacle is profoundly human and, like most such spectacles, seems never to end or to lose its fascination.

The interaction of doctors and pharmaceutical companies is also extremely consequential for patients, doctors, and the larger society. The drug industry manufactures, distributes, and publicizes powerful chemical and biologic agents that have proven benefits and that physicians sometimes fail to use as often as they should, or in sufficient doses. In this sense, industry’s efforts to encourage the use of some agents by physicians can be seen as contributing to the public health. At the same time, the marketing by the drug industry of its products to physicians is manifestly aimed also at improving industry profits; in the process, such marketing may contribute to less savory social consequences, including increasing drug costs and the misuse or overuse of medications in ways that may adversely affect patients.

Several recent developments have focused renewed attention on the relationship between drug companies and doctors. One is the surge in spending on prescription drugs, which totaled $162.4 billion in 2002 after years of double-digit percentage increases. A second is the publicity surrounding a number of prominent legal cases in which drug manufacturers have been convicted of crimes related to their marketing of drugs to physicians or have made huge payments in the settlement of civil suits for similar noncriminal violations. A third is an increasing recognition by both pharmaceutical companies and physicians that, in certain respects, the relationships between drug companies and doctors have become embarrassing to both parties and need to change.

This report reviews the salient aspects of the relationships between physicians and drug companies at the turn of the 21st century. I examine the nature and extent of drug-company interactions with physicians and review what is known about the consequences of those interactions for physicians’ clinical decisions, as well as the cost and quality of the care they provide. I then briefly note some recent attempts by private organizations and government agencies to manage or regulate the interactions between physicians and drug companies in an effort to prevent perceived abuses, and I conclude with a discussion of how the relationships are likely to evolve in the future.

Interactions between drug companies and doctors are pervasive. Relationships begin in medical school, continue during residency training, and persist throughout physicians’ careers. The pervasiveness of these interactions results in part from a huge investment by the pharmaceutical industry in marketing. In 2002, the industry expended 33 percent of its revenues on “selling and administration.” In 2001, one company, Novartis, reported spending 36 percent of its revenues on marketing alone. The marketing expenditures of the drug industry have been estimated variously at $12 billion to $15 billion yearly, or $8,000 to $15,000 per physician. In 2001, the industry’s sales force of drug detailers, whose job is to meet individually with physi-
cians and promote company products, numbered nearly 90,000 in the United States\textsuperscript{3,8} — 1 salesperson for every 4.7 office-based physicians.\textsuperscript{8}

Moynihan\textsuperscript{14} catalogued 16 different ways in which drug companies relate directly or indirectly with doctors. These range from the seemingly trivial (e.g., the ubiquitous dispensing of gifts such as pens and pads with drug names inscribed) to the much more troubling (e.g., the ghostwriting of articles for academic physicians, the payment of large honoraria and consulting fees to prominent physicians who extol the virtues of company products, and the support of lavish trips and entertainment for physicians who commonly prescribe company products).

Surveys of residents indicate that they receive an average of six gifts from pharmaceutical companies annually.\textsuperscript{15} In a survey of 106 directors of emergency-department programs in 2002, 41 percent responded that their programs allowed residents to be taught by representatives of drug companies, 35 percent reported that residents received free industry samples at work, and 29 percent said that residents’ travel to meetings was sometimes dependent on the availability of company support.\textsuperscript{16} According to another report, residents in a psychiatry program in Toronto attended up to 70 lunches that had been sponsored by drug companies and received 75 promotional items over the course of one year.\textsuperscript{17}

As physicians mature, their relationships with drug companies also change, becoming more likely to involve consulting and honoraria and less likely to involve luncheon seminars. A 2001 survey of a random sample of U.S. physicians by the Henry J. Kaiser Family Foundation found that 92 percent of physicians received free drug samples from companies; 61 percent received meals, tickets to entertainment events, or free travel; 13 percent received “financial or other in-kind benefits”; and 12 percent received financial incentives to participate in clinical trials.\textsuperscript{18} A 1997 study by Ferguson and colleagues found that 83 percent of internists with the Department of Medicine at the University of Maryland had met with drug-company representatives in the previous year.\textsuperscript{19} Wazana reports that, on average, practicing physicians meet with drug-company representatives four times a month.\textsuperscript{15}

