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National Health and Hospital Reform Commission

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Contents

Executive Summary

- This submission considers proposals for reform in some major areas affecting Australian health and hospital policy. These include the balance between private insurance and public hospital services, health technology safety and cost-effectiveness assessment, encouraging health innovation as an evidence-based concept and a balance between branded and generic pharmaceutical products.
- In the background to such discussions is whether Australian health technology policy should support a conception of **health technology innovation driven by lobbying and advertising** (the US "competitive markets" approach to pharmaceutical innovation mentioned in Annex 2c.1 of the AUSFTA) OR a **scientific evidence approach to health technology innovation** (the Australian 'objectively demonstrated therapeutic significance approach to pharmaceutical innovation mentioned in Annex 2c.1 of the AUSFTA).
- A central part of this submission's health technology recommendations is the need for a multidisciplinary body to oversight "me-too" and incremental patent claims and distinguish them from the impending avalanche of 'evergreening' or 'me-too' ploys with minimal additional community benefit over existing comparitor products, supervising a single list of recognised pharmaceutical patents (that makes searching by intending generic entrants easier) and facilitating rapid hearing and clearance of related patent claims. This would be modelled on the Office of Patented Medicines and Liaison in Health Canada.
- The submission recommends that too encourage a growing generic pharmaceutical sector, the first company to achieve market entrance (often after defeating an 'evergreening' claim) should receive a period of market exclusivity and capacity to have refunded a portion of TGA and PBAC costs.
- The submission recommends that to foster a biologics and nanotherapeutics industry in Australia with regional export opportunities discussion items be included (after prolonged consultation with leading Australian industry and academic stakeholders) in the trade in goods sections of bilateral trade deal negotiations with China, India and Japan.
- The submission recommends the insertion in the Australian constitution (after a general human rights or specific referendum) of a constitutional right to emergency health care, (as in the South African and India constitutions amongst others)

This Submission in Relation to NHHRC Terms of Reference

This submission focuses in particular on practical reforms proposals and benchmarks to maintain equitable and sustainable access to hospital services, given the growing burden of chronic disease, population ageing, costs and inefficiencies generated by blame and cost shifting. It also focuses on proposals to maintain equitable and sustainable access to and the escalating costs of new health technologies. It takes into account the need to

a. reduce inefficiencies generated by cost-shifting, blame-shifting and buck-passing;
b. better integrate and coordinate care across all aspects of the health sector, particularly between primary care and hospital services around key measurable outputs for health;
c. bring a greater focus on prevention to the health system;
d. better integrate acute services and aged care services, and improve the transition between hospital and aged care;
e. improve frontline care to better promote healthy lifestyles and prevent and intervene early in chronic illness;
f. improve the provision of health services in rural areas;
g. improve Indigenous health outcomes; and
h. provide a well qualified and sustainable health workforce into the future

The proposals in this submission are focused on maintaining the principles of universality of Medicare and the Pharmaceutical Benefits Scheme, and public hospital care.

The submission takes into account the NHHRC principles as set out below:
Proposed design principles
(generally what we as citizens and potential patients want from the system).

1. **People and family centred:**
2. **Equity**
3. **Shared responsibility:**
   Strengthening prevention and wellness:
4. **Comprehensive:**
5. **Value for money:**
6. **Providing for future generations**:
7. **Recognise broader environmental influences shape our health:**
8. **Taking the long term view:**
9. **Safety and quality:**
10. **Transparency and accountability:**
11. **Public voice:**
12. **A respectful, ethical system:**
13. **Responsible spending on health:**
14. **A culture of reflective improvement and innovation:**

The Role of Private Health Insurance in Australia

Private health insurance (PHI) in Australia currently plays a prominent duplicate role in health care cover, providing private alternative coverage for the same set of services supplied in the public health system.

The economic arguments in favour of duplicate PHI stated in the literature are as follows:

- PHI increases consumer choice by:
    - providing enrolees with more choice regarding the timing of care or
    - a broader choice of providers

This is possible since it reimburses the cost of care in private hospitals that are partially or not publicly funded, providing access to services that may not be covered by the public system. Also, private insurers generally do not selectively contract with providers in these countries, thereby typically providing unrestricted choice of doctors and hospitals across the private sector. (Lokuge, Denniss and Faunce 2004)

- For those that obtain PHI, it allows for faster access to treatment in the private system, which in turn decreases the pressure upon the public system and reduces waiting times for those who remain.

- It increases the resources available on a per capita basis in the public system, as those who purchase private health insurance still continue to pay taxes. (Madore 2008)
- It is increasingly viewed as the main vehicle to channel finances towards private hospital care, shifting demand and cost from public to private hospital providers. PHI is considered necessary to sustaining a viable and dynamic private care sector, thus maintaining individual choice and reducing pressures on public hospitals (OECD 2003)

How well has PHI met these goals?

The evidence in the literature suggests that although PHI has been successful in addressing some policy goals, many challenges remain. In fact, a number of authors question the ability of PHI to achieve the objectives expected by policy makers, viewing PHI as contributing to the problem rather than mitigating it. Some of these concerns are summarised below.

Although PHI has improved individual choice, either by individual tailoring to preferences by selecting among different products or choice over providers (public or private) and their timing of care[4], it has been shown that the availability of more coverage options does not necessarily bring to more effective consumer choice. PHI markets in Australia and the United States, for example, are characterised by a broad choice of covered benefits and levels of cost sharing, often making it difficult for consumers to understand their options. Furthermore, product choice can undermine risk pooling within the market. This indicates that a wide selection of health care insurance products may not be necessary in order to provide consumers with meaningful and satisfactory choices (OECD 2004)

Where PHI has facilitated the development of private delivery services and additional capacity, it has enhanced access to timely elective care for privately insured individuals. This though has not resulted in the expected reduction of waiting times in the public system as PHI has also increased overall demand of health services. In addition, privately insured patients appeared to be using the public sector for complex and urgent procedures and the private sector for less complex and non-urgent procedures (Dawkins et al 2004) These findings are consistent with experiences in New Zealand and Ireland. ((Blumberg 2006)

It has also been noted that incentives have been created by higher payment levels in PHI markets that have encouraged providers to

maintain long queues in the public system or refer patients to their own private facilities in order to sustain their private practice.

Cost containment – value for money

The expansion of PHI in Australia over the past decade was expected to reduce the pressure on public hospitals in relation to waiting lists, as well as reduce the financial burden on the public system. In addition, by allowing market forces to dictate the decisions of players in the health care market, PHI was expected to bring about greater efficiencies and therefore increased value for money. However, the evidence indicates that this has not occurred due to both inherent failures in the market and disincentives created by particular government policies.

Firstly, PHI has removed little of the cost pressures from public health financing systems. As noted above, the privately insured patients continue to use publicly financed health services, even if they hold private coverage, with private providers typically concentrating on elective treatments. PHI also tends to have a moral hazard effect. PHI coverage of cost sharing on publicly financed health services removes price signals and incentives to consume health care sparingly. Furthermore, the shift towards PHI has come at considerable cost to the Australian Government by the implementation of subsidies such as the 30 per cent rebate.

This trend is not unique to Australia, as many commentators have pointed out that PHI has increased total health expenditure, and at times public expenditure, in several OECD countries, resulting in increased overall health expenditure (OECD 2004)

Compounding the problem, in most countries, private health insurers have not been subject to such centralised, governmental controls of health care costs. This has generally resulted in less tight control over privately financed activities and prices. Private insurers do not have the same bargaining powers over the price and quantity of care provided to insurees as public systems do. Thus, expenditure control

is harder to achieve in systems with multiple payers, which includes most PHI markets, and those with fragmented relationship between providers and payers. Purchasers have a weaker bargaining position relative to providers than single-payer or integrated national health systems do, especially when insurers do not bargain collectively with providers.

Secondly PHI has not resulted in the value-based competitive markets as hoped. The lack of readily understood comparative information about available products and high transaction costs has hindered movement between insurers. Also, competition itself may not develop on price and quality; rather, insurers tend to compete by selectively marketing certain benefit packages to applicants who represent "better risks" – i.e. risk selection. The inability of insurers to compete on price and quality grounds very much depends on their relative power over providers. Market forces driving efficiency can be greatly inhibited if providers exercise dominant market power, leading them to enforce high health services prices and shielding them from insurer-pressure to improve quality and cost effectiveness of care. Thus, in general private insurers have not served as an impetus for quality improvement within the health care system. An important exception to this trend, however, has occurred in the United States, where certain insurers and self-funded employer-sponsored health plans, particularly "managed care" plans, have been very involved in directing and overseeing certain aspects of care delivery. By exerting more leverage over the care they purchase, insurers seek to secure a competitive advantage through products offering good quality and value for money.

Finally the extent to which PHI enhances equity is debatable. There is strong evidence that a larger number of households of higher income and socio-economic standings are more likely to have PHI even without the government incentives such as the rebate. These latter households enjoyed deadweight benefits, "in the sense they needed no such benefits to purchase PHI to begin with. Given that households

who took up PHI ought, by their revealed preference, to be better off, it can be concluded that households with high income and socio-economic standings are the main beneficiaries of the policy changes. The lower uptake of PHI in rural areas is an example of how policies directed at increasing the uptake of PHI can exacerbate disparities between sections of the community. Since PHI uptake is lower in regional areas relative to urban and the fact that private facilities are clustered around cities, policies that funnel public money into private health services (such as the PHI rebate) are unlikely to reduce the load on the public system in regional areas as private facilities are often not available as substitutes. Additionally, regional Australians who are encouraged to take up PHI by the tax systems (for example the Medicare Levy) are essentially subsidising the PHI industry at the expense of local public health services.

Policy recommendations

There is a reasonable argument for a scaling down of the 30 per cent rebate, given that its distortionary effect on the market has not achieved its aim of taking the pressure off the public system. The recent increase in the Medicare Levy threshold in the 2008 Federal budget and the associated savings highlight the fact that the money spent on the rebate could have been better used elsewhere, for example directly subsidising the supply of important health services that will directly take pressure off the public system. If these monies were spent in regional areas, this would have the additional effect of reducing the disparities between urban and rural health acre currently experienced.

However, for the continued viability of the PHI industry in Australia constraining regulatory features need to be relaxed. Partial reform may include insurers to experience rate on the basis of age and gender reducing the need for younger people to balance the risk pool. Concurrent to this would be a subsidy that results in insurers being

indifferent between the elderly and young – maintaining private coverage for a large section of the population.

Of greater importance is a clear determination by policy makers of the role PHI and private providers are to play within the health system. This will involve better integration of the health system, in particular the private and public funding and private and public hospital systems. There is a strong case for PHI to plays a more complementary role with the public system, where Medicare and the public system provide a base coverage for all health needs of Australians. PHI would then become a form of top up to the public system.

To enhance the possibility of increased efficiencies in the health system, a greater degree of competition needs to be injected into the health. A possible option is to introduce some form of managed care into the system via, for example, the establishment of budget-holding entities. Although such arrangements may be inhibitory on choice, it allows for the vertical integration of funding and provision and enhances pressure on providers to reduce costs and maintain or improve upon quality.

The Balance Between Public Hospital and Private Health Insurance Systems;

The US Approach

United States Health expenditures are projected to double and consume 20 percent of national income over the next decade, with increasing numbers of people losing their insurance.(Schoen et al 2008) Much of the debate on how to move forward to achieve universal coverage centers on the relative roles of privately and publicly sponsored insurance. In the United States, more than 60 percent of the under-sixty-five population now receives insurance through employer-sponsored health plans to which employers contribute an estimated $420 billion per year. In the general United States population, however, support for public insurance is also strong—with 40–50 percent supporting a

public approach. The reasons relate to the fact that a change in jobs or job status can trigger a gap in health insurance and to volatility in private insurance markets where market competition often results in practices to avoid adverse risk selection. As a result, the U.S. insurance industry is characterized by high overhead costs for marketing, underwriting, and administration, but high profit margins. In recent decades in the US, Medicare, Medicaid, and the State Children's Health Insurance Program (SCHIP) public health programs, while states such as Massachusetts have enacted a combined approach that offers a choice of publicly sponsored and private plans.

