Learning how not to do the pharmaceutical industry tango: Raising student awareness of ethical conflicts of interest

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In order to respond in a thoughtful manner to an ethically challenging situation, one must first perceive that the situation has a troubling dimension. This point seems almost too obvious to be worth making. Unfortunately, however, in the real world of doctors, pharmacists and pharmaceutical company representatives, many ethically fraught situations go largely unrecognised as such, or have become accepted as normal. This problem - failure to recognise even the existence of an ethical red flag – arises for medical and pharmacy trainees long before they become qualified practitioners.

The purpose of this chapter is to raise a warning flag around the issue of pharmaceutical industry gifts to students and health professionals. Empirical data are provided which illuminate the function of the gift relationship between giver and recipient. Two related issues are also discussed: (a) the payment of fees to health professional 'opinion leaders' whose positive assessment of a product can help to stimulate prescribing and sales, and (b) the underlying question of conflict of interest between a professional's obligation to his or her patients and relations with pharmaceutical companies.

Aims of this chapter

By the end of the session based on this chapter you should be able to:

- Identify key ethical challenges in the relationship between health professionals and the pharmaceutical industry;
- Define a conflict of interest situation and describe why such situations are especially troubling in medical practice.

The impact of gifts – large and small

Bellin and her colleagues (2004) found that medical students have extensive exposures to pharmaceutical industry marketing during their training and that these exposures increase dramatically when the students progress from the preclinical to the clinical setting. Approximately 72% of students in their clinical years recalled over 20 exposures compared to 33% of preclinical students.

What is meant by the term 'exposures'? Mostly, we are talking about sponsored events, gifts, free meals and samples of medicines. In short, most medical (and some pharmacy) students benefit in a number of ways from industry generosity. Pizza, and the beer that helps to wash down the pizza at medical school or pharmacy parties, are often supplied by kindly pharmaceutical sales representatives. Gifts of expensive textbooks and pocket texts are not uncommon (Bellin et al.,

2004). Overall, gifts to US health sciences students ranged in value from a nominal value, for example, for monogrammed pens, to a value of up to US$800 for travel subsidies, with a median estimated value of US$20 (Hodges, 1995). However, frequently even small gifts are highly prized by the students.

A recent report (Sierles et al., 2005) showed that US medical students receive a gift or attend a company-sponsored activity surprisingly often: on average once a week. When asked whether such gifts would influence their prescribing patterns, approximately 70% replied "no". In a similar vein, Hodges (1995), found, paradoxically, that the more gifts that students, interns and residents in Toronto psychiatric hospitals accepted, the less they felt that their judgement would be influenced. (For more on the use of gifts in pharmaceutical promotion, see Chapter 2.)

Existing evidence strongly indicates that exposure to pharmaceutical industry marketing has a significant influence on physicians' practice and prescribing patterns (Lexchin, 1993). Bluntly put, gifts *do* influence behaviours, despite the widespread belief by health care trainees and professionals that they are personally invulnerable to such blandishments (Madhaven et al., 1997; Banks et al., 1992).

Although there is a degree of variability because some countries and some institutions restrict the gifts that companies may offer, the practice of providing gifts to health professionals in widespread. Most important to keep in mind is that the shower of coffee mugs and free lunches, pen lights, knapsacks, stethoscopes and pocket textbooks teaches young doctors and pharmacists that accepting gifts from the pharmaceutical industry is a normal part of professional life. Medical or pharmacy school is where gift-giving begins, but scarcely where it ends. The 'gift economy', whether in the setting of the hospital or the doctor's office, on the golf course or in a restaurant, wins the sales representative 'face time' with health professionals and establishes a bond between the representative and the professional.

Doctors often cite free samples as the main reason they see sales representatives. This is a special type of gift as it allows the physicians in turn to give to their patients. As is discussed in Chapter 4, free samples are a form of market seeding, generally for new, expensive medicines that are usually no better than less costly older treatments. Thus, free samples lead inexorably to higher costs for patients and insurers in the long term.

The culture of gift-giving by the companies and gift-taking by physicians and pharmacists, hospitals and universities is viewed by most health-care professionals as benign and perfectly legitimate. As one noted physician and journal editor has aptly commented: "*I don't criticise the marketers for behaving like marketers. What they do is make people feel entitled - so it's not a bribe; it's their due. And you end up with a situation where doctors won't walk fifty yards at a big medical meeting without being transported in a drug company bus.*" (Rennie, 2003).

