Medical law reporter

Editor: Thomas Faunce*

THE VIOXX PHARMACEUTICAL SCANDAL: PETERSON v MERKE SHARPE & DOHME (AUST) PTY LTD (2010) 184 FCR 1

In early March 2010, Federal Court Justice Jessup in Peterson v Merke Sharpe & Dohme (Aust) Pty Ltd (2010) 184 FCR 1 ruled that Merke Sharpe & Dohme Pty Ltd had produced a defective product contrary to the Trade Practices Act 1974 (Cth), the anti-arthritic drug Vioxx. Promoted as relieving arthritic pain without the side effect of gastric ulceration, the drug also doubled the risk of heart attack in those prescribed it. The court also heard that the manufacturing company had engaged in misleading practices to promote the prescription and usage of Vioxx, including "fake" journals and guidelines to "drug reps" that minimised the adverse cardiovascular risks. The manufacturer had already settled a class action in the United States for more than US$7 billion for those harmed by the drug but this was the first such case to be decided in Australia. The court awarded the applicant, Graeme Peterson, A$300,000 in damages. This column examines this judgment and analyses evidence there presented that Merck may have misled the scientific community, the medical profession and Australia's drug regulation system to get Vioxx on the market and keep it there. It considers whether the case reveals the need for more rigorous post-marketing surveillance and other changes to Australia's drug regulatory system, including a replacement of self-regulation in pharmaceutical promotion with a United States-style system of rewarded informant-led criminal penalties and civil damages claims.

INTRODUCTION

Peterson v Merke Sharpe & Dohme (Aust) Pty Ltd (2010) 184 FCR 1 was a representative proceeding under Pt IVA of the *Federal Court of Australia Act 1976* (Cth). The applicant, Graeme Robert Peterson, alleged that the consumption of the medication rofecoxib (whose commercial brand name was Vioxx) from May 2001 contributed materially to the onset of a heart attack he sustained in December 2003. The first respondent was Merck Sharpe & Dohme (Aust) (MSDA) and the second respondent its United States parent company Merck & Co Inc (Merck).

Merck developed Vioxx in the 1990s as a member of a new class of non-steroidal anti-inflammatory drugs (NSAIDS) derived from the rofecoxib molecule.[1] This new drug was supposed to enable sufferers of arthritic pain to consume the pain reliever without experiencing the gastrointestinal side effects (including gastric ulceration) often found in older drugs designed for this purpose.[2] The March 2000 VIGOR (Vioxx Gastrointestinal Outcomes Research) trial had suggested that there was an elevated cardiovascular risk (particularly acute myocardial infarctions or heart attacks due to spasm of the coronary arteries) associated with the consumption of Vioxx.[3] It demonstrated "a five-fold higher incidence of myocardial infarction in the rofecoxib group compared

* BA LLB (Hons), B Med, PhD; Australian Research Council Future Fellow. Associate Professor, ANU College of Law and Medical School.

Correspondence to: Fauncet@law.anu.edu.au.

[1] Avorn J, "Dangerous Deception" (2006) 355(21) NEJM 2169.

[2] Hampton T, "Experts Point to Lessons Learned from Controversy over Rofecoxib Safety" (2005) 293(4) JAMA 413.

[3] Bombardier C, Laine L, Reicin A et al, "Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis" (2000) 343 NEJM 1520.

to the naproxen".[4] The identified difference in cardiovascular risk, however, was attributed to "a cardioprotective effect of naproxen, rather than a cardiotoxic effect of rofecoxib", an interpretation which was also made in several later studies.[5] Vioxx was marketed and sold in Australia by MSDA between late 2000 and September 2004. In early 2000 Merck commenced a major placebo-controlled clinical trial of Vioxx (the APPROVe trial) among patients with a history of colorectal adenomas. It was the results of the VIGOR and APPROVe trials that were to be pivotal to the result in this case.

In December 2005 Curfman et al[6] published a critique of the VIGOR trial prompted "by evidence that the VIGOR article did not accurately represent the safety data available to the authors when the article was being reviewed for publication" and that more than four months prior to publication "at least two of its authors were aware of critical data on an array of cardiovascular events that were not included in the VIGOR study". Of specific concern was the fact that three myocardial infarctions were not included in the data submitted to the NEJM because they were reported after a pre-specified cut-off date for the reporting of cardiovascular events. Significantly, this date was selected by the research sponsor and was one month earlier than the cut-off date for adverse gastrointestinal events. These and other concerns relating to the data and communication of critical information culminated in the assertion that the conclusions presented in the Bombardier et al article "regarding the safety of rofecoxib were misleading" and that the cut-off date was "an untenable feature of the trial design, which inevitably skewed the results".

There were two responses to Curfman et al's expression of concern. One (from the "non-Merck authors") argued that the original article had followed appropriate clinical trial principles, the trial was performed according a pre-defined plan and "the article did not require a correction". Further, "in order that the results of clinical trials be valid and unbiased the research plan must not be changed once the randomization code is broken and the study unblinded". They alleged an independent committee charged with overseeing safety concerns had recommended to Merck that "a data analysis plan be developed for serious cardiovascular events" though at that time reportedly did not feel it appropriate to bring this issue to the VIGOR steering committee.[7] Following this, Merck developed a cardiovascular data analysis plan.

