The Physician's Relationship with the Pharmaceutical Industry: *Caveat Emptor*...Buyer Beware!

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ABSTRACT: Historically physicians have had close relationships with the pharmaceutical or other medically related industry. This has come under close scrutiny by the public, with articles appearing in medical journals and the lay press. The reality is that physicians depend on industry to bring products to market as well as to assist in research and education, leaving physicians questioning what their relationship with industry should be. This review deals with this complex relationship, identifying ways that industry might affect decision making in the clinical context. We will highlight areas of potential concern in this relationship, identify attendant moral dilemmas, and provide some recommendations. Our intention in raising the consciousness of physicians and medical institutions to these potential areas of concern is to aid physicians in their efforts to provide the best medical care for patients and to practice with integrity.

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The era of burgeoning medical development has thrown the medical profession, often unaware, into areas of interaction with the pharmaceutical or other medically related industry (referred to here as Industry). These interactions raise numerous moral dilemmas that must be fully appreciated in order to best approach them with integrity. Although these relationships have many dimensions, this review will focus on the relationship between physicians and Industry in the major areas of interaction, clinical practice, research, and education; discuss ethical considerations involved in those relationships; and provide recommendations.

THE INTERACTIONS

The relationship between Industry, the physician, the patient and governing bodies – namely, hospitals, academic institutions and professional organizations – is complex. However, prior to considering these relationships it is important to clarify the duty of physicians, the duty of governing bodies, and the duty of Industry. The primary duty of physicians and hospitals is to care for their patients. For the physician this includes direct care of individual patients based on best clinical judgment, informed by the available medical literature. The problem is that a significant number of interventions in medicine are not evidence-based and, therefore, are subject to individual interpretation [1]. If doctors do not provide the best care for their patients, patients will lose trust in doctors. Doctors also work to improve knowledge of disease states, investigate new treatment modalities, and educate patients and others in the health care system. The duty of academic institutions is to seek the truth, and if they do not do so they will lose their credibility. The duty of professional organizations is to provide regulation of its members, and if this is not accomplished the risk is that government will intervene. The duty of Industry is to bring products to market and thereby to make money for their shareholders; if they do not do so, they will go out of business [2,3]. Industry has a large financial stake in health care and, in a free-market economy, a legitimate interest in promoting its products.

However, it is important to realize that physicians also derive direct benefit from Industry. What should the relationship be between physicians and Industry? One of the more visible daily interactions of doctors and Industry involves pharmaceutical company representatives (drug reps). Carl Elliott describes this relationship as "a delicate ritual of pretense and self-deception" [4]. He states that drug reps pretend they give impartial information, while doctors pretend they take it seriously. Drug reps try to influence doctors, while doctors tell themselves that they are not being influenced. For this encounter, drug reps act as if they are not salespeople, while doctors act as if they are not customers. Despite this practice of pretense, the priority of Industry is 'to sell the product'. This means that marketing the product is extremely important, as it is with all products. This is of particular concern for doctors who rely on drug reps as a primary source of information. The more a drug is promoted the more it will be prescribed [5]. The purpose of marketing is to inform doctors and patients of new treatments, train doctors in the use of the products, and identify the potential complications or hazards related to the products. There is also a motivational

component to marketing: to encourage potential customers. This interaction of potentially competing interests is associated with potential pitfalls.

POTENTIAL PITFALLS FOR THE CLINICIAN

Most doctors have some type of relationship with Industry, with a significant number receiving food or financial support from it, as shown in the study by Campbell et al. [6]. When we receive a gift the usual reaction is to be grateful, and this creates a sense of obligation to the giver of the gift. Industry is aware that providing free food makes any message more palatable, and more likely to be favorably received [1]. Wall and Brown comment that "… free lunch, pens, notepads, and coffee mugs are highly effective means by which to influence physician judgment and increase pharmaceutical sales" [5]. Doctors in general are not too concerned about the impact of free food; they do not feel that their relationships with Industry in any way compromise their integrity as doctors [7]. However, Steinman and co-authors [8] observed that although 61% of internal medicine residents did not think that their own prescribing practices were being influenced by Industry promotions and contacts, only 16% thought that it did not affect other physicians' prescribing practices. We tend to see others as more easily influenced and more susceptible to bias than we see ourselves [9], though this has been shown not to be the case [10].