The not-so-free lunch

Health sciences students are often asked or required by their teachers or clinical preceptors to attend sponsored lunches or rounds. Pharmaceutical companies spend vast sums of money on gifts for practising physicians, but they also spend millions more sponsoring and providing free meals for 'educational events' aimed at trainee physicians and pharmacists (Bellin et al., 2004).

Working lunches on the ward and quite often lavish restaurant dinners, are regularly paid for by the sales representative. Senior physicians with a national or international reputation benefit financially in even more substantial ways: for example, first class winter travel to the Caribbean or to some luxurious ski resort (Angell, 2004). Consultancy and speaking fees, together with paid positions on advisory boards, often add significantly to the doctor's income (IMS Health, 2005). Industry codes vary from country to country and what is prohibited in one may be permitted in another. In practice, when industry codes prohibit certain kinds of gifts, for example, expensive meals, the prohibition is undermined by such expedients as 'unrestricted grants' from the companies to medical education providers, who then use the money to sponsor lavish meals (Angell, 2004).

The free food has two main functions at these 'educational' events: to attract an audience, of course, but also to create an atmosphere of goodwill, which the sponsoring company expects will extend to the sponsor and the promoted medicine – if only subconsciously.

"I can't be bought for"…

In justifying (or excusing) their acceptance of pharmaceutical company gifts and meals, students often argue that it is permissible to accept these benefits because, as medical or pharmacy students, they are burdened with sizeable debt but blessed with only minimal income. Since a medical or pharmacy education is expensive and stressful, the availability of such benefits seems to most students to be a good thing. Who but a killjoy could object?

"I can't be bought for" … (you fill in the blank: free pizza, a laptop computer, a consultancy fee, free tickets to a concert or sporting event, travel to an exotic destination). Employing these or similar words, physicians, residents, medical students, pharmacists, pharmacy students, pharmaceutical researchers, all indignantly affirm that there is no harm done – and certainly no harm to their own integrity – by the acceptance of pharmaceutical company gifts and sponsorships.

Only a deeply corrupt doctor or pharmacist would consciously and deliberately prescribe a medicine to patients when that medicine is known to be sub-optimal. Virtually all health-care professionals (and trainee professionals) feel confident that they are not corrupt in this way. Unfortunately, however, there is a good deal of evidence provided by social science research that demonstrates that "*even when individuals try to be objective, their judgements are subject to an unconscious and unintentional self-serving bias*." (Dana and Lowenstein, 2003).

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Companies spend a significant part of their marketing budgets on lunches, gifts and recreation for health professionals because they know that such spending brings in extra sales. As Rawlins (1984) pointed out more than two decades ago:

"…few doctors accept that they themselves have been corrupted. Most doctors believe that they are quite untouched by the seductive ways of industry marketing men [and women]; that they are uninfluenced by the promotional propaganda they receive; that they can enjoy a company's 'generosity' in the form of gifts and hospitality without prescribing its products. The degree to which the profession, mainly composed of honourable and decent people, can practice such self deceit is quite extraordinary. No drug company gives away its shareholders' money in an act of disinterested generosity."

Independent education or 'peer-to-peer' marketing?

Department chairs and star researchers are sometimes referred to by the pharmaceutical industry as key opinion leaders and are courted assiduously. In an article in *Pharmaceutical Executive,* Dorfman and Maynor (2006) describe why this marketing technique is used:

"*Doctors don't respond well to the traditional sales and marketing push. But, they do respond well to each other. In fact, there are doctors who wield tremendous power of persuasion over their peers. These doctors have earned the respect and attention of other prescribers and have been recognized for their expertise and knowledge of innovative, emerging therapies. But more important, they are likely to try, adopt, and advocate for new products.…From a marketing standpoint, these doctors represent the top tier of the physician hierarchy—the ultimate key opinion leaders."*

Internal company documents that surfaced in a US court case, concerning illegal promotion of gabapentin (Neurontin) for unapproved uses, confirm the importance of physician-to-physician marketing as a promotional strategy. Parke-Davis identified 40 potential 'thought leaders' in one US region, more than half of whom were current or future university departmental chairs, vice-chairs or directors of academic clinical programmes. Thirty-five of these 40 'thought leaders' participated in Parke-Davis- sponsored activities, and 14 of them received honoraria, research grants or educational grants from the company (US$10,000 to $158, 250 per 'thought leader') (Steinman et al., 2006). This is by no means the only company to pay large fees to 'thought leaders'. The US state of Minnesota, e.g., which requires pharmaceutical companies to disclose payments to individual physicians, reported payments up to US$76,350 for advisory board membership and US$334,180 for consulting activities (Ross et al., 2007).