One of the most common ways in which the pharmaceutical industry now interacts with practicing physicians is through continuing medical education. As of 2003, according to Dr. Murray Kopelow, president of the Accreditation Council for Continuing Medical Education, pharmaceutical companies were providing about $900 million of the $1 billion spent annually on continuing medical education in the United States.\textsuperscript{20} In fact, new, for-profit companies have arisen, called medical education and communication companies, whose purpose is to provide educational offerings to physicians. These organizations are sometimes subsidiaries of public-relations firms that also conduct advertising for the pharmaceutical industry.\textsuperscript{2,21}

Drug companies do not relate to physicians only as individuals. The pharmaceutical industry also maintains relationships with the organizations to which physicians belong and for which they work.\textsuperscript{10} Drug companies are frequent financial sponsors of the annual meetings of physician organizations, and they also support special projects by those organizations.\textsuperscript{2} For example, the American Medical Association has received industry funding, including support to publicize its own guidelines for how physicians should relate to the drug industry.\textsuperscript{22} As many as 59 percent of the authors of clinical guidelines endorsed by many professional associations have had financial relationships with companies whose drugs might be affected by those guidelines.\textsuperscript{23}

Drug companies also have attempted to influence the pharmaceutical agents that are available for use by physicians who work with and for certain organizations. Some of these practices are widely accepted in the business world both inside and outside of medicine. For example, pharmaceutical companies offer discounts to managed-care organizations and their agents — pharmaceutical-benefit managers — in return for favorable treatment of their products in the formularies used by these organizations. Some pharmaceutical companies, however, have engaged in ethically, and perhaps legally, questionable efforts to affect the drugs that health care organizations allow or encourage their physicians to use. Studdert et al. review several instances of this behavior in another article in this issue of the Journal.\textsuperscript{24}

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**Consequences of the Relationships**

The relationships between drug companies and doctors would be of little interest if they did not have potential consequences for patients, doctors, and the larger society. Explicitly or implicitly, much
of the debate about these relationships revolves around the question of whether drug companies influence physicians’ behavior and, if they do, whether the results are, on balance, positive or negative for the quality and cost of health care and for the profession of medicine itself.

Most physicians are quite tolerant of, and even have a positive attitude toward, their interactions with drug companies.15 Many physicians believe that their interactions with drug companies have educational value for themselves and also provide benefits for patients, both because physicians are kept informed about available therapeutic agents and because the free samples they are given can be distributed to patients.25,26 Physicians also tend to be confident that they themselves are invulnerable to any bias inherent in the educational content offered or supported by drug companies. A study of residents found that 61 percent believed that they were not influenced by the marketing efforts of pharmaceutical companies (although only 16 percent were equally confident about their colleagues).25 Brett and colleagues found in a small survey of residents and faculty members at a U.S. medical school that a majority of respondents tended to view a wide variety of interactions between drug companies and doctors as ethically acceptable.26 Examples included the receipt of pencils, pads, and expensive textbooks (valued at $500 apiece), company-funded dinners at which the company’s products were favorably mentioned, free drug samples for physicians’ offices, free lunches for residents, and the presence of drug representatives during clinic hours and during company-supported “happy hours.” Respondents were more likely to view interactions as problematic when the value of the gift or entertainment increased, when it involved recreational as opposed to professional activities, and when information provided to physicians during the interaction was biased or self-serving.26

Despite the confidence of physicians in their ability to resist efforts by drug companies to affect their behavior — especially in ways that may serve company purposes rather than their own or those of their patients — a substantial body of theoretical and empirical literature (as well as physicians’ own concern about their colleagues) suggests that many physicians may be mistaken. Some of this literature focuses on what might be called the gift relationship — that is, the manner in which gifts influence human behavior and the role they play in human relationships. According to Katz et al., “When a gift or gesture of any size is bestowed, it imposes on the recipient a sense of indebtedness. The obligation to directly reciprocate, whether or not the recipient is conscious of it, tends to influence behavior. . . . Feelings of obligation are not related to the size of the initial gift or favor.”13

The idea that small gifts may be as influential as large gifts seems counterintuitive but is supported by substantial research in social science.13,27 Among the most important influences on behavior are the simplest and most fundamental: food, friendship, and flattery. Indeed, these have constituted the basis of human relationships since the beginning of time.13 Also supported by research is the observation that humans are vulnerable to a powerful, unconscious “self-serving bias”; that is, they have trouble seeing themselves as biased when the bias serves their needs or advances their own perceived interests.27

The social-science literature, therefore, suggests that it would be surprising if doctors were not influenced by the small and large services and tokens of appreciation and interest provided by pharmaceutical companies. Furthermore, if many physicians find the blandishments of drug companies gratifying and rewarding, then physicians in general would be systematically handicapped in detecting any bias in decision making caused by these interactions. To posit otherwise would imply that physicians are different in fundamental ways from their fellow human beings.