The OECD Approach

A recent OECD health system report (2004) has stated that many OECD countries have started to monitor indicators of health-care quality, often for benchmarking purposes as part of broader efforts to track and improve health-system performance. In most countries, attention has first focused on the quality of hospital care, but initiatives to evaluate other health and long-term care settings are also under way. Such efforts can be strengthened by developing tools like clinical practice guidelines and performance standards that promote the practice of evidence-based medicine, provided that those standards are not designed to produce statistics that drive ideologic pro-privatisation agendas.

Paper medical records, prescriptions, and test reports do not support accuracy, access or sharing of information. Hospitals in Australia and the United States that have adopted automated systems for placing medication orders in hospitals have achieved marked reductions in the rate of medication errors and related patient injuries, resulting in measurable improvements in quality and shorter lengths of stay. The next big step will be to integrate hospital outcome data with prescription data to prevent "leakage" from PBAC recommendations and to allow post-approval claw-backs or reduction of subsidy for underperforming patented F1 medications.

Concerns have been voiced in a number of OECD countries that a gap may be looming between demand for and supply of the services of physicians and

nurses. Indeed, shortages have already appeared in a number of OECD countries. Despite increasing demand for services, supply is projected to fall, or at best to grow slowly (in the absence of countermeasures) as a result of societal trends to reduce work hours and retire early, physician workforce ageing, and diminished interest in nursing, relative to other professions. Increasing salaries and financial incentives (salary packaging of a wider number of items) is only one step towards a solution. One idea to increase the prestige and career prospects of nurses is to allow them to collect adverse incident data on both doctors and nurses for their own nurse-controlled data base, charging fees for access to the data and supporting nursing PhD's to analyse it.

Inequities in service use persist in some countries. These reflect factors such as the impact of user fees on lower-income groups, differences in insurance coverage across the population, the extent to which politicians have been influenced and conflicted by industry and the extent to which citizens are able to bring constitutional actions against inequitable health policies. The outcome can be poorer population health, which further fuels economic isolation and social exclusion and unrest.

Medical technological advances offer chances to improve patient care and health outcomes, but they can increase aggregate costs as well. Uncertainty regarding costs and benefits, which is often the case, creates a dilemma for decision makers. Countries differ greatly in how decisions to adopt and pay for new heath-related technology are made, and these in turn affect diffusion. The United States has been waging a global campaign against reference pricing which is one of the few effective tools available to ensure the price for underperforming technologically new medicines reflects their actual community value. Australian policy makers to date have lacked the will, insight or interest to oppose this.

Some emerging technologies, such as gene therapies, pose ethical challenges that can make decision-making even more difficult. The conditional approval of promising technologies, pending further study is a frequent lobbying ploy of industries desperate for venture capital and prepared to trade off public safety and the precautionary principle for that. Rigorous technology assessment safety, quality and efficacy practices are

undermined by the client-relationships created by user fees and pressure to 'fast-track'. The use of transparent processes for decision-making is regularly undermined by industry 'commercial-in-confidence claims.

In at least a dozen OECD countries, waiting times for elective surgery are viewed as excessive. Often this is exaggerated as part of the pressure exerted by managed care organizations to dismantle public health care. Moderate waiting times do not appear to have negative effects on health outcomes, but they do affect quality of life; also, those waiting in discomfort are less likely to be fully productive in their work. If the supply of surgery is judged to be adequate, waiting times can also be reduced by ensuring that patients are not added to waiting lists unless (or until) their need exceeds a threshold level, while those with greatest need are assured of timely services. A number of countries are experimenting with policies to provide patients with more choice in long-term care services and to help patients get care at home, rather than in an institution, when feasible. Some countries provide funds to be spent upon such care, rather than payment for covered services, and such funds may be used to support family caregiving in most cases. This yields increased flexibility and control over services received, and reduced feelings of dependency. However, consumer-directed spending policies are likely to be more expensive than traditional approaches.

Cost-sharing requirements for users of health services can reduce the burden on public financing systems. But major savings from user fees are unlikely, particularly as vulnerable populations must be exempted to avoid restrictions on access that could be costly in the long run. Such exemptions impose administrative costs. Apart from this, patients are likely to skimp on preventive care and appropriate treatments unless they are given incentives to do otherwise. Complementary private health insurance can help to ensure access to care where cost-sharing requirements are large. But it can drive up patient demand and overall costs at the same time.

Private health insurance premiums are a regressive source of financing compared with income-based taxes or social insurance contributions. Policy makers should carefully craft regulations and/or fiscal incentives to ensure that policy goals are met. Absent such interventions, private health insurance markets will fail to promote access to coverage for people with chronic

conditions and other high-risk persons – as well as those with lower incomes. Additional interventions, such as standardisation of insurance products or other steps to help consumers understand the costs and benefits of insurance, can increase the potential of private insurance markets to make a positive contribution to health-system performance. People need protection against the risk of incurring large expenses for long-term care, as for acute health-care and disability. Different approaches can work, such as mandatory public insurance (as in Luxembourg, Netherlands and Japan), a mix of public and mandatory private insurance (as in Germany), tax-funded care allowances (as in Austria) and tax-funded in-kind services (as in Sweden and Norway). The market for private long-term care insurance is small, but could increase with the right policy support.

Countries have slowed cost growth using a combination of budgetary and administrative controls over payments, prices and supply of services. The health sector is typically characterised by market failures and heavy public intervention, both of which can generate excess or misallocated spending.

In systems where both financing and delivery of care is a public responsibility, efforts to distinguish the roles of health-care payers and providers, so as to allow markets to function and generate efficiencies from competition, have proved generally effective. In systems of any type, shifts in responsibility in health-care management or administration can also reduce waste and increase productivity. For instance, certain qualified nurse practitioners might undertake certain duties that are also performed by physicians, where safe and appropriate.

Nurses or general-practice physicians can serve as gatekeepers, assessing need for treatment and directing patients to the most appropriate care provider. With the Internet, patients can be better informed about the costs, risks and expected outcomes for treatments. This could either temper or increase their demand. To promote value, patient cost-sharing requirements might be employed in a more discriminating manner, letting patients benefit financially from making cost-effective treatment choices.

The PBS and Science or Evidence-Based Methods of Valuing the Community Value of Innovation

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 (Department of Health 2007a). The success of the PBS pricing and listing mechanisms can partly be appreciated through lower average pharmaceutical prices for the government compared with other developed countries (Australian Government Productivity Commission 2001). It is also popular with the public as listed medicines are available for a relatively low co-payment of approximately AU$30 (Department of Health 2007b).

The low costs of medicines are achieved through the PBS pricing and listing mechanisms, parts of which were radically amended in mid 2007. (Faunce 2007a) 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))).

Working through a hierarchy of evidence, the PBAC and its and its advisory subcommittee assess the cost-effectiveness of the submitted product against its best already marketed comparitor. This is the core of the PABC's evidence-based approach to assessing ***the community value of health technology innovation, a concept known as 'health innovation'*** to distinguish it from lobbying and adversting-based approaches to establishing the innovation credentials of new health technologies. If the product is deemed not cost-effective, in a cost-minimisation exercise its price is referenced down to that of the comparitor. Reference pricing, in its most fundamental sense, then applies post-listing when new competitors (with lower prices) enter six groups presently established under the Therapeutic Group Premium (TGP) Policy. In this TGP system, the unusual criterion of "individual interchangeability" assists patients wishing to obtain an alternative to a drug in one of these groups whose price has a high additional premium.

If the PBAC recommends against listing a particular pharmaceutical, the manufacturer can still access the market and promote its product, however the consumer will have to pay a higher out-of-pocket price. The PBS process is thus not a non-tariff barrier to trade. It also facilitates a more science-based approach to pharmaceutical pricing. The Pharmaceutical Benefits Pricing Authority (PBPA) uses the PBAC recommendation to negotiate a maximum amount the government will reimburse to pharmacists. (Sansom 2004). It, as mentioned, is an evidence-based system of evaluating pharmaceutical 'health innovation' on the basis of objectively demonstrated therapeutic significance, in line with the four main objectives of Australia's ***National Medicines Policy*** (Department of Health 2007c):

- 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.

Australia's Pharmaceuticals Policy in a Global Context

Worldwide, generic pharmaceutical manufacturers comprise a large segment of the global pharmaceutical industry, and are collectively expanding at a faster rate than the so-called 'innovative' or 'brand name' sector, as a consequence of systematic regulatory encouragement, mergers and acquisitions, as well as the growth of a new market for 'biosimilars'.[1] Generics sales (in the top eight national markets) in 2005 were about US$55 billion, which represents about one tenth of the total global prescription drug market.[2] A UK-based business forecaster has predicted the Australian generic pharmaceuticals market, with appropriate regulatory support, should have doubled in value to $2.4 billion a year by 2009 on the back of three per cent rise in market share from the current estimate of 12.8 per cent.[3] As we shall see, for a variety of structural and regulatory reasons, such estimates now are being conservatively revised.

Under the Pharmaceutical Benefits Scheme (PBS) cost-effectiveness reimbursement system, as it operated between the late 1990's and 2004, Australian generic pharmaceutical firms competed not on PBS price, but for deals with retail pharmacists (by offering convenient supply arrangements and, most significantly, large discounts, in the order of 30% or more). They also benefited (as did the Australian public and Federal government) from the process of reference pricing and cost-effectiveness assessments involved in the

[1] Lofgren H. *Generic Drugs: International Trends and Policy developments in Australia. Working paper 10*. Centre for Strategic Economic Studies. Melbourne 2002.
[2] Gray N. **Changing Landscape: A Special Report on the World's Top 50 Pharma Companies**. *Pharmaceutical Executive* 2006, **May**: 78-88.

Australian PBS listing process. This ensured relatively favourable prices for 'brand-name' medicines, but slightly higher prices for generics, compared to the US and some other developed countries.[4] The way the PBS operated, however, provided little incentive for the generic suppliers to engage in price competition.[5] 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.[6]

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 Pharmaceutical Benefits Advisory Committee (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). If the submitted product is proven to be substantially more costly than such comparitors, then a significant improvement in efficacy or reduction in toxicity has to be established to justify listing. This provision provides the legislative basis for reference pricing under the Australian PBS.

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[3]Business Monitor Australia *Pharmaceuticals and Healthcare Report.* Available at: http://www.pharmainfocus.com.au/news.asp?newsid=1143 (last accessed 8 May 2006)

[4] Productivity Commission 2001. *International Pharmaceutical Price Differences: Research Report.* Ausinfo Canberra. 2001

[5] Sweeny K. *Review of Findings: Australian Pharmaceutical Pricing in a Global Context, Working Paper No. 19,* Centre for Strategic Economic Studies, Victoria University, Melbourne 2004.

[6] Neville W, Unpublished PhD Thesis 2007. Globalisation and Health Project. Centre for Governance of Knowledge and Development, Regulatory Institutions Network, Australian National University.

Reference pricing is perhaps the central component of the basic architecture of the PBS system.[7] Reference pricing is government price reimbursement mechanism which at the core of most definitions compares a new pharmaceutical on grounds of objectively demonstrated therapeutic significance related to measured outcomes on its primary clinical indication, when compared against already available products and therapies in the same therapeutic group.[8] Prices of all drugs in such a group are tied to that of the lowest, or in some cases the average, price. [9] This does not necessarily mean that the reference price becomes the market price for all drugs in the same therapeutic class, rather the reference price becomes a benchmark.[10] Manufacturers can set prices higher than the reference, but in doing so they need to genuinely compete in the open market against equivalent lower priced medicines. The resultant expert recommendation may allow the creation of either positive or negative lists for government reimbursement of pharmaceutical prices.[11]

Between 1990 and 2004, a succession of Australian governments funded a variety of regulatory initiatives, to obtain greater public benefit from the PBS system, pharmaceutical R&D and the generic pharmaceuticals sector. Reference pricing and the capacity it gave government reimbursement to reward innovation scientifically proven to be of objectively demonstrated therapeutic significance, was central to capacity of these policy initiatives to fulfil the core elements of the thoroughly debated approach to competitive markets encapsulated in the Australian National Medicines Policy. **The four principles of the**

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[7] Sansom, L**. The subsidy of pharmaceuticals in Australia: Process and challenges.** *Australian Health Review*, 2004. **28(2):** p. 194-205

[8] Ioannides-Demos L; Ibrahim J; McNeil J. **Reference-Based Pricing Schemes: Effect on Pharmaceutical Expenditure, Resource Utilisation and Health Outcomes. Review Article** *Pharmacoeconomics*. 2002; **20(9**):577-591.