It can be very flattering as well as lucrative to be recognised as a local, national or international expert or 'rising star' in one's field, and to be invited onto advisory boards and speakers' bureaus. Clinicians justify this work as reflecting their expertise and their own opinions. Nevertheless, they are part of a marketing plan, the effectiveness of which depends in no small part on message delivery by a seemingly neutral clinical expert.

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The companies also provide substantial amounts of money to subsidise continuing medical education (CME), (Lexchin, 1993) professional conferences and professional journals (Smith, 2003). As Relman (2003) notes, since many jurisdictions require that doctors undertake postgraduate education as a condition of keeping their license, regular attendance at CME meetings is an integral part of doctors' lives. Over 60% of the cost of CME in the US is paid for by the pharmaceutical and medical device industries. In 2006, these industries spent US$1.45 billion on accredited CME (Hébert, 2008). Would the general public be shocked to learn, one wonders, that continuing education of doctors is not paid for by the doctors themselves but, instead, by pharmaceutical companies or, often, by for-profit firms hired by pharmaceutical companies?

Can industry funding predict research results?

Health professionals also receive funding from pharmaceutical companies to carry out research. These relationships can raise a number of ethical concerns, especially if the sponsor is involved in the design and analysis of clinical trials and reporting of results.

One of the most influential studies of how researchers' objectivity might be compromised by pharmaceutical industry sponsorship appeared in the *New England Journal of Medicine* in January 1998. Stelfox and colleagues (1998) set out to examine published articles on the safety of calcium channel antagonists. Their goal was to answer the question: to what extent is there an association between industry support of medical research and the research findings of investigators? Stelfox divided authors according to their relationships with pharmaceutical companies and then, independently, classified their research findings on the medicine's safety as "supportive", "critical" or "neutral". The conclusion reached by Stelfox et al. must be of serious concern to every supporter of industry university partnerships: "*Our results demonstrate a strong association between authors' published positions on the safety of calcium channel antagonists and their financial relationships with pharmaceutical manufacturers.*"

It may be worth spelling out just how influential pharmaceutical company sponsorship appears to have been: "*Ninety-six per cent of supportive authors had financial relationships with the manufacturers of calcium channel antagonists, as compared with 60 per cent of the neutral authors and 37 per cent of the critical authors.*"

It should be noted, however, that there is a *caveat* in the Stelfox study: they were unable to establish a timeline. Did the authors first have a financial relationship with the company and then write the positive article or did they initially write a positive article and then develop the financial relationship? Obviously neither is acceptable but from the point of view of research integrity, the first is probably worse than the second.

More recently, Bero and colleagues (2007) examined the influence of funding sources on study methods and outcomes for 192 studies comparing statins (cholesterol-lowering medicines) with other statins or different therapies. Studies funded by the manufacturer of the test medicine were 20 times as likely to report results favourable to the test medicine than studies funded by

the manufacturer of the comparator (95% confidence interval 4-93). Studies with adequate blinding were also less likely to report favourable results than those that were not blinded or in which blinding was inadequate.

Lexchin and colleagues (2003) carried out a meta-analysis of studies that examined the relationship between industry funding and research results. Studies funded by the industry were four times as likely as non-industry funded research to report outcomes favourable to the industry. This bias reflects a number of factors. Sismondo (2008) points out that one of these is the relationship between researchers and the sponsor: *"Sponsorship, then, creates subtle influences through the building of relationships that lead researchers to see the pharmaceutical companies with which they interact, and their products, in a more favourable light than they would otherwise."*

A related problem is that of 'ghost' and 'guest' authorship on clinical trial reports. A 'ghost' author is someone who has written the report but is not listed as an author; this is often a company employee or a contract medical writer. A 'guest' author is listed but has not contributed; usually an academic clinician whose name may be used to lend weight and credibility to sponsored trials. Both relationships run counter to principles of accountability and responsibility of authors of published trial reports.

Several US court cases have revealed internal company documents listing trial reports with authors 'to be determined' (Ross et al, 2007). A contract medical writing company, Current Medical Directions, was responsible for management of 85 papers on Pfizer's antidepressant, sertraline (Zoloft), 55 of which resulted in published reports (Healy and Cattell, 2003). Unsurprisingly, given the funding source, all of the included clinical trials and economic analyses were favourable to Pfizer.

The same bias, sometimes conscious but most often unconscious, that afflicts investigators whose research is funded by the pharmaceutical industry also afflicts doctors, pharmacists, trainee doctors and trainee pharmacists who accept gifts from industry. Unconscious bias is pervasive and has a seductive tendency to undermine a doctor's commitment to put the patient's interests ahead of all others. For this reason, respect for professional ethics places an obligation on all health-care practitioners not to put themselves in conflict of interest situations.

Box 1: The 'Olivieri case': a cautionary tale about sponsored research

"The issue is not about whether their inconvenient findings were correct. It is about individual conscience in conflict with corporate greed. It is about the elementary right of doctors to express unbought medical opinions and their duty to acquaint patients with the risk they believe to be inherent in the treatments they prescribe."

– John Le Carré, *The Constant Gardener*, 2001

The Olivieri case raises questions about the influence of pharmaceutical industry sponsors on investigators' ethical obligations to disclose risks to clinical trial participants, and researchers' ability to publish findings that are counter to the financial interests of sponsors. It has implications not only for academic freedom, but also the integrity of the scientific literature on the safety and effectiveness of medicines.

In 1995, Nancy Olivieri was the lead researcher in a study of a new medicine for thalassemia, a hereditary form of anaemia. Deferiprone, was the first oral treatment for thalassemia, an important potential advance over subcutaneous infusions. The trial was carried out at a University of Toronto teaching hospital where Dr Olivieri was a clinical faculty member. The sponsor was a Canadian pharmaceutical company, Apotex.

During the trial, Dr Olivieri and a colleague became concerned about risks from iron accumulation in the livers of some patients on deferiprone. They wanted to carry out more monitoring and to warn patients of this potential risk. Apotex officials disagreed with their concerns, threatened legal action, stopped the trial and removed Dr Olivieri from a second deferiprone safety trial in Europe.

In the bitter controversy that followed, neither the university nor the hospital supported Dr Olivieri against Apotex. She was initially removed from her clinical faculty position, but was later reinstated after an independent inquiry found no evidence of wrongdoing. In 2002, she and her colleagues reached a mediated settlement with the hospital and university, providing them with substantial redress for grievances over unfair treatment. A settlement against Apotex remains in dispute, more than ten years later.

For an in-depth discussion of this and a related case, see:
Schafer A (2004). Biomedical conflicts of interest: a defence of the sequestration thesis—learning from the cases of Nancy Olivieri and David Healy. *Journal of Medical Ethics*;30:8–24. doi: 10.1136/jme.2003.005702.

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Schafer A (2004). Biomedical conflicts of interest: a defence of the sequestration thesis—learning from the cases of Nancy Olivieri and David Healy. *Journal of Medical Ethics*; 30:8-24.

Thompson J, Baird P, Downie J (2001). The Olivieri report: The complete text of the report of the independent inquiry commissioned by the Canadian Association of University Teachers. Toronto: Lorimer, (http://www.dal.ca/committeeofinquiry, accessed 17 April 2009).

Washburn J (2005). University inc.: The corporate corruption of higher education. New York: Basic Books.

[end of box 3]

Conflicts of interest

Health-care professionals are understandably concerned with advancing their own careers. Closely related to this, they are also concerned to promote the well-being of their families, which hinges to some considerable extent on their income. None of these motivations is illegitimate. But the essence of being a health-care professional is that you commit yourself to put the life and health of your patients first, ahead of every other consideration.

When patients consult a health-care professional, they should be able to trust the independence and objectivity of the professional's judgement. The doctor-patient relationship depends heavily upon patient trust in the doctor's integrity and altruism (Wynia et al., 1999). The same is true of the pharmacist-patient relationship.

When doctors or pharmacists, medical students or pharmacy students, accept gifts or benefits from the pharmaceutical industry, they are putting themselves in a conflict of interest situation:

"A person is in a conflict of interest situation if s/he is in a relationship with another in which she has a moral obligation to exercise her judgement in that other's service and, at the same time, s/he has an interest tending to interfere with the proper exercise of judgement in that relationship." (Davis, 1982).

Gifts create a sense of obligation, often unconscious, to 'return the favour' (see Chapter 2 on influence techniques). Since the doctor may also hope to receive future gifts, perhaps fairly substantial ones, from this company or from other pharmaceutical companies, self-interest reinforces the principle of reciprocity, and both conspire to bias the doctor's judgement and to distort his/her clinical practice. If doctors understood this clearly, they would never permit themselves to compromise the integrity of their judgement. If patients understood this clearly, they would be much less tolerant of the practice whereby their physician or their pharmacist was beholden to the pharmaceutical industry.

Box 1 lists four key principles of bioethics that underlie health professional-patient relationships. A tension exists between adherence to these ethical principles and financial links between health professionals and the pharmaceutical industry. Similar tensions exist in the link between the industry, medical and educational institutions and research.

Codes of conduct

Restrictions on gifts are generally covered under industry self-regulatory codes. (PhRMA, 2002) (see Chapter 7). However, these codes leave an enormous loophole in the form of an exemption for so-called educational or research activities. Additionally, they often allow small gifts or gifts that are related to patient care. For the most part, it is the companies themselves which decide what counts as education or research.

As described, most health-care professionals sincerely believe they are unaffected by gifts. But the companies know better. When they invest so many billions of dollars buying gifts and other benefits for doctors and pharmacists their goal is clearly to increase sales of their high-profit-margin products. And this strategy works. A number of published studies have demonstrated that free gifts induce physician reliance on pharmaceutical sales representatives as a source of 'objective' information (Brennan et al., 2006). When doctors rely on pharmaceutical company representatives for their information about new medicines they are much more likely to prescribe new medicines for their patients (Wazana, 2000). The prescription of expensive new patented medicines, when there are equally good or better generic medicines available, not only adds dramatically to the financial burden on patients (and the health-care system generally) but often results in sub-optimal health results.

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Box 2: Key principles of bioethics

1. **Respect for autonomy**

Respect for autonomy requires that patients should be encouraged and assisted, whenever possible, to make informed and voluntary decisions about their health care. It is the basis for *informed consent* in interactions between health professionals and patients.

2. **Nonmaleficence**

This is the principle *to do no harm*. Doctors should strive not to cause needless harm or injury to the patient, either through the treatment that is provided or by not providing needed care.

3. **Beneficence**

Health-care providers have a duty of care to benefit patients to the maximum extent possible in the circumstances. This goal applies both to individual patients, and to the good of society as a whole, for example, in efforts to prevent antibiotic resistance.

4. **Justice**

Justice in health care is usually defined as *distributive fairness*: to provide to each according to his or her needs, regardless of ability to pay. It supports the sharing of resources to provide health care for all.

(Adapted from: http://depts.washington.edu/bioethx/tools/princpl.html)

Vioxx: did conflicts of interest affect the benefit/harm appraisal?

Vioxx (rofecoxib) became a blockbuster product after a clinical study, known as the VIGOR Trial, was published in the *New England Journal of Medicine* (Bombardier et al., 2000). This trial demonstrated that patients who took Vioxx for arthritic pain suffered somewhat fewer stomach bleeds than patients who were given the generic medicine naproxen. Armed with this study, Merck's sales force fanned out across North America and Europe to 'educate' doctors about the advantages of this new 'miracle' anti-inflammatory medicine. Vioxx was heavily promoted to doctors and to consumers (through direct-to-consumer advertising, permitted in the US, but not in most other countries; see Chapter 5). This medicine, one of a class of medicines known as COX-2 inhibitors, quickly became a financial blockbuster for Merck, with annual sales in the region of US$2.5 billion.

However, the VIGOR Trial - on the basis of which Vioxx flew into the commercial stratosphere - also revealed that the patients who received Vioxx suffered five times as many heart attacks and strokes as those who were randomised to naproxen. One would think that this life-threatening adverse side effect would have inhibited doctors from prescribing Vioxx to any of their patients or would have led doctors to prescribe Vioxx only to the small group of patients who were at extremely high risk of stomach bleeds and extremely low risk of heart attack and stroke. Sadly, no such inhibition occurred. Doctors wrote millions of prescriptions for Vioxx. The sales juggernaut did not grind to a halt until Merck removed Vioxx from the market. This happened only after a trial meant to test Vioxx as a preventative medication for bowel cancer confirmed, instead, that Vioxx caused a significant level of heart disease.

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We now know that - notwithstanding the early evidence of elevated risk of serious adverse consequences - Merck instructed its sales reps to mislead doctors about the safety of Vioxx. They code-named their 'educational' campaigns 'Offense' and 'XXceleration' (FxClub.com, 2006). The company's representatives distributed pamphlets that ignored the cardiovascular results from the *New England Journal of Medicine* VIGOR Trial (Curfman et al., 2005, 2006) and instead presented a range of scientifically inferior studies (with inadequate subject numbers and/or inferior design) which purported to show that Vioxx users were at **lower** risk for heart attacks rather than, as was the really the case, at much **higher** risk. Had doctors been properly informed about the evidence, they would have limited their prescribing of Vioxx. The VIGOR study was itself later exposed as underreporting the data on the cardiovascular risks associated with Vioxx (Curfman et al., 2005).

This evidence of deliberate pharmaceutical company manipulation of doctors – under the banner of 'education' - only emerged (in documents submitted to the US Congress) after Vioxx was withdrawn from the market (Brownlee and Lenzer, 2005). On 30 September 2004, after more than 80 million patients had taken this medicine and annual sales had topped US$2.5 billion, the company withdrew the medicine because of an excess risk of myocardial infarctions and strokes (Topol, 2004). Tragically, by the time the product was withdrawn, it is estimated that tens of thousands of patients had already died unnecessarily from heart attacks and strokes induced by Vioxx (Graham et al., 2005).

In this connection, it may be worth quoting a typical passage from the compelling testimony offered by Dr David Graham of the US Food and Drug Administration (FDA) at a US Congressional hearing:

"Let me begin by describing what we found in our study, what others have found, and what this means for the American people. Prior to approval of Vioxx, a study was performed by Merck named 090. This study found nearly a 7-fold increase in heart attack risk with low dose Vioxx. The labelling at approval said nothing about heart attack risks. In November 2000, another Merck clinical trial named VIGOR found a 5-fold increase in heart attack risk with high-dose Vioxx. The company said the drug was safe and that the comparison drug naproxen, was protective. In 2002, a large epidemiologic study reported a 2-fold increase in heart attack risk with high-dose Vioxx and another study reported that naproxen did not affect heart attack risk. About 18 months after the VIGOR results were published, FDA made a labelling change about heart attack risk with high-dose Vioxx, but did not place this in the "Warnings" section. Also, it did not ban the high-dose formulation and its use. I believe such a ban should have been implemented." (Graham, 2004).

Conclusion

The experience with Vioxx raises questions about pharmaceutical industry marketing practices, but also about grossly inadequate performance by the regulatory authority. These questions have been extensively discussed in both the medical and the general media. Millions of patients received this medicine before it was withdrawn from the market despite the predominance of

evidence indicating that the risk-benefit ratio of this medicine was significantly unfavourable. Although the evidence that harms outweighed benefits was present from the outset in the medical literature, it was widely ignored by physicians, with the honourable exception of a hardy minority of independent clinicians, who issued appropriate warnings long before the product was finally withdrawn in 2004 (Wright, 2002).

Less has been said about the role of health professionals. Did gifts, free samples, speakers' honoraria and a host of other financial relationships between health professionals and the manufacturer play a part in stimulating prescriptions of this medicine? No one would suggest that physicians knowingly prescribed an unnecessarily harmful product to patients because of a free dinner or round of golf. However, as this chapter points out, acceptance of pharmaceutical industry gifts can subvert professional practice in a variety of ways, many unconscious. Ultimately, it is the patient who suffers. As Dana and Loewenstein (2003) point out, "*Pharmaceutical companies know that gifts influence physicians, which is why many restrict their own employees from accepting even small gifts*." Moreover, when patients discover the full extent of the gift relationship which exists between physicians and the pharmaceutical industry, a second major casualty is likely to be the bond of trust between doctor and patient.

In short, doctors and other health-care providers should recognise the applicability of the old saying, "There is no such thing as a free lunch". Accepting gifts or other benefits from pharmaceutical companies and their representatives carries a heavy ethical price, namely, the sacrifice of one's professional integrity. Ethical health-professionals-in-training should say "no" to all pharmaceutical company gifts and benefits and should continue to say "no" when they become fully qualified health professionals. At the same time, one should recognise that saying "no" when one's fellow students are saying "yes" carries risks. One not only feels badly when one loses the material rewards that come to those who say "yes", but one risks being seen as a threat by one's colleagues. Those who publicly reject illegitimate benefits risk being seen as killjoys. Critics of pharmaceutical company marketing may become estranged from the very people with whom they need to form bonds of mutual support and community. Thus, when one is considering taking a stand on principle one ought also to consider the possibilities of collective action. Self-education, followed by discussion and dialogue with colleagues, has the possibility of leading to a group response. At the end of the day, one has to act according to one's conscience; but if one is able to act collectively with like-minded others, then the impact of one's action is likely to be exponentially greater.

Student exercises

1. Debate on ethical conflicts among health professionals

Divide students into debating teams of 4 to 6 people. The first debate will be on the following question:

Team 1: *There is no ethical conflict in physicians and pharmacists accepting money from pharmaceutical companies.*

Team 2: *It is ethically unacceptable for physicians and pharmacists to accept money from pharmaceutical companies.*

Students should try to debate each side of this question regardless of their initial opinions. They can meet as a team to discuss how they will approach the debate and divide the content they will cover among team members. For example, one person might want to deal with small gifts or free lunches, another with being a member of a company advisory board, etc., yet another with sponsored research or institutional support.

Debate of this topic should include citation of some highly publicised cases of the interactions of industry with research scientists who have raised issues of uncertainty.

Background reading:

Schafer A (2004). Biomedical conflicts of interest: a defence of the sequestration thesis-learning from the cases of Nancy Olivieri and David Healy. *Journal of Medical Ethics,* 30(1):8-24.

Rennie D (1997). Thyroid storm. *Journal of the American Medical Association,* 277(15):1238-43.

Moynihan R (2003). Who pays for the pizza? Redefining the relationship between doctors and drug companies. Part 2: Disentanglement. *British Medical Journal,* 326:1189-1192.

Topol EJ (2004). Failing the public health-rofecoxib, Merck, and the FDA. *New England Journal of Medicine*, 351(17):1707-9.

Katz D, Caplan A, Merz J (2003). All gifts large and small: toward an understanding of the ethics of pharmaceutical industry gift-giving. *American Journal of Bioethics*, 3(3):39-46.

Dana J, Loewenstein G (2003). A social science perspective on gifts to physicians from industry *Journal of the American Medical Association*, 290(2):252-5.

2. Questions on the Olivieri case:

"My ethical obligation as a clinical researcher was to inform patients and the trial ethics committee of any perceived risks. As the physician responsible for the care of many of these patients, I also had duty to 'do no harm'. When I indicated my intention to inform patients and their parents, regulatory agencies and the scientific community, of my concerns, the company disputed both the risk associated with the drug, and the need to inform patients."

– *Nancy Olivieri, personal communication*

- If a clinician suspects that a medicine is leading to harm to patients during a clinical trial, must they inform the patients even if they are not sure?

- What steps can regulatory agencies, academic institutions and journals take to ensure that all of the results of a sponsored clinical trial – both beneficial and harmful – are reported in published articles?

- If industry sponsors stop studies when suspected harmful effects begin to emerge, how is the scientific literature as a whole affected? What does this mean for the information on benefits and harmful effects of medicines that physicians and pharmacists are able to access?

3. This situation happened to a leading researcher in her field, in a wealthy industrialised country. How do you think it might have differed if she was just starting her career? What if she were based in a developing country?

4. In press coverage of 'the Olivieri case', the public hospital and university involved came under greater criticism than Apotex. Do you agree with this? Why or why not?

5. Do you know of a similar case involving researchers from your own country or region?

6. Discussing conflict of interest policies

In this exercise, students should break into teams that will interview medical or pharmacy faculty officials about institutional conflict of interest policies.

They can either use the PharmFree scorecard developed by the American Medical Students Association (AMSA) or use this scorecard as a model to develop their own, more locally appropriate scorecard. For information on the AMSA rating system, see: http://amsascorecard.org/methodology

They should report on the results of these interviews, their faculty's letter grade and any recommendations they have for a change in policies.

Background reading:

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