Margaret Allars is a Professor in the Faculty of Law of the University of Sydney and a member of the New South Wales Bar. She teaches postgraduate courses in administrative law and her practice at the bar is also in that area. In 1993 she was appointed by the Federal Government to chair the Inquiry into the Use of Pituitary Derived Hormones in Australia and Creutzfeldt-Jakob Disease, which reported in 1994. More recently, she has appeared in cases involving merits reviews in the Administrative Appeals Tribunal, in decisions relating to the registration of therapeutic goods.

Thank you very much for the invitation to speak on what is a very interesting topic. I should say at the outset that two of the cases that I am going to mention this evening are cases where I represented the Therapeutic Goods Administration (**TGA**), but of course what I have to say tonight is said in my personal capacity.

Relevant decision-maker?

The TGA is the key regulator of therapeutic goods in Australia but we can't really assess its role without also looking at some other decision-makers. Those are the Administrative Appeals Tribunal (**AAT**) and the Federal Court. When you look at the Federal Court its role in both public law and private law needs to be considered. It is clear when we do consider these decision-makers, that the TGA has no monopoly on setting standards for therapeutic goods. However, the key and critical question is whether the TGA is the sole decision maker that may legitimately set those standards.

Standard setting by the Therapeutic Goods Administration

Turning to the TGA first of all, section 25(1)(d) of the *Therapeutic Goods Act* 1989 (Cth) (the **Act**) gives a role to the Secretary of the Department, and hence to the Secretary's delegates within the TGA, of evaluating the quality, safety and efficacy of therapeutic goods for the purposes for which they are used, and to evaluate in order to see whether those matters are satisfactorily established.

There is no general standard as to safety. There is no definition of that term in the Act, nor would it be appropriate for there to be such a definition. The standards that have been developed are directed to the particular kinds of medicines where registration or listing is sought.

The TGA has developed policies, usually called guidelines. These are the *Australian Regulatory Guidelines for Prescription Medicines* (**ARGPM**), the *Australian Regulatory Guidelines for Over-the-Counter Medicines* (**ARGOM**), and so forth. More specific guidelines apply to the evaluation of particular types of medicines. To supplement the guidelines which the TGA has developed itself, the TGA has approved certain guidelines issued by the European Medicines Agency (**EMEA**). The TGA does not adopt the guidelines of the United States Food and Drug Administration (**FDA**).

The guidelines complement each other, sometimes overlap and their coverage of matters relating to quality, safety, efficacy and timely availability of therapeutic goods, those being the three objects of the *Therapeutic Goods Act*, are addressed in that way. No provision of the Act, or the regulations made under it, requires that any particular guideline be applied in any particular case.

Application of standards by the Therapeutic Goods Administration

So that explains what happens at the planning or policy level. At the operational level there is room for flexibility in the application of the guidelines. Indeed, section 1.7 of the ARGPM specifically refers to the flexibility that's available in applying those Guidelines.

The need for flexibility can be understood when you look at an example of the application of the guidelines in *Re Sylvan and Department of Health and Ageing* [2009] AATA 814. That case concerned Cholesen, a product manufactured as an extract of red yeast rice, a naturally occurring substance that is used as a colouring agent in food, as a preservative and in traditional medicine. If you always suspected that Peking duck was good for you, you were right. Although in a sense Cholesen is a complementary medicine, it contains an active ingredient identical to that found in statins, which are prescription medicines listed in Schedule 4 to the *Standard for the Uniform Scheduling of Drugs and Poisons* 2008 (**Poisons Standard**).

Applying its *Guidelines for the Levels and Kinds of Evidence* and applying the ARGPM, the TGA found that Cholesen differed in some important respects from traditional red yeast rice available in Asia. Its cholesterol lowering effects were not accounted for simply by the level of the active ingredient. The TGA decided not to give registration under section 25(1)(d) because safety had not been satisfactorily established. That decision was affirmed by the AAT, but one can see that the *Australian Regulatory Guidelines for Complementary Medicines* (**ARGCM**) were not directly applicable. Other guidelines came into play.

The TGA has other functions apart from the function under section 25(1)(d). An important one is listing of products on the register. The system is a co-regulatory framework for listing of therapeutic goods and that allows for speedier marketing. From 2000 this co-regulatory framework allowed for a product to be listed under section 26A of the Act by the sponsor giving a certificate which indicated that certain matters were satisfied: the product was eligible for listing; it was safe for the purpose for which it was to be used; its presentation was not unacceptable.

The TGA engages in post-marketing monitoring of listed medicines and the Secretary has power to cancel a listing, just as she has power to cancel registration of a registered product. That can be done for a variety of reasons that include the presence of an imminent risk of death, serious injury or illness, or if it appears to the Secretary that quality, safety or efficacy of the goods is unacceptable.

