SENATE STANDING COMMITTEE ON COMMUNITY AFFAIRS

LEGISLATION COMMITTEE

Inquiry into the National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010

SUBMISSION

SUBMISSION NUMBER: **13**

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20 October 2010

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Terms of Reference

On 25 November 2009 the Senate referred the following matter to the Community Affairs References Committee for inquiry and report by 30 June 2010:

Consumer access to pharmaceutical benefits and the creation of new therapeutic groups through the Pharmaceutical Benefits Scheme (PBS), including:

a. the impact of new therapeutic groups on consumer access to existing PBS drugs, vaccines and future drugs, particularly high cost drugs;

b. the criteria and clinical evidence used to qualify drugs as interchangeable at a patient level;

c. the effect of new therapeutic groups on the number and size of patient contributions;

d. consultation undertaken in the development of new therapeutic groups;

e. the impact of new therapeutic groups on the classification of medicines in F1 and F2 formularies;

f. the delay to price reductions associated with the price disclosure provisions due to take effect on 1 August 2009 and the reasons for the delay;

g. the process and timing of consideration by Cabinet of high cost drugs and vaccines; and

h. any other related matters.

The *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* was reintroduced into the House of Representatives on 29 September 2010. On 30 September 2010 the Senate, on the recommendation of the Selection of Bills Committee, re-referred the provisions of the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* to the Community Affairs Legislation Committee for inquiry and report by 16 November 2010.

Executive Summary

- The *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* will not facilitate a more economically sustainable Pharmaceutical Benefits Scheme (PBS) (as is claimed in the explanatory memorandum) chiefly because:
  - The Bill's price reductions to generic pharmaceuticals in the F2A category and F2T categories are excessive and undermine the sustainability of a profitable, independent generic pharmaceuticals industry in Australia,
  - The Bill's generic medicines price reductions will reduce pharmaceutical price competition in the long term
  - The Bill's generic medicines price reductions compromise industry innovation policy by inhibiting the creation of niche Australian-owned biologic and nanogeneric companies whose cost-effective products would otherwise have flowed through to the PBS.
  - The Bill's generic price medicines reductions do not mesh with a coherent policy of fostering a research-based generic medicines industry in Australia and instead encourage a Wallmart-type repackaging model of generic pharmaceuticals in Australia
  - The Bill's generic medicines price reductions are not coherently linked with measures to reduce the most significant factor threatening sustainability of the PBS- the rise in cost of the brand name (patented) F1 originator medicines (whose companies Medicines Australia primarily represents) which has more than doubled (from $2.8 billion in 2005/6 to $4.8 billion in 2009/10.

- To assist sustainability of the PBS the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* should permit the creation of new therapeutic groups to enhance ongoing consumer access to high

cost patented drugs by restraining costs associated with new drugs whose manufacturers have failed the PBAC test of "health innovation" by being unable to prove cost-effectiveness over comparable marketed products with a lower price.

- The consultation undertaken in the development of *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* in its current form was adequate. Consultation with industry interest and lobby groups (particularly Medicines Australia) should not be viewed as facilitating their capacity to covertly and without democratic accountability shape or veto federal health policy.
- The Bill should include measures to prevent monopolistic and anti-competitive behaviour in the Australian pharmaceutical industry in the manner of the False Claims legislation in the United States.

Recommendations

- That the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* require no changes to the F2 PBS pricing arrangements without without reaching agreement with the Generic Medicines Industry Association (GMiA).
- That the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* provide for the expansion of the Therapeutic Group Policy as an essential part of the evidence-based approach to pharmaceutical pricing that has made Australia a world leader in rational pharmacoeconomics and an important factor in ensuring the intergenerational sustainability and survival of the Pharmaceutical Benefits Scheme (PBS) and in fulfilling the National Medicines Policy.
- That the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* include amendments to the *National Health Act 1953 (Cth)* repealing the fracturing of the PBS formulary into F1 and F2 categories.

- In the alternative, that the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* reduce the size of the mandatory price drops for generic medicines in the F2 formulary, balancing the amount of revenue loss by expanding the therapeutic groups premiums and tightening the science-based criteria of 'health innovation' ('objectively demonstrated therapeutic significance' as per Annex 2C of the AUSFTA) that allow patented drugs to enter and remain in the F1 PBS category..
- That the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* repeal the amendments to the *National Health Act 1953 (Cth)* creating the vague standard of 'interchangeable on an individual patient basis' as adding nothing useful to the PBS process of cost-effectiveness 'health innovation' assessment, but only leading to confusion with the more science-based concept of bioequivalence and inhibiting the creation of an Australian biologic generic pharmaceutical industry.
- That the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* include measures to encourage investment in the generic pharmaceutical industry in Australia including: export under patent provisions, protection of the research-use exemption from patent royalties and other measures to discouraging 'evergreening' and anti-competitive practices in the Australian pharmaceutical industry
- That the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2010* include provisions that allow whistleblowers from within the pharmaceutical industry reporting fraud on the Federal government to receive a percentage of the triple damages recovered by the Federal Government in the manner of operation of the False Claims legislation in the United States.

Background and General Comments

The PBS has unquestionable democratic legitimacy. It is one of the few pieces of public policy in Australia that has been approved in a Constitutional referendum by a majority of citizens in a majority of States. It has survived challenges to its implementing legislation in the High Court of Australia and been improved by a series of federal governments over more than fifty years of intense health policy debate.

The core regulatory component of the PBS system is section 101 (3A&B) of the *National Health Act 1953 (Cth)*. This, in broad terms, requires that pharmacoeconomic experts on the PBAC, recommend PBS listing (after a central government price negotiation) of a pharmaceutical submitted by its manufacturer after a positive determination of its cost-effectiveness in relation to alternative therapies (whether or not involving drugs).