In 2004 Merck instigated a worldwide withdrawal of the drug after receiving a recommendation from the United States Food and Drug Administration (FDA) that it had detected a statistically significant occurrence of adverse cardiovascular events among patients in the Vioxx arm of the APPROVe trial which was twice that of those in the placebo arm.

Jessup J concluded that on the probabilities the applicant's consumption of Vioxx had contributed to the damage to the artery as a result of the disturbance in balance of prostacyclin (a vasodilator substance that inhibits blood clot formation) and thromboxane (a vasoconstrictor and hypertensive factor that facilitates clot formation) thereby leading to the formation of a thrombus or thrombi (clot or clots) which would likely cause an occlusion of major blood vessels supplying oxygen to the heart (at [772]). Jessup J found that the consumption of Vioxx had indeed doubled Mr Peterson's risk of heart attack:

> Having regard to what is now known about the relationship between the consumption of Vioxx and cardiovascular disease, and to the applicant's own condition at the time, I am satisfied that Vioxx contributed to his heart attack.

[4] Juni P, Nartey L, Reichenbach S, Sterchi R, Dieppe PA and Egger M, "Risk of Cardiovascular Events and Rofecoxib: Cumulative Meta-analysis" (2004) 364 *The Lancet* 2021.

[5] Juni et al, n 4, citing Konstam MA, Wier MR, Reicin A et al, "Cardiovascular Thrombotic Events in Controlled, Clinical Trials of Rofecoxib" (2001) 104 *Circulation* 2280; Rahme E, Pilote L and LeLorier J, "Association Between Naproxen Use and Protection Against Acute Myocardial Infarction" (2002) 162 *Archives of Internal Medicine* 1111; Watson DJ, Rhodes T, Cai B and Guess HA, "Lower Risk of Thromboembolic Cardiovascular Events with Naproxen Among Patients with Rheumatoid Arthritis" (2002) 162 *Archives of Internal Medicine* 1105.

[6] Curfman GD, Morissey S and Drazen JM, "Expression of Concern Reaffirmed" (2006) 354(11) NEJM 1193.

[7] Bombardier C, Laine L, Burgos-Vargas R, Davis B, Day R, Bosi Ferraz A, Hawkey CJ, Hochberg MC, Kvien TK, Schnitzer TJ and Weaver A, "Response to Expression of Concern Regarding VIGOR Study" (2006) 354(11) NEJM 1196.

Mr Peterson alleged that Merck knew, or ought to have known before 2004 that the consumption of Vioxx increased the risk of heart attacks and should have appropriately warned him of the risk. This formed the basis of Mr Peterson's action (and that of the group of similar patients he represented) for compensation on grounds of both common law negligence and under the *Trade Practices Act 1974* (Cth). The proceeding was transferred to the Federal Court pursuant to an order made by the Supreme Court of Victoria in April 2006. The order outlined that, in advance of all other issues in the proceeding, the following issues were to be determined (App A):

- the issues of fact and law in the claim brought by Mr Peterson in his personal capacity; and
- those issues of fact and law set out in the Schedule attached to the Order that the Court finds to be common to the claims of the group members.

This column considers the implications of this case for Australian pharmaceutical regulation. It raises questions, eg, about how a drug that had been recommended for use and designated safe by the Therapeutic Goods Administration (TGA) in 1999 was in fact harmful. It also considers implications, raised by evidence in the case, that the current self-regulatory system may be encouraging pharmaceutical companies to fail to inform doctors about all the known risks of the drugs they manufacture or to engage in a range of behaviours promoting such a product in their own interest at the expense of patients' health.

GRAHAM PATERSON'S PROBLEMS WITH VIOXX

Graham Peterson was born in June 1950. He had been a smoker but had stopped in 1980. He had had a medical checkup as part of a pre-employment process in the late 1990s which did not identify any particular problems (at [692]). While working in the Navy, he began to suffer from back pain, which he managed with anti-inflammatory medication (at [695]). A side effect of taking this medication long term was the development of some gastrointestinal pain for which he took Mylanta and had had some investigative procedures including a barium meal and a gastroduodenoscopy that identified some stomach inflammation (at [696]). He continued to manage his condition with a range of therapies, including some alternative medications like fish oil and glucosamine. Mr Peterson had met his doctor, John Dickman, while they were both in the Navy.

Dr Dickman stated to the court that, in gathering information about new drugs to prescribe for his patients, he would rely on several sources, including specialists, sales representatives, journal articles and the medical press, other general practitioners, product information and patient feedback. He said it was usual for educational meetings about new drugs to be conducted and sponsored by the manufacturer over dinner at a local restaurant. He understood that specialists speaking at these dinners were often paid by the pharmaceutical company but he assumed they would still give "unbiased" and "truthful" information about the drug. Attendance at these meetings also often gave doctors a number of continuing medical education (CME) points that are required to maintain professional registration (at [705]).

In late 1999 or early 2000 Dr Dickman attended a dinner hosted by MSDA promoting Vioxx. A local rheumatologist was speaking and Dr Dickman remembers him saying that he believed Vioxx was safer than traditional NSAIDs. Largely as a result of this specialist's endorsement, Dr Dickman decided to prescribe Vioxx to his patients (at [714]). He believed that he would have been at greater risk of being negligent if he hadn't prescribed it because it had a lower risk of inducing a potentially life-threatening gastrointestinal bleed in a patient than the old NSAIDs did (at [715]). Dr Dickman also stated (at [717]) that he recalled that during meetings with Merck sales representatives about Vioxx, "the sales representatives' emphasis was primarily on Vioxx's safety".

In May 2001 Dr Dickman prescribed Vioxx to Mr Peterson. Mr Peterson found that Vioxx provided relief from the pain without the gastrointestinal side effects he had experienced with other drugs (at [730]). In December 2003 Graeme Peterson had a heart attack. It did not occur to Mr Peterson or Dr Dickman that Vioxx could have been a causative agent in this adverse cardiovascular event. It was not until the drug was withdrawn from sale on 30 September 2004 that Mr Peterson considered that there might be a connection (at [4]). As a result of his heart attack

Mr Peterson was unable to continue his existing employment and was only able to work around 8-10 days per month because he became easily tired (at [778]). He had to give up his recreational activity of diving (at [781]).

The cardiologist who treated Mr Peterson after he suffered his heart attack identified his risk factors as hypertension, hyperlipidemia, obesity and the presence of left ventricular hypertrophy. It was agreed that he was "highly likely to have had coronary atherosclerosis that was clinically silent at the time". He was also a former smoker, male, 51 years old and was therefore at a moderate to high risk of a cardiovascular event within five years (at [764]). The cardiologists were unable to say if the consumption of Vioxx had increased the applicant's blood pressure because of a lack of data (ie blood pressure readings) taken after the administration of Vioxx (at [765]). They also agreed that, in a patient with multiple risk factors such as Mr Peterson, there was no definitive way of knowing which risk factor or combination of factors caused the heart attack (at [767]). The specialists also agreed, though, that Vioxx at least doubled Mr Peterson's risk of having a heart attack and this was based on data collected from the clinical trials but most specifically the APPROVe trial (at [768]).

Mr Peterson sought compensation from the respondents under the *Trade Practices Act 1974* (Cth) and more specifically against the second respondent (Merck) in negligence.

ACTIONS AGAINST MSDA AND MERCK IN NEGLIGENCE

Jessup J accepted the applicant's argument that Merck, as a manufacturer of a product intended for human consumption, owed a duty to intended consumers to take reasonable care to prevent the product from causing injury or loss to those consumers (McHugh J in *Dovuro Pty Ltd v Wilkins* (2003) 215 CLR 317 at 328).[8] Such a manufacturer's duty, he held (at [782]), included responsibility for ensuring that appropriate and necessary information about the product is communicated to persons who will use or consume the product, and who, it can be foreseen, may suffer loss or damage.

Mr Peterson argued that Merck had fallen short of discharging that duty by failing to withdraw Vioxx from the market in 2000 after the results of the VIGOR clinical trial became known and by failing to carry out sufficient research and investigation in response to those results. Mr Peterson also argued that the first respondent had acted negligently in relation to the ways in which Vioxx was promoted to prescribing doctors in Australia. The applicant claimed, eg, that MSDA failed to provide any or any adequate information, advice or warning on packets or labelling to the effect that the consumption of Vioxx tablets materially increased the risk of sustaining a cardiovascular condition. He alleged that no such information was provided to pharmacists, medical practitioners and other health care professionals, either in the marketing or in the distribution and supply of Vioxx (at [817]).

The respondents (MSDA and Merck) relied on three arguments to demonstrate that they had met and discharged their duty of care. Their first position was that they had complied with the TGA regulatory regime for marketing and that such approval was official recognition they had met the "quality, efficacy and safety" standards required of a prescription medicine.[9] The respondents, in what is now a standard lobbying tactic of the patented pharmaceutical industry, also maintained that the Australian prescription drug regulatory system's requirement to protect the public from harm must be tempered by the public's need to be promptly supplied with innovative new medicines. They further argued (at [790]) that it would be inconsistent with the law of negligence to impose a duty of care upon prescription drug manufacturers which required any more than that they participate in the scheme in a "bona fide" way and fulfil their statutory obligations under the scheme.

Jessup J was not impressed with such arguments. He found (at [193]), [194]) that, if they were accepted, then, provided that the pharmaceutical manufacturer complied with the statute in good faith, it

> could, it seems, engage in all manner of negligent promotion, communication or presentation without being exposed to claims of the kind that the applicant now brings … The manufacturer's obligation is

[8] And in *Graham Barclay Oysters Pty Ltd v Ryan* (2002) 211 CLR 540 at [106].

[9] *Therapeutic Goods Act 1989* (Cth), s 25.

> not, in my view, exhausted upon compliance with the statute – no more so than the motorist's obligation to take care in the driving of his or her vehicle is exhausted upon compliance with road traffic regulations: see *Sibley v Kais* [1967] HCA 43; (1967) 118 CLR 424 at 427.

The respondents' second defence was the "learned intermediary" defence which attempted to establish that the manufacturer's duty is discharged once they warn the prescribing doctor of the known benefits and risks of the product, it is then a matter for the doctor to pass this information onto the patient and thus shift the liability to the doctor. This defence has not previously been accepted in Australia and Jessup J did not believe that it offered anything more than was provided for in the existing framework of negligence law (at [796]).

The third and final defence by the respondents effectively dealt with the issue of foreseeability. On this issue Jessup J made reference to Mason J's judgment in *Wyong Shire Council v Shirt* (1980) 146 CLR 40 at 47-48:

> The perception of the reasonable man's response calls for a consideration of the magnitude of the risk and the degree of the probability of its occurrence, along with the expense, difficulty and inconvenience of taking alleviating action and any other conflicting responsibilities which the defendant may have.

Jessup J then asked: what would the reasonable manufacturer and supplier do by way of response to the risk identified? Jessup J did not think that the respondents' attempts to avoid liability by placing blame on Dr Dickman were appropriate given that, unlike a doctor and patient, the respondent drug manufacturers did not enjoy a one-on-one relationship with the consumers of Vioxx. They supplied a mass-produced product, packaged and labelled by them that should have provided a general warning (at [801]).

Jessup J found that the respondents' case was conducted without discrimination between Merck and MSDA on matters of scientific knowledge and understanding. He held (at [819]) that, on the back of the VIGOR study, it was reasonable for Merck to have undertaken a cardiovascular outcomes study, but it was not required to withdraw Vioxx from the market. The court also determined (at [820]-[823]) that MSDA should have included a warning in the product information in or around October 2000 and that the warning should have been in relation to cardiovascular risks. Jessup J held that MSDA could have notified the TGA and sent out a "Dear Doctor" letter as a way of raising awareness about the cardiovascular issues identified in the VIGOR study (at [840]). By November 2001 the product information had been amended but relying on the product information alone when the drug had been on the market for over 12 months at that point, according to Jessup J (at [849]), was insufficient. Jessup J found that Merck had a common law duty of care that meant that it should have warned Mr Peterson's doctor of the cardiovascular signal which had alerted them to a potential risk to patient safety with ongoing use of the drug and, as such, they ought not to have emphasised the safety of Vioxx.

Having established a breach of duty, Jessup J then turned to the issue of causation. This is where the applicant's case in negligence failed. The question was whether MSDA's failure to warn, and/or its emphasis upon safety, caused Dr Dickman to prescribe, and to continue to prescribe, Vioxx to the applicant, and caused the applicant to continue to consume it. Jessup J found that even if Dr Dickman had been not been exposed to the sales people making representations that Vioxx was safe, he would have still prescribed Vioxx to the patient and that Mr Peterson would have taken it (at [873]).

As a result of the applicant's failure to make out the element of causation, the case in negligence against MSDA and Merck was dismissed (at [874]). Jessup J then considered the applicant's submissions concerning alleged breaches of the *Trade Practices Act 1974* (Cth).

ACTION AGAINST MSDA FOR MISLEADING PROMOTION UNDER THE TRADE PRACTICES ACT

Mr Peterson's claim for compensation for breaches of ss 52, 75AD, 75AC, 74B and 74D of the *Trade Practices Act 1974* (Cth) involved allegations that the drug manufacturers engaged in misleading or deceptive conduct;[10] traded in defective goods causing injuries or loss to the injured individual;[11] traded in goods not reasonably fit for purpose;[12] and traded in goods of unmerchantable quality.[13]

Section 52(1) of the Act provides as follows:

> (1) A corporation shall not, in trade or commerce, engage in conduct that is misleading or deceptive or is likely to mislead or deceive.

The applicant's central case here was that the Vioxx promotional product information did not contain any adequate information, advice or warning to the effect that the consumption of rofecoxib or Vioxx tablets materially increased the risk of suffering the adverse cardiovascular conditions and that MSDA knew or ought reasonably to have known that the consumption of rofecoxib or Vioxx tablets materially increased the risk of suffering the (pleaded) cardiovascular conditions. In more detailed terms, the applicant alleged that in packaging and labelling, or in marketing, or in distributing and supplying for sale Vioxx tablets, MSDA failed to provide any adequate information, advice or warning on packets of Vioxx tablets or the labelling thereon to the effect that the consumption of Vioxx tablets materially increased the risk of suffering the adverse cardiovascular conditions.

The respondent's case here was that the conduct alleged by the applicant was not made in trade or commerce as required by s 52 of the Act. They relied on *Concrete Constructions (NSW) Pty Ltd v Nelson* (1990) 169 CLR 594 in which it was held that that the section was concerned with the conduct of a corporation towards persons with whom they may have commercial or trade dealings and this relationship did not correspond with that relied upon by the applicant (at [885]).

The respondents then claimed that their marketing representations were largely directed at prescribers (doctors) and providers (pharmacists) of the medication and were not directly aimed at consumers involved in trade and commerce in Australia. Ms Dobson gave evidence about the MSDA marketing team (at [886]):

> The role of MSDA's marketing team is to make prescribers aware of the features of its prescription medicines so that they will prescribe them to the broadest group of suitable patients. This is good for patients and good for MSDA, which is a for-profit company. This was our objective with Vioxx.

However, the MSDA sales representatives did use the product information in their "sales pitch" to doctors and this would, Jessup J held (at [887]), be considered conduct in trade or commerce. He relied (at [604]) on the High Court's statement in *Concrete Constructions* that:

> Such conduct includes, of course, promotional activities in relation to, or for the purposes of, the supply of goods or services to actual or potential consumers, be they identified persons or merely an unidentifiable section of the public.

LIABILITY FOR DEFECTIVE PRODUCTS (SECTION 75AD) AND SAFETY (SECTION 75AC)

Section 75AD of the Act provides:

> If
>
> (a) a corporation, in trade or commerce, supplies goods manufactured by it and
> (b) they have a defect; and
> (c) because of the defect, an individual suffers injuries;
>
> then

[10] *Trade Practices Act 1974* (Cth), s 52.

[11] *Trade Practices Act 1974* (Cth), s 75AD.

[12] *Trade Practices Act 1974* (Cth), s 74B.

[13] *Trade Practices Act 1974* (Cth), s 74D.

(d) the corporation is liable to compensate the individual for the amount of the individual's loss suffered as a result of the injuries; and
(e) the individual may recover that amount by action against the corporation; and
(f) if the individual dies because of the injuries – a law of a State or Territory about liability in respect of the death of individuals applies as if
  (i) the action were an action under the law of the State or Territory for damages in respect of the injuries; and
  (ii) the defect were the corporation's wrongful act, neglect or default.

The applicant submitted that Vioxx tablets were goods manufactured by MSDA, that the goods had a defect and that the group members suffered injuries because of the defect. To establish that Vioxx tablets had a "defect", the applicant invoked s 75AC alleging that the safety of Vioxx tablets was not such as persons generally were entitled to expect. Under s 75AC the defect must exist in the *particular* goods which cause injury to the individual (at [912]). Section 75AC(1) provides that goods have a defect if their safety is not such as persons generally are entitled to expect. In determining this issue, regard is to be given to all relevant circumstances (s 75AC(2)). Hence there were two questions for the court (at [913]):

- what was the safety of the goods; and
- was that safety such as persons generally are entitled to expect?

The applicant submitted that the consumption of Vioxx materially increased the risk of suffering adverse cardiovascular conditions. Jessup J rejected this allegation for all of the "Vioxx cardiovascular conditions", with the exception of myocardial infarction. His Honour held that, across a population, the consumption of Vioxx did involve an increase in myocardial infarction; however, he noted (at [916]) that the question of "whether there was a risk in the case of a particular patient, and how troubling that risk was, were matters which involved a professional judgment by his or her practitioner".

In the absence of the provision of any information, advice or warning, the risk of myocardial infarction made the safety of Vioxx less than what persons generally were entitled to expect (at [917]). The withdrawal of Vioxx from the market implied as much (at [917]). No warning as to cardiovascular results of the VIGOR trial were communicated by MSDA to the applicant's general practitioner, Dr Dickman, before at least November 2001. His Honour held that until November 2001 the safety of Vioxx (as purchased and consumed by the applicant) was not such as persons generally were entitled to expect (at [918]).

Evidence of the amendment of the Vioxx product information in November 2001 was not a factor that changed this finding. Although this amounted to a warning within the meaning of s 75AC(2)(d), MSDA had available information to the effect that, in the VIGOR trial, the myocardial infarction rate had been 0.5%, though it had not communicated this to medical practitioners "by a means no less likely to capture their attention than the means employed in October 2000": a general "Dear Doctor" letter referring to side effects (at [920]). Thus, in the context of all the relevant circumstances, the amendments were insufficient to make the safety of Vioxx such as persons generally were entitled to expect (at [921]). On the basis of this reasoning, Jessup J concluded that after November 2001, when MSDA supplied the Vioxx tablets that were consumed by the applicant, those tablets had a defect within the meaning of s 75AD of the *Trade Practices Act*.

MSDA submitted that, under s 75AK(1)(b), the goods had that defect only because they complied with a mandatory standard. This submission was rejected. Jessup J reiterated (at [924]) that

> the safety of Vioxx was less than what persons generally were entitled to expect because, as a matter of composition, the consumption of Vioxx had the potential to increase the risk of suffering a myocardial infarction, in circumstances which included the absence of any relevant information or warning communicated to the applicant's doctor. It was not because of a mandatory standard that the composition of Vioxx was as it was.

His Honour did, however, accept (at [926]) MSDA's defence under s 75AK(1)(c). Section 75AK(1)(c) provides a defence if it is established that the state of scientific or technical knowledge at the time when goods are supplied by their actual manufacturer was not such as to enable that defect to be discovered. The relevant question therefore was when did MSDA become aware of

the cardiovascular data from the APPROVe study because it would not have been until then that Merck would know or ought reasonably to have known that the consumption of Vioxx increased the risk of the occurrence of cardiovascular events. This information was not available until September 2004.[14] Jessup J decided (at [930]) that "the defence should be available, notwithstanding that enough was suspected about the product to activate an implied obligation to give warnings of the kind mentioned in s 75AC(2)(d)". The applicant's claim under s 75AD of the Act was thus rejected.

REASONABLY FIT FOR PURPOSE (SECTION 74B)

Under s 74B, the applicant alleged that Vioxx tablets were not reasonably fit for the purpose because Vioxx materially increased the risk of suffering that cardiovascular condition (at [932]).

Jessup J noted (at [941]) that s 74B(1)(c) of the *Trade Practices Act* allowed for a situation "in which the acquirer makes known his or her purpose by implication". The authorities show that "the putative acquirer does not need to have freedom from the particular defect consciously in his or her mind at the time of acquisition". Thus, in *Grant v Australian Knitting Mills Ltd* [1936] AC 85 the plaintiff, Dr Grant, "was not required to prove that he had in mind purchasing a pair of underpants that would *not* give him dermatitis". As his Honour explained (at [942]), "the fact that he contracted dermatitis from a chemical contained in the material of the garment which he wore justified the conclusion that the garment was not fit for the purpose of being worn as intended (ie against the skin)". Following this, in the present case, if the applicant's purpose was only to obtain relief from the pain associated with arthritis, "he need not also demonstrate that he had it in mind that Vioxx would not cause heart attacks".

Jessup J also considered implied communication of "purpose" between the manufacturer and the consumer because the communication between those two parties is rarely direct: he asked (at [947]), "what communication of purpose as between the consumer and the manufacturer should be implied?" Section 74B(1)(c) of the Act is expressed as follows (emphasis added):

> the goods are acquired by the consumer for a particular purpose that was, expressly or by implication, *made known to the corporation*, either directly, or through the person from whom the consumer acquired the goods or a person by whom any antecedent negotiations in connexion with the acquisition of the goods were conducted.

Jessup J stated (at [946]) that the consumer's purpose was not merely to achieve the effects of the medication but also the achievement of that effect in accordance with the terms of the prescription and any advice or instructions that may be assumed to have been given by the doctor. Jessup J added that it would be wrong to exclude the communications made to the doctor by the manufacturer regarding the use of the drug and any adverse consequences associated with taking it. The court relied on Keifel J in *Carey-Hazell v Getz Bros & Co (Aust) Pty Ltd* [2004] FCA 853 and concluded (at [948]):

> The purpose which the consumer implicitly makes known to the manufacturer will necessarily take account of risks that were known to medical practitioners generally.

Jessup J did not find that the medical practitioners or MSDA were aware of the risks and therefore they were unable to pass this information onto their patients or practitioners respectively.

The respondent also relied on s 74B(2)(b) as a defence arguing that s 74(1) cannot apply where "the circumstances show that the consumer did not rely, or that it was unreasonable for the consumer to rely, on the skill or judgment of the corporation".[15] This means that the applicant does not have to establish that he relied on MSDA's skill or judgment but the respondent did not put this proposition to the applicant and as such the court rejected the respondent's reliance on the defence. In relation to the allegations that Vioxx was not reasonably fit for the purpose implicitly made known by him to the first respondent, or of merchantable quality (ss 74B and 74D of the Act), Jessup J accepted that Vioxx involved an approximate doubling in risk of heart attack and was not fit for the purpose of being used for the relief of arthritic pain which was the purpose implicitly for which Mr Peterson bought the goods.

[14] Jessup J referred to his conclusion in Pt V of the decision as carrying the consequence that he makes this conclusion on this point.

[15] *Trade Practices Act 1974* (Cth).

MERCHANTABLE QUALITY (SECTION 74D)

The applicant alleged that Vioxx tablets were not of merchantable quality, and thus were supplied by MSDA in contravention of s 74D (at [969]). Branson J in *Medtel Pty Ltd v Courtney* (2003) 130 FCR 182; [2003] FCAFC 151, to which Jessup J referred (at [962]), said that s 74D of the Act

> calls for quality, or fitness for purpose, of the goods to be measured against what it was reasonable to expect in that regard at the time of the supply of the goods to the consumer. That measurement must be undertaken, in my view, in the light of information concerning the goods available at the time of trial. However, the issue remains whether the goods were fit for the relevant purpose as it was reasonable to expect at the time of their supply to the consumer.

The central question arising under s 74D was whether Vioxx tablets were fit for the purpose (or purposes) for which goods of that kind were commonly bought as it was reasonable for the applicant to expect. Jessup J found that because Vioxx increased the risk of heart attack twofold and that Vioxx was primarily prescribed for the purpose of arthritic pain relief, then the goods were not fit for purpose. As a result (at [984]), the applicant was entitled to compensation under s 74D(1).

In summary, Jessup J concluded that:

- Although MSDA's failure to warn and its emphasis on the drug's safety amounted to misleading conduct under s 52, the applicant's myocardial infarct did not occur by reason of that conduct.
- Vioxx was a defective good under s 75AD, in the sense that its safety was not what a person, such as the applicant, was entitled to expect.
- Under s 74B, Vioxx was not reasonably fit for the purpose implicitly made known to the applicant – the relief of arthritic pain. No arthritic pain medication should carry a twofold increase for the risk of myocardial infarction.
- Under s 74D, Vioxx was not of merchantable quality and it was reasonable for Mr Peterson to expect that a medication for the relief of arthritic pain would not carry a twofold increased risk of a heart attack (at [975]).

THE VIOXX STORY IN THE CONTEXT OF PHARMACEUTICAL REGULATION

Prior to the launch of Vioxx, which made US$2.5 billion a year for the company between 1999 and 2004, Merck had been struggling for some years to develop a new "blockbuster" drug that would generate big profits.[16] Between 1999 and 2001 Merck had also lost patent protection over five of its best-selling drugs, Vasotec, Pepcid, Mevacor, Priloxed and Prinivil and two more, Zocor and Prayachol, were due to lose their protection in 2007.[17]

The respondent drug manufacturers claimed that it was controversial whether there was sufficient evidence in 2000 from the VIGOR trial to justify withdrawal of Vioxx from the market.[18] Yet one cumulative meta-analysis of the risk of cardio-events associated with rofecoxib in patients with chronic musculoskeletal disorders, published in 2004, encompassing 18 randomised controlled trials and 11 observational studies, concluded that an increased risk of myocardial infarction in patients taking Vioxx was evident from 2000 onwards. Further, "this effect was substantial and unlikely to be a chance finding". As for the possible cardioprotective effect of naproxen, analysis of data from observational, pharmaco-epidemiological studies indicated that, "if there was an effect it was small", and "not large enough to explain the findings of the VIGOR study".[19]

As mentioned, the findings which eventually prompted Merck's voluntary withdrawal of Vioxx on 30 September 2004 were those from the APPROVe study. APPROVe involved 2,600 patients and was designed to evaluate the efficacy of rofecoxib in preventing the recurrence of colorectal polyps in

[16] Culp D and Berry I, "Merck and the Vioxx Debacle: Deadly Loyalty" (2007) 22(1) *St John's Journal of Legal Commentary* 1.

[17] Culp and Berry, n 16.

[18] Editorial. "Vioxx Controversy" (2004) 292(23) JAMA 2827; Hampton, n 2.

[19] Juni et al, n 4.

patients with a history of colorectal adenomas. A 3.9-fold increase in the incidence of serious thromboembolic adverse events in the group taking 25 mg of rofecoxib per day was identified when compared with placebo.[20]

In the United States, cardiovascular risks associated with Vioxx during its market life translated into an estimated 88,000 to 140,000 excess cases of serious coronary heart disease, including many fatalities.[21] Extrapolation of APPROVe data to Australia equates to a potential excess of several thousand cardiovascular events cause by rofecoxib.[22] This estimate does not include the fact that patients with inflammatory arthritis are likely to "be at higher baseline risk of cardiovascular event than the 'low risk' population included in the APPROVe trial".[23]

Given this evidence about potential safety problems with this new innovative medicine, much of the significance of Jessup J's decision in this case relates to its implications for how the pharmaceutical industry uses scientific research as a marketing tool.[24]

In December 1999 the United States Food and Drug Administration informed Merck & Co that they objected to Merck's dissemination of promotional materials for Vioxx that misrepresented Vioxx's safety profile.[25] In September 2001 the FDA recognised that Merck & Co were engaging in pharmaceutical marketing behaviour promoting Vioxx that was in violation of several sections of the *Federal Food, Drug and Cosmetic Act* (US) and that review by the Division of Drug Marketing, Advertising and Communications (DDMAC) had determined that those marketing materials were "false, lacking in fair balance or otherwise misleading" and that they minimise "the potentially serious cardiovascular findings that were observed in the VIGOR study and thus misrepresent[s] the safety profile for Vioxx".[26]

The potentially misleading marketing, advertising and communication that Merck engaged in included six promotional audio conferences which promoted Vioxx as a safe effective drug, promoted it for unapproved uses in unapproved doses and, in addition, minimised or omitted to provide information on the risks associated with the use of the drug. Merck also released a press statement entitled *Merck Confirms Favourable Cardiovascular Safety Profile of Vioxx* (22 May 2001) which claimed that Vioxx had a "favourable cardiovascular safety profile". Merck even went so far as to publish a study it had its own people conduct in a peer-reviewed journal without any disclosure of their interest. That article, "Cardiovascular Thrombotic Events in Controlled, Clinical Trials of Rofecoxib" was published in *Circulation*, the Journal of the American Heart Association.[27] Alise Reicin, one of the authors of the paper, was vice-president for clinical research at Merck. The article concluded:

> Data from >28000 patients in 23 studies representing >14000 patient-years at risk demonstrated that rofecoxib was not associated with excess CV thrombotic events compared with either placebo or non-naproxen NSAIDs. The data suggest, but are insufficient to ascertain, the cardioprotective benefits of naproxen.

Perhaps even more disturbing was the allegation made in evidence during this case of ghostwriting of articles. Dr Jeffrey R Lisse, a rheumatologist, was listed as the lead author on an

[20] Hampton, n 2.

[21] Graham D, Office of Drug Safety at the United States Food and Drug Administration, cited in Mayor S, "Rofecoxib Caused Excess Heart Disease" (29 January 2005) 330 BMJ 212.

[22] Langton PE, Hankey GJ and Eikelboom JW, "Cardiovascular Safety of Rofecoxib (Vioxx): Lessons Learned and Unanswered Questions" (2004) 181(10) MJA 524.

[23] Langton et al, n 22, citing DoHA, *Media Release* (30 June 2004).

[24] Avorn, n 1; Jelinek GA and Neate S, "The Influence of the Pharmaceutical Industry in Medicine" (2009) 17 JLM 216.

[25] Department of Health and Human Services, *Warning Letter to Raymond Gilmartin CEO Merck & Co, Inc* (2001), http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCcompanies/UCM166383.pdf viewed May 2010.

[26] Department of Health and Human Services, n 25.

[27] Konstam et al, n 5.

article discussing a Vioxx study. The article was published in the *Annals of Internal Medicine* but Dr Lisse stated that "Merck designed the trial, paid for the trial, ran the trial … the initial paper was written by Merck and sent to me for editing".[28]

In Australia, the training of "drug reps" to minimise physician concerns about the adverse cardiovascular effects of Vioxx indicates considerable problems with self-regulation as the chief mode by which such activities are regulated. A publication of MSDA called the *Australian Journal of Bone and Joint Medicine* was found by Jessup J (at [296]) to have

> the setup of a peer-reviewed, independent, journal, and much of the material in it had been written by professional contributors (whether or not acknowledged). However, it was neither peer-reviewed nor independent. It was effectively a highbrow means of promoting some of MSDA's products (including Vioxx) within the medical profession. The journal ostensibly had an editorial board, but there is reason to be sceptical about the reality of that institution: Dr Bertouch was named as a member of it, but he was unaware of that membership, and had never attended a meeting of the board.

Evidence was given (at [281]) that MSDA used specialists and senior physicians in "education cascades" or a "communication cascades" to promote products.

Such revelations must call into question whether the dominant self-regulation model in relation to pharmaceutical promotions to the medical profession is adequate to protect the public interest.

CONCLUSION: THE FAILURE OF AUSTRALIAN PHARMACEUTICAL SELF-REGULATION

Jessup J found that the applicant Graeme Peterson suffered a heart attack in 2003 after consuming Vioxx manufactured by the respondents which doubled the risk of such an event and was thus not reasonably fit for the purpose under the Act. Mr Peterson was awarded compensation in the sum of $300,000.

Although misleading conduct was not a material part of the decision, the publicity associated with this case provided the Australian public and medical profession with a rare window into the types of practices that multinational pharmaceutical companies are prepared to engage in to promote the sale of their products.

Nothing much has changed in terms of Australian pharmaceutical regulation since this case was decided. Medicines Australia, the lobby group for the multinational patented and mixed patented-generic pharmaceutical manufacturers, continues to coordinate a self-regulation system based on a voluntary code of conduct in relation to pharmaceutical advertising to the public and lobbying to the profession. Companies appear to consider that the fines imposed are outweighed by the increase in sales and continue to violate both the spirit and letter of such guidelines. What is needed are stronger anti-fraud and anti-collusion laws in Australia targeted at the pharmaceutical industry, as well as systems providing financial incentives for whistleblowers who reveal fraud by such companies on the public purse.

The problematic role of the pharmaceutical industry in sponsoring and controlling clinical trials and influencing the submission and publication of their data continues to increase. Reviewers with ties to pharmaceutical companies still seek, eg, to prevent the publication of evidence that might be deleterious to their interests. In the May 2010 federal budget Medicines Australia announced that it had signed a Memorandum of Understanding (MOU) to accept compulsory price drops in the generic drugs made as a component of its members' business in return for a commitment by the government to restrain policy development in the area of new therapeutic groups for the PBS, a crucial mechanism in controlling the cost of new patented medicines. As a result of such policies, the wholly generic drug industry (which used to be predominantly Australian-owned firms) has largely closed its research and manufacturing arms and is in the process of moving the bulk of its activities (except for packaging and distribution) offshore to the detriment of Australia's science base as well as our capacity to respond to a public health emergency by rapidly scaling up production of essential medicines under compulsory licence.

[28] Berenson A, "Evidence in Vioxx Suits Shows Intervention by Merck Officials", *New York Times* (24 April 2005), http://www.nytimes.com/2005/04/24/business/24drug.html?pagewanted=print&position viewed May 2010.

The Vioxx litigation highlights the failure of the self-regulation model for promotion of drugs by the Australian pharmaceutical industry. It is also significant that Mr Patterson had to rely on Trade Practices legislation and not tort law to provide some form of protection for him against the unethical practices of the pharmaceutical companies. The case confirms the need for amendments to the *Therapeutic Goods Act 1989* (Cth) creating an independent statutory authority with powers to impose fines, criminal penalties and enter into civil litigation (with the assistance of financially rewarded information from corporate insiders based on United States False Claims legislation) to reclaim fraudulently obtained public moneys (eg, due to pharmaceutical promotions knowingly or recklessly avoiding licensing or safety marketing requirements as well as national health policies and safety regulations and standards).[29] Such behaviour should include failing to log a pharmaceutical clinical trial protocol onto a public register at inception (linked to the World Health Organisation's International Clinical Trials Registry Platform (WHO ICTRP)). It should likewise be considered an actionable fraud against the federal government for pharmaceutical sponsors to encourage individual health care providers and consumer and patient support groups, their institutions or agents, by either cash or in-kind transfers, packaging, labelling and promotional material including use of sales representatives, to encourage use of a PBS-listed medication for off-label or unapproved uses.

Associate Professor Thomas Faunce
ARC Future Fellow, The Australian National University

Ruth Townsend
Lecturer, College of Law and Medical School, The Australian National University
and

Alexandra McEwan
Research Assistant, College of Law, The Australian National University

[29] Faunce TA, "Submission on the Position Paper on the Promotion of Therapeutic Goods", Department of Health & Ageing, *Inquiry into Industry Codes of Conduct* (27 July 2010).