A reasonable response might be that the professional training of physicians does differentiate them from others, rendering them resistant or immune to influences that might affect other Homo sapiens and enabling them to appraise their patients’ interests objectively and put those interests before all other considerations. However, the evidence suggests that physicians are unable to transcend their humanity in their daily practices.

In a very thorough review of the literature on the effects of interactions with drug companies on physician behavior, Wazana15 identified 16 relevant studies. These studies found that a wide variety of interactions — meetings with company representatives; the receipt of gifts, free drug samples, and free meals; company support for travel to and lodging at educational events; attendance at lectures by representatives of pharmaceutical companies; acceptance of honoraria; and other relationships — were associated with changes in physicians’ use of
medications. Involved physicians were more likely to request the inclusion of the company’s drugs on hospital or health maintenance organization formularies, more likely to prescribe the company’s products, and less likely to prescribe generic medications. The resulting changes in the use of medication were often costly and “nonrational” in that the newly prescribed or requested drugs had no therapeutic advantage over the alternatives. Interestingly, several studies have found that the larger the number of gifts that physicians received, the more likely they were to believe that gifts did not affect their prescribing behavior.\textsuperscript{15,28} Wazana found no studies that directly measured the effects of relationships between physicians and drug companies on patients’ outcomes or on the aggregate costs of health care.\textsuperscript{15}

Interactions between physicians and drug companies may also affect another important consideration: the credibility of the medical profession in the eyes of patients and the public. In rewriting its own guidelines on physician–industry relationships, the American College of Physicians noted, “A perception that a physician is dispensing medical advice on the basis of a commercial influence is likely to undermine a patient’s trust not only in the physician’s competence but also in the physician’s pledge to put patients’ welfare ahead of self-interest.”\textsuperscript{10} Obviously, such perceptions among patients, if widespread, could erode the public’s collective trust in the profession. The limited research on the attitude of patients toward the receipt by physicians of gifts and other considerations from the pharmaceutical industry suggests that patients are more likely than doctors to believe that gifts may influence prescribing behavior and that patients tend to view gifts that influence prescribing behavior as inappropriate.\textsuperscript{29}

### Efforts to Manage Relationships

What is clear is that physicians’ organizations, drug companies, and the government have become uncomfortable in recent years with the nature, extent, and potential consequences of interactions between physicians and pharmaceutical companies. This discomfort reflects a growing consensus that some drug companies have been offering, and some physicians accepting, financial and other benefits that are ethically and even legally inappropriate.\textsuperscript{4-6,30,31} In response, professional, industry, and government groups have attempted to clarify standards that differentiate appropriate from inappropriate relationships and thereby to reduce the frequency of suspect interactions.\textsuperscript{32} The content of several of these new sets of guidelines and regulations is summarized by Studdert and colleagues.\textsuperscript{24}

Taken together, this series of private and public pronouncements seems to embrace the view that relationships between some drug companies and physicians are ethically appropriate, often beneficial, and certainly unavoidable and that the challenge for the medical profession, drug companies, and the government is to contain those relationships within acceptable boundaries and to avoid certain egregious and possibly illegal practices. As such, new and existing policies seem to be generally consistent with the views of most physicians, who have indicated in studies cited here that they view as appropriate the provision by drug companies of modest gifts, free drug samples, support for educational programs (including associated modest meals), and a number of other services for doctors. Physicians are less likely, however, to view as acceptable the receipt of gifts and services that are either very valuable (though there is no consensus on the dollar amount) or unrelated to a professional purpose (e.g., a golf bag or tickets to a sporting event).

A number of critics find the efforts to preserve and manage relationships between drug companies and physicians to be ill conceived and impractical. Two former editors of the \textit{Journal}, Arnold Relman and Marcia Angell, find the American Medical Association guidelines to be “general and vague.”\textsuperscript{32} Joseph Gerstein, an internist from Massachusetts and a former managed-care executive who first notified federal officials about illegal activities at TAP Pharmaceutical Products,\textsuperscript{24} believes that it will be difficult for physicians to avoid biases introduced by even modest marketing activities by drug companies. “Maybe there are some physicians who are so morally stout . . . that they can be sure they weren’t affected,” commented Gerstein in an interview. “I would like to meet that person.” He noted further that the Office of the Inspector General (OIG) of the Department of Health and Human Services “has put out some pretty firm guidelines, but there are an awful lot of people working to get around them.”

Sidney Wolfe, director of Public Citizen’s Health Research Group and a perennial critic of the drug industry, is skeptical that current guidelines will
have any meaningful effect on behavior. “The problem,” said Wolfe in an interview, “is that there is no detection mechanism and no enforcement mechanism.” The only practical approach to dealing with interactions between drug companies and physicians, in the view of many critics, is for physicians not to accept anything of financial value, no matter how trivial, from drug companies. The only professional group to support this viewpoint is the American Medical Student Association, which has called on physicians to sever their relationships with the pharmaceutical industry.33

FUTURE DEVELOPMENTS

It is far too early to assess the ways in which recent efforts to manage physician–industry interactions have influenced the nature, extent, or effects of those relationships. Anecdotal reports attest both to a reduction in some perceived excesses, such as lavish entertaining of physicians at expensive resorts, and to their persistence in the face of new guidelines.34,35 M. Therese Crouse, director of compliance, health care, and marketing at Eli Lilly, asserts that OIG guidance in particular “absolutely affected the way we are doing business. . . . Entertainment is significantly cut down. . . . [There is] no more golf; no more movie nights.” Having just revisited or revised their policies, professional, government, and pharmaceutical groups and agencies seem likely to await the verdict of time before attempting additional interventions.

The one exception may be state governments, which have become much more active on a number of health policy fronts in recent years, including lawsuits against tobacco companies, the regulation of managed care, and, most recently, the scrutiny of behavior by drug companies. As of March 1 of this year, four states — Maine, Vermont, Nevada, and New Mexico — had begun requiring companies to report how much they were spending on the marketing of their products to physicians working in their states.34 Vermont, which requires the disclosure of any marketing expenditures in excess of $25, reported in February of this year that 44 pharmaceutical companies spent $2.47 million in “fees, travel expenses and other direct payments to Vermont physicians, hospitals, universities and others for the purpose of marketing their products” in the year ending June 30, 2003.36

Whether these and other external controls on the interactions between physicians and drug companies will fundamentally change those interactions over the long run, however, remains far from certain. Doctors and leaders of drug companies are mature, consenting parties in relationships that both are highly motivated to maintain — for drug companies because the relationships are vital to selling their products, and for physicians because they value, wisely or not, the information, gifts, and services that companies provide in the course of their marketing activities. From a social standpoint, it is difficult to argue that the relationships are totally without redeeming value, since some of them seek to increase the dispensing of drugs and biologic agents that physicians currently underprescribe, with major adverse consequences for public health. Professional and company attitudes, together with the rationale that marketing by drug companies could in some ways enhance public health, will make it politically impractical for governments to adopt the kind of draconian ban on relationships between doctors and drug companies that their strongest critics favor. And as long as such relationships are legal, the parties involved will face constant temptations to test the limits of professional and industry codes and government regulations. One can predict, therefore, that there will be ongoing cycles of scandal and reform for the foreseeable future.

In many ways, the ultimate arbiter of the nature, extent, and consequences of interactions between drug companies and physicians is the medical profession itself.21 As a for-profit business, the pharmaceutical industry should be expected to market its products aggressively within legal boundaries. It is then up to physicians to decide whether to accept the proffered information and enticements. It is unlikely that professional organizations, as representative bodies, will move far out ahead of their members in making policy on these issues. As its president, Murray Kopelow, notes, the Accreditation Council for Continuing Medical Education “must reflect the values of the profession.” So too, in the end, must the interactions between drug companies and physicians.

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References (For full references, see the original article.)