Australia's PBS is highly respected nationally and internationally as a successful articulation of a scientific approach to ensuring maximum public benefit from government expenditure on medicines. Now solidly based on principles of the *National Medicines Policy*, it has been operating for over half a century to provide evidence-based, cost-effective and equitable access to healthcare for Australians. Efficient operation of the PBS in the present rapidly changing regulatory environment and with much more problematic claims to innovative status by originator companies, requires a well-financed cost-effectiveness regulatory system with robust protections of its independence.

Before a new patented drug is listed, it must obtain safety, quality and efficacy marketing approval from the Australian *Therapeutic Goods Administration* (TGA). Once this is done, the supplier may apply to have it listed on the PBS, to an independent statutory committee – the *Pharmaceutical Benefits Advisory Committee* (PBAC) set up under the *National Health Act 1953*. The PBAC is required to consider applications against certain criteria set out in the legislation. The PBAC cannot recommend a new drug for listing if it is

'substantially more costly than an alternative therapy' unless it 'provides a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies' (*National Health Act 1953* (Cth), section 101(3B(a))). This is an onerous public responsibility on the highly expert members of the PBAC who to date have been inadequately compensated financially for their substantial effort.

The PBAC must now operate in a highly complex regulatory environment. In August 2007 (after minimal parliamentary debate lasting no more than two week for both houses combined), the *National Health Amendment (Pharmaceutical Benefits Scheme) Act 2007* was passed, amending key provisions of the *National Health Act 1953*. In implementing what I have called 'in substance, the Medicines Australia policy proposals' for changes to the PBS reference pricing system, the legislation effectively created two PBS pricing formularies. F1 comprises single brand, mostly patented and 'innovative' drugs and F2 comprises multiple brand, mostly generic medicines. Reference pricing no longer occurs between the two formularies. The pricing of new 'innovative' medicines in the F1 formulary risk diminishing the extent to which the PBS processes now can be said to be based on objectively demonstrated therapeutic significance. In outlining the changes late last year, the then Australian Health Minister Tony Abbott admitted that 'Generics Medicine Industry Association is not, as I understand it, especially happy with these changes.'

Although explained as derived from the need to allow lower cost generic medicines into Australia, these F1-F2 legislative changes to the PBS appear to substantially reflect the position on the PBS articulated by US negotiators during the AUSFTA negotiations (and in the AUSFTA Medicines Working Group (MWG)) on the 'elimination' of PBS reference pricing mechanisms (as supervised by the PBAC) has been successful to a significant degree, altering a core aspect of the Australian national medicines system that provided Australian citizens with timely and affordable access to medicines.

The Australia-United States Free Trade Agreement (AUSFTA) came into force on 1 January 2005. Australia's medicines pricing system has undergone significant regulatory change as a result of the AUSFTA. Before negotiating the substantive details of the AUSFTA, US negotiators were provided with clear objectives regarding Australia's pharmaceutical regulation and specifically the PBS. These included the 'elimination of government measures such as price controls and reference pricing'. Another US negotiating objective emerging from the IFAC-3 industry-trade advisory committee was that reward for market-based (not evidence-based) conceptions of 'innovation' would become a major principle of Australian pharmaceutical regulation through linkage with a non-violation nullification of benefits (NVNB) lobbying provision. Australian negotiators took an essentially defensive stance. They sought no direct and specific reciprocal changes to US pharmaceutical policy (which they could have done) but instead placed greater emphasis upon preserving the essential elements of Australia's pharmaceutical cost-effectiveness regulatory system.

> We went into these negotiations with an absolutely clear mandate to protect and preserve the fundamentals of the PBS. That is what this agreement does, there is nothing in the commitments that we have entered into in Annex 2C or the exchange of letters on the PBS that requires legislative change.

Australia expected that the competing definitions of pharmaceutical 'innovation' in Annex 2C would not override Australia's *National Medicines Policy*. Australia also had an expectation that NVNB provisions, particularly those linked to AUSFTA obligations related to Australian domestic health and medicines policy, would be restricted by the international law principle of good faith treaty interpretation.

The AUSFTA resulted in many well acknowledged statutory changes to Australian medicines policy. A more problematic area was the potential

influence of the competing definitions of pharmaceutical 'innovation' inserted in AUSFTA Annex 2C.1. The then Australian Minister for Trade (Mark Vaile) stated in relation to Annex 2C of the AUSFTA that "the core principle that we both agree on in this area ... is recognising the value of innovation." This begged the question, however, as Annex 2C.1 contained two competing definitions of pharmaceutical innovation. The first such definition required valuing pharmaceutical innovation through competitive markets (the US approach). The second permitted valuing pharmaceutical innovation through the operation of objectively demonstrated therapeutic significance (the Australian approach). The creation of new Therapeutic Groups fits squarely within this approach.Australia's overall expectation in this respect (that domestic medicines policy would continue to be governed by the four principles of the *National Medicines Policy*) has not altered. The four key pillars of the Australian *National Medicines Policy* remain:

> * timely access to the medicines that Australians need, at a cost individuals and the community can afford;
> * medicines meeting appropriate standards of quality, safety and efficacy;
> * quality use of medicines; and
> * maintaining a responsible and viable medicines industry.

The creation of new Therapeutic Groups is consistent with Australia's evidence-based concept of community value from pharmaceutical innovation underpinning all four points of the *National Medicines Policy*.

A Freedom of Information application concerning the AUSFTA Medicines Working Group (MWG) inaugural meeting points to an AUSFTA connection with 2007 Australian legislation limiting PBS reference pricing. It revealed, for example, that an opinion editorial had been discussed at the MWG which argued that innovative new pharmaceuticals submitted for PBS listing should be reference priced against innovation in other classes, rather than against

generics. The second meeting of the MWG on 30 April 2007 discussed the new F1 category, which as a result of intervening Australian legislation had now been structured along the lines proposed in the editorial the MWG had discussed at their previous meeting.

As a result of the 2007 Howard government legislative amendments, from August 2008 new sections 85AB and 85 AC to the *National Health Act 1953 (Cth)* fractured the PBS formulary into an F1 category (for prescription medicines with no 'bioequivalent brands-mostly patented medicines) and an F2 category-for mostly generic medicines. Compulsory price drops were imposed for drugs in the F2 category. There was to be no reference pricing between the two categories and new reference pricing groups would have to satisfy the criteria of "interchangeable on an individual patient basis" (new sections 84AG and 101 [3BA]).

Under the F1-F2 PBS system, reference pricing still operates for specific categories of single brand drugs 'interchangeable on an individual patient basis' with multiple brand medicines: for example ACE inhibitors, angiotensin II receptor antagonists, calcium channel blockers, H2 receptor antagonists, proton pump inhibitors, HMG Coenzyme A reductase inhibitors (pravastatin and simvastatin only). Reference pricing also continues to operate where enhanced cost-effectiveness is not established for a new drug submitted for PBS listing, the PBAC moves to cost-minimisation and the comparator happens to also be in the F1 (this happened recently for the sidenifil for pulmonary hypertension). But if one of those F1 drugs later moves to F2 (with compulsory price drops), there will be no reference pricing and Australian taxpayers could well end up paying differing amounts for drugs with the same cost-effectiveness. New therapeutic groups for reference pricing can still be created and this happened in a recent Federal budgetary measure for atorvastatin and rosuvastatin. This capacity to create new Therapeutic Groups is an important component of modifying the fiscal inequities associated with the reduced reference pricing between the F1 (patented) and F2 (generic) medicines classes.

Need to Expand Therapeutic Groups (Rather than cut Generic Prices) to Assist Sustainability of the PBS

The argument that the F1-F2 system and its reduction of reference pricing has led to higher medicines prices in Australia is predicated on the assumptions that these AUSFTA-promoted F1-F2 PBS changes have put in place a mechanism designed by the multinational pharmaceutical industry that lobbied for them through Medicines Australia and the AUSFTA MWG, in time to lead to higher Australian medicines prices for the primary reason of corporate greed.

The most obvious place to find such a potential AUSFTA-initiated difference is to look at cost-minimised F1 drugs (no proven cost-effectiveness) that have been through the PBAC process with an F2 comparitor since the PBS formulary was fractured into the F1 and F2 categories. Thus, we looked at the PSDs to discover examples of PBS-approved F1 drugs with F2 cost-minimisation comparators (be they F2A or F2(T)) over the period from July 2008 until June 2009. These times were chosen since the major price effects of the *National Health Amendment (Pharmaceuticals Benefits Scheme) Act 2007* came into effect from August 2008.

Using Medicare Australia's public data, the aggregate services (based on the number of prescriptions filled) and overall Government contribution for the service of these specific drugs (the F1 approved drug and its F2 comparator) products was collected and analysed for such examples. An Average Cost to the Government was discerned based on Total Government Cost divided by Total Services. The analysis of these results included an examination of the equi-effectiveness of each cost-effective pair and more importantly, the clear differences in average price to the Government. This analysis thus aimed to provide case studies of differences in the potential Government cost that could have been saved under the previous reference pricing system prior to the F1/F2 bifurcation process in 2007.

Tables 1.1 and 1.2 provide illustrative examples of two such cost-minimisation drugs approved for PBS F1 listing after the F1/F2 reforms: Levetiracetam and Pamipexole. Levetiracetam was approved for extension of listing in the PBS F1 category to include treatment of primary generalised tonic clonic seizures and generalised myoclonic seizures in November 2008. Pramipexole was approved for listing without restriction in the PBS F1 category to allow use as monotherapy (early stage) or in combination with levodopa (advanced disease) in July 2008.

Both drugs were and progressed initially through expert PBAC evidence-based evaluation of their 'health innovation' (objectively demonstrated therapeutic significance) with close comparators in the F2(T) category (Lamotrigine for the former and Bromocriptine for the latter). Levetiracetam was found to have a therapeutic equivalency of 2887mg to every 296mg of Lamotrigine. Parmipexole was determined to possess a therapeutic equivalency of 2.8mg to every 20.8mg of Bromocriptine.

Table 1.1	**Volume of Prescriptions**	**Total Government Cost**	**Average Cost to Government per unit**
Levetiracetam (F1)	160994	20,448,127	127.0117334
Lamotrigine (F2(T))	184092	16,034,860	87.10242705

Table 1.2	**Volume of Prescriptions**	**Total Government Cost**	**Average Cost to Government per unit**
Pramipexole Hydrochloride (F1)	43079	2,750,903	63.85716939
Bromocriptine (F2(T))	14062	564,320	40.1308491

As may be seen from Tables 1.1 and 1.2, each F1 drug had an overall higher average cost per unit to the Australian Government (and thus the Australian taxpayer) than drugs which expert assessment of pharmacoeconomic evidence had shown offered clinically equivalent efficacy and safety. This is not a rational divergence, that is, there is no logical or transparent reason for this divergence in price. If such divergence becomes a significant feature of the PBS then (given the assumptions mentioned earlier) it will confirm a significant negative impact on the evidence-based nature of Australian medicines policy and potentially on the prices to government (the Australian taxpayer) for F1 category PBS-listed prescription medicines. This is a negative impact that maintaining the capacity to create new Therapeutic Groups can reduce.

Additionally, the following two graphs (Figures 1.1 and 1.2) show changes in overall Average Price of major drugs in different Anatomical Therapeutic Chemical (ATC) groups. Here, Average Price represents Total Cost to government and patients (the latter collectively via co-payments), divided by Total Number of Prescriptions. The figures depict the differences in Average Price trends within one ATC group between those classified as F1 and F2 drugs.

(Figure 1.1)

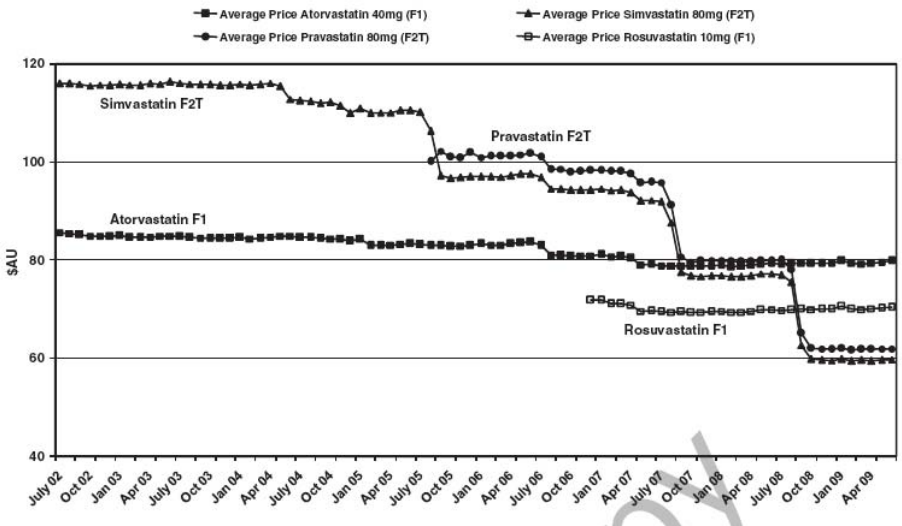

Figure 1: Lipids in PBS average price, 10–14 July 2002 to 10–14 June 2009.

Figure 1.1 shows the Average Price changes in Serum Lipid Reducing drugs. Of these, Atorvastatin and Rosuvastatin are F1 drugs, whereas Simvastatin and Pravastatin have been classified within F2(T). Remembering that these are medications with closely aligned clinical and cost-effectiveness, it can be seen that over time government and patients have been paying an increasingly disproportionate amount for the F1 classified medications without the necessary (according to the *National Health Act 1953* (Cth)) expectation that they are paying for increased cost-effectiveness (or a greater level of objectively demonstrated therapeutic significance).

(Figure 1.2)

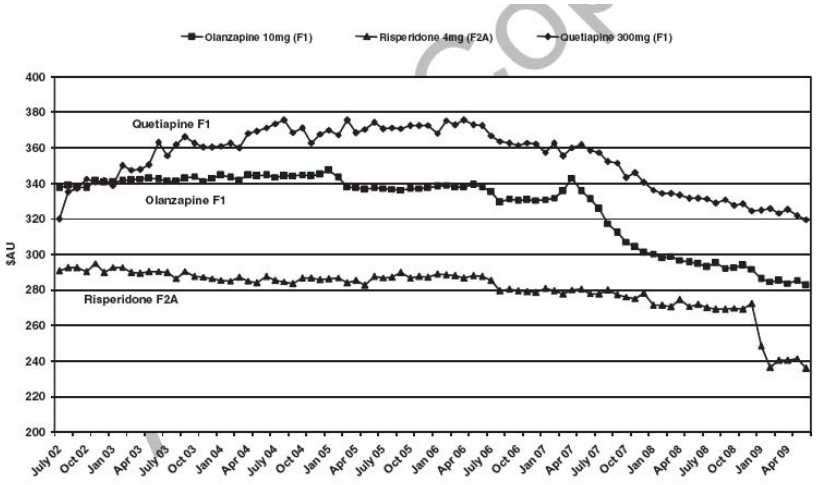

Figure 2: Psycholeptics in PBS average price, July 2002 – June 2009.

Figure 1.2 shows the Average Price changes in Psycholeptic drugs. Of these, Olanzapine and Quetiapine are F1 drugs, while only Risperidone is an F2(T). Figures 1.3 and 1.4 show changes in overall Average Price of major drugs in different Anatomical Therapeutic Chemical (ATC) groups.

Here again, Average Price is Total Cost to government and to patients (via co-payments) divided by Total Number of Prescriptions. The figure depicts the differences in Average Cost trends within one ATC group between those drugs in this class classified as F1 and F2. The increasing divergence once more is due to the creation of the F1-F2 category and is not an outcome of increased scientifically proven cost-effectiveness of drugs in the F1 category.

Other Issues

PBS as World Standard in Cost-Effectiveness

Despite the AUSFTA and the lobbying efforts of Medicines Australia, the Australian PBS system remains a world class example of evidence-based pharmaceutical cost-effectiveness analysis. Nevertheless, in relation to the fracturing of the PBS formulary and reduction of reference pricing we are left supporting the conclusion that the creation of the F1 category is likely to, over time, result in higher prices for some patented drugs than would have been the case under previous pricing arrangements.

In the face of ongoing lobbying by the multinational patented pharmaceutical industry strong ongoing Australian governmental, administrative and academic vigilance is required to protect its essential elements, particularly that of seeking a fair balance between price and proven community benefit in relation to public expenditure on medicines under section 101(3B[a]) of the *National Health Act 1953 (Cth)*.

Market and Evidence-Based Definitions of Innovation

One benefit of the AUSFTA to global medicines policy (probably unexpected by the multinational patented pharmaceutical industry) is that Annex 2C.1 emphasized a choice of alternate definitions of pharmaceutical innovation. The first was the principle of valuing pharmaceutical innovation through the operation of competitive markets. This was the US negotiating position which requires (and permits) strong anti-trust laws to be effective. Strengthening of Australian laws against fraud and anti-competitive behavior in the pharmaceutical industry could be a particularly positive outcome of the 'competitive markets' definition of pharmaceutical innovation of Annex 2C.1 of the AUFSTA.

The second (the Australian position) was that pharmaceutical innovation could also be valued by adopting or maintaining procedures that appropriately value objectively demonstrated therapeutic significance

(requiring and permitting regulatory processes for expert evaluation of pharmacoeconomic evidence related to such 'health innovation'). As such, AUSFTA Annex 2C.1 now not only helps preserve the core science-based processes of the PBS system, but helps frame the global debate on determining health technology innovation.

One illustration of this can be seen in Article 5.2 of the Korean-US Free Trade Agreement (KORUSFTA). The Koreans, having witnessed the debate over the PBS in the AUSFTA, determined to create regulatory space in the KORUSFTA for subsequent creation by them of a similar cost-effectiveness pharmaceutical evaluation process. Article 5.2 KORUSFTA, after recognising each nations' differing approach to medicines policy, indicates that if South Korea establishes a reimbursement system for pharmaceuticals or medical devices where the amount paid is not based on Competitive market-derived prices, then it has to appropriately recognize the value of patented pharmaceutical products (Article 5.2 [b][i]). KORUSFTA article 5.1 (c) and (e) respectively mention PBS-type sound economic incentives as a method of facilitating access to patented medicines and PBAC-style transparent and accountable procedures as a means of promoting health innovation.

The 2009 Kennedy Report on Valuing Innovation in NICE Assessments is directly relevant to debates such as that under the KORUSFTA about how to value pharmaceutical innovation. It strongly promotes, for example, what is in effect the Australian, PBS evidence-based approach to assessing and valuing innovation through expert assessment of objectively demonstrated therapeutic significance. The Kennedy Report recommends disinvestment or compensation to the government if an alleged innovative product fails to offer value or meet expectations made when being evaluated for public funding. It recommends a working definition of pharmaceutical innovation emphasising scrutiny of whether the relevant product significantly and substantially improves the way that a current need (including supportive care) is met. Other commentators have recently reinforced this approach by supporting the

view that empirical research suggests that patents are an ineffective incentive for innovation generally.

A recent academic survey of drug regulation is the US, Europe and Australia, for example, recommended that "well defined and consistent comparative effectiveness research is a much more rational and predictable way for payers to make purchasing decisions than for administrators to impose price cuts arbitrarily, to shift costs to individual patients, or to ration needed technologies and services according to ability to pay."

F1-F2 PBS Categories and Evergreening

A central method is use of the patent system by innovator companies to delay the appearance of generic competitors. In terms of the PBS this would involve strategies to keep drugs in the F1 PBS category and prevent them being transferred to the F2 category. The PBAC may be heavily involved in such PBS category disputes. Briefly, other evergreening tactics the PBAC may encounter include introducing once a day versions of a drug just before patent expiration to replace a three times a day form or bringing a single isomer version of a drug that was previously marketed as a racemic isomer (e.g., esomeprazole replacing omeprazole). Recently drug companies have used doctors to attack generic products in academic journals. Another recent development involves contractual agreements in which the generic manufacturer agrees not to enter the market in return for financial remuneration from the brand name manufacturer. Brand name companies will sometimes enter into agreements with a single generic company to allow that company to produce a generic version ("authorised" generics) of a drug that is soon to go off-patent.

Data exclusivity may end up being another evergreening strategy. Generic companies are unable to use the original safety and efficacy data for a period of time. If they want to bring a product to market while data exclusivity is being enforced they would have to conduct their own set of clinical trials to establish safety and efficacy. The cost of these trials would be prohibitive.

Making data exclusivity long enough could significantly delay the appearance of generics.

Problems with Patented Pharmaceutical Industry Policy in Australia

Pricing of new pharmaceuticals is non-transparent at best, and an exercise in global profit-gouging in the name of innovation at worst. The Australian Government has done a vast amount to encourage innovation in the pharmaceutical sector in Australia, with little reward.

Between 1990 and 2004, a succession of Australian governments funded a variety of regulatory initiatives, to obtain greater public benefit from pharmaceutical R&D and the pharmaceuticals sector. These have largely been unsuccessful and have too often resulted in wasteful subsidy of inefficient originator industries with Australian taxpayer funds.

On 29 May 2001, for example, the then Minister of Industry, Tourism and Resources announced a Pharmaceuticals Industry Action Agenda with an Implementation Group under the Chairmanship of Dr Graeme Blackman. Its key policy recommendations were to "promote increased investment and exports of pharmaceuticals goods and services" (action 2); "identify opportunities and facilitate growth in the export of pharmaceuticals industry" (action 7) "promote two-way movement between industry and academia" (action 11) and "align industry activity with the National Innovation Awareness Strategy" (action 14).

As part of this Action Agenda, and following on from similar programs dating from the late 1980s, the Department of Industry, Tourism and Resources between 1999 and 2004 operated the $300 million Pharmaceutical Industry Investment Program which rewarded manufacturers undertaking research and development in Australia. This program channelled support to nine companies, including one generics firm, FH Faulding & Co Limited (subsequently Mayne Pharma). It was replaced from 1 July 2004 by the Pharmaceuticals Partnerships Program worth $150 million over five years.

These policies focused on subsidising research and development and not on making the types of structural and regulatory changes that would support the sustainability of the regulatory components (particularly the TGA and PBAC) critical to a pharmaceutical industry in Australia. These policies of pharmaceutical industry development, in retrospect, paid insufficient attention to supporting and developing the PBS or enhancing the PBAC.

New Generics Industry policy and Therapeutic Groups Needed for Challenges of Biologics and Nanomedicine

The industry challenges that the PBAC and Australian industry policy will soon be facing are extremely challenging. It is estimated that several hundred new 'biologic' drugs are now in development pipelines, many by generic medicine companies. These include, for example, growth hormone, insulin, granulocyte-macrophage colony-stimulating factor (GM-CSF), or erythropoietin. Such drugs are distinctively derived from living cells and their manufacturing companies often prefer to call themselves 'discovery generics', to highlight the amount of innovative research required for successful product development of these generic products. The current worldwide market for protein-based biotech. drugs, is over $20 billion. Biotech. patents increased substantially in most nations in the period 1991-2002, including Australia (19 to 100), Canada (53-136), Sweden (24 to 93), US (1160 to 2342) and EU (650 to 2025). India (3 to 28), China (0 to 49) and Ireland (6 to 7) increased by comparatively small amounts, but achieved the strongest gains in the most recent years.

In the bio/nanopharma sector, Australia retains a leading role in the Asia-Pacific region and ranks number sixth the world in terms of number of firms. Without careful policy attention this positive situation may not continue. Remove Australia's three largest biotech companies (CSL, Cochlear and ResMed), for example, and the sector as a whole suffered a 14.6% decline of share price in 2006 (the NASDAQ Biotech Index falling 14.3 per cent in the same period).

Most medical ethics guidelines preclude clinical trials on a product that is demonstrably inferior to the current standard of care. Yet the PBAC may have to evaluate with such products without the capacity to require head-to head RCTs against the best already marketed therapeutic comparitor (instead of having to do modelling placebo RCTS).

A proposed US Federal Access to *Life-Savings Drugs Bill* is intended to alleviate such problems. It allows abbreviated approval of biological products that share the "principal molecular structural features" of previously approved brand-name products. Approval for pharmacy substitution is conditional on regulators approving a biologic as a clinically "interchangeable" product, rather than a "follow-on" (or "me-too'). The Bill grants the secretary of the Department of Health and Human Services (DHHS) the extraordinary discretion (and responsibility) of determining on a case-by-case basis, whether additional clinical trials are required. Such developments are likely to impact on a PBAC process that as a result of the F1-F2 legislative changes must now address the vague and subjective standard of 'clinical interchangeability (rather than the more robust and objective biological equivalence).

In Australia, nanomedicine is a rapidly growing industry sector. Hasty regulatory approval to the F1 PBS category of nano-versions of existing drugs (as is the case with generic 'biologicals') could place expenditure burdens of public health systems and risk damage to public health. In this context, given the presumptive claims that nanomedicine manufacturers will make for reimbursement reward of their 'innovation', the maintenance of a robust system of PBS reference pricing will be critical to ensuring that the Australian public obtains value for its nanomedicine expenditure. A recent European Science Foundation report recommends that the flexible enabling functions of nanotechnology in medical applications may be lost if coordinated policies facilitating investment and efficient regulation are not developed. At present, however, most regulatory concern in Australia seems to be focused generally on the safety of nanotechnology, rather than its cost-effectiveness. This will

change. At that time the PBAC process will need to have capacity to deal with much more complex evaluations.

Challenge of Pharmacogenetics

Pharmacogenetics (the science of studying genetically-determined responses to medicinal drugs) is another area that will provide particular challenges for the PBAC. Based on recent UK and US studies, about 1 in 15 admissions to Australian hospitals are due to or involve adverse drug reactions, many of these directly leading to adverse health outcomes. Such harmful side effects vary between individuals and range from failure to respond therapeutically, to minor illness and even death. A few Australian companies are already starting to invest in this area. One prominent example is Genetic Technologies Ltd, which is licensed by Myriad Genetics (USA) to carrying out BRCA breast cancer genetic screening. Australia, generally, has a strong related skills base in genetic sequencing.

Predicted developments in pharmacogenetics include (1) recording of individual patient pharmacogenetic profiles (2) establishment of prescribing guidelines, that will relate dose to genotype and highlight the possibility of adverse drug interactions (3) development of new drugs for patients with specific genotypes (drug stratification). This latter area could be of particular policy value in the context of Australian biopharma industry renewal. Pharmaceutical industry interest may extend to 'packaging' drugs along with genetic tests and takeovers or licensing of genetic test manufacturers.

If pharmacogenetics is to minimize drug expenditure by reducing wastage and simplify post-marketing surveillance, then both Therapeutic Goods Administration (TGA) and the PBS officials will need to be actively involved in policy development. Under definitions of reference pricing prior to the F1-F2 categories, for example, new patented drugs seeking PBS listing in conjunction with a genetic test would still need to be evaluated for comparative cost-effectiveness against existing marketed products (without linked genetic tests). Clinical trials are becoming increasingly expensive and

pharmacogenetics could provide a seemingly attractive way of reducing industry dependence on them for regulatory approvals and post-marketing surveillance. The Novartis Institutes of Biomedical Research has recently been promoting use of biomarkers to select research subjects with the idea of improving the efficiency of pharmaceutical clinical trials. Despite cautious present investor interest, linking medicines with a genetic test could facilitate valuable long term diversification in the Australian bio/nanopharma industry.

Tougher Laws to Prevent Monopolistic, Fraudulent and Anti-Competitive Behavior in the Australian Pharmaceutical Industry

It is estimated that, in the United States, as much as 10% of general public health expenditure could be eroded by some form of fraud or anti-competitive behaviour, even where appropriate laws and regulations are in place. In the health care area, legislation such as the *False Claims Act 1986* (US), the *Fraud Enforcement and Recovery Act 2009* (US), the *Stark (Physician Self-Referral) Statute 1995* (US), the *Anti-Kickback Statute 1972* (US), the *Food, Drug and Cosmetic Act 1938* (US), the *Social Security Act 1965* (US) and the *Patient Protection and Affordable Care Act 2010* (US) has created systematic processes whereby the Federal Government has recovered billions of dollars in fraudulently made claims. In the financial year 2009, eg, the government recovered US$2.43 billion as a result of anti-fraud actions, 67% of this involving health care and 81% of such actions being initiated by whistleblowers who received a percentage of the public moneys ultimately recovered. As well as the federal *False Claims Act*, 25 State jurisdictions in the United States now have legislative mechanisms allowing relators (whistleblowers), many of whom are corporate insiders, to reveal to law

enforcement officials fraudulent practices involving public moneys in return for a percentage of the damages amount ultimately recovered.

The federal *False Claims Act* allows a private citizen to file an action on behalf of the government, known as a "qui tam" action, and claim a share of the funds recovered.[1] A qui tam action can be brought by anyone who has knowledge of fraud on the government, provided that it is not based on already publicly disclosed allegations or transactions in a criminal, civil or administrative hearing; in a congressional, administrative or Government Accounting Office report, hearing, audit or investigation; or from the news media and the person is not an "original source" of the information. These limitations are designed to avoid "parasitic claims" by individuals who have made no material contribution to uncovering the fraud or providing the factual basis of the case. A qui tam action is filed under seal, and a "disclosure statement" containing all the relevant and material facts is served (in the case of federal *False Claims Act* filings, which may also include pendant State *False Claims Act* claims) on the Department of Justice (DOJ) in Washington, DC, the local attorney in whose district the case is filed, and (if State *False Claims Act* claims are included) designated State government officials.[2] Following a preliminary investigation, if the relevant government decides to intervene within the statutory time period, it takes over the running of the case. The individual who initially made the disclosure remains as a "relator" to the proceedings. If the government declines to intervene, the individual through her or his lawyers can still proceed themselves;[3] however, this type of action is far less successful. When a qui tam action is successfully prosecuted, the relator is allowed a 15% to 20% share of the recovery if the government intervenes;[4] and between 25% and 30% where the government does not.

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[1] 31 USC § 3730 (b)(1), (d).
[2] 31 USC § 3730(b)(2).
[3] 31 USC § 3730(b)(4).
[4] 31 USC § 3730(d)(1).

Under the "American rule", each party to an action generally pays their own costs; however, a successful qui tam relator is entitled under the statute to have attorneys' fees and costs reimbursed by the defendant, in addition to receiving a percentage of the recovery. Crucial differences from the Australian position are that a criminal prosecution is no bar to civil proceedings (in fact, parallel criminal and civil investigations and recoveries are common) and that the government obtains triple the damages it sustained because of the false claim as well as a civil penalty of between US$5,500 and $11,000 per false claim. The United States Government can recover *False Claims Act* penalties even where it can prove no damage.[5] Where the government paid for goods that were never received, or services, such as medical treatment, which were not actually performed, the single damages (ie, before trebling) are equal to the full amount paid by the government for the non-existent goods or services.[6] Where, due to under-delivery or under-performance, the government was overcharged, the general rule is that the single damages are measured by the difference between what the government paid for the items or services and what it should have paid. Where the government has been overcharged as a result of collusive bidding or bid-rigging, the single damages are calculated as the difference between the amount the government actually paid, and the amount it would have paid in an open and competitive bidding environment.[7] The government can recover full *False Claims Act* damages where the goods or services were provided as a result of some underlying fraudulent conduct such as false statements or violations of the *Anti-Kickback Statute 1972* (US). The United States Government's *False Claims Act* damages are trebled before any offset or compensatory payments received by that government are taken into account.

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[5] *United States ex rel Hagood v Sonoma County Water Agency* 929 F 2d 1416 at 1421 (1991).
[6] *United States v Pani* 717 F Supp 1013 (1989).
[7] *Brown v United States* 524 F 2d 693 at 706 (1975).

The legislative scheme has allowed recovery of damages for a range of common fraudulent practices in the United States pharmaceutical, medical device and health care sectors that are likely to exist also in Australia. These include:

- making claims for government money involving a false certification;
- over-utilisation of clinical laboratory and diagnostic services;
- inflating the price used for government reimbursement above that charged to pharmacists and other private payers;
- concealing discount prices afforded to non-government payers and otherwise improperly pricing drugs, misbranding, providing defective and poor-quality health care items and services;
- billing for medicines or health services not provided or inadequately or inappropriately provided;
- colluding to inflate price, "off-label" promotion of drugs (ie marketing for unapproved uses);
- providing kickbacks to doctors and institutions that prescribe or purchase products; and
- discounting medicines to hospitals which then charge the Federal Government a higher price.

In response to the global financial crisis, Congress enacted the *Fraud Enforcement and Recovery Act* in 2009, which included amendments to the *False Claims Act* strengthening the legislative scheme by overturning certain court rulings that did not reflect the original intent of the *False Claims Act*. It is now clear that the *False Claims Act* reaches all recipients of government funds, including subcontractors, private contractors administering government health programs and recipients of federal block grants. It is enough that a false statement made by a contractor or subcontractor was "material" to the government's decision to pay, regardless of the entity to whom the false statement is made. The *Fraud Enforcement and Recovery Act* also amended the

False Claims Act to make it actionable to retain (or conspire to retain) for more than 60 days, public funds known to have been paid in error.

A terminated whistleblower's signing of a release of all claims against her or his former employer does not bar the subsequent filing of a qui tam suit against the employer putting the government on notice of a fraud. However, where the government was sufficiently aware of the alleged wrongdoing prior to the qui tam filing, a pre-filing release signed by the relator will be upheld and the qui tam action will not be permitted. Although the *False Claims Act* prohibits the settlement (or voluntary dismissal) of a qui tam action without the government's consent, this only applies to settlements reached after a qui tam action has been filed.

Another tool the United States Government has used to seek recompense from the pharmaceutical industry is an anti-trust statute, the *Hart-Scott-Rodino Antitrust Enforcement Act 1976* (US). This Act is administered by the Federal Trade Commission (FTC) and the Antitrust Division of the United States Department of Justice (DOJ). The FTC recently filed a case, *FTC v Ovation Pharmaceuticals Inc*, seeking to recover profits relating to Ovation's 2006 acquisition of a monopoly over medications to treat a serious heart condition that primarily affects low birth-weight infants. Once a monopoly was obtained, Ovation raised the price for NeoProfen and Indocin, the only FDA-approved drugs to treat the condition.

Recent examples from Europe highlight the global significance of the problem of collusion in the pharmaceutical industry and the difficulties associated with detecting, investigating and prosecuting fraud in these sectors. In 2008, the Competition Commissioner of the European Commission coordinated unannounced raids on the offices of leading pharmaceutical companies, including GlaxoSmithKline (United Kingdom), AstraZeneca (United Kingdom), Sanofi-Aventis (France), Pfizer (United States) and Novartis AG (Switzerland). The raids were considered to be the only practicable option

available to gather evidence that fraud and anti-competitive practices, such as strategic "evergreening" of patent clusters in the sector, had stalled innovation and blocked the entry of cheap generics into the market. Like Australia, the European Union lacks civil fraud recovery provisions similar to the United States *False Claims Act*'s qui tam mechanism.

As an example of a *False Claims Act* case in the United States pharmaceutical sector, the pharmaceutical company Eli Lilly pleaded guilty in 2009 to a criminal charge of promoting the anti-psychotic Zyprexa for use outside FDA guidelines and was required to pay a criminal fine of $US515 million, plus a US$100 million forfeiture, for a total criminal resolution of US$615 million. In addition, the company agreed to pay up to US$800 million, to be split between the Federal Government and participating States, to settle civil claims of Medicaid and Medicare fraud. Altogether, the settlement yielded a total recovery of US$1.415 billion. The company promoted Zyprexa as a sedative in nursing homes, despite known risks of heart failure and pneumonia; and for use in disruptive children, despite known risks of severe weight gain. In this case, over US$78 million of the government's civil recovery was shared among six *False Claims Act* relator employees. Most of Zyprexa's United States sales (which have totalled $US39 billion since FDA approval in 1996) have been paid for by federal government programs, as the drug is largely prescribed among indigent or disabled populations. The crucial factor in the case was hundreds of internal Eli Lilly documents and email messages among top company managers that showed that the company had sought to play down Zyprexa's tendency to cause weight gain and metabolic disorders, including diabetes, over a long period of time, while promoting the drug for unapproved uses.

The Australian legal system has developed considerably since 1989, when a federal committee on insider trading recommended that qui tam laws were "incompatible" with accepted principles and practice in the Australian legal

system. Over the past 20 years, anti-competitive behaviour has increasingly been regarded as a serious crime by Australian regulators. Champerty has been abolished in most jurisdictions, and litigation funding companies are permitted to back public interest class actions. It is undisputed that large-scale corporate fraud and anti-competitive behaviour are incompatible with Australian values.

While Medicare Australia, within the Federal Department of Health and Ageing, has an anti-fraud program, it is primarily focused on discovering fraud by individual health care professionals. Further, the pharmaceutical and medical device sector has not been listed by the ACCC as one of its regulated industries. The ACCC's anti-trust model in this area is based on an immunity policy, and tight controls on a voluntary code of conduct. Its effectiveness in comparison with United States anti-trust laws has never been systematically investigated. There could be significant benefits to the Australian Government, and community more broadly, by implementing qui tam reforms and new evidentiary techniques for discovering fraud and anti-competitive behaviour in these sectors.

The amount of public money that reforms in this area could recover is significant. It is estimated that the return to the United States Government is $15 for every $1 spent on qui tam investigations and litigation. In 2009, the United States DOJ announced that it had recovered over US$24 billion for the Federal Government since 1987, $15.6 billion of which resulted from qui tam actions. These numbers are actually understated, as they do not include civil *False Claims Act* recoveries by the States or criminal fines arising from parallel criminal/civil cases. For example, the official DOJ total for 2009 is $2.4 billion. When State recoveries and criminal fines are included, the total is $5.6 billion. Since 1987, relators who made public interest disclosures in qui tam proceedings have been paid approximately US$2.4 billion.