[9] Lipsy RJ. **Institutional formularies: the relevance of pharmacoeconomic analysis to formulary decisions.** *Pharmacoeconomics* 1992;**1(4):**265-81

[10] Jacobzone S. 2000 *Pharmaceutical policies in OECD countries: reconciling social and industrial goals.* Paris, OECD. DEELSA/ELSA/WD (2000)1.

[11] Giuliani G, Selke G, Garattini L **The German Experience in Reference Pricing** *Health Policy* 1998; **44(1):** 73-85

National Medicines Policy reflect a fair balance of stakeholder concerns:

> 1. timely access to the medicines that Australians need, at a cost individuals and the community can afford;
> 2. medicines meeting appropriate standards of quality, safety and efficacy;
> 3. quality use of medicines; and
> 4. maintaining a responsible and viable medicines industry.[12]

One such recent Australian pharmaceutical industry initiative involved the minimum pricing policy, introduced in December 1990. This encouraged patients to switch from innovator brands to corresponding generic products. The effect, however, was marginal, since pharmacists could only dispense the brand prescribed by the doctor, and the average surcharge or brand premium was only about $1 per prescription. Brand substitution by pharmacists was introduced on 1 December 1994, when generic medicines constituted only 2% of PBS expenditure. This policy allowed supply of less-expensive generic medicines at the request of the patient, regardless of which brand the doctor had prescribed. In February 1998, the government introduced the therapeutic group premiums scheme (TGPs). Its objective was to introduce greater competition into the pricing of medicines judged to have an equivalent therapeutic effect, even though they were not identical chemical compounds. The availability of cheaper generics was then supposed to have flow-on positive effects in decreasing PBS reimbursement of all products in such groups (despite the extent of brand premiums).

On 29 May 2001, 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).[13]

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).[14] 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 a generic pharmaceutical or nano/biotech. industry in Australia. Crucial to such sustainability is a system of high rewards for genuine innovation objectively demonstrated by expert comparison of outcomes on core clinical indications against all competitors. PBS reference pricing provides this high reward for success in true competition on a level playing field. These policies, in retrospect, paid insufficient attention to supporting and developing PBS reference pricing.

Industrial Renewal: Biologic Generics

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[12]Commonwealth of Australia. National Medicines Policy. Available at: http://www.health.gov.au/internet/wcms/publishing.nsf/Content/nmp-objectives-policy.htm (last accessed 6 Feb 2007)

[13] Australian Government, Department of Industry, Tourism and Resources. 2001. *Pharmaceuticals Industry Action Agenda* Accessible at: www.industry.gov.au (last accessed 22 Oct 2006)

[14]Pharmaceutical Industry Investment Program (PIIP) 1999-2004. Available at: http://www.industry.gov.au/content/itrinternet/cmscontent.cfm?objectID=FDBCC43B-898E-4433-AFCA84E5DF7D417D .

It is estimated that several hundred new 'biologic' drugs are now in development pipelines. 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.[15]

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.[16] 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).

One main obstacle to generic investment in such biologics, is the difficulty in obtaining regulatory quality, safety and efficacy approval for marketing. To achieve such marketing approval, a generic 'biologic' manufacturer must uniquely prove to a regulator use of the same protein expression system, purification protocol, and delivery

[15] Lawrence S. **Biotech Patenting Upturn** *Nature Biotechnology* 2007; **24 (10):** 1190.
[16] Economist Intelligence Unit. *Benchmarking Study of the Characteristics of the Australian and International Pharmaceuticals Industry*. Sept 2005. Australian Government. Dept. of Industry, Tourism and Resources Lofgren H, Benner M: **Biotechnology and Governance in Australia and Sweden: Path Dependency or Institutional Convergence**. *Australian Journal of Political Science* 2003, **38(1):** 25-43.

technology as in the original patent. Unusually stringent aseptic production techniques are required to guard against contamination.

Safety, quality and efficacy regulators also consider that there are significant unresolved scientific issues about how to establish bio-equivalence between complex biological macromolecules. A protein, for example, can be folded, glycosylated, and methylated in quite different ways if expressed in mammalian or bacterial cultures. Likewise, a generic monoclonal antibody may bind to the same antigen, but through an alternate binding site and with an altered affinity from the original antibody. All of this may alter a product's pharmacokinetics and pharmacodynamics from the brand name competitor. The source material in biologic manufacturing is likewise not as readily classified as involving chemicals or standard generic pharmaceutical active product ingredients.

Most medical ethics guidelines preclude clinical trials on a product that is demonstrably inferior to the current standard of care. Under current regulations, as long as a company can continue making medically significant improvements on a therapeutic protein, it may be able to retain an exclusive market indefinitely without having to repeat full-scale clinical trials. Amgen appears to have used that approach in developing an improved version of its blockbuster treatment for anaemia, Epogen (Aranesp). In Europe, the Schering company likewise has gained approval for a version of interferon-alpha called PEG-interferon alpha, in which a polyethylene glycol (PEG) moiety increases the half-life of the protein in the body, reducing dosing frequency.

Similarly, new generic production facilities often generate biologics with increased purity from the original, placing pressure on 'discovery generic' manufacturers to perform additional clinical trials. These, through inconvenient and a substantial additional expense, are likely

to be less risky to patients, however, than the original studies, because the underlying principle of the drug's action has already been proven and the clinical end point is known. Some 'biologic' manufacturers have even filed for a new patent after significantly altering the production process. Eli Lilly, for example, developed a new manufacturing process for its human growth hormone and had the protein approved as a new orphan drug (Humatrope). Overlapping product patents, process patents, use patents and purity patents are likely to spur litigation for product exclusivity in this area.[17]

Such regulatory problems contributed to the fact that, in 2004, 2005 and 2006, only 5, 2 and 4 biopharmaceuticals respectively, were transferred from the US Center for Biologics Evaluation and Research to the Center for Drug Evaluation and Research for successful biologics license applications.[18] A proposed US Federal Access to *Life-Savings Drugs Act* 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.[19]

Yet, in 2006, the European Medicines Agency (EMA) following new guidelines, recommended approval of Sandoz's Omnitrope, a generic version of an existing growth hormone pharmaceutical. The EMA, unlike the US Food and Drug Administration (FDA) has guidelines assisting generic manufacturers wishing to market 'biogenerics'

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[17] Dove A. **Betting on biogenerics** *Nature Biotechnology* 2001; **19**: 117–120.
[18] Owens J. **2006 drug approvals: finding the niche** *Nature Reviews Drug Discovery* 2007**;6**: 99-101.
[19] Vastg B. **The Policy Outlook from the Hill** *Nature Biotechnology* 2007; **25(1):** 13-16

Further, companies such as Momenta Pharmaceuticals are utilising technologies that analyze the structure of complicated sugar molecules and possibly proteins, smoothing regulatory safety, quality and efficacy approval of these replicant pharmaceuticals.[20]

Certain geographic and political areas are racing ahead with biologic development. In Denmark, for example, strengths in clinical science base, management and established indigenous pharmaceutical companies are supported by policies facilitating start up and collaborations (for example Novo Nordisk and Leo Pharma (diabetes) and Lundbeck (psychiatric and neurological disorders)). A particular element in Scandinavian success in this area may be 'Medicon Valley', (around Copenhagen and Malmö in Sweden), which, along with Cambridge in the UK and Basel, is one of Europe's top three biotech clusters. [21]

Australian pharmaceutical policy makers need to learn the lessons of the industry renewal policies that have been applied, or are being attempted, to achieve such results with biologic generics. Breaking the reference pricing linkage between 'innovative' and 'generic' drugs may not be useful in this context.

Industrial Renewal: Pharmacogenetics

Another biopharma area where carefully organized policies, building on existing skills and facility strengths, could promote Australian industrial renewal, is pharmacogenetics (the science of studying genetically-determined responses to medicinal drugs). 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

[20] Heuser S. **European decision presages era of generic biology drugs**. *Boston Globe* February 13, 2006 Available at: http://www.boston.com/business/healthcare/articles/2006/02/13/european_decision_presages_era_of_generic_biology_drugs/ (last accessed 1 Feb 2007)

leading to adverse health outcomes.[22] Such harmful side effects vary between individuals and range from failure to respond therapeutically, to minor illness and even death.[23] 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.[24]

The US FDA's approval of the AmpliChip CYP450 (Roche and Affymetrix) for *in vitro* diagnostics represented a significant regulatory advance for pharmacogenomics Yet, as with 'biologicals,' regulatory changes necessary to facilitate uptake of (and public benefit from) such pharmacogenetic developments have yet to be systematically considered by Australian health policy makers.

Privacy laws, for example, will need to mesh with the capacity of a simple finger prick, mouth wash, or hair sample to obtain genetic information enabling a doctor to rapidly determine the likelihood of a drug's efficacy and side effects. If pharmacogenetics is to minimize

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[21] Moran N **Danish biotech outperforms its European counterparts** *Nature Biotechnology* 2006; **24**: 1460 - 1461

[22] Lazarou J, Pomeranz BH, Corey PN. **Incidence of adverse drug reactions in hospitalised patients: a meta-analysis of prospective studies**. JAMA. 1998;**279**:1200–1205

[23] Weber, WW. *Pharmacogenetics*. Oxford University Press; Oxford 1997

[24] Wolf CR, G Smith, RL Smith. **Pharmacogenetics** *BMJ*. 2000; **320(7240)**: 987–990.

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.

Industrial Renewal: Nanotherapeutics

Medical nanotechnology involves the development of drug/invasive therapeutic device products controllable at atomic, molecular or macromolecular levels of approximately 1-100 nanometers. Nanostructures have much greater strength, stability and surface area per unit mass than standard materials and those below 10nm possess quantum effects where size may control, for example, the specific wavelength of emitted light.[25]

Nanotechnology is a rapidly expanding area of medical research and development globally.[26] Over 200 companies are actively involved in this area, viewing nanotechnology is having a powerful enabling function that enhances the effectiveness and market competitiveness

[25] J Sone J Fujita, Y Ochiai *et al* **Nanofabrication toward sub-10 nm and its application to novel nanodevices** *Nanotechnology* 1999; **10**: 135-141
[26] Brower V. **Is Nanotechnology Ready for Primetime?** *J Natl Cancer Inst* 2006; **98(1):** 9-11.

of existing health technologies.[27] Peptide nanotubes, for example, have been investigated as the next generation of antibiotics[28] and as immune modulators[29] Nanomedical applications been investigated in neurosurgery,[30] cardiac surgery[31] and blood disorders[32] Most major pharmaceutical companies have substantial investments in nanotechnology.[33]

In Australia, nanomedicine is a rapidly growing industry sector. Nanotechnology is a priority area for Australian Research Council (ARC) funded research (A$53,013,909 in 2002-03), many collaborations being promoted by the ARC Nanotechnology Network (ARCNN).[34] Starpharma, for example, (with US-based Dendritic NanoTechnologies) and Australian government and US National Institutes of Health (NIH) funding, is developing VivaGel™ as an HIV-prevention dendrimer-based microbicide gel. VivaGel™ represents bottom up nanotechnology and involves a well-defined synthetic polymer, made by adding monomers in a branching manner, binding to glycoproteins on the surface of HIV and thus preventing, in a dose-response manner, HIV binding to receptors on T-cells. VivaGel™ is the world's first dendrimer-based drug to be approved for human trials by US FDA (phase 1 study completed 2004). pSividia has developed

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[27] Wagner V, Dullart A, Bock A-K, Zweck A: **The emerging nanomedicine landscape** *Nature Biotechnology*; 2006; **24(10):** 1211-1218.
[28] Ghadiri MR. **Antibacterial Agents Based on the Cyclic D, L Peptide Architecture** *Nature* 2001; **412**: 451-455
[29] Bottini M, Bruckner S, Nika K et al, **Multi-Walled Carbon Nanotubules Induce T Lymphocyte Apoptosis** *Toxicology Letters* 2006; **160 :** *121-126.*
[30] Leary SP, Liu CY, Yu C et al **Toward the Emergence of Nanoneurosurgery: Part I-Progress in Nanoscience, Nanotechnology and the Comprehension of Events in the Mesoscale Realm** *Neurosurgery* 2005; **57(4):** 606-633
[31] Kong DF, Goldschmidt-Clermont PJ. **Tiny Solutions for Giant Cardiac Problems** *Trends Cardiovasc Med* 2005; **15(6):** 207-11.
[32] Hulstein JJ et al. **A Novel Nanobody that Detects the Gain-of-function Phenotype of von Willebrand Factor in ADAMTS13 Deficiency and von Willebrand Disease Type 2B** *Blood* 2005; **106(9):** 3035-42.
[33] Prestidge CA. **Nanoscience facilitating the development of novel pharmaceutical delivery systems.** Abstract of oral presentation Australian Research Council Nanotechnology Network International Conference on Nanoscience and Naotechnology Brisbane Convention Centre 3-7 July 2006
[34] Australian Academy of Science *Nanotechnology Benchmarking Project.* Available at: http://www.science.org.au/policy/nano-exec.htm [last accessed 28 Jan 2006]

Brachysil™ a nanostructural, porosified, biosilicon platform technology for controlled drug delivery and already have a licensing agreement for it with a US company based in China.

