Medicine and 'Big Pharma'

President's Introduction

We usually attempt to have presentations from at least two speakers at our scientific meetings. Indeed, we attempted to obtain another speaker. I am certainly not being critical of anybody in regard to the fact that we couldn't get someone, but I should let you know that initially Julian Lee, our Vice President, obtained an indication that Medicines Australia, the national association representing the prescription medicines industry, was prepared to provide a speaker. Unfortunately, that person subsequently became unavailable and Medicines Australia was not able to provide another speaker. It seemed to me that, in the absence of that body being able to provide a speaker, it was preferable that we proceed with Professor Henry on the basis that I had noticed that some of the people on his task force were, in a sense, representatives of the pharmaceutical industry. So I want to assure everyone that there was no bias, intended or otherwise, on the part of the Committee in organising this evening's presentation.

Professor David Henry is Professor of Clinical Pharmacology, Faculty of Health, University of Newcastle. He is the director of the World Health Organisation's Collaborating Centre for Training in Pharmacology and Rational Drug Use. In 2002 he worked on the availability of anti-AIDS drugs in the Essential Drugs and Medicines Policy Department of the World Health Organisation in Geneva, Switzerland. His interests include evaluation of drugs, the medical profession and pharmaceutical industry, lay news reporting of new drugs, availability of drugs in developing countries and the development of drug-pricing models based on cost-effectiveness.

I regret that Big Pharma is not here to act as a counterpoint to some of the things I am going to say. I have enjoyed some robust exchanges with them over the years, including a couple of visits to Federal courts. So we both have form in that regard. But tonight I want to look at the bigger picture, to look at the evidence and at the data on the relationships between doctors and the drug industry. I will start with the international scene and then move on to examine some recent Australian data. We can then look for possible problems, responses and solutions. I am not going to present extreme views about the behaviour of certain companies. So if you were looking for blood on the floor tonight, I am going to disappoint you a little.

My talk is about the important relationship between Medicine and Big Pharma. Big Pharma has been the main source of new medical products, which have more clearly defined our understanding of disease processes and have provided significant advances in the treatment and prevention of major illnesses. Its relationship with the medical profession is important to us and to our patients. The most thoughtful writer on this quite complex multi-faceted topic, David Blumenthal, published a nice review in October last year in the New England Journal of Medicine, in which he wrote:

> "On display in the relationship between doctors and drug companies are the grandeur and weaknesses of the medical profession - its noble aspirations and its continuing inability to fulfill them. Also on display are the power, social contributions, and occasional venality of a very profitable industry whose products contribute in important ways to health and longevity ... but that at times employs methods that are deeply troubling and even criminal."

He highlights the potential conflicts between two legitimate institutions, the medical profession and the industry. Both have great virtues, both are largely well-intentioned, but there are inevitable tensions. At times, the behaviours that arise from those relationships are undesirable,

unethical and, in some cases, illegal. The negative impacts of these have been felt in the last few years. I am going to look at some of these as a background, not making any judgment about who is at fault, but just recording the fact that they occurred.

What is driving this relationship?

What Blumenthal says, very much from an American perspective, is that the renewed attention to this relationship is being driven by three major factors: the rising cost of drugs, the costs of legal settlements and the embarrassment following the disclosure of confidential documents which reveal the extent to which information was withheld from the profession and the public. In this country, the rising cost of drugs falls largely on the Pharmaceutical Benefits Scheme, but in the United States, it falls on private insurers and on individual patients. Increases in drug expenditure have generally risen at a rate substantially higher than the growth in overall health spending and have created problems in funding. We now have drugs for treating quite large numbers of patients at a cost of $20,000 to $30,000 per patient per year. In my hospital, the average cost of a hospital admission (which we used to regard as very expensive) is a fraction of the annual cost of some of these drugs. You could buy a rather nice new car each year just on the acquisition costs of one of these medications.

A second factor, particularly in the United States, is massive settlements of legal (mainly anti-trust) cases, tending to centre, as you would expect, around organised health care, rather than on individual physicians. These have involved large organisations, such as health maintenance organisations and the federally funded programs, Medicare and Medicaid. The corrupt and anti-competitive behaviour uncovered by these investigations has led to penalties of up to a billion Australian dollars. These have been some of the largest penalties in the history of corporate crime. Of the top ten corporate crimes listed regularly, I think six involve pharmaceutical companies. Other legal cases have come down to the level of police breaking into doctors' surgeries to find evidence of corrupt behaviour. There has been a great deal of mutual embarrassment at the public disclosures that followed these events. In consequence, the industry has been seen in a progressively more negative light, particularly in the United States. This has not been helped by instances of serious drug toxicity with drugs like the COX-2 inhibitors, (Vioxx being the trade name of one) and the perceived problems with some of the new antidepressant drugs. I am not quite sure why there has not been a greater media reaction in Australia.

The widespread publicity

A number of well-publicised incidents have involved hundreds of thousands of patients. I don't mean hundreds of thousands were harmed, but hundreds of thousands have taken those drugs, with, potentially, a large number of serious events, ranging from heart attacks to suicides. While we accept the inevitability that efficacious drugs will cause harm, the punitive component of the legal damages awarded so far has been because of a lack of disclosure on the part of the companies. The companies have been seen to be culpable in that they had the knowledge, and, like the tobacco industry, they hadn't made that information clear. They knew (say) that Vioxx caused heart attacks; they knew that, under certain circumstances, selective serotonin re-uptake inhibitor antidepressants could cause suicidal ideation. It is that knowledge, and the subsequent failure to act, that have darkened the picture.

The other very significant event occurred in the 1990s, when thirty-seven drug companies decided to take Nelson Mandela to the High Court in South Africa to try to overturn the

Medicines and Related Substances Act. This sought, amongst other things, to bring cheaper drugs to the people and to allow a large amount of generic substitution. The companies were very unwise to try to block it, perhaps not realising that the first respondent in that court action was Nelson Mandela himself. I remember receiving the affidavit for that case. When one saw Mr Nelson Mandela as the first respondent, lined up against thirty-seven drug companies, you knew that this would not go anywhere.

Some US Statistics

I will now move along and deal with some hard facts relating to the extent of the industry's investment in marketing and hence of its relationship with the medical profession, based on figures from the United States. When preparing a review we looked at the data from quite a large number of multinationals. More than 30 percent of their revenues are consistently spent on 'marketing and administration'. They never separate these out, but you can be sure that most of it has gone on marketing. In the United States, one company will spend more on marketing one antihistamine drug to the profession and to the public than the Coca-Cola company spends on all of its product marketing. That is the size of this endeavour.

They spend between $8,000 and $15,000 annually on contacting each doctor in the country. Nationwide, one representative will service up to five physicians. This is a huge business with huge numbers of staff. Shareholders might think that the money could sometimes be put to better use.This is probably the most comprehensive list of their marketing activities, published by Ray Moynihan two years ago in the British Medical Journal..

- Face-to-face visits from drug company representatives
- Acceptance of direct gifts of equipment, travel or accommodation
- Acceptance of indirect gifts, through sponsorship of travel
- Attendance at sponsored dinners and social or recreational events
- Attendance at sponsored educational events, continuing medical education workshops or seminars
- Attendance at sponsored scientific conferences
- Ownership of stock or equity holdings
- Conducting sponsored research
- Company funding for medical schools, academic chairs or lecture halls
- Membership of sponsored professional societies and associations
- Advising a sponsored disease foundation or patients' group
- Involvement with or use of sponsored clinical guidelines
- Undertaking paid consultancy work for companies
- Membership of company advisory boards of 'thought leaders' or 'speakers' bureaux'
- Authoring 'ghostwritten' scientific articles
- Medical journals' reliance on drug company advertising, company purchased reprints and sponsored supplements

The contentious areas

I want to highlight a few of those which are clearly contentious:

- acceptance of gifts or equipment;
- travel support;

- attendance at sponsored educational events-the way that education is framed around the interests of the company, thus affecting the perceived value of drugs discussed in an educational setting;
- ownership of stock equity holdings; we haven't found this so much in this country, but it is quite a big issue in the United States. The doctors may have a large investment in the company that makes the drugs they are prescribing;
- undertaking paid consultancy work for companies: open-ended arrangements that sometimes involve payment, such as a US$50,000 annual retention for a senior cardiologist to be available to 'consult' or lobby for the company;
- membership of company advisory boards, which usually assist them to position a product, in terms of its regulatory decisions, (how to approach the FDA, or the TGA in this country) and also how they are going to sell this product to the profession; which buttons to press when you want to argue that this new anti-hypertensive or anti-cancer drug is a real winner and should be prescribed. You need people who understand the thinking of the profession to make that successful; and
- less frequently, but important, is the practice of authoring ghost-written scientific articles. That is where a study is done with industry money; it may involve the clinician in recruiting patients into the study, but the clinician does not analyse the data, nor actually write the manuscript. It is authored by a competent medical writer. The clinician, who has really had nothing to do with the writing of the paper, puts their name on it and the medical writer doesn't.

So there are a lot of different relationships, many of which are grounds for concern. Let me say, however, that there are positive aspects to these relationships. Governments and non-government organisations do not have a good history of providing us with new drugs, although they may fund the early research. New drugs tend to come from private industry, from the patented drug industry, usually trans-national corporations; these drugs have to be trialled and be developed in the clinical workplace, and, as clinicians, we have to work with those companies. So there is much good coming out of those relationships.

Entanglement: multiple open-ended relationships

The term 'entanglement' has been used by a number of researchers. We have used it recently in a paper in the Archives of Internal Medicine (Nov 28 2005;Vol 165(21):2493-6). We were interested in the fact that the development of one tie between medical specialists and drug companies often leads to other ties. These might be open-ended, with some sort of continuing commitment or obligation, whether conscious or unconscious. There is friendship and even a degree of socialisation in some of these relationships. Bear in mind that public hospitals can be quite hostile work environments with a lot of stress. So going to a nice hotel and meeting some rather nice people who wine and dine you, is a welcome relief. While there is nothing illegal or actually immoral about that, you can see how this leads to closer ties.

Medical specialists can be involved in an advisory panel with other senior clinicians in the area. You can meet them and communicate with them on a one-to-one level. That may be harder in a hospital setting or within a professional society. There is a blurring of boundaries with our responsibilities to patients. Over time, through these processes, those obligations start to shift. Through repetitive contact, we start to make decisions more in the interests of the company than of our patients.

The outcomes of these forms of engagement have been well documented by some fairly rigorous studies. Doctors' clinical judgements are affected by those relationships. Although the majority of doctors feel that they are not affected, most think that their colleagues are! Prescribing behaviour is changed by contact with the industry. It has been shown repeatedly in the case of face-to-face detailing, from attending sponsored seminars, and even from academic 'grand rounds' in teaching hospitals, where a particular commercial product has been mentioned in the presence of a representative of the industry. When you look at subsequent prescribing (based on data or self-reporting) you find a higher occurrence of the prescribing of that particular drug. The US studies have been consistent and quite unambiguous in showing large effects. The other side to the argument is that industry wouldn't do it if it weren't effective in changing our prescribing behaviours.

The Australian experience

I want now to shift to Australia to examine the current situation and what might be done to change it. To a degree this involves a series of perverse behaviours. Dr Peter Mansfield, an Adelaide GP and director of MaLAM (Medical Lobby for Appropriate Marketing), now Healthy Scepticism [http://www.healthyscepticism.org/]), has pointed out that drug companies are actually rewarded consistently for doing the wrong thing. I will examine some of these perverse influences before reviewing Australian data.

The inappropriate promotion of drugs

I served on the Pharmaceutical Benefits Advisory Committee for several years. When we listed a drug at an agreed price for a well-defined group of patients, the company would sometimes promote that drug for a much broader set of clinical indications than listed in the Pharmaceutical Benefits Scheme. We used to call it 'leakage'. For instance, a drug might be listed for severe oesophageal ulceration, but it would get widely used for symptomatic oesophageal reflux (acid reflux), and the company could actually legally promote the drug for a much broader set of indications. So the PBS listing, governed by the National Health Act did not prevent a company promoting the use of the drug for a wider set of indications than were permitted by the Therapeutic Goods Act. That is a problem with having two sets of legislation. The companies are able to sell, at the agreed price for a more severe clinical condition, at the margins of its appropriate use, a much larger amount of the drug. It is essentially a windfall for them. It is perverse in that we are not rewarding outcomes, we are rewarding sales and their ability to promote the product. The financial implications of that behaviour are huge.

The other aspect is education itself. Much of post-graduate medical education has been handed over to the industry. So there are some more very strong perverse influences.

'Evergreening'

Some of these perverse behaviours can be traced to our current system of patent protection. All members of the World Trade Organisation (an increasingly large part of the world) have set minimum levels of patent protection, generally providing 20 to 25 years of marketing exclusivity for a specific drug. The system was designed to encourage innovation and financial risk-taking in research. However, once a company gets 20 years of exclusive marketing, it is actually encouraged to take a low-risk track of making minor modifications to the molecule they have already sold for the last 10 to 15 years. They make a minor alteration to the drug and persuade the Patents Office, which appears not to be hard, that this is 'novel'. They then get a patent for another 20 years. Of course, the development track and costs for that new, modified molecule are

much less than those for the original work. They are rewarded by getting full patent protection. Then they can try to block the entry of cheaper generic equivalents and sell their own drug at a higher price.

So the profitability of what we call 'me too' drugs is really very high. Their development costs are relatively low, the time for development is quite short, they get full patent protection. They are often drugs for very common conditions: heart disease, cholesterol, acid reflux, erectile dysfunction and asthma, where there are very large markets and where it pays to spend a lot on promotion. Promotion then becomes the largest part of the company's business.

Marketing becomes the company's dominant activity

This has been well-documented in the United States. The industry on average has been reducing the numbers of researchers, while increasing the number of marketers and lawyers; they need lawyers to defend their patent actions. So they become companies that invest in and rent out intellectual property. It is not that they don't do research, but their corporate business has shifted. The system rewards this perverse behaviour.

The other point is that health care is not organised in this country; it is disorganised. There are several thousand individual small medical businesses. So the industry is forced to deal with a very large number of clients. If we had only one health system or four or six, then big Pharma would deal with them as large buying entities. Instead, it has to deal with 10,000 small businesses and send an army of salesmen out there to make sure that we doctors are aware of their products. So, again, the companies are encouraged by the system to undertake an awful lot of marketing.

Of course, one shortcut is just to market straight to the public, which is occurring in the United States and New Zealand, but not in Australia. Of course, to a degree it is happening everywhere, through the world-wide web.

When examining these perverse behaviours, looking for perpetrators as criminals is a waste of time. The people involved are not immoral. They work in a system that encourages the wrong sorts of behaviours. It does not reward health outcomes; it does not reward companies for making people better; it rewards them for selling their products. Of course, along the way, there has to be a demonstration of evidence of efficacy and safety, but ultimately, once you get into the market place there is a huge reward for doing the wrong thing.

What contacts does the industry have with Australian doctors? How do they compare with studies overseas?

To address this, I wish to review a survey we did of medical specialists. By that I mean doctors who have completed the higher examinations of the Royal Australasian College of Physicians and who are practising in one or other of the recognised divisions of 'internal medicine'. Surgeons, anaesthetists, radiologists, pathologists, psychiatrists and other specialists are not included in the term 'medical specialists'. The study group was led by Prof Ian Kerridge (haematologist and bio-ethicist) and comprised clinicians, population health researchers and behavioural scientists, including a senior member of one of Australia's leading research-based pharmaceutical companies. I won't speak much to the methodology. Some of it has been published, some of it is in the press; most of it was standard. Details are at http://www.mja.com.au/public/issues/182_11_060605/hen10805_fm.html. This study is not unique. It is just the largest recent study done in Australia.

The basic statistics are that we surveyed 2,120 medical specialists, of whom 823 completed a comprehensive questionnaire regarding all aspects of their relationships with the pharmaceutical industry. The first set of results concerns gifts:

Item offered	Number & Percentage offered (N = 823)	Number & Percent offered who accepted
Food	792 (96%)	761 (90%)
Items for the office	777 (94%)	702 (90%)
Items for personal use	421 (51%)	240 (57%)
Journals/textbooks	412 (50%)	240 (58%)
Reimbursement of travel	320 (39%)	224 (77%)
Payments (honorarium, retainer, salary, trust funds)	311 (38%)	247 (79%)
Equipment	146 (18%)	87 (60%)
Grant/s for untied financial support	73 (9%)	51 (70%)

Gifts are the very essence of these contacts. I use the word 'gift' in a generic sense. It is not just pens or mugs; it is anything that potentially confers a benefit to the recipient. Let me say again that this is largely an activity of the patented medicines industry; gifts are not commonly offered by the manufacturers of generic drugs, who are (or should be!) working on smaller margins. They don't promote their products very heavily and they don't develop gift relationships.

There are some familiar items there, ranging from food through to equipment and grants. The really common gifts are, as expected, food, items for the office, some items for personal use. We even found boxer shorts with a big 'V' on them. You guessed right if you thought it advertised an item for personal use. Journals and text books rated lower: 39% of respondents reported-in the last 12 months-offers of reimbursement for travel. Nearly 20% had received an offer of equipment in the last year. This can range in value up to several thousands of dollars. Some untied grants were quite large; it is not absolutely clear what they were for.

The reported acceptance rate for these gifts was generally high. It is a little depressing that the lower acceptance rates included journals, text books and equipment that might actually have been quite useful.

Attendance at meetings

The next chart is slightly more complex because it includes a range of activities related to meetings. I will make some general points: the majority have received such invitations to meetings. They included educational meetings with company promotion, accredited continuing medical education (CME) meetings, and even straight product launches. Three quarters had received invitations to the latter, where there was no purpose other than the commercial launch of a new product.

Item offered	Number & percent offered (N = 823)	Number & percent of those offered who accepted	Number & percent of those offered who accepted as speakers	Number & percent of those offered who accepted as audience
Invitations to sponsored symposium	673 (84%)	358 (53%)	87 (21%)	332 (79%)
Invitations to educational meetings with promotion	628 (79%)	412 (66%)	109 (24%)	343 (76%)
Invitations to educational meetings with no promotion	607 (76%)	473 (79%)	159 (28%)	392 (71%)
Invitations to CME meetings	604 (75%)	463 (77%)	139 (27%)	379 (73%)
Invitations to product launch meetings	608 (75%)	299 (49%)	82 (24%)	260 (76%)

Product launches have become infrequent in the last few years because, as you may have noticed, there are not many new products around. Industry is not producing many new drugs. It is a worry that the introduction of new drugs has fallen by half since the mid-1990s. This has nothing to do with rising regulatory standards. The pipeline has diminished, hopefully temporarily. The acceptance rates are for invitations are fairly high, even for straight commercial product launches: about 50%.

Look at the two right-hand columns, "What was your role at this meeting? Were you there as a speaker or were you there as a passive member of the audience?" Passive learning can be a good thing, but we see that some of these meetings are unashamedly promotional and commercial. Despite that, three quarters of those respondents are saying "I was in the audience, sitting there listening". It doesn't involve a great amount of participation And the educational content is questionable.

Support for interstate or international travel

Now we look into one of the more contentious areas. Let's pick on some activities that I think everybody agrees are inappropriate: you are travelling, your partner is going with you and the company is paying for both of you. As far as I am aware, all organisations, including Medicines Australia, the Colleges and the AMA agree that this is wrong. However, somewhere between 5% and 15% of the medical specialists reported such offers in the last year (for national or international travel). These trips were not often being made as a speaker but as a passive member of the audience.

Item offered	Number & percent offered (N = 823)	Number & percent of those offered who accepted	Number & percent of those offered who accepted as speakers	Number & percent of those offered who accepted as audience
Travel support to a national or international conference	428 (52%)	282 (66%)	70 (22%)	243 (78%)
Travel to conference in Australia for Dr	324 (40%)	177 (55%)	45 (24%)	146 (76%)
Travel in Australia which includes partner	123 (15%)	30 (24%)	6 (20%)	**24 (80%)**
International travel to conference for Dr	263 (32%)	186 (71%)	44 (22%)	**154 (78%)**
International travel which includes partner	35 (4%)	13 (37%)	1 (8%)	**12 (92%)**

How much is Big Pharma spending on these "gifts"?

The next table presents the estimated dollar values for some of these activities.

$10,000	Overseas conference support as attendee
$10,000	Travel to international meeting
$10,000	Travel subsidy
$10,000	Sponsorship to attend/present at international meeting flight/hotel
$12,000	Travel and accommodation to USA
$12,000	Overseas travel support to a conference
$15,000	Business class return trip to Hamburg for industry conference
$15,000	Attendance at international meeting
$18,000	Sponsorship of clinical meeting 3x $6,000
$40000	Air travel to attend meetings where I have been speaking

One person reported, in the last year, receiving offers of $40,000 worth of air travel to attend meetings.

Doctors asking Big Pharma for gifts

The other side to this story is that the profession quite often requests gifts from the industry (next table). The dollar values of gifts requested can be large. Perhaps I should emphasise that the $60,000 was requested as a donation to a hospital department in return for time spent seeing representatives of a company. It is difficult to find a legitimate reason for such an offer.

$20,000	Specialist society meeting function
$30,000	Conference travel and accommodation x2
$30,000	Nursing positions
$35,000	Sponsorship of international congress
$40,000	Symposium for costs of international speakers x2 and national speakers x5
$60,000	Donation to the department in return for time spent seeing reps
$75,000	Salary for nurse co-ordinator
$80,000	Sponsorship of Bone and Joint decade in Australia (as National Co-ordinator)
$80,000	Nursing support for patient care
$100,000	As part of a local organising group for a national scientific meeting

Our collection of items given to doctors

We were interested in what types of gifts actually turned up in doctors' mail. We recruited 51 of the specialists who participated in the other part of the survey. We gave them a 'bin', a special receptacle and said, "Don't bother analysing it. Just stick everything you get into the bin. We will collect it. We will analyse it and we will give it back to you." (The giving back was actually harder than the taking: they didn't want this stuff back.) Over an eight week period, 51 specialists received, on average, 42 gifts: five gifts per week. A lot of them were simple items: minor office equipment, pen sets.

Gifts: 'Bin Collection'

- 51 randomly selected specialists collected all material over 8 weeks
- 2,117 items - 42 gifts/respondent (5 gifts/week/person)
- Promotional items (1,052); drug samples (420); office gifts (258); invitations (174); clinical practice aids (148); personal gifts (65)

Drug samples

Drug samples are regarded as quite valuable. Doctors hand the patient the 'starter pack' of the drug, and the patient has nothing to pay. Of course, that is a 'seeding' arrangement for the

industry. Their hope is that the patients will stay on the drugs and that they will then be prescribed through the PBS. Doctors like drug samples, because they are convenient, patients like them because they are free and don't involve going to a pharmacy. Companies like them because they are a cheap way of promoting their products.

Public and professional perception of these 'gifts' to doctors

We asked doctors whether they agreed or strongly agreed with the statement that it was appropriate to accept a range of gifts with various monetary values. These ranged from items of potential clinical value: patient leaflets, drug samples, equipment, (sometimes of substantial monetary value)-to items clearly of no direct clinical benefit, such as theatre tickets, a dinner without educational activity, a lap-top computer, a refrigerator (not for drug samples), equipment for the staff tea room, and so on. You will see that there is a fairly clear ranking in the minds of doctors. They are not much worried by low monetary value items. Where there is a greater monetary value or it is clearly purely social and has nothing to do with the practice of medicine, then their approval rates were a lot lower.

With the public, however, for methodological reasons, we asked the question in a slightly different way. There is a much higher general acceptance: up to two or threefold higher than for doctors. They were less influenced by the dollar values than were the doctors. The public was less impressed with dollar values if they could see a benefit to them, as patients, from the 'gift'. They made it very clear that, if it was a spirometer or a blood pressure machine, or something that was clearly going to educate their doctor, then it was quite appropriate.

	Percentage of General Public agree: 'Sometimes' + 'Always' appropriate to accept	Percentage of Medical Specialists 'Agree' or 'Strongly Agree' appropriate to accept
Patient leaflets ($10)	96	63
Drug samples ($100)	92	75
Lunch for doctor and staff+ ($100)	83	25
Spirometer/ECG Machine ($2500)	80	26
Stethoscope ($100)	80	33
Conference with partner ($1200)	76	20
Conference doctor only ($1000)	75	40
Dinner & Lecture with partner ($100)	60	44
Chocolates ($10)	54	36
Electric scales for patients ($100)	35	50
Computer for surgery ($2500)	34	8
Dinner with partner social ($100)	34	28

Big Pharma, practising doctors and research

We also examined research relationships with the industry.

- 823/2,120 medical specialists completed questionnaires;
- 49% of salaried physicians and 33% of private physicians reported involvement in industry-sponsored research in the previous 12 months;
- 216 had been approached by industry, compared with 117 who had approached industry; and
- 8.6% or respondents (21% or those with research relationships) reported potentially serious breaches of research integrity

About half of the salaried physicians and about a third of the private physicians had some research relationship with the industry in the last 12 months.

This is two-way traffic: 216 had been approached by industry, but 117 had approached the company. About 8.6% of respondents (equivalent to nearly 20% of researchers) reported that there had been potentially serious breaches of research integrity. These breaches took the form of delayed or non-publication of data, particularly data which they felt reflected negatively on the product. Our respondents felt that the information should have been in the public domain, but it hadn't got there or got there very late. There were also instances where data had been modified and where the wording of manuscripts had been changed to make a drug look better.

'Entanglement' of Australian medical specialists.

I mentioned the question of multiple open-ended ties earlier in this talk. In analysing our data, we were interested in whether or not a research relationship with industry leads to other ties, such as being on an advisory panel, holding shares, or being offered travel support to an overseas conference. We were particularly interested in the development of multiple ties.

Specific interactions with industry ('ties')

Acted as member of an advisory panel	193 (23%)
Acted as an expert speaker about a product	131 (16%)
Provided input into professional educational materials	133 (16%)
Acted as paid consultant to industry	46 (5%)
Held shares in pharmaceutical company	56 (7%)
Offered payments (e.g. honoraria)	313 (38%)
Offered item or activity of value >$AU500	418 (51%)
Offered travel support to a national conference	328 (40%)
Offer travel support to an overseas conference	259 (31%)

When we looked at the number of *additional* ties beyond the existing research relationship, there is a clear gradient: the researchers were much more likely than non- researchers to seek to develop multiple ties. People with six or more ties have a pretty substantial relationship on multiple levels with major companies; the odds of this are 42 times higher in those in research compared with those who did not report a research relationship. There is a very strong multiplier effect of those research relationships.

Number of industry ties	Research relationship with industry	No research relationship	Odds Ratio (95% CI)
0	32	181	1.0 (reference)
1	42	107	2.2 (1.2, 3.8)
2	67	92	4.1 (2.4, 6.9)
3	58	52	6.3 (3.5, 11.1)
4	58	33	9.9 (5.4, 18.2)
5	44	15	16.5 (7.8, 35.6)
6+	37	5	41.8 (14.5, 143. 4)

The attitudes of the medical specialists

Understanding attitudes is essential to any analysis of the behaviour of doctors. The social scientists we worked with did some in-depth interviews on the attitudes of the medical specialists. The analysis of the transcripts identified some clear-cut qualitative differences between groups with differing attitudes.

In-depth interviews with 50 medical specialists

- 10% were 'avoiders'
- 40% were 'ambivalent engagers'
- 50% were 'confident engagers'

They categorised about half into what they called 'confident engagers', who felt they could engage with the industry and not be influenced. Somewhat fewer were 'ambivalent engagers'. They felt "I have to do this, but I have some reservations". Ten per cent said, "No, I am not really having anything to do with these relationships at all".

Some verbatim comments

I will end this presentation with some quotes from the qualitative study: At one end of the spectrum: "It's just corruption"; at the other end: "Everybody else does it". To get a sense of the ambivalent engagers: "I don't actually have any outright opposition towards companies because of the role they have in research and development", and "The conflict I have is (with) their ability to influence what I prescribe". This highlights the tension felt by this ambivalent group. A quote from a confident engager: "They sponsor medicine, so the least I can do is give them ten or 15 minutes of my time a couple of times a year as a trade-off", "I have been offered several overseas trips, etc.". Confident engagers feel, no matter what emerges from analysis of their interviews, that their thinking about their behaviour is not going to be influenced by the opinions of people in the social sciences.

Conclusions

In Australia, there are high levels of engagement between medical specialists and the pharmaceutical industry. Not surprisingly, it is probably not at the levels seen in the USA and probably does not involve the very large sums of money seen there. I have tried to describe some of the types of engagement observed in a study of Australian medical specialists. In concluding, there are three aspects that I would like to highlight:

- *Gifts*: I would like to highlight generous travel support, particularly when it involves partners; but also any significant international travel where the recipient is just going to

be sitting in the audience. As doctors we are not badly paid and I don't think that drug companies should be paying for our travel or our education.

- *Research relationships*: these are necessary and desirable so long as they are carefully managed. But they can lead to multiple open-ended ties. Individuals can become enmeshed in the company's activities and interests. Maybe ethics committees should identify this and draw limits around the other relationships developed by researchers.
- *Attitudes*: despite the publicity given to relationships between doctors and drug companies in the last few years, qualitative research indicates that a large proportion of medical specialists still believe that they can engage with the industry without ill effects. This is despite a large number of studies showing clear-cut effects, and despite the views of the doctors themselves that their colleagues are likely to be affected, but not they themselves.

How do we respond to all of this?

What are the correct responses to this? The professional organisations have all developed guidelines and most have been tightened up in the last year or two. These are valuable in setting standards, but I don't think that guidelines alone are sufficient.

It is inevitable and desirable that medical specialists work with the pharmaceutical industry. Personally, I would prefer that the majority of these relationships were in the form of contracts. Such contracts would lay out the obligations of both parties, would be open to scrutiny and could be supervised by an independent body. A contract would not proscribe certain activities but if (for instance) you are going to a cardiology meeting in Alice Springs to sit in the audience, I think that your professional organisation should know about that. I think you and the company should sign a contract, so that it is very clear what you are expected to do and what the company's obligations are.

The other more challenging question is whether we can reward companies differently, in other words, not reward them only for the volume of sales. This is a whole area of academic enquiry that is too extensive to review here. A closely related concern is that the patent system for drugs has perverse effects. It has been proposed by Love and Hubbard [http://www.ita.doc.gov/td/health/phRMA/Consumer Project on Technology Response2.pdf] that if we repealed patents and had an international research and development treaty, then we could pay the proportion of drug expenditure that goes into research and development into a large fund; companies would compete for this fund in return for researching drugs that society needs.

In closing, let me say I think there are a number of problems with doctor-company relationships in Australia. Current solutions are probably not adequate, but at least the causes of the behaviours and of the attitudes are now well understood. I think it is probably time to move away from the moralising position which so many of us have adopted. These activities have been going on for a long time and the behaviours are quite resistant to change. In seeking solutions, we cannot stop at guidelines promulgated by the professional organisations. We have to move further, and that includes looking at the whole system of organised health care and the removal of some of the perverse incentives that currently exist for companies and for physicians.

Acknowledgements

I am grateful to many colleagues who contributed to the research described in this talk. I am simply representing the work of others, but opinions expressed here should not be attributed to anyone else. The work described here was supported by the NHMRC.