The influence of the pharmaceutical industry in medicine

George A Jelinek and Sandra L Neate*

Pharmaceutical companies are known to be among the most profitable companies in the world. Proceedings of legal cases and published research provide insights into the nature of the influence of drug companies on research and publication practices relating to the drugs they manufacture, on marketing disguised as "education" and on doctors who prescribe their drugs. The influence of drug companies extends further to sponsorship of opinion leaders who promote their drugs and groups that produce clinical guidelines. More rigorous regulation of the relationship between the pharmaceutical industry and medicine is required.

INTRODUCTION

There is widespread concern within the medical profession and the community about the conflict of interest that exists between for-profit drug companies – with their obligations to maximise sales of their products for the benefit of shareholders – and members of the medical profession who recommend these products to patients. This article explores the influence of the pharmaceutical industry on medical research and practice. It seeks to discover from the medical literature the extent of such conflict of interest, and the effects of that conflict on the conduct and outcomes of research and its publication, and hence clinical practice.

THE PHARMACEUTICAL INDUSTRY

The pharmaceutical industry is highly profitable. Some pharmaceutical companies are among the world's largest and most profitable companies. Marcia Angell, former Editor-in-Chief of the *New England Journal of Medicine*, has described the industry as being "awash with money" and as consistently being the most profitable industry since the 1980s. Her book, *The Truth About the Drug Companies*,[1] noted that in the 2002 Fortune 500, which outlined the takings of the top 500 companies in the United States, the combined profits for the top 10 drug companies (US$35.9 billion) outweighed the combined profits of the other 490 companies (US$33.7 billion). Further, she found that the drug companies' profits comprised 17% of sales, compared with 4.6% for the other companies. These are highly profitable, powerful multinational companies, and it is worth bearing this in mind when considering their influence in medicine.

The pharmaceutical companies state that such profits are necessary, as much of the profit in the pharmaceutical industry is ploughed back into research and development because drug development is so costly. Angell laid this claim to rest, noting that the marketing budgets of these corporations far outweigh their research and development budgets, by a factor of around three-to-one. Further, the salaries of drug company executives are enormous, and disturbingly, a considerable amount of money is spent on "educating" doctors. The education of doctors by the companies that sell the products they are educating doctors about creates the potential for profound conflicts of interest.

* Professor George A Jelinek MD DipDHM FACEM, Professorial Fellow, Department of Medicine, University of Melbourne (St Vincent's Health), Fitzroy, Victoria; Dr Sandra L Neate MBBS DA DipObsRACOG FACEM, Senior Staff Specialist, Department of Emergency Medicine, St Vincent's Health, Fitzroy, Victoria, and Honorary Fellow, Department of Medicine, University of Melbourne (St Vincent's Health), Fitzroy, Victoria. Conflict of interest: Professor Jelinek was remunerated by Slater & Gordon for providing testimony on behalf of the plaintiff in the case of *Peterson v Merck Sharpe & Dohme (Aust) Pty Ltd (No 3)* [2006] FCA 875 awaiting judgment in the Federal Court of Australia in 2009. The authors declare no other conflicts of interest.

Correspondence to: Professor George A Jelinek, Department of Medicine, University of Melbourne (St Vincent's Health), Victoria Parade, Fitzroy, Vic, Australia.

[1] Angell M, *The Truth About the Drug Companies. How They Deceive Us and What to Do About It* (Random House Trade, New York, 2005) p 11.

INFLUENCE OF THE INDUSTRY ON RESEARCH FINDINGS

Drug company-sponsored research is known to be inferior to independent research in a number of ways. The association between positive findings in randomised trials and industry funding appears to have first been documented in 1986.[2] It has since been shown that industry-sponsored research is significantly more likely to reveal positive findings in cancer[3] and orthopaedics[4] journals and in randomised controlled trials published in the *British Medical Journal*[5] and five general interest medical journals.[6] Systematic reviews have found that drug company-sponsored research is around 3.6[7] to four[8] times as likely to be favourable to a company's product as independently funded research. Research has concluded that such trials may be more positive due to the biased interpretation of results.[9]

Further, authors of company-sponsored research are more than five times as likely as independent authors to recommend the company's drug.[10] Researchers with industry connections have been shown to be far more likely to publish papers favourable to company products than those without such connections. In the case of calcium channel blockers, eg, 96% of authors of papers favourable to a particular drug had financial ties to the company that made the drug compared to 37% of those whose papers had been critical.[11]

INFLUENCE OF THE INDUSTRY ON RESEARCH CONDUCT, REPORTING AND DRUG APPROVAL

It is likely that the drug industry, through its control of much of the research into pharmaceuticals, is able to persuade regulatory authorities such as the Food and Drug Administration (FDA) in the United States and the Therapeutic Goods Administration (TGA) in Australia that drugs should be licensed when the evidence supporting their licensing is, in reality, less than compelling. In approving a drug for clinical use, the FDA accepts the results of clinical trials run by the drug company which produces the drug. These studies do not necessarily have to have been published in peer-reviewed journals.

[2] Davidson RA, "Source of Funding and Outcome of Clinical Trials" (1986) 1 J Gen Intern Med 155.

[3] Djulbegovic B, Lacevic M, Cantor A et al, "The Uncertainty Principle and Industry-sponsored Research" (2000) 356 *The Lancet* 635; Friedberg M, Saffran B, Stinson TJ et al, "Evaluation of Conflict of Interest in Economic Analyses of New Drugs Used in Oncology" (1999) 282 JAMA 1453; Hartmann M, Knoth H, Schulz D et al, "Industry-sponsored Economic Studies in Critical and Intensive Care Versus Studies Sponsored by Nonprofit Organizations" (2003) 18 J Intensive Care Med 265; Knox KS, Adams JR, Djulbegovic B et al, "Reporting and Dissemination of Industry Versus Non-profit Sponsored Economic Analyses of Six Novel Drugs Used in Oncology" (2000) 11 Ann Oncol 1591; Peppercorn J, Blood E, Winer E et al, "Association Between Pharmaceutical Involvement and Outcomes in Breast Cancer Clinical Trials" (2007) 109 *Cancer* 1239.

[4] Khan SN, Mermer MJ, Myers E et al, "The Roles of Funding Source, Clinical Trial Outcome, and Quality of Reporting in Orthopedic Surgery Literature" (2008) 37 Am J Orthop E205, discussion at E212.

[5] Kjaergard LL and Als-Nielsen B, "Association Between Competing Interests and Authors' Conclusions: Epidemiological Study of Randomised Clinical Trials Published in the BMJ" (2002) 325 BMJ 249.

[6] Yaphe J, Edman R, Knishkowy B et al, "The Association Between Funding by Commercial Interests and Study Outcome in Randomized Controlled Drug Trials" (2001) 18 Fam Pract 565.

[7] Bekelman JE, Li Y and Gross CP, "Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review" (2003) 289 JAMA 454.

[8] Lexchin J, Bero LA, Djulbegovic B et al, "Pharmaceutical Industry Sponsorship and Research Outcome and Quality: Systematic Review" (2003) 326 BMJ 1167.

[9] Als-Nielsen B, Chen W, Gluud C et al, "Association of Funding and Conclusions in Randomized Drug Trials: A Reflection of Treatment Effect or Adverse Events?" (2003) 290 JAMA 921.

[10] Als-Nielsen, Chen, Gluud et al, n 9.

[11] Stelfox HT, Chua G, O'Rourke K et al, "Conflict of Interest in the Debate Over Calcium-channel Antagonists" (1998) 338 NEJM 101.

In the case of antidepressants, researchers examined the 42 FDA reviews for the six most widely used antidepressants approved from 1987 to 1999.[12] Interestingly, most of the 42 trials lasted six weeks, despite the fact that these agents are generally promoted and prescribed for long-term use. The studies showed that in the randomised controlled trials, placebos were in fact 80% as effective as the drugs. The difference in drugs versus placebos averaged to two points on a 62-point scale of mood. This was a statistically significant difference; whether it was clinically significant is a different matter. The researchers found that the effect was really only of clinical significance for those who were very severely depressed.[13] If there was, in fact, so little additional benefit of the antidepressants over placebos, why are so many patients, most of them not severely depressed, prescribed them?

While the FDA assesses all these studies in making its determination of whether to license the drugs, many of the studies are not subsequently published. In fact, a substantial bias has been shown to exist in what is published and what is not. Selective reporting may mean that clinicians have an unrealistic view of the efficacy of such drugs. To take the antidepressants again, researchers showed that of 74 studies registered with the FDA to license antidepressants, 38 had positive results; of these, 37 were published.[14] Thirty-six had negative or questionable results; of these, 22 were not published, 11 were published in a way that made them appear positive, and only three were published accurately according to the researchers. Overall, the published literature suggested that 94% of studies were positive, whereas FDA literature showed that 51% were positive. Meta-analysis of published literature versus FDA literature showed a one-third greater effect size in published data. Selective reporting can clearly inflate our estimate of the benefit of these drugs.

The drug industry also has a significant influence on research conduct and reporting. In a national Australian survey of 823 medical specialists, 12.3% reported that industry staff wrote first drafts of their papers for publication.[15] Further, 6.7% reported delayed publication, 5.1% non-publication of key negative findings, and 2.2% concealment of results. Overall, 71 respondents (8.6%) experienced at least one event that could represent a breach of research integrity.

While doctors who may be sceptical about drug company marketing usually trust the peer-reviewed medical literature,[16] this trust may sometimes be misplaced, because of drug company manipulation of publishing practices. Research reporting has been profoundly affected by drug company sponsorship in several well-publicised cases. In the case of Merck's Vioxx (rofecoxib), researchers have shown that many articles written in-house by the company's own researchers or by commercial medical writing firms were published with "guest authors" who were academic investigators recruited by the company.[17] Further, it has been reported that the company obscured the mortality risks associated with the drug in published trials despite being aware of them from in-house reports.[18]

In Australian legal proceedings it has been revealed that Merck funded leading medical publisher Elsevier to produce a publication that appeared to be, but was not, a peer-reviewed medical journal

[12] Kirsch I, Moore TJ, Scoboria A et al, "The Emperor's New Drugs: An Analysis of Antidepressant Medication Data Submitted to the US FDA. Prevention and Treatment" (2002) 5 ArtID 23.

[13] Kirsch I, Deacon BJ, Huedo-Medina TB et al, "Initial Severity and Antidepressant Benefits: A Meta-analysis of Data Submitted to the Food and Drug Administration" (2008) 5 PLoS Med e45.

[14] Turner EH, Matthews AM, Linardatos E et al, "Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy" (2008) 358 NEJM 252.

[15] Henry DA, Kerridge IH, Hill SR et al, "Medical Specialists and Pharmaceutical Industry-sponsored Research: A Survey of the Australian Experience" (2005) 182 MJA 557.

[16] Angell M, "Industry-sponsored Clinical Research: A Broken System" (2008) 300 JAMA 1069.

[17] Ross JS, Hill KP, Egilman DS et al, "Guest Authorship and Ghostwriting in Publications Related to Rofecoxib: A Case Study of Industry Documents from Rofecoxib Litigation" (2008) 299 JAMA 1800.

[18] Psaty BM and Kronmal RA, "Reporting Mortality Findings in Trials of Rofecoxib for Alzheimer Disease or Cognitive Impairment: A Case Study Based on Documents from Rofecoxib Litigation" (2008) 299 JAMA 1813.

(the *Australasian Journal of Bone and Joint Medicine*) promoting the benefits of Vioxx,[19] further eroding the ability of clinicians to differentiate marketing from science.

THE RELATIONSHIP BETWEEN DRUG COMPANIES AND DOCTORS

Drug companies reward doctors who undertake research for them. In the Australian survey of 823 medical specialists previously discussed, 41% of these doctors reported involvement in industry-sponsored research in the previous year.[20] These doctors were around three and a half times more likely to have been offered industry-sponsored items over $A500, and nearly five and a half times more likely than others to have been offered support for attending international conferences. For doctors who were members of advisory boards, this latter figure rose to seven fold, and nine fold for paid consultants to industry.

A variety of inducements is offered to doctors. The same Australian survey showed that:

- 96% had been offered food;
- 94% had been offered items for the office;
- 75 to 84% had been invited to product launches, symposia or "educational events";
- 52% had received offers of travel to conferences; and
- 50% had been offered personal gifts, journals or textbooks.[21]

The authors reported that 66 to 79% of offers were accepted.

These problems are widespread. A United States study reported that 94% of physicians reported a relationship with the industry, with 83% accepting food and 78% free samples.[22] Further, 35% had received money as reimbursements, with 28% receiving direct payments for lectures, etc. The survey demonstrated that marketing was focused on opinion leaders likely to influence prescribing by other doctors. Cardiologists were twice as likely to receive inducements as other physicians.

This conflict of interest is widespread throughout the profession. An example of the extent was reported in a study examining the drug company associations of the committee members of the Committee on Safety of Medicines in the United Kingdom.[23] This committee advises the United Kingdom regulatory agency on new drug approvals. Of 29 committee members, 23 had financial conflicts of interest. Thirteen of the members had associations with five companies, four with 10 companies, and three with 20 companies.

It may surprise that even clinical guidelines, widely thought to be objectively and independently produced, have on occasion been shown to be sponsored by the company producing a drug advocated in the guidelines,[24] authors to have received speakers' fees and travel assistance from that drug company[25] and dissemination of the guidelines to have been sponsored by the drug company.[26]

The extent of this conflict of interest can be further appreciated when one considers that the *New England Journal of Medicine*, widely considered to have the most stringent policy of general medical journals for restricting and declaring potential conflicts of interest of authors, was forced in 2002 to

[19] *Peterson v Merck Sharp & Dohme (Aust) Pty Ltd (No 3)* [2006] FCA 875.

[20] Henry D, Doran E, Kerridge I et al, "Ties that Bind: Multiple Relationships Between Clinical Researchers and the Pharmaceutical Industry" (2005) 165 Arch Intern Med 2493.

[21] McNeill PM, Kerridge IH, Henry DA et al, "Giving and Receiving of Gifts Between Pharmaceutical Companies and Medical Specialists in Australia" (2006) 36 Intern Med J 571.

[22] Campbell EG, Gruen RL, Mountford J et al, "A National Survey of Physician-Industry Relationships" (2007) 356 NEJM 1742.

[23] Abraham J, "The Pharmaceutical Industry as a Political Player" (2002) 360 *The Lancet* 1498.

[24] Millar JA, "Genesis of Medical Thromboprophylaxis Guidelines in Australia: A Need for Transparency and Standardisation in Guideline Development" (2009) 190 MJA 446.

[25] Fletcher JP, "Genesis of Medical Thromboprophylaxis Guidelines in Australia: A Need for Transparency and Standardisation in Guideline Development" (2009) 190 MJA 450.

[26] Millar, n 24.

reverse a 12-year policy of precluding anyone with financial ties to industry from writing editorials or reviews, because it could not find enough authors without ties.[27]

THE INFLUENCE OF CONFLICT OF INTEREST ON PRESCRIBING

It may be argued that this widespread conflict of interest is not a problem if it does not actually change doctors' prescribing behaviour. If pharmaceutical industry involvement does not translate into changed prescribing practice, one wonders why drug companies would waste their resources on such activities. Social science research shows that even small insignificant gifts influence the recipient.[28] While doctors generally deny that they are influenced,[29] physicians attending pharmaceutical events are more likely to use the product, even without scientific evidence.[30] It has been reported that promotional activities lead to increased prescribing, non-rational prescribing and acceptance of commercial rather than scientific views.[31]

HOW DRUG COMPANIES INCREASE THEIR SALES

The industry uses a variety of techniques to increase sales. Information from legal proceedings documents some of these practices. One such practice is to encourage doctors to use a drug approved for one condition "off label" for other conditions by "educating" doctors about its supposed benefits in the secondary condition. The pharmaceutical industry is not required to convince regulatory authorities that a drug is effective if it is being prescribed off-label. Doctors can prescribe for any condition, not just those approved by regulators. The companies can enlist (pay) opinion leaders to lecture other doctors about the benefits of a drug licensed for one condition being used off-label for others, resulting in a shift of prescribing to include the off-label indications.

Take the example of Neurontin™ (gabapentin). This drug was FDA-approved in 1994 for "epilepsy when other drugs have failed, in combination with another", that is, it was a third line epilepsy drug. In 1996, David Franklin, a Parke-Davis employee, sued, alleging there had been a massive illegal scheme to promote Neurontin for off-label use. Court evidence showed that the company had paid academics to put their names on flimsy research to show that the drug worked in other conditions (bipolar disorder, post-traumatic stress disorder, insomnia, restless legs, hot flushes, migraines, tension headache, etc). This "research" was widely disseminated to practising doctors through "educational meetings" conducted by doctors paid to lecture about the benefits.[32]

Interestingly, the company tracked the prescribing of doctors after these meetings and found a 70% increase in prescribing.[33] Suffice to say, Neurontin became a "blockbuster" (>US$1 billion pa) drug with sales of $2.7 billion in 2003, an astonishing result for a third line epilepsy drug. Eighty per cent of sales were for the "off-label" conditions. In effect, Neurontin had become a general restorative for chronic discomfort in patients with conditions that would last for years. In May 2004, Pfizer, which had taken over Parke-Davis, pleaded guilty to "illegal marketing" and paid US$430 million in damages, a small percentage of the annual takings from sales of the drug.[34] This raises the important question of what happened to all the people still on Neurontin, a drug known to have a variety of side effects. And what about all the doctors who kept prescribing it, unaware of the court findings?

[27] Drazen JM and Curfman GD, "Financial Associations of Authors" (2002) 346 NEJM 1901.

[28] Katz D, Caplan AL and Merz JF, "All Gifts Large and Small: Toward an Understanding of the Ethics of Pharmaceutical Industry Gift-giving" (2003) 3 Am J Bioeth 39.

[29] Brett AS, Burr W and Moloo J, "Are Gifts from Pharmaceutical Companies Ethically Problematic? A Survey of Physicians" (2003) 163 Arch Intern Med 2213.

[30] Lexchin J, "Interactions Between Physicians and the Pharmaceutical Industry: What does the Literature Say?" (1993) 149 CMAJ 1401.

[31] Wazana A, "Physicians and the Pharmaceutical Industry: Is a Gift Ever Just a Gift?" (2000) 283 JAMA 373.

[32] Steinman MA, Harper GM, Chren MM et al, "Characteristics and Impact of Drug Detailing for Gabapentin" (2007) 4 PLoS Med e134; Steinman MA, Bero LA, Chren MM et al. "Narrative Review: The Promotion of Gabapentin: An Analysis of Internal Industry Documents" (2006) 145 Ann Intern Med 284.

[33] Peterson M, "Doctor Explains Why He Blew the Whistle", *New York Times* (12 March 2003).

[34] Quoted in Angell, n 1, p 161.

Indeed, a new industry seems to be growing out of this practice of off-label promotion of drugs. In March 2008, the 6th Annual Off-Label Usage Conference on "Minimizing the Legal Risk Associated with Off-label Marketing" was held at the Hilton Philadelphia Airport. According to brochures, conference highlights included (from the flyer):

> [L]atest enforcement indicating FDA's priorities and initiatives, review of multi-million dollar settlements, identify what triggers government inquiry: Learn to identify the red flags, best practices by pharmaceutical companies to remain compliant with self-regulatory processes to avoid government scrutiny and maximize privilege, dos and don'ts of promotion through third parties, ensuring internal compliance for effective sales force training and monitoring programs to reduce liability.

A completely novel approach to maximising company profits was demonstrated by Astra Zeneca's "shark fin" project. Again court proceedings allow us a rare insight into the dubious practices of drug companies. This came about because omeprazole was nearing the end of its patent in 2001 after earning US$26 billion as a treatment for indigestion. The company knew that profits would plunge (like the other side of a shark's fin) with generic drugs becoming available when the patent ended. A "think tank" was assembled to deal with this. They decided on marketing one of the two isomers of omeprazole separately (esomeprazole) as Nexium; that is, this "new" drug was in effect a repackaged version of their old medicine. Despite the drugs being equipotent, they then compared 40mg Nexium with 20mg omeprazole. Naturally, esomeprazole, at twice the dose of omeprazole, appeared more effective and it was subsequently marketed as a superior drug. Astra Zeneca filed a patent for Nexium in February 2001, and spent $0.5 billion on marketing to physicians and direct to consumers, a practice allowed in the United States. Nexium became a blockbuster drug, in the United States selling for $4.09 per tablet versus 67c for the old omeprazole.[35]

This conduct became the subject of a proposed class action in the United States District Court in Delaware in early 2005.[36] The suit alleged false, misleading and deceptive advertising. The suit was dismissed. The judgment concluded that the advertisements complied with FDA-approved labelling; therefore federal law pre-empted State law. A subsequent appeal to the Third United States Circuit Court of Appeals in June 2007 was also dismissed,[37] on the grounds that the FDA had "exclusive authority" to regulate drug advertising. One dissenting judge (Cowen J) noted that such "implied conflict pre-emption" of State law was unwarranted since the FDA had no power to require pre-approval of advertisements and lacked resources to police advertisements.

VIEWS OF PROMINENT MEDICAL JOURNAL EDITORS

Medical journal editors generally have a closer view than most of the issues surrounding conflict of interest between doctors and the pharmaceutical industry. For the most part, they have no particular axe to grind, and one might expect their views to be dispassionate. However, drug company purchasing of large numbers of reprints of their own published research, a large source of income for medical journals, may create a conflict of interest even for journal editors.

It is disturbing to see the widespread documented concern about these relationships from the editors of some of our most influential journals. Marcia Angell, former Editor-in-Chief of the *New England Journal of Medicine*, has written:

> Now primarily a marketing machine to sell drugs of dubious benefit, this industry uses its wealth and power to co-opt every institution that might stand in its way, including the US Congress, the FDA, academic medical centers and the medical profession itself.[38]

[35] Gladwell M, "High Prices. How to Think About Prescription Drugs", *New Yorker* (25 October 2004).

[36] *Watters v AstraZeneca Pharmaceuticals LP* (Delaware District Court, Case No 1:2005cv00196, filed 5 April 2005) and *Macken v AstraZeneca Pharmaceuticals LP* (Delaware District Court, Case No 1:2005cv00220, filed 14 April 2005).

[37] *Pennsylvania Employees Benefit Trust Fund, etc v Zeneca, Inc; AstraZeneca Pharmaceuticals, LP* (United States Court of Appeals for the Third Circuit on appeal from the District of Delaware (Providence County), Case No 05-5340, 23 August 2007).

[38] Angell, n 1, p xxx.

According to Richard Horton, Editor-in-Chief of *The Lancet*, "Journals have devolved into information laundering operations for the pharmaceutical industry".[39]

Richard Smith, respected former Editor-in-Chief of the *British Medical Journal* for 25 years, has been particularly critical: "I must confess that it took me almost a quarter of a century editing for the BMJ to wake up to what was happening." "Medical journals", he said, are "an extension of the marketing arm of pharmaceutical companies."[40] He noted that potential profits from reprints of just one trial can run to US$1 million (£0.5m), and that this potential income has a corrupting influence on a journal because many editors are charged with ensuring their journal makes a profit. Thus, conflict of interest is an issue with wider ramifications than authorship and sponsorship of studies. Smith continued:

> How did we reach a point where so many doctors won't attend an educational meeting unless it's accompanied by free food and a bag of "goodies"? Something's wrong, and medical journals are part of what's wrong.

He took particular issue with the effect of drug company influence on randomised controlled trials: "What is happening is that this major scientific invention – the randomised trial – is being debased for marketing reasons." He summed up by saying that "The industry dominates health care, and most doctors have been wined and dined by it".

We should be particularly concerned when independent journal editors conclude, as Marcia Angell did:

> As I saw industry influence grow, I became increasingly troubled that much published research is seriously flawed, leading doctors to believe new drugs are generally more effective and safer than they actually are.[41]

She noted that "In many drug-intensive medical specialties it is virtually impossible to find an expert who is not receiving payments from one or more drug companies".[42] Both Angell and another former Editor-in-Chief of the *New England Journal of Medicine*, Dr Jerome Kassirer, have written books about the corrupting influence of the drug companies.[43] Kassirer was particularly scathing of his medical colleagues, going as far as saying that "It shouldn't have to be patients' responsibilities to protect themselves against the medical profession". Angell concluded that bias permeates the whole system and is not just confined to isolated instances.[44]

POSSIBLE SOLUTIONS

Australian authors have proposed a number of possible solutions to the increasing influence of the pharmaceutical industry on medical research and practice.[45] They argue for increased transparency, including the potential for strict independent auditing of funding sources as is required for politicians and company directors. Further, they argue that journals should require opinion leaders to be free from conflicts of interest.

More radically, they suggest that it may be in our long-term interest to develop a culture within medicine where opinion leaders are expected to provide their expertise to drug companies pro bono, and that academic medical centres should create independent offices of medical education to oversee funding, potentially with bans on gifts, food and travel. There has been a recent call to extend practical

[39] Horton R, "The Dawn of McScience" (2004) 51 *New York Review of Books* 7.

[40] Smith R, "Medical Journals are an Extension of the Marketing Arm of Pharmaceutical Companies" (2005) 2 PLoS Med e138.

[41] Angell, n 1, p xxx.

[42] Angell, n 1, p 142.

[43] Kassirer JP, *On the Take: How Medicine's Complicity with Big Business can Endanger Your Health* (Oxford University Press, New York, 2005).

[44] Angell, n 16.

[45] Haines IE and Olver IN, "Are Self-regulation and Declaration of Conflict of Interest Still the Benchmark for Relationships Between Physicians and Industry?" (2008) 189 MJA 263.

guidelines for interaction with the pharmaceutical industry to all health professionals.[46] It is hard to argue that these changes would not have a beneficial effect on the integrity of scientific research, teaching and publication.

In the United States, Angell has argued for direct government control via an Institute for Prescription Drug Trials, contending that it is absurd to look to these companies for unbiased evaluations of their own products.[47]

CONCLUSIONS

Drug companies are among the most profitable companies in the world. The drug industry is a powerful force in medicine, driving research and publication, and influencing clinical practice through education and marketing. Drug companies have been prosecuted for and have admitted to illegal marketing. Widespread conflict of interest results in over-prescribing of many medicines of dubious benefit. This conflict of interest can lead doctors to neglect genuine health in favour of pharmaceuticals.

Individually, doctors should consider whether to accept anything from drug companies, including gifts, research funding or honoraria. Collectively, there is a strong case for greater regulation of the relationship between the industry and the profession. Our dependence in medicine on pharmaceuticals leaves us open to manipulation by a for-profit industry that is responsible to its shareholders rather than to our patients.

[46] Shipp DH and Mallarkey G, "Liaison Between Public Hospital Staff and the Pharmaceutical Industry: Guidance from the NSW Therapeutic Advisory Group" (2009) 190 MJA 406.

[47] Angell, n 16.