At present, however, most regulatory concern in Australia seems to be focused generally on the safety of nanotechnology, rather than on facilitating venture capital for a nanomedicine industry systematically focused, through good regulatory architecture, on public health outcomes. A major concern is that highly reactive and mobile engineered nanoparticles (ENPs) may present unique health risks when used in medical applications.[35] There are currently no effective methods to monitor ENP exposure risks[36] Research suggests that the health risks of nanostructures cannot be predicted *a priori* from their bulk equivalent. In animal studies, short term exposure to ENP's has produced dose-dependent inflammatory responses and pulmonary fibrosis. Some engineered nanoparticles have also been shown to preferentially accumulate in mitochondria and inhibit function, others may become unstable in biological settings and release elemental metals [37]

Despite such findings, the US FDA appears to have assumed that macroscale safety may translate to that at the nano level.[38] A nanoparticulate reformulation of an existing drug, for example, has been deemed by the FDA not to require an Abbreviated New Drug Application (ANDA) because bioequivalence was established.[39]

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[35] Institute of Occupational Medicine for the Health and Safety Executive. 2004. *Nanoparticles: An Occupational Hygiene Review*. Available at: http://www.hse.gov.uk [last accessed 14 Aug 2006]]

[36] Department of Employment and Workplace Relations Australian Government, *Submission to Senate Inquiry Into Workplace Exposure to Toxic Dusts and Nanoparticles* Canberra August 2005.

[37] Flinders Consulting Pty Ltd. A review of the potential occupational health and safety implications of nanotechnology Australian Safety and Compensation Council 2006. Avaliable at: http://www.ascc.gov.au/ascc/AboutUs/Publications/ResearchReports/AReviewofthePotentialOccupationalHealthandSafetyImplicationsofNanotechnology.htm (last accessed 28 August 2006)

[38] Baluch AS. **Angstrom Medica: Securing FDA approval and commercializing a nanomedical device** *Nanotechnology Law and Business* 2005; **2**: 168-173.

These developments suggest that the Australian government should take a stronger long term policy interest in public benefit-focused industry renewal in the nanotherapeutics sector. A recent Senate Inquiry recommended creation of a working party to consider creation of a distinct, permanent regulatory body for nanotechnology.[40] The latter approach was taken with gene technology under the *Gene Technology Act* 2000 (Cth).[41] Such a broad licensing approach, encompassing regulatory industrial, agricultural and therapeutic applications may not be the best vehicle for encouraging renewal in the uniquely complex Australian bio/nanopharma sector.

Appropriate regulatory changes could favour the development of a biopharma industry where existing off-patent products are re-badged to become more profitable with a more effective nano-based delivery system. On the other hand, hasty regulatory approval 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.[42] One of the best models for facilitating

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[39] Till MC, Simkin MM, Maebius S. **Nanotech meets the FDA: A success story about the first nanoparticlate drugs approved by the FDA.** *Nanotechnology Law and Business* 2005; **2**: 163-167.
[40] Commonwealth of Australia Senate Inquiry into Workplace Exposure to Toxic Dusts and Nanoparticles *Final Report* 31 May 2006 Canberra. Faunce TA, Walters H, Williams T, Bryant D, Jennings M, Musk B. **Policy challenges from the "White" Senate Inquiry into workplace-related health impacts of toxic dusts and nanoparticles**".*Aust New Zealand Health Policy*. 2006; **17;3(1):**7-12
[41] Homer JB and Hirsch GB **System Dynamics Modeling for Public Health: Background and Opportunities.** *AJPH* pre-published Jan 31 2006, 10.2105/AJPH.2005.062059.
[42] European Science Foundation *Nanomedicine: An ESF-European Medical Research Councils (EMRC) Forward Look Report (*European Science Foundation, Strasbourg 2005).

community value from nanotechnology research may be the Nanotechnology Victoria (Nanovic) consortium (Universities of Melbourne, Swinburne and RMIT with the CSIRO) receiving start-up funding from the Victorian Government.[43]

New Approaches to Medicines Policy in the Trade Negotiations

Learning from the AUSFTA passive approach

There is much Australian policy makers and trade negotiators should be able to learn form the US approach to medicines provisions in the AUSFTA. The US position to 'eliminate' PBS reference pricing through the AUS-FTA negotiations was part of a legislated agenda that had been carefully worked up with US industry through prolonged meetings in the IFAC-3 committee. For example, §2102(b)(8)(D) of the (US) *Bipartisan Trade Promotion Authority Act* of 2002 lists, as one of its principal negotiating objectives, '*to achieve the elimination of government measures such as price controls and reference pricing which deny full market access for United States products.*' US negotiators had for some time worked closely with senior members of the US patented-pharmaceutical industry on the Industry Functional Advisory Committee on Intellectual Property Rights for Trade Policy Matters (IFAC-3) to develop draft AUS-FTA provisions that would achieve this end. (Industry Functional Advisory Committee 2004) The philosophical position expressed in public to ostensibly explain this stance was that reference pricing in the PBS allowed the Australian government to 'free ride' on US research and development (for example see Shiner 2004). Although this free market ideology is little supported by facts and ignores the scientific basis of PBAC evaluations (Lexchin and Light 2005), as will be shown, it is still influential in US policy and has strongly influenced the KORUS-FTA.

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[43] Australian Government. Invest Australia. *Australian Nanotechnology. Capability and Commercial Potential 2nd ed Cth Australia 2005.*

The Australian government, on the other hand, had a much more defensive approach to medicines in the AUS-FTA negotiations. It stated that the major concern for its negotiators to the AUS-FTA was to be simply the preservation of the PBS. Stephen Deady, Australia's chief negotiator highlighted this passive approach in stating:

> "… 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." (Deady 2004)

The Senate Select Committee report stated that most submissions to its inquiry were explicitly against the PBS being a part of such trade negotiations. Its report cited statements from some members of the US Congress who clearly considered that trade negotiations should not be used to interfere with national health systems of other countries, and that domestic health policy should not be a part of any trade agreements (p102). The Senate Select Committee concluded that 'as a core social policy in Australia, the PBS should never have been on the negotiating table' (p102). The committee also noted that although the Australian public was assured that the PBS was never going to be on the negotiating table, there is evidence to suggest that it was an issue from the very first round of negotiations or 'discussions' (p103). Yet, having been surprised the US had sought and succeeded in including the PBS in the negotiations, Australia, though clearly entitled to do so, sought corresponding no changes at all in US medicines regulation, even despite the tactical advantages this might have produced.

There is also evidence to suggest that in preparing to negotiate the intellectual property chapter 17 of the AUS-FTA, Australian-based stakeholders in generic pharmaceutical industry were not consulted with anything like the care and detail utilised by the US in the IFAC-3 system. (Faunce 2007b). This is particularly evident in light of the

apparent ready acquiescence by Australian negotiators to some of the chapter 17 TRIPS-plus patent term extensions, data exclusivity and 'linkage evergreening' provisions which directly opposed the commercial interests of the Australian generics industry.

Competing Definitions of 'Innovation' in Annex 2C

Australian negotiators, as mentioned, claimed that they went into negotiations 'with an absolutely clear [purely defensive] mandate to protect and preserve the fundamentals of the PBS.' (Senate Select Committee 2004, p105). The resulting agreement, however, as encapsulated in Annex 2C, contains provisions which (by facilitating industry lobbying through various established committee structures) were likely to directly impact the policy and function of the PBS. Three out of four of the Agreed Principles in Annex 2C, for example, mention the need to recognise and promote 'innovative pharmaceuticals,' although this term is not generally taken to refer to generic medicines which provide significant cost savings to the PBS (Annex 2C 1(a), (c), (d)).

Despite its manifest importance, the term 'innovative' lacks an express definition in the AUS-FTA text. The Annex 2C text allows the word to be interpreted either through the US position of 'competitive markets' (so-called 'market-valued innovation') or the Australian position of 'adopting or maintaining procedures that appropriately value the objectively demonstrated therapeutic significance of a pharmaceutical' (so-called 'evidence-based health innovation'). The potential for conflict arising from this was recognised by the Senate Select Committee and by others since (Senate Select Committee 2007, p107; Faunce *et al.* 2005). Annex 2C's statement of agreed principles has also been criticised for not mentioning equitable and affordable access to medicines as encapsulated in the Australian Medicines Policy, as well as being required by the *Doha Declaration on the Trade Related*

Intellectual Property Rights Agreement (TRIPS) Agreement and Public Health to promote public health by facilitating access to affordable medicines (WTO 2001).

The 'transparency' provisions under Annex 2C.2 contain requirements that listing PBS proposals are completed within a specified time, that procedural rules, methodologies, principles, and guidelines used to assess a proposal be disclosed, and that applicants are given opportunities to provide comments. These obligations are imposed only on Australia. Australia, as mentioned, sought to impose no reciprocal requirements on US authorities. Furthermore, PBS applicants and the public are to be provided with detailed information about the determinations made, and an 'independent review process' is to be available to an applicant directly affected by a recommendation or determination. The legislative form that this review process initially took framed it more as a quality assurance exercise for PBAC decisions, with no new evidence and no overturning of PBAC decisions permitted (Harvey *et al* 2004, p257; Faunce 2005).

Annex 2C also established a 'Medicines Working Group' (MWG) which is to 'promote discussion and mutual understanding of issues relating to this Annex' (Annex 2C 3(b)). This has been viewed as creating the potential for patented pharmaceutical companies to lobby for or against existing medicines policies, thereby diminishing the growth of the generics industry (Faunce 2007b, p4), for example, through the role of Medicines Australia, the lobby group representing the 'innovative medicines industry in Australia' in the MWG.

Although Australian representatives maintained that this group would not influence policy formulation, there is evidence from the first two MWG meetings that specific Australian legislative reforms that would support the US 'competitive markets' approach to valuing pharmaceutical 'innovation' were encouraged. After the first meeting of

the MWG in Washington, in a press conference at the office of the US trade representative in Washington, Australia's trade minister Mark Vaile stated that:

> "the core principle that we both agree on in this area and that is recognising the value of innovation and the importance of ongoing innovation as far as pharmaceuticals are concerned as the fundamental central principle in what we're doing. We continue to monitor a number of different areas in the operations of our system in Australia, our PBS, or as you call it here in the United States, our formulary." (Vaile 2006)

This is best interpreted as a statement supporting Australia's position on 'health innovation' in Annex 2C: that it is best determined scientifically by evidence of objectively demonstrated therapeutic significance, rather that by the operation of so-called 'competitive markets'. (Faunce 2007b, p5).

Impact of the AUSFTA on the July 2007 F1-F2 PBS Reforms

The impacts of the AUS-FTA on national medicines policy and the PBS can arguably now be clearly seen. In August this year (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 have been called 'in substance, the Medicines Australia policy proposals' (Faunce 2007b, p6) for changes to the PBS reference pricing system, the legislation effectively creates 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. (Faunce 2007a) 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. (Faunce and

Lofgren 2007) In outlining the changes late last year, the Australian Health Minister admitted that 'Generics Medicine Industry Association is not, as I understand it, especially happy with these changes.' (Abbott 2006).