Role of the Administrative Appeals Tribunal

General principles

Let me turn to merits review by the AAT. The AAT reviews what are called "reviewable decisions". These are decisions that are made within the TGA on reconsideration of the initial decisions made by the Secretary's delegate. Both levels – reconsideration by the TGA and then review by the AAT - are concerned with a re-exercise of all the powers and discretions of the decision of the original delegate.

When we come to the AAT, the AAT exercises the same power as the Secretary under section 25(1)(d) and as well, based on some case-law concerning the AAT's function generally, we say that its role is to make the correct or preferable decision on all the material before it. Merits review involves simply doing over again what the Secretary was required to do.

What happens with the guidelines? The AAT case-law, in particular the *Drake* litigation (*Re Drake and Minister for Immigration and Ethnic Affairs (No 2)* (1979) 2 ALD 634), indicates that the AAT, whilst having power to review policy that is applied by the decision-maker in the decision under review, nonetheless will only depart from guidelines cautiously, where there are cogent reasons and individual justice requires it.

Ego

It is interesting then to see how the guidelines of the TGA are approached by the AAT. An illustration of those is found in *Re Ego Pharmaceuticals Pty Limited and Minister for Health and Ageing* (2010) 120 ALD 71. In that case the AAT found that the guidelines were due for an overhaul. There were four relevant EMEA guidelines adopted by the TGA for dealing with locally applied products, corticosteroids and so forth. There was also a *Question and Answer Guideline* of the EMEA which hadn't been expressly adopted by the TGA but which operated as an interpretation of some of the applicable EMEA guidelines. That did not dispel the lack of clarity.

In response to the comments of the AAT, the TGA commenced a review of the guidelines. *Ego* illustrates, however, that the AAT in practice may make a decision inconsistent with the TGA's guidelines without actually formally acknowledging that it is doing so, and without clearly addressing the principle about cautious departures from policy where there are cogent reasons.

In *Ego* the TGA refused registration of a generic product Zatamil, which is a topical corticosteroid cream, lotion and hydrogel for the treatment of dermatitis. The TGA was not satisfied as to the safety of this product. The studies that were provided were vasoconstrictor studies and the TGA required other types of studies in order to be satisfied as to therapeutic equivalence with the originator product. In doing so the TGA applied the ARGPM, the ARGOM and the EMEA guidelines, in particular the *Question and Answer Guideline* that I mentioned.

The difficulty was that the *Question and Answer Guideline* referred to an FDA guidance on vasoconstrictor studies. In the AAT, on the basis of the evidence that was before it, the AAT accepted that a vasoconstrictor assay (**VCA**) was an adequate methodology for testing the bioequivalence or indeed the therapeutic equivalence of a topical corticosteroid.

The AAT, however, remitted the matter to the TGA for a further decision to be made after a long period of time, indeed allowing 14 months before the sponsor was required to submit a further VCA study, the first one having been flawed and failing to comply with the FDA guidance. The matter remained pending before the AAT throughout this period but subsequently the product was registered.

What does that case mean? The AAT certainly applied standards which differed from those of the TGA, standards relating to safety. However, it did so only for the purpose of the particular case before it. In that sense we could say it departed from the TGA's standards of safety in a particular case but did not actually make new standards for the future for all sponsors.

Aspen

Let me turn to a different kind of decision reviewed by the AAT, a cancellation decision. Again, the AAT differed from the TGA in this instance. The case is *Re Aspen Pharmacare Australia Pty Ltd and Minister for Heath and Ageing* [2012] AATA

362. The TGA cancelled the registration of Di-Gesic and Doloxene. These were grandfathered medicines, but a study called the multiple ascending dose study, or the MAD study, suggested toxicity of an ingredient dextropropoxyphene. As a result of the MAD study, action was taken by regulators in the UK, the US, the European Union and New Zealand to remove these two products from general availability. The TGA also took action.

In the AAT, experts gave evidence on behalf of the TGA and on behalf of the sponsor. The issue was ultimately determined by which expert the AAT preferred. The AAT preferred the experts who gave evidence for the sponsor. The AAT also indicated, in surprisingly strong language, the reasons why it gave less weight to the TGA's experts' evidence. Again in this case, surprisingly, the AAT did not make a final decision but remitted the matter to the TGA for reconsideration, expressing the view that safety concerns could be met by imposing conditions under section 28 of the *Therapeutic Goods Act*.

On 12 September 2012 the TGA made an announcement that it had decided to affirm its original cancellation decision. However, because the AAT had granted a stay of the original cancellation decision, the products remain on the register until the matter is finally determined when it comes back to the AAT.

There are no guidelines for cancellation decisions. The decision is a little bit different from a registration decision under section 25(1)(d). Safety issues are decided on the basis of the available evidence. By its assessment of the evidence, the AAT set a standard for these products that was different from the standard set by the TGA. In my view, this case is different from the *Ego* case, in that it does involve the AAT in setting a standard rather than just departing from one.

Role of the Federal Court: Public law

Let me turn to the Federal Court. In its public law jurisdiction the Federal Court can hear appeals on questions of law from the AAT or it can engage in judicial review under, for example, the *Administrative Decisions (Judicial Review) Act* 1977 (Cth) (**ADJR Act**). In both contexts the Court only looks at legal issues. It doesn't delve into the merits of the choice of the guidelines or indeed the merits of safety issues as they have been determined by either by the TGA or the AAT.

The Federal Court does, of course, tangentially look at some safety issues and issues about presentation of products and advertising when it applies the usual judicial review grounds in an ADJR Act application, and a recent example of that is *Swisse Vitamins Pty Ltd v The Complaints Resolution Panel* [2012] FCA 536.

Role of the Federal Court: Private law

The Federal Court also exercises jurisdiction in the private law context in a way which does involve it, I believe, in setting standards. The most important areas where that occurs appear to be in actions for damages for negligence and in consumer protection cases. The interesting example of that in recent times is *Peterson v Merck Sharp & Dome (Australia) Pty Ltd* (2010) 184 FCR 1 (***Vioxx case***).

This was a representative action brought by a group that included Mr Graeme Peterson who had been prescribed Vioxx in 2001 for relief of his arthritic pain. Two and a half years later he suffered a serious heart attack. The sponsor Merck Sharpe & Dohme (Australia) (**Merck**) had attained registration and commenced marketing the product in February 2001.

Two studies followed. One was the VIGOR study in 2000 and that prompted Merck to apply to the TGA for a variation of the product information. That application was approved by the TGA. The product information was varied. In September 2004 early results of the second study, the APPROVe trial, showed that there was a statistically significant risk - an increased risk - of cardiovascular thrombotic events in patients taking Vioxx. A week later Merck withdrew Vioxx from the market.

Mr Peterson's case in negligence was that at the time he was prescribed Vioxx, Merck knew or ought to have known that its use increased the risk of myocardial infarction and that Merck failed adequately to warn of the risk. So it was an argument about failure to disclose an increased risk.

The variation in the product information, according to the argument, did not constitute reasonable steps by Merck to warn medical practitioners. What was argued to be required (by those in the representative action) was a "Dear Doctor" letter from Merck advising of the results of the VIGOR study.

The trial judge found that negligence was not established in Mr Peterson's case. This finding turned on the evidence of the treating doctor that he would have continued to prescribe Vioxx and Mr Peterson would have continued to take his advice. Mr Peterson gave evidence that if his treating doctor told him that Vioxx would double his risk of a heart attack he would not have taken it. The trial judge did not accept that evidence.

While Peterson failed in part on his treating doctor's evidence, Merck appealed against findings that were favourable to Peterson on the issue of breach of duty by Merck. This was because other members of the representative group might not face similar difficulties with their treating practitioner's evidence.

One important issue where the findings made were favourable to Merck was the issue of causation. Mr Peterson was a former smoker, aged 51. He had hypertension, hyperlipidemia and left ventricular hypertrophy. The trial judge nonetheless concluded that Vioxx made a material contribution to his heart attack. At the same time the trial judge concluded that he could not find the heart attack would not have occurred but for the consumption of Vioxx. His overall conclusion, however, was that Vioxx was the cause of Mr Peterson's heart attack because it increased his risk.

The Full Federal Court allowed the appeal, reversing the trial judge's finding on causation: *Merck Sharp & Dome (Australia) Pty Ltd v Peterson* (2011) 196 FCR 145. The causal test is whether it is more probable than not that consumption of Vioxx caused or materially contributed to the occurrence of the heart attack. Within this test there is a "but for" test, operating as a negative criterion: that is, taking Vioxx had to be a necessary factor in the heart attack: (2011) 196 FCR 145 at [98] – [99].

As a negligence action that depended upon causation, of course the focus here wa upon one individual and the way the particular case was run. It is not upon general rules, which are what the standards are that we are concerned with in relation to safety. However, the *Vioxx case* was important in raising issues about the relationship between conclusions about duty of care, causation and negligence actions, and the regulatory scheme administered by the TGA.

At first instance and on appeal Merck argued that compliance with the regulatory scheme administered by the TGA demonstrates that a product meets safety

standards and hence precludes any common law action in negligence. The short answer given by the Full Court was that while the *Therapeutic Goods Act* establishes minimum safety standards for the availability and use of regulated medicines in the public interest, it does not show a legislative intention to abrogate the common law right to bring an action in negligence.

That common law right remains in place where a sponsor fails to meet a duty of care. The Full Court agreed with the more detailed treatment of this topic undertaken by the trial judge in rejecting the argument: (2011) 196 FCR 145 at [161]. If Merck's argument were accepted, a sponsor would be able to engage in negligent promotion or presentation of a product, without exposure to common law claims. Those claims could be "snail in the bottle" claims about poor manufacture of a particular batch, or a failure to disclose knowledge of an increased risk, as in the present case. However, at common law, a manufacturer has a relationship of proximity to a consumer, giving rise to the duty of care which is the foundation of a negligence action.

So what we gain from this is the response that the standards set within a regulatory scheme in order to lawfully market a product co-exist with the common law duty to meet relevant standards of care. Further, the common law duty of care is not limited by those statutory requirements or by the standards that we find in the guidelines applied by the TGA. The common law might require more. At the same time, compliance with some of the TGA's guidelines might provide evidence relevant to the question of whether a sponsor has met the common law standard of care.

The *Vioxx case* raised other issues about the interface between the *Therapeutic Goods Act* and another regulatory scheme, consumer protection under the former *Trade Practices Act* 1974 (Cth), now the *Competition and Consumer Act* 2010 (Cth). Merck contended that the provisions of the *Trade Practices Act*, or some of them, were impliedly repealed by provisions of the *Therapeutic Goods Act*. Their focus was in particular on the prohibition in the *Therapeutic Goods Act* upon publication of advertisements about therapeutic goods that are listed in Schedule 4 to the Poison Standards, dealing with prescription medicines.

The trial judge rejected this contention shortly, referring to the presumption in statutory interpretation that where there is more than one regulatory scheme applying to the same subject matter, Parliament intended that both regulatory schemes should apply.

I will move on from the particular provision which triggered that argument, section 52 of the *Trade Practices Act* (misleading and deceptive advertising), because that wasn't really discussed in the Full Court decision.

The provisions which were discussed and that are of interest in exploring this interface between regulation by the TGA and private law litigation are, firstly, section 75AD of the former *Trade Practices Act* dealing with defective products. In the appeal the Full Court upheld the conclusion of the trial judge that the claim that this was a defective product failed: (2011) 196 FCR 145 at [190], [201]. It accepted that Vioxx had a defect for some people. However, the problem here was the same as the problem in the negligence claim: causation was not established. Mr Peterson hadn't established that he suffered any injury “because of the defect” within 75AD.

It was interesting to note that the Explanatory Memorandum for the bill that inserted 75AD into the *Trade Practices Act* in 1992 specifically addressed the circumstance of a defect in the context of prescription medicines. It stated that circumstances to be

taken into account in applying what is said to be an objective test in the *Trade Practices Act* include circumstances about the product information.

The sponsor provides this complex information in the product information to the medical practitioner. It includes reference to side effects and so forth. It is not provided directly to consumers. However, the Explanatory Memorandum stated that the medical practitioner is an intermediary who decides whether or not it is appropriate to prescribe the medicine.

Another claim under the *Trade Practices Act* was under 74B - was the product reasonably fit for its purpose, and also 74D - was it of merchantable quality? Again, there were difficulties with causation here. However, the trial judge concluded these claims were established and awarded Mr Peterson $330,000 in damages. The Full Court reversed that conclusion.

In relation to 74B, reasonably fit for purpose, the difficulty for Mr Peterson apart from causation was that he had not expressly or impliedly made known to the supplier of the product, the pharmacist, his requirement that Vioxx had a quality of absolute safety or complete absence of adverse side-effects: (2011) 196 FCR 145 at [172]. All he had implicitly made known to the pharmacist was that he wanted to acquire Vioxx for the purpose of using it to treat his arthritic pain without gastro-intestinal side effects.

Section 74B was not engaged. The Full Court said almost all medicines have side-effects and are contraindicated for a particular patient or group of patients. In addition, the inferences drawn from the evidence in the Full Court were that Vioxx did not double the risk of Mr Peterson having myocardial infarction in any event: (2011) 196 FCR 145 at [173], [174]. The claim relating to merchantable quality was disposed of in a similar manner.

Conclusions

What do we conclude from all of this? The TGA does set standards and it applies them. The AAT has a role of re-exercising those powers. So as a matter of law it is entitled in a sense to set standards, but it is only expected to depart from the standards of the TGA cautiously, where there are cogent reasons to do so. It appears to be ready to do so in some cases, and arguably in the cancellation case of *Re Aspen* it did so.

The Federal Court does not have a role of setting standards as to safety in its public law jurisdiction. By contrast, in its private law jurisdiction it does have such a role. It sets standards in a way which is rather unpredictable. as common law actions for negligence evolve in terms of the principles applicable, and also as consumer protection legislation changes, as we see it changing now.

Thank you.