Doctors should disclose the nature of any relationships they have with Industry, particularly financial relationships, which may influence or may be perceived to influence decisions about Industry products

As to the magnitude of the Industry, in 2003 estimates of the average cost for developing a new drug was US$802 million [11], and one can only expect costs to increase over time. However, the great majority of drugs are not original, but similar or identical to available drugs – the "me-too" drugs. Even these drugs are expensive to bring to market, costing more than $100 million [2]. Therefore, it is essential for Industry to charge the highest possible price, and to persuade doctors, pharmacists, and the public that an equivalent drug is actually better than the one on the market. The need for and prototype of this form of marketing is seen in other large corporations, such as automobile or beer companies. With regard to marketing, according to 2007 data from the United States Department of Health and Human Services and the Bureau of Labor Statistics there are 90,000 pharmaceutical sales representatives in the United States selling their product to 567,000 physicians, and Industry spends $12 billion per year on physician marketing [5]. According to Gagnon and Lexchin [12], in 2004 in the U.S., whereas 13.4% of sales dollars went to research and development, nearly twice as much (24.4%) was spent on promotion. The difficulty, therefore, relates to the influence, or the perceived influence, of this marketing on doctors. This may result in the physician compromising his or her integrity due to a conflict of interest. Conflicts of interest arise when an individual has two conflicting roles that should not be performed at the same time, such as involvement in the selection of medications for the hospital formulary or the infant formula contract for the hospital, while receiving money for research from one of the contending companies. Although the physician involved is an expert as evidenced by the fact that she is a prominent researcher in this area, having a financial arrangement with one company may very well influence this physician. Some conflicts of interest in medicine are more substantial, where a physician directly profits from sales, than others, such as being an Industry employee, stockholder, member of a board of directors, a regular consultant, or owning a patent. However, there are other situations where there may also be a conflict of interest, such as being an occasional Industry consultant or speaker, receiving an honorarium, or receiving financial support for research from Industry [13]. How common is a conflict of interest? Sheldon Krimsky [14] evaluated 789 articles appearing in leading research and medical journals from universities in Massachusetts; he found that in one out of three articles at least one author had a conflict of interest, and the prevalence would have been even higher if consultancies and honoraria were considered.

Is the monetary value of the "gift" connected to the perception of conflict of interest? Is it acceptable, for example, to take a free pen provided at a medical conference if you do not listen to the drug pitch, do not make eye contact, and are not in relationship with or in any other way influenced by the drug rep? How about a "gift" from a drug company not related to one's own scope of practice, such as a pathologist using a pen with the logo from a company that manufactures infant formula? If a drug company does not attempt to influence your work, is there anything wrong with taking their "gift"? Is this in any way different from the acquisition of a pen that has a logo from a hotel or conference center? A physician who appears with an array of Industry pens and other paraphernalia in his white coat or spends time with drug reps may cause his patients to question how Industry is influencing the physician in other prescribing practices, and this may engender distrust. The importance of transparency for patients, and of not advertising for Industry was recently confirmed by Tattersall and colleagues [15] and by Edwards and Ballantyne [16].

Medical school and residency training programs should provide education about relationships with Industry and how to interact with drug reps

A question we must ask ourselves is why a drug company wishes to 'give' us something in the first place. Industry has an

obligation to provide the public with safe and effective medications, and to make money for their stockholders. In Industry drug reps must demonstrate that expenditure will provide some advantage to the company and result in improved sales, or the company will not spend the money. Industry actively pursues physicians in positions of authority, or who are influential within their own clinics or communities, to provide expert opinion that will promote their product [17].

POTENTIAL PITFALLS FOR THE RESEARCHER

Michael Wilkes [18] noted that physicians who receive financial support from Industry generally do not inform patients, whom they enroll in research studies, of this conflict of interest. Furthermore, Industry-sponsored studies are more likely to have favorable outcomes and are more likely to be supportive of a therapy than independently funded research [19,20]. In a landmark study on the association between author attitudes to calcium-channel antagonists and their financial relationships with drug companies, Stelfox et al. [21] found statistically significant differences between authors who had financial relationships with the drug companies and those who did not. Most authors supportive of the drug were more likely to have financial relationships with the drug companies involved in the studies, as compared to authors who were neutral or critical of the drug. All supportive authors had financial interactions with at least one drug company, which was statistically more when compared with neutral or critical authors [21].

In addition, a study demonstrating a positive effect is easier to publish than a study demonstrating no effect or even a negative effect [22]. This concept – publication bias – was first identified by Francis Bacon, who wrote: "...the human intellect…is more moved and excited by affirmatives than negatives" [2]. Liss [20] and Halkin [23] found that Industry promotes positive and suppresses negative results. This is evidenced by restrictions on publication and data sharing [24], as well as by selective reporting of results [25]. This partial disclosure of truth, if only positive results are published, compromises the honesty of researchers who are all too aware of the publication bias of editors.

There are examples in the public domain of clinician-researchers who have published concerns related to their findings despite threats from the drug companies who supported the research and legally "owned" the data [22,26]. For a researcher the orientation is to do what is best for her patients, to seek the truth through research, to prevent harm and to educate others, specifically through publication. For the drug company the orientation is to market drugs that will make money for the company shareholders, to recoup drug development costs, and certainly to prevent litigation with its attendant costs [2]. In response to recent ethical and legal fiascos in Canada and the United States, serious pitfalls have been identified in the relationship between researchers and Industry, resulting in the establishment by academic institutions of ethically justifiable regulations related to contracts [22]. However, it is not a simple black and white picture of Industry (portrayed as the "bad guys") pressuring doctors (the "helpless victims") under the vigilance of scientific and medical journals (the "good guys").

POTENTIAL PITFALLS FOR THE EDUCATOR

In the area of continuing education, in 2004 American pharmaceutical companies provided $1.1 billion for continuing medical education. To maintain licensure, doctors in North America must attend these courses [27]. The question is who should sponsor these activities? Given the costs entailed and the historical involvement of Industry, who can and who will pay if Industry does not? Moreover, Industry conducts research on how best to sell products. Carl Elliott found that physicians attending lectures by another physician wrote nearly four times more prescriptions compared with prescription practices following lectures given by drug reps. Even after taking into consideration the presenting physician's fees, this still resulted in a doubling of the profit margin [4].

Since academic institutions and government do not appear to be funding more research or providing more support for continuing medical education, our relationship with Industry will continue and we cannot just call Industry the "bad guys." We also must be cognizant of the potential tarnish of the medical journals, also not clearly the "good guys." Editors of medical journals claim that they cannot find experts who do not have a conflict of interest as "…most of the top medical authorities in [the U.S.], and virtually all of the top speakers on medical topics, are employed in some capacity by one or more of the country's pharmaceutical companies" [28].

Hospitals, academic institutions and professional organizations should develop guidelines on interactions with Industry, including gifts of any value, free samples, advertising, and sponsorship of educational events

A major concern identified in journals is that of ghostwriting, pertaining to journal articles authored by a medical writer who is employed directly or indirectly by Industry. There are medical education and communications companies that contract with Industry to ensure that the company's medical publications support its "marketing plan" [29]. They commission academics to "author" journal articles in collaboration with medical writers (*ghostwriters*), and the contributions of ghostwriters and Industry are hidden [30]. One might anticipate that an article written by a professional medical writer would have a higher likelihood of acceptance by a reputable journal. Not surprisingly, according to the former editor of the *British Medical Journal*, "[t]he quality of the journal will bless the quality of the drug" [29]. However, a potential pitfall is that adverse

side effects may not be described, such as suicide attempts in children taking Zoloft®, a selective serotonin reuptake inhibitor (Pfizer Inc. USA) [29,30]. Therefore, for a myriad of reasons the facile injunction "Just say *no* to drug reps" is not enough. For the "no-see physician," the doctor who will not see drug reps, the potential pitfall is in being "naïve" to the fact that Industry has other tactics to engage "no-see" doctors [31].

ETHICAL CONSIDERATIONS

Edmund Pellegrino speaks of the importance of the moral character of the physician in instructing their conscience, which results in the provision of the best care for patients [32]. The virtues include honesty, fidelity, courage, justice, prudence, wisdom, and compassion [33]. These virtues relate to professionalism, which can be seriously eroded if we do not mindfully enter into relationships with Industry [Table 1].

The context of this interaction is important in determining the ethical dilemmas encountered and in identifying the system problems that provide fertile ground for ethical misconduct. In narrative ethics the details of the situation, through which we identify the values and motives of the individuals involved, are important. Physicians are human, and the demands on physicians are increasing while respect for physicians appears to be waning. Physicians generally have very busy practices with a multitude of urgent demands every day. When the drug rep comes into your office and asks how you are (possibly the first person to say something nice to you all day) and wants to give you something, whether it is easily digested information or a pen or a pad of paper, you react kindly. However, Industry utilizes the skills of professionals to teach drug reps how to get the physician's attention, how to get their message across effectively in 5 or 10 minutes, and how many times to repeat the message in whatever time frame is available.

When money is given or a favor promised in order to influence judgment or conduct of a person in a position of trust, this is a bribe [34]. There is a philosophical concept of "clean hands" which addresses how far away from a conflict, or in this case a conflict of interest, one must be seen to be "clean." Those in positions of public trust, such as policemen, judges or doctors, cannot have a financial interest in violating or potentially violating their professional duties. They must be financially disinterested and must also be seen to be financially disinterested, or they may compromise the trust placed in them and in their professions [35]. Journals and educational venues address this by ensuring a declaration of a conflict of interest. However, this does not resolve the ethical dilemma, and the perception of a conflict of interest can endure. Furthermore, we suggest that an acknowledgment of a conflict of interest at the beginning of a presentation, which addresses the requirements of the regulatory bodies, does not influence the impact of the take-home message, particularly when it is presented by a prominent researcher or influential physician.

Some doctors claim that they are immune to marketing and therefore can engage in whichever activity they wish as they are not in a conflict of interest position [36], but it is clear that marketing *does* affect physician practice [37]. However, we need Industry, which brings products to market, and this is essential [11]. It is unlikely in the foreseeable future that government or non-profit organizations will provide adequate funding for ongoing research and education. Therefore, there is, and will continue to be, an ongoing relationship of doctors with Industry.

Table 1. Ethical dilemmas that may influence the integrity of the physician

Considerations	Benefits	Potential risks/harms
Relationships with drug reps	• Provide information	• Conflict of interest • Erode patient trust • Jeopardize integrity of physicians • Misleading information that might harm patients
Research & development of new technologies	• Bring drugs to market • Research funding	• Industry control data • Publication bias • Increase costs for patients
Continuing medical education	• Educational opportunities • Support of academic meetings	• Adversely influence doctors • Lack of disclosure • Belief that disclosure is merely a formality
Ghostwriters	• Research is published	• Lack of disclosure • Lack of transparency

RECOMMENDATIONS

We support the following recommendations in providing the best care for our patients and promoting the maintenance of professional integrity:

- Committees deciding about Industry products should be "clean" (i.e., derive recommendations from unbiased sources) [31]. Therefore, doctors who receive funding from Industry should recuse themselves from decision making about those Industry products
- Industry may provide Unrestricted Educational and Research Grants, but there should be transparency in the allocation of these funds
- The presence of drug reps should be restricted in clinical areas where there are patients
- Doctors should disclose any conflicts of interest, particularly financial interests: at presentations, at meetings about Industry products, to patients when prescribing medications that fall into this category, and when enrolling patients in research
- Training programs should develop teaching sessions to identify:
  - the relationship between doctors and Industry [38,39]
  - critical appraisal and discussion of Industry studies and advertising materials
  - tools to interact with drug reps

- ▹ ethical considerations in relationship with Industry, to maintain the integrity of the doctor
- Hospitals, academic institutions or professional organizations should have guidelines addressing educational programs, advertising (including gifting and free sample distribution), and research [40].

In our relationship with Industry there will be times when we may wonder how best to utilize the potential benefits while minimizing the risks. As in other types of interaction with any business one must approach carefully, with the warning *caveat emptor*, let the buyer beware. The relationship between doctors and Industry is not a privileged relationship but rather a business relationship necessary for the provision of the best care possible for our patients, with whom we *do* have a privileged relationship. Our recommendations will not solve all of the moral dilemmas related to our interactions with Industry, but if we can continue to critically appraise the products being sold and question our relationship with Industry, we will go a long way in upholding our personal and professional integrity.

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