Although explained as derived from the need to allow lower cost generic medicines into Australia, (Abbott 2006) these F1-F2 legislative changes to the PBS appear to substantially reflect the position on the PBS articulated by US negotiators during the AUS-FTA negotiations (and in the AUS-FTA MWG) on 'innovation' in Annex 2C of the AUS-FTA described earlier.(Faunce and Lofgren 2007) This suggests that although assurances to the contrary were given, the US policy on the 'elimination' of PBS reference pricing mechanisms has been successful to a significant degree, altering a core aspect of the Australian national medicines system.

A Comparison of Medicines Provisions in the AUSFTA and the KORUS-FTA

The pharmaceuticals chapter of the KORUS-FTA is described by the US Trade Representative as 'a shared commitment on access to innovative medicines.' (USTR 2004). It is recognised as having been modelled on Annex 2C of the AUS-FTA, but has been described as even more restrictive (Flynn and Palmedo 2007). The main issues seen to impact medicines, and thus the areas which have garnered criticism, are the restrictions on formulary pricing, and the intellectual property provisions, which are seen to go beyond what is accepted under the TRIPS agreement. However, the KORUS-FTA can also be seen to have broader implications for Korean medicines and health technologies policy.

Medicines and medical devices

While the AUS-FTA Annex 2C is entitled 'Pharmaceuticals' and deals exclusively with this, the equivalent KORUS-FTA provision is entitled 'Medicines and Medical Devices' (chapter five). This broad category is defined in article 5.8 as "pharmaceutical, biologic, medical device, or diagnostic products" and potentially encapsulates much more than its Australian equivalent, by including expensive 'medical devices' which could range from cochlear implants to nanotechnology in health care.

Restricting drug formularies

Korea announced its intention to create a 'positive list' for government reimbursement of the price of pharmaceuticals in May 2006. This move met by strong opposition from KORUS-FTA US negotiators who refused to attend a Pharmaceutical and Medical Device Working Group meeting. In a public statement by a US trade representative, the US saw the decision to create the list as 'inconsistent with both the mandate of the Pharmaceutical Working Group and the market-opening spirit of the FTA.' (Cutler 2006). In reality, the US negotiators had been surprised that a developed nation had adopted a similar approach to themselves and sought to use FTA negotiations to fulfil its own national interests in medicines policy.

This is not the first time that the US has used trade negotiations with Korea to impose higher drug prices. Since 1999, the US has been negotiating market access in the pharmaceutical sector with Korea (USTR 2004b). One aspect of the negotiations was to pressure Korea to adopt the "A-7 pricing system" for all new innovative medicines, that is the average ex-factory price in the A-7 countries – US, UK, Germany, France, Italy, Switzerland and Japan (USTR 2004b, p168). This had been widely criticised, as the result required Koreans to pay much higher prices relative to their average income per person than any of the other A-7 countries. Furthermore, Korea also paid more for

patented drugs than the US did in absolute terms (Flynn and Palmedo 2007).

Korea's price mooted reimbursement system is to be part of its universal National Health Insurance (NHI) system, which relies heavily on its generics industry to control the costs of medicines. It is likely to be quite similar to the Australian PBS in that it uses a formulary (referred to as a 'positive list') and reference pricing – aspects which the US also saw as barriers to trade (Flynn 2007a).

Article 5.2 of the KORUS-FTA deals with the issue of pharmaceutical innovation in a somewhat similar manner to Annex 2C of the AUS-FTA. In determining price reimbursements, the KORUS-FTA requires a Party's determination must be 'based on competitive market-derived prices' (article 5.2(b)), (which can be viewed as the US' preferred position) or if it is not, the Party must then 'appropriately recognize the value of the patented pharmaceutical product or medical device in the amount of reimbursement it provides.' The crucial focus in this context must be on the word 'value'. It is likely that the Koreans will argue, after they have set up a science-based positive list formulary like the PBS, that the term 'value' in this alternative must mean something different than "competitive market-derived prices." As such it would be a legitimate expectation that it referred to a process of evidence-based determination of 'objectively demonstrated therapeutic significance' as mentioned in AUSFTA Annex 2C.

Article 5.2 of the KORUS-FTA allows the use of comparators in pricing (in allowing manufacturers to apply for an increased amount of reimbursement based on relative safety or efficacy (article 5.2 (b)(ii)). There is, however, no explicit support for pre-AUS-FTA PBS model of reference pricing as expressed in the TGP policy.

It is also interesting to note that before the final text of the KORUS-FTA was released, there was some concern regarding its potential impact on US state drug formulary programs (see for example Shaffer 2007). These are used extensively to negotiate drug prices by US state governments, as well as by private insurance companies. Many US agencies such as Department of Defense, and Veterans Administration and Medicaid purchase drugs through cost-effectiveness-based price negotiating programs. Medicaid is run through state governments under federal guidelines providing health insurance.

However, due to concern expressed by the US public during the negotiations, these US state programs were exempted (for example see Flynn 2007b). For example, 'government procurement of pharmaceutical products for healthcare' (referring to the US Department of Defense and Veterans Administration drug procurement programs) appear to be exempt by a footnote under article 5.2. This section also explicitly refers to 'health care programs operated by its [the Party's] central level of government' thereby excluding, and thus protecting Medicaid which is run on the state level. For even greater clarification, article 5.8 contains a definition of 'health care programs operated by a Party's central level of government', which includes a footnote stating that 'Medicaid is a regional level of government health care program in the United States, not a central level of government program.'

The result is that the provisions do not apply to US government pricing programs, thereby protecting access to affordable medicines within the US, while continuing to apply to the Korean 'positive list' formulary. This highlights even more starkly than AUS-FTA Annex 2C, the clear preferential nature of the medicines provisions in these bilateral trade agreements.

Transparency

Both Annex 2C of the AUS-FTA and Chapter 5 of the KORUS-FTA address the US conception of 'transparency' in any healthcare program reimbursing pharmaceuticals. As discussed earlier, the Annex 2C provisions created mechanisms allowing further review of PBAC decisions, calling into question the authority of well established government healthcare institutions.

The KORUS-FTA transparency provisions are similar, but go further than AUS-FTA Annex 2C in providing additional requirements, for example that the parties "within a reasonable, specified period, provide applicants with meaningful, detailed written information regarding the basis for recommendations or determinations."

Article 5.7 requires the establishment of a "Medicines and Medical Devices Committee" similar to the AUS-FTA MWG. It is likely this committee will play a similar role in help to shape the US medicine agenda into conformable domestic legislation.

A major difference in the texts is the requirement that Korea establish an independent review process which appears to allow pharmaceutical companies to challenge decisions regarding pricing or formulary listing (article 5.3 5(e)). While this initially appears similar to the Annex 2C equivalent, a confirmation letter from the Korean government to the US trade representative states that in implementing this section, Korea will establish an independent review body (Kim 2007). This body will be entirely separate to government health care authorities that are involved in price reimbursement schemes and decisions, and will be comprised of 'professionals with relevant expertise and experience' with no pecuniary or personal interest in the outcome of the decisions. It is unclear whether this body will have the power to overturn pricing decisions, however it can be assumed that it

is unlikely for it to have been established to serve a purely advisory role.

Intellectual Property Provisions

The KORUS-FTA includes what have been described as 'TRIPS-Plus' intellectual property protections, which in general terms work to delay generic competition and allow their royalty life span to be increased for the owners of the multiple patents that now cluster around such products. These include changes to data exclusivity (art 18.9.1), linkage requirements (linking safety approval and patent status) (art 18.9.4), mandatory extensions of patents (art 18.8.6), and patent requirements for new uses of known products (art 18.8.1). 'TRIPS-Plus' is a controversial term which appears to carry an implicit value judgement about the positive value of these changes. An opposing point of view would consider them more deleterious for public health as so (from that perspective) 'TRIPS-minus."

KORUS-FTA Article 18.9 allows for five years of data exclusivity for new pharmaceutical products and three years for those containing 'a chemical entity that has been previously approved'. This prevents generic manufacturers from accessing the data from clinical trials conducted by the patented equivalent, which would allow them to prove that their product is 'bioequivalent' to the brand name drug. Bypassing the need to repeat stage III and IV clinical trials, generic manufacturers can use data from the original safety and efficacy submission to prove that their drug will behave in the same way. Their early access to the data allows generics to obtain marketing approval, and be ready to market their product as soon as the patent term expires. Data exclusivity provisions prevent generic manufacturers from applying for approval based on the original data during the period of exclusivity, thereby delaying their access to the market. This could become a major hindrance to government compulsory licensing

of generic manufacture in a public health emergency. While the TRIPS agreement allows for protection of data from 'unfair commercial use' it has been argued that there are other ways in which this can be done (Flynn 2007b, p4). These provisions once again hinder the Korean government's ability to further the Korean generic industry. There existence in the KORUS-FTA text, however, appears to be due solely to aggressive negotiating by the US, rather than lack of a systematic pro-generics negotiating agenda as was the problem for Australia in the AUS-FTA context.

The KORUS-FTA text also contains 'linkage' provisions, which function to prevent safety, quality and efficacy regulatory authorities from giving market approval to generic drugs while the brand name is still under patent. A number of Special 301 Reports issued by the USTR show that the US had a primary goal of forcing Korea to adopt linkage provisions:

> The United States encourages Korea to address its lack of an effective coordination system between its health and patent authorities to prevent the issuance of marketing approvals for unauthorized patent-infringing copies of pharmaceutical products. The United States will work with Korea to make progress on these and other IPR issues through the upcoming Free Trade Agreement negotiations. (USTR 2006)

Article 18.9.4 provides a similar mechanism to the AUS-FTA equivalent, whereby a patent owner is required to be notified of a generic manufacturer's request for marketing approval and for the prevention of marketing approval if a patent rights are asserted. However, unlike the corresponding AUS-FTA article 17.10.4, the patent holder must first have notified the regulatory authority as covering the particular product. This encourages regulatory oversight of a list of approved pharmaceutical patents, helping to avoid patent 'evergreening' and reducing much uncertainty and patent search costs for generic manufacturers.

Recent US Democrats deal with USTR on Medicines Provisions in Bilaterals

In May 2007 a new deal regarding recent US bilateral trade agreements and their adverse impact on public health was reached between the US Democrats and the Bush Administration (USTR 2007a). The Democrats negotiated concessions in a number of areas including patent extensions, linkage provisions, and to some extent in data exclusivity – thereby eliminating some of the most egregious 'TRIPS-plus' provisions (Committee on Ways and Means Republicans 2007). This deal was predicted to have an impact on the KORUS-FTA as well as other forthcoming trade agreements (Weisman 2007). For example, patent extensions were to be made optional, using terms such as 'may' instead of 'shall', the *Doha Declaration on TRIPS and Public Health* and the so-called 'Paragaph 6 Solution' were to be mentioned explicitly (Love 2007).

Although it was reached prior to the completion of the KORUS-FTA, it is believed that the negotiated concessions did in fact influence the final KORUS-FTA agreement (Sweeney 2007; Joo 2007). Chapter 16 of the United States – Peru Trade Promotion Agreement, however, does appear to have taken on these changes (USTR 2007b). Under this revised agreement, the intention of both parties appears to be that patent extensions for brand drugs are not mandatory, and generic drugs will become available in Peru no later than they are made available in the U.S. In addition, patent disputes may be permitted to be resolved solely through the legal system, rather than through notification systems in the drug safety approval process. Article 16.3 of this agreement also allows Peru to take advantage of the so-called 'paragraph 6' solution under the *Doha Declaration on TRIPS and Public Health* which allows compulsory licences issued by nations with limited manufacturing capacity to be satisfied by more developed nations. Rwanda recently became the first country to invoke this

TRIPS provision when it announced plans to import a generic HIV drug from Canada. (Anonymous 2007)

If subsequent US bilateral trade agreements do incorporate the concessions gained through this deal, this must surely also send a signal about how little national benefit Australia achieved by the passive approach Australian medicines negotiators took to the AUS-FTA.

Toward a positive Australian medicines agenda for the China and India FTAs

On 18 April 2005, after the completion of a joint FTA Feasibility Study showing potential for significant economic benefits, Australia and China agreed to begin negotiations on an FTA (DFAT 2007). While so far pharmaceuticals have not been considered in the discussions, there are compelling reasons to believe that the inclusion of a chapter on pharmaceuticals in the final FTA will be greatly beneficial to both countries.

As one of the world's largest manufacturers of generic pharmaceuticals, China has a pharmaceuticals industry predicted to become the world's 5th largest by 2010, and largest by 2050 (PWC 2004, p2). Foreign drug investors see the Chinese drug market as having great scope for growth, with a population of over 3.1 billion, ageing at a projected 3% a year, as well as a very low relative research base, with approximately 97% of manufactured drugs being copies of foreign products or 'generics' (PWC 2004, p2-3). Currently, all the top 20 multinational pharmaceutical companies have set up wholly owned subsidiaries or joint-ventures in China (Zhou 2007). While the Chinese market holds huge potential for a large pharmaceutical research and development (R&D) base, the market is currently quite fragmented, partly due to bureaucratic obstacles in centralising the

industry, as well as inconsistent intellectual property standards deterring both local and foreign manufacturers (PWC 2004, p4). The result is that currently China has only patented two “innovative” drugs (China Economic Information Agency 2002).

Conversely, Australia possesses the regulatory expertise (through the well established mechanisms of the TGA), high quality research institutions, and a strong and growing R&D base (DITR 2007). As well as great potential to enhance the generics industry in Australia, there is much scope to develop the “innovative” pharmaceutical market, leading to large global exports.

As with Australia, but unlike many parts of Europe and the US, China has not only invested heavily in biopharmaceutical sciences, but has also ensured liberal policies towards globally contentious issues such as therapeutic cloning. This is an area which still lacks global consensus, making international collaborative research difficult. As Australia has recently legalised therapeutic cloning by lifting the ban on somatic cell nuclear transfer (SCNT) last year, there is much potential for collaborative research and development in this area through partnerships and joint ventures, which could be greatly facilitated by an FTA.

China is already showing great promise as a potential market for the Australian biotechnology and nanotechnology industries, for example through the patenting in China of BioSilicon™, a nanotech silicon drug delivery system manufactured by the Australian publicly listed company, pSivida Ltd. Furthermore, the CSIRO has been developing and acquiring patents for RNA interference (RNAi) gene silencing technology. Already holding patents in China, representatives from the CSIRO have stated that they see ‘a major market for its RNAi technology in China’ (O’Neil 2005).

The rise of an Indian multinational pharmaceutical industry with strong intellectual property protection and interest in rapid marketing of safe biologic generics, is a phenomenon that can hardly be disregarded by Australian negotiators to any trade agreement with that nation. India's pharmaceutical industry now ranks fourth in the world and its firms produce 20% of the worlds APIs. (Lofgren 2007) Interestingly from Australia's point of view, Indian firms meet 70% of that nation's pharmaceutical demands. (Lofgren 2007) The international competitiveness of top-tier Indian medicines firms now attracts the best national graduates and Indian firms have begun to make significant foreign acquisitions. (Lofgren 2007) Both India and China, also with high relevance to Australian interests, are actively investing in a 'modular' model of decentralised biotech R&D involving global distribution and semi-autonomous activity (Goodall et al 2006)

It has previously been suggested that in establishing a pharmaceuticals chapter within a CHINA-AUS-FTA, a Medicines Working Committee could be set up to facilitate dialogue about cooperative research, manufacture and distribution of pharmaceuticals (Faunce 2005). The value of such a committee would be even more apparent in an INDIA-AUS-FTA. The parties through such a committee could facilitate ongoing discussions at the highest policy levels about establishing, for example, regulatory mechanisms similar to Australia's PBS, sharing expertise, data, assessments and methods of comparing effectiveness and objective therapeutic significance of existing and new medicines. The traditional of public health focus in government policy could make this an attractive proposition for Australia, India and China. The operation of the similar MWG under the AUS-FTA provides a precedent. It will be quite a peculiar circumstance from the Australian point of view if the AUS-FTA allows contains such a medicines committee. Intellectual property provisions reflecting the new pro-global public healh position negotiated in the US, also could be included in the medicines

provisions of the trade agreements between Australia and India and China respectively.

There are thus a variety of significant factors suggesting the value of Australia now taking a more active role in using these trade deals to negotiate for positive national and transnational benefit in health technology areas where it maintains a competitive advantage (such as bio and nanobiotechnology basic research).

The Australian and Korean trade agreements with the US were the first to include pharmaceuticals chapters. During negotiations for both, the US expressed a strong agenda to change certain aspects of the domestic health policies of each country, particularly by getting rid of reference pricing mechanisms in the Australian PBS and limiting their capacity for introduction in the Korean positive list formulary. Recent legislative changes to Australia's price referencing mechanisms show that despite assurances from Australian negotiators, some core aspects of the PBS, and in turn Australian health policy, were in fact negatively affected by the AUS-FTA. Whether or not a similar adverse impact on domestic health policy is observed in Korea remains to be seen.

Unless changes in Australian policy towards enhancing national and transnational benefit through health technology provisions in trade agreements are made soon, then regardless of the bipartisan deal negotiated by the US democrats, the AUS-FTA and KORUS-FTA may provide the unfortunate model for future medicines provisions in FTAs entered into by Australia. The new Australian government, with its apparent agenda of transparency in government, may see the value in a clear articulation of domestic trade agenda in legislation (such as that of the US), which ensures that particular national and transnational goals in health technology policy are developed, maintained and promoted during trade negotiations. This could

include, for example, the establishment of similar advisory bodies to the US IFAC committees and the AUS-FTA MWG, which could monitor and report on the protection of Australian interests both during and after trade negotiations such as those with China and India.

A Multilateral Treaty on Health Technology Cost-Effectiveness Assessment

One approach, advocated by the author in a variety of publications, to overcoming the problems of disjunction between the global burden of disease and the direction of health technology R&D involves aggregating and formalising at the global level existing networks of national assessors scrutinising the safety and cost-effectiveness of new health technologies, while supporting and expanding domestic legislative arrangements whereby governments subsidise to citizens the cost of new health technologies through centralised public-funded price negotiation schemes involving closed-bid competitive tender for therapies urgently required to meet identified public health needs. This Cost-Effectiveness Assessment and Competitive Tender model involves a multilateral treaty establishing basic principles and procedures for price negotiations between governments (or UN agencies) and manufacturers of new health technologies based on expert assessment of safety and cost effectiveness. (Faunce 2006)

Unlike the proposed R&D Prize Treaty recently discussed at the World Health Organisation (WHO) Intergovernmental Working Group (IGWG) meeting, it leaves the existing patent system intact and does not require nations to allocate a large proportion of their GDP to a system several steps removed from their direct control. It is has advantages over the Advance Market Commitments (APC) model where calculating in advance the amount of R&D reimbursement is a major issue (Hollis 2008).

What the Cost-Effectiveness Assessment and Competitive Tender Treaty requires instead is a combination of 1) formalisation in a

multinational treaty of the basic principles by which urgently required, new health technologies are assessed for safety and cost-effectiveness and then 2) linkage through the same mechanism with domestic regulatory processes in which public funds are allocated to subsidise expenditure by citizens on new health technologies, for example by closed-bid competitive tender.

One value of Cost-Effectiveness Assessment and Competitive Tender Treaty is that states are more likely to commit themselves to facilitating a public goods agenda in the area of medicines policy if they can convince themselves that it is financially responsible and does not cut across existing intellectual property protections, or strongly protected areas of state sovereignty. In effect, there is a chance they could be persuaded that such a treaty merely moves to a global stage successful science-based systems of equitably allocating public funds for health technology purchase such as the Australian Pharmaceutical Benefits Scheme (PBS) and New Zealand's PHARMAC system. (Faunce 2007 ch7) It is designed to ensure that markets operate most competitively to deliver best community value on criteria of objectively demonstrated therapeutic significance. A political advantage of the Global Cost-Effectiveness Assessment and Tender Treaty is that central government price negotiation on evidence-based criteria with the relevant patent holder/manufacturer can be strategically presented as a form of expenditure minimisation, or a fiscally responsible way of obtaining community health value for public expenditure. Increased tendering for active pharmaceutical ingredients and generic medicines will create significant savings in developing nation health budgets. Post-tender, the winning company will have a new, larger, market share, be able to buy chemicals in bulk and exploit economies of scale in production. (OXERA 2001)

Multinational pharmaceutical manufacturers may well view any process of using expert assessment of published cost-effectiveness

evidence about their products, particularly if linked with a competitive tender process, as challenging the role of advertising and monopolistic practices to control the market place to their advantage under the 'market fundamentalist' philosophy outlined earlier. One of their major counter arguments is likely to be that such mechanisms (whatever their apparent value in terms of distributive justice, global ethics and international human rights) allow foreign nations to free ride on US research and development and so promote high domestic US drug prices. (Faunce 2007b). (Kolitch 2006). As a 'pull' mechanism they could claim it will not be specific enough (unless globally endorsed through a Treaty) to encourage their R&D to flow in directions required by the global burden of disease.

It could likewise be argued that repetition of tendering rounds may increase the likelihood of market concentration if the same suppliers win contracts, so that competitors let their expensive product licence expire. Tendering may also drive the price down rapidly once a drug comes off patent, but facilitate the market exit of unsuccessful generic suppliers and further price increases. While securing supply has been a problem in isolated cases in New Zealand (where the tender system is utilised widely), this problem tends to be exaggerated by multinational pharmaceutical interests. (Faunce, Lofgren, Harvey and Johnston, 2006) Concerns that tendering may cause difficulties in planning production for generic manufacturers, would be minimised if the process involved an open tender for generics below a government set price, especially if it was linked to tax incentives for companies to create head to head clinical trials of their generic products against brand name and other generic competitors, and a systematic program of physician education.

For tendering contracts to function properly as a 'pull' mechanism for health technology R&D, enforceable penalty clauses for failure to deliver or other contract default are crucial. The simplest such clause

would specify that a defaulting contractor should reimburse the relevant government positive list for the extra cost of obtaining supplies from elsewhere. The contract between the supplier and the relevant government should allow, however, for some flexibility in the agreed volume if demand turns out lower than forecast, or a supplier fails to deliver. (Faunce, Lofgren, Harvey and Johnston, 2006)

This Cost-Effectiveness Assessment and Competitive Tender Treaty model further differs from the R&D Prize Treaty model in that it aims to enhance the global scope of fully mature regulatory processes already existent in many jurisdictions (few nations currently have domestic prize fund or patent prize systems in place). It can provide a clear incentive system for pharmaceutical manufacturers to seek to develop innovative medicines for developing world populations, by providing a transparent pathway to a large pool of mixed charitable, United Nations and domestic government funds allocated to being spent, under a competitive tender process, upon pharmaceuticals for otherwise 'research-neglected' diseases in the developing world.

Another advantage of the Cost-Effectiveness Assessment and Competitive Tender Treaty model is that its requisite involvement of experts in the regulatory process will ensure that the whole process is less likely to be captured by the multinational health technology industry to its own advantage. The goal of a global framework treaty on the principles and procedures to guide safety and cost-effectiveness evaluation of new health technologies could also be a more politically achievable one than the earlier discussed proposals if all the different interests are taken into account and weighed in a balanced manner. Working out a road map toward such a treaty would involve discussions about principles on assessor reimbursement (possibly a tax on global financial transactions) and liability protection, rationalisation of commercial–in-confidence protections, post-marketing surveillance and performance indicators for conditional

approvals and strategies to obtain information on marginal cost of production and price setting.

Once sufficient ratifications of such a treaty have been achieved, the course of pharmaceutical R&D would be shaped over time as firms compete to make large profits by having their products placed on the treaty list. (Faunce, 2006 p8). Its carrot is to provide manufacturers and patent holders with potential access to a flat playing field of large and reliable sources of domestic funding once they have met the requisite evidence-based standards. Although the democratic deficit inherent in the international law-making will not be perfectly rectified under this model, the involvement of experts in the regulatory process will assist the likelihood that the whole process will be more transparent and accountable to global health needs.

Restricting Non-violation Nullification of Benefits Complaints

Article 21.2 of the AUSFTA outlines when a party to the agreement may avail themselves of the dispute settlement process. In addition to the traditional complaints when one party feels the letter of the agreement has been violated, the dispute resolution process is also available to a party that feels the spirit of the agreement has been breached, regardless of whether there has also been a breach of the letter of the agreement.[44] This so called non-violation nullification of benefits (NVNB) clause only applies to specified sections of the agreement, including Chapter 2 and Annex 2C on pharmaceuticals and Chapter 17 on intellectual property.

The NVNB clause has long been a feature of the General Agreement on Tariffs in Trade (GATT) but has rarely been invoked.[45] A similar clause was controversially included in the Agreement on Trade Related

[44] Article 21.2(c).
[45] GATT article XXIII.1(b). *US-Japan Film* panel noted only eight cases where NVNB claims were substantially discussed in 50 years.

Aspects of Intellectual Property (TRIPs) but has been the subject of a moratorium.[46] Despite the overwhelming reluctance on the part of WTO members to extend the operation of the NVNB clause beyond the GATT, the US has pushed aggressively for its inclusion in TRIPs and each of the bilateral trade agreements it has negotiated with it trading partners.

Despite this, there is little international jurisprudence on the operation of the NVNB clause. An analysis of the available GATT jurisprudence reveals four elements of a NVNB claim.[47] Firstly, there must be a measure applied by a party. This may include laws, regulation and policy statements of the party and its officials. Secondly, there must be a benefit that was reasonably expected to accrue to another party under the agreement. Thirdly, the effect of the measure must be to nullify or impair the benefit. Finally, the nullification or impairment of the benefit must be contrary to the reasonable or legitimate expectations of the complaining party. It is important to note that in the WTO *Korea-Procurement* case the panel held that NVNB claims were available note only against parties who had failed to implement its obligations in good faith, but also against parties who had not negotiated in good faith. Thus, the conduct of the parties during the negotiation process may give rise to legitimate expectations that a benefit will be conferred by the final agreement that can be enforces via an NVNB claim. Article 26 of the WTO DSU importantly requires a complaining party to provide a detailed justification of a NVNB claim. That is, the complaining party must address each of the four elements and provide evidence that each element has been fulfilled.

Of particular relevance in this context are the requirements that the complaining party show that a benefit was due to accrue to it under

[46] TRIPs Article 64.
[47] Faunce et al, NVNB article.

the agreement and that the measure and its effect on that benefit was contrary to the legitimate expectations of the complaining party. Previous NVNB cases under the GATT have involved claims where the benefit was increased market access arising from tariff concessions.[48] However, the PBS does not deny or inhibit any US pharmaceutical manufacturers accessing the Australian market. Manufacturers may still sell their products to Australian consumers at a price of their own choosing irrespective of the operation of the PBS. Thus, the US would have to claim that a benefit it legitimately expected to accrue to it under the AUSFTA was to have drugs listed on the PBS at a higher price or that all innovative drugs would be listed on the PBS, regardless of whether they were deemed cost-effective for the Australian community.

The benefit then impaired would be the difference in the actual reimbursement paid to the pharmaceutical manufacturer and the reimbursement the manufacturer would have received if it had not had to reduce the price at which is was offering the drug in order to make it cost-effective. On the other hand, Australia could potentially file a counterclaim that it legitimately expected that the cost-effectiveness criterion, the reference pricing mechanism and the independence of the PBAC process would not be included in the AUSFTA. The benefit nullified would be the increase in cost incurred by the Australian taxpayer when the cost-effectiveness criterion is not applied. This has been estimated to be between AU$1.5 and 2.5 billion. The central issue then becomes whether each party can establish that they had a legitimate expectation that the identified benefit would not be nullified by the other party. Thus, a party must show it did not, and could not, reasonably have anticipated the measures that nullified the expected benefit.[49] This requires an extensive analysis of the public statements of negotiators and

[48] *US-Japan Film.*
[49] *US-Japan Film; Korea-Procurement.*

government officials during negotiations, at the time the agreement was concluded and throughout the passage of the implementing legislation.

Restriction of Bilaterals Limiting Choice of Forum

Article 21.4 of the AUSFTA contains a choice of forum provisions, which provides that where a dispute arises under the AUSFTA and another agreement, the complaining party can chose the forum in which to settle the dispute, to the exclusion of all other potential dispute settlement proceedings. This choice may be important in the outcome of a dispute because different fora may offer different parties different advantages.

In addition to the AUSFTA, Australia and the US are also parties to a number of other international agreements relating to trade through membership of the WTO. In the case of trade in pharmaceuticals, Australia and the US are governed by obligations arising under both the AUSFTA and TRIPs. In several cases, the AUSFTA contains provisions that simply mirror and reinforce existing obligations. In such cases, a dispute may be initiated either under the AUSFTA Chapter 21 or under the Understanding on Dispute Settlement (DSU) in the WTO.

There are several similarities between the WTO dispute settlement process and the procedures outlines in Chapter 21 of the AUSFTA. Both seek to resolve a potential dispute initially through consultations between the disputing parties. In the event that consultations do not resolve the issues between the parties, a three-member panel is convened, comprising experts chosen by the parties. The panel ultimately decides the issue between the parties. However, there are some critical differences between the two processes.

The WTO dispute resolution process provides a 'rule-oriented' approach to interpreting and enforcing treaty obligations.[50] Such as approach emphasises the importance of formal rules in a formal procedural setting in determining obligations rather than case-by-case diplomacy between the parties. Thus, the WTO dispute resolution process includes an appellate body to which parties may appeal from a panel decision on a point of law. The rulings of the appellate body operate as a body of jurisprudence to which future panels must have regard. In addition, the WTO process allows third parties to participate in the dispute settlement process in order to ensure the best interpretation and application of the rules. In such a system, the relative power of the disputing parties becomes less important. Smaller or weaker parties can form coalitions where their interests align and, backed by a system designed to give effect to rules rather than reputation or economic power, can protect those interests better than they could alone.

In contrast, the bilateral forum under the AUSFTA allows the differences in the parties' bargaining power and economic strength play a greater role. There is no appeals process, no accepted body of jurisprudence and no chance for the smaller party, Australia, to offset its bargaining weaknesses by joining forces with other nations. The differences in the parties' relative power are further enhanced by the creation of working groups or joint to committees to monitor the operation of the agreement, including dispute resolution. Of particular concern here is the establishment of the Medicines Working Group to oversee Annex 2C on pharmaceuticals. The precise composition, role and authority of these working groups are not defined in the agreement but are to be determined later between the parties. These working groups represent a shift away from a rule-oriented system towards a negotiation or diplomacy-oriented system in which the ability of the US, as the stronger party, to apply

[50] Drahos article 'The Bilateral Web of Dispute Settlement'.

diplomatic pressure to Australia is protected. The operation of the Medicines Working Group will also allow private industry to have direct access to this negotiation process. Australia needs to take an active and firm role in the establishment of the working group, the definition of its terms of reference and constitution of its membership to ensure that the group functions as a forum for discussion only, not the renegotiation of obligations.

In relation to NVNB claims, the procedural rules and limitations established in the DSU do not apply to NVNB claims under the AUSFTA. This includes the requirement for a detailed justification. The procedures governing dispute resolution, including NVNB claims, under the AUSFTA are to be determined between the parties.

In a dispute with the US, Australia, as the weaker of the two disputants, is likely to be better off under the WTO dispute settlement proceedings because the multilateral process will go some way to minimising the differences in power between Australia and the US. This is particularly so in the event of a dispute over pharmaceuticals and the PBS. While the AUSFTA focuses on recognition for innovation, TRIPs expressly recognises the need for timely and affordable access to medicines that underpins the PBS. Further, since most WTO members are net importers of intellectual property, Australia is likely to find allies in a dispute with the US.

On the other hand, the US is likely to prefer to deal with a dispute with Australia in the bilateral forum where its power will be more effective. The threat of large compensation claims or cross-retaliation in other industries by the US may be sufficient to induce Australia to change its domestic legislation or policy to suit the US. Thus, if, and indeed when, the US wishes to bring dispute proceedings against Australia, it is likely to chose the AUSFTA dispute settlement process. Australia must be aware of its weaknesses in this forum and push for

a rule-oriented focus in the establishment of rules of procedure for panels and terms of references for joint committees and working groups so as to minimise the effect of the power imbalance between the two parties.

Promoting Experimental Use Patent Exemption for Public-Funded Universities

The decision by the United States Court of Appeals for the Federal Circuit (and the refusal of the US Supreme Court to reconsider that decision) in *Madey v. Duke University* rendered the 'experimental use' defense to patent infringement practically ineffective for most US researchers[51]. In the European Union many member states have similar exemptions to patent infringement, usually introduced by statute. Commonwealth countries such as Canada also have statutory exemptions, whereas others such as New Zealand have a common law exemption. [52]

In Australia, there is no authoritative case law, nor any explicit statutory exemption from patent infringement for experimental use. The Australian Law Reform Commission (ALRC) and Advisory Council on Intellectual Property (ACIP) have recently considered the issue and supported the creation of such an exemption in Australian law. Such a change would not be contrary to any provision in the Australia-United States Free Trade Agreement. This is particularly true of IP harmonisation provisions. These are "best endeavour" provisions.

[51] 307 F3d 1351 (2002). The US Supreme Court refused an appeal in June 2003

[52] Section 60(5)(b), Patents Act 1977 (UK); Section 55.2(6), Patent Act 1985 (Canada). *Monsanto Co. v. Stauffer Chemical Co. (NZ)* [1984] FSR 559; *Smith Kline & French Laboratories Ltd v. Attorney-General (NZ)* [1991] 2 NZLR 560. Australian Law Reform Commission. *Issues Paper 27*, December 2002 (http://www.austlii.edu.au/au/ other/alrc/publications/issues/27) at 226. ALRC. *Discussion Paper 68*, February 2004 (http://www.austlii.edu.au/au/other/alrc/publications/dp68). Advisory Council on Intellectual Property. *Patents and Experimental Use Issues Paper*, February 2004 (http://www.acip.gov.au/library/patentsexpuse.PDF). Dwyer, J.W., Dufty, A., Lahore, J. & Garnsey, J. *Patents, Trade Marks & Related Rights* (Butterworths, Sydney; 1996) Walsh, J.P., Arora, A. & Cohen, W.M. Effects of research tool patents and licensing on biomedical innovation, in *Patents in the Knowledge-Based Economy* (eds Cohen, W. M. & Merrill, S.) 285−340 (National Academy Press, Washington; 2003).

They exist in the body of chapter 17 of the agreement and not a side-letter or annex. They thus do not create a unilateral obligation on Australia to make its IP laws identical with those of the US. Association of this IP harmonisation provision with a non-violation nullification of benefits (NVNB) provision (article 21.2(c)) does not alter this conclusion. NVNB provisions, which activate the full panoply of trade dispute measures where the "spirit" of the agreement has been broken, can only apply to completely unambiguous obligations. To hold otherwise would fundamentally undermine the principle of *pacta sunt servanda* or good faith treaty interpretation set out in the *Vienna Convention on the Law of Treaties*.

The biotechnology industry is one sector of the pharmaceutical industry where Australia has the opportunity to develop innovative products. An experimental use exemption allowing researchers in Australia's great public universities to experiment with molecules and processes without the inhibiting effect of paying royalties, will be vital to this process.

Constitutional Right to Emergency health Care

Australia's have has little experience, until comparatively recently of being persecuted or endangered by their government. Nonetheless such an eventuality has been an inevitable circumstance in other jurisdictions and is immeasurably enhanced by the increased capacity of corporate oligarchies to influence governments. Whilst many human rights initiatives are unlikely to be warmly embraced by the notoriously conservative Australian electorate, this may not be true of a constitutional right to emergency health care. Such a right has worked effectively in India and South Africa and jurisprudence offers governments a margin of appreciation taking into account their limited resources. Such a constitutional provision would provide a rational limit to health care privatisation in Australia, would be widely supported as an accepted part of our egalitarian social structure.

Limiting Evergreening of Pharmaceutical Patents

Certain pharmaceutical patent "anti-evergreening" amendments that were made in 2004 to the *Therapeutics Goods Act* 1989 (Cth) as part of the implementation process required to commence the AUSFTA. It has been argued by Medicines Australia in its submission to this Inquiry, that such provisions are unnecessary for a variety of reasons unsubstantiated by evidence, including the claim that article 17.10.4 of the AUSFTA will not promote "evergreening" of blockbuster brand name patents. Some commentators have also claimed that such amendments are a "dead letter," either because generic manufacturers are unlikely to litigate using the amendments (due to the costs as well as industry cross ownership) or the facility by which reasonable exceptions can be claimed.

This submission argues, however, that the amendments may play a very important role in any subsequent trade dispute with the US involving the pharmaceutical-related provisions of the AUSFTA. This role involves the clarification of Australia's "legitimate expectations" with regard to the non-violation nullification of benefits (NVNB) provision in Article 21(2) (c) of the AUSFTA.

Pharmaceutical patents allow a company that has developed a drug to market it free from competition for a fixed period[53], in return for making public its original clinical data demonstrating safety and efficacy. This data is later available to generic companies when the drug comes off patent. It is a system that balances reward of innovation in research and development with the public benefit of dispersed knowledge. It is a separate system from pharmaceutical approval by the Australian Therapeutic Drug Administration (TGA),

[53] Under the terms of the Trade Related Aspects of Intellectual Property Rights (TRIPS) agreement patents are issued for 20 years from the time of filing. However the actual monopoly period for

which is designed to check whether a new drug has demonstrated an adequate level of safety and efficacy.

Ch 7 of the *Patents Act 1990* (Cth) dealing with patents of addition bears upon the evergreening question. It provides that, even if what is proposed is a true improvement in or modification of the main invention, and not merely instructions as to use of it, a consequent patent of addition should not extend beyond the life of the base patent. Under s 81(1) of the Act, when a patentee, applicant or an authorised person may apply for a further patent for an improvement or modification of the main patent. Failing an extension of term under the provisions of pt 3 of ch 6, the term of a such a patent of addition is generally only coincident with the term of the patent for the main invention.[54]

Forms of Evergreening

So what is "evergreening" and what will preservation and promotion of such amendments achieve? Pharmaceutical patents allow a company that has developed a drug to market it free from competition for a fixed period (20 years under the TRIPS agreement), in return for making public its original data. It is a system that balances reward of innovation in research and development with the public benefit of dispersed knowledge. It is a separate system from pharmaceutical approval by the Australian Therapeutic Drug Administration (TGA), which is designed to check whether a new drug is safe, of consistent quality and efficacious.

Drug patent "evergreening" is an important strategy that multinational pharmaceutical companies have been using since 1983 in the USA (and since 1993 in Canada) to retain rent-profits over "blockbuster"

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medicines is about 12-14 years after taking into account the time taken to conduct clinical trials and get the product through the regulatory system.

[54] As Gyles J commented in the context of this case '[e]ven if it could qualify as a patent of addition pursuant to ch 7 of the Act it would have been limited to the term of the salt patent.'

(high sales volume) drugs by extending patent monopolies for as long as possible. In its most simplistic form evergreening works like this: when the original patent over the active compound of a large sales volume brand name drug is due to expire, its manufacturing company gets regulators to notify it that a generic copy is getting ready to enter the market.

Laws are enacted requiring generic manufacturers to notify brand name competitors of their intention to enter the market. Such laws also require government regulators not to give marketing approval for a generic medicine unless no contrary patent claims can be established. Having received notification of a possible market entry by a generic product, a threatened brand-name manufacturer then seeks to dissuade such competition by claiming what are sometimes large numbers of complex and often highly speculative patents, for example over the capsule or gel of the drug, instead of its contents. [55] Where a generic manufacturer has limited resources, a threat of patent litigation is often enough to make it remove a drug from application. Even if litigation is commenced, the brand name owner enjoys sustained sales from its blockbuster till all proceedings are completed.

The problem is a severe one in the US. Evergreening began in the US in 1983 with the so-called Hatch-Waxman legislation.[56] In 2002 an extensive and lengthy inquiry by the US Federal Trade Commission (FTC) found that as many as 75% of new drug applications by generic drug manufacturers suffered legal actions under patent laws by the original brand name patent owner. These were driving up US drug costs by keeping the cheaper generic versions off the market. The FTC recommended that only one "evergreening" injunction against a

[55] Michael Burdon, Kristie Sloper 'The Art of Using Secondary Patents to Improve Protection' Special Issue June 2003 Vol. 3, 3 *International Journal of Medical Marketing* 226

[56] *Waxman-Hatch Act* (35 USC §156), Gerald Mossinghoff, 'Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process' (1999) 54 *Food and Drug Law Journal* 187.

potential generic market entrant be permitted per product[57] and this change was implemented in legislation in December 2003.[58] The US legislature passed its *Medicare Prescription Drug Improvement and Modernisation Act* 2003. This included, in section 1101 a complicated process of early declaratory relief to assist remedying the problem of brand name pharmaceutical patent "evergreening." This implemented a specific recommendation in the report of the US Federal Trade Commission ("FTC") in 2002. The FTC recommendation was that only one "evergreening" injunction against a potential generic market entrant be permitted per product.[59]

In Canada, to be discussed in more detail subsequently, a similarly extensive investigation by the Competition Bureau revealed similar problems with drug patent "evergreening" arising from the Patented Medicines (Notice of Compliance) Regulations in 1993 required as an obligation of entering the North American Free Trade Agreement ("NAFTA"). It found that over 200 legal actions involving "evergreening" claims had been brought and that this was having an adverse effect on the sustainability of the Canadian generic drug industry and drug prices in that country.[60]

"Evergreening" is more a multifaceted strategic and tactical process, rather than any particular technique of prolonging patent life over "block-buster" medications. Such tactics already blooming worldwide and in Australia. In India, for example, only 215 generic drugs received marketing approval during 1998-2004, despite nearly 5,000 patent "claims" being made in the same period through a "mail box" system. One reasons was that the Indian government passed

[57]. Lara Glasgow, 'Stretching the limits of intellectual property rights: has the pharmaceutical industry gone too far?' (2001-2002) 41 *Journal of Law and Technology* 227
[58] Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* Federal Trade Commission (2002)
[59]. Lara Glasgow, 'Stretching the limits of intellectual property rights: has the pharmaceutical industry gone too far?' (2001-2002) 41 IDEA –Journal of Law and Technology 227
[60] Canadian Competition Commission

legislation required by the World Trade Organisation (WTO) Trade-Related Intellectual Property Rights (TRIPS) agreement, allowing brand name patent claims for new "uses," rather than new chemical entities.

Even states as small as Nicaragua have not escaped "evergreening" attention. That government's recent legislation facilitating access by all citizens to affordable generic medicines was immediately challenged by the US. On the other hand, in South Africa, Trade Minister Mandisi Mpahlwa has recently refused a demand by EFTA Countries (Switzerland, Norway, Iceland and Liechtenstein) to include provisions facilitating pharmaceutical patent "evergreening" in the Free Trade Agreement with SACU (South Africa, Botswana, Namibia, Lesotho and Swaziland).

US regulatory authorities have been subjected, as previously mentioned, for some time to brand name medicine patent "evergreening" tactics.[61] The US Food and Drug Administration ("FDA"), for example, was recently asked to approve the marketing of Pfizer's new drug, called torcetrapib, which increases good (or HDL) cholesterol, in the same capsule with Pfizer's high sales volume "blockbuster" Lipitor (that lowers LDL cholesterol). Lipitor, which loses its original patent protection in 2010, is the world's top-selling medicine, with sales of almost $11 billion last year. Unfortunately, the US lacks an equivalent to our Pharmaceutical Benefits Scheme, so that if Pfizer's "evergreening" combination is backed by plausible research, the FDA may have to approve it, protecting Pfizer from actions under antitrust laws.

In Australia, the *Patents Act* 1990 (Cth) since 1998, already permits non-use-related patent extension for up to five years (section 77) for

[61] Mike Hutchins, 'Using interlocking additional early stage patents to improve and extend protection' Special Issue June 2003 Vol. 3, 3 *International Journal of Medical Marketing* 212, 215

delayed pharmaceutical marketing approval and the AUSFTA has "locked-in" this monopoly protection (article 17.9.8(b)).[62]

Although evergreening encompasses a wide variety of tactics, a central method is use of the patent system by innovator companies to delay the appearance of generic competitors. When the original patent over the active compound of a large sales volume brand name drug is due to expire, its manufacturing company gets regulators to notify it that a generic copy is getting ready to enter the market. Laws are enacted requiring generic manufacturers to notify brand name competitors of their intention to enter the market. Such laws also require government regulators not to give marketing approval for a generic medicine unless no contrary patent claims can be established. Having received notification of a possible market entry by a generic product, a threatened brand-name manufacturer then seeks to dissuade such competition by claiming what are sometimes large numbers of complex and often highly speculative patents, for example covering the capsule or gel of the drug, instead of its contents. [63] Where a generic manufacturer has limited resources, a threat of patent litigation is often enough to make it remove a drug from application. Even if litigation is commenced, the brand name owner enjoys sustained sales from its blockbuster till all proceedings are completed.

Briefly, other evergreening tactics 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 involese contractual agreements in which the generic manufacturer agrees not to enter the market in return for financial remuneration

[62] ss 70-79A (div 2 of pt 3 of Ch 6)

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.[64] 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.

The Canadian Experience with Evergreening under NAFTA

To Canadians observing the developments in the AUSFTA requiring regulatory linkage of medicines safety evaluation with patent status, must have involved a significant element of *déjà vu.* In 1993, over a decade earlier, the *North American Free Trade Agreement* (NAFTA) had required the Canadians to implement a similar process. They did so in the Patented Medicines Notice of Compliance Regulations. The Canadians have since developed considerable regulatory experience in dealing with the problems of "evergreening." The Canadian situation with evergreening provides a particularly useful example of what may happen in Australia because of the similarities between the two countries: roughly the same size and population, similar levels of development and comparable medical systems and finally the absence of an indigenous multinational brand name industry.

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[63] Michael Burdon, Kristie Sloper 'The Art of Using Secondary Patents to Improve Protection' Special Issue June 2003 Vol. 3, 3 *International Journal of Medical Marketing* 226

[64] Andrew Teuten, 'Strategies for extending the period of exclusivity of a pharmaceutical product' (2004) *Sagittarius Intellectual Property Consultants* <http://www.sagittariusipc.co.uk/AT_presentation_Jan04.pdf> accessed July 2005.

Under the *Notice Of Compliance* (NOC)[65] regulations Health Canada cannot issue a NOC until the all of the relevant patents on a brand name product have expired. As a result when the generic company submits its application to get a product approved it also sends a Notice of Allegation (NOA) to the patent holder claiming that no patents are being infringed. If the patent holder challenges the NOA then that automatically triggers a 24-month regulatory stay which prevents the Minister of Health from granting approval to the generic and the matter then may proceed to a court hearing. The stay expires either at the end of the 24 months, when the patent expires, or when the court case is decided whichever comes first.

The effect of these linkage regulations is a subject of intense disagreement between the generic and brand name companies. The Canadian Generic Pharmaceutical Association (CGPA) claims that "not only is this abuse of Canada's patent regime extremely harmful to Canada's generic pharmaceutical industry, the Canadian public loses out on millions of dollars in savings by having to pay for the higher-priced brand-name version for an extended period of time. The delays caused by these needless court battles have cost Canadians, their governments and private insurers hundreds of millions of dollars." Canada's Research-Based Pharmaceutical Companies (Rx&D), the peak brand name industry association, counters that these regulations are necessary because "generics do not have to concern themselves with a possible interlocutory injunction to prevent infringing sales once an infringing generic product is on the market. Statistics show that this remedy is available in pharmaceutical cases approximately half as often as in other industry patent cases. Indeed, as a result of the inability of pharmaceutical patentees to obtain interlocutory injunctions to prevent the complete destruction of their intellectual property rights and market share, the "linkage" regulations are the only means for Canada to meet its international

[65] A Notice of Compliance is official Canadian terminology for market authorization.

obligations to provide an effective enforcement mechanism for patents[66] The 80% success rate for the generic companies translates into 4 out of 5 cases won. There are 125 cases where there was no hearing, in 20 cases where the NOA was withdrawn this is counted as a win for the patentee but the 100 cases where the innovator either accepted the NOA or the case was otherwise settled are not counted as wins for the generic.[67]

A second area of contention is the use of multiple patents to delay the appearance of a generic product. The CGPA maintains that the brand name companies continually list new patents on a product, each of which can trigger a new NOA and an additional stay on the appearance of a generic. In this way, competition is delayed.[68]

The brand name companies dispute this interpretation. Their position is that there is always ongoing research into drugs and that it is natural that new patents will be filed, reflecting improvements such as moving from a three pill a day regimen to once a day dosing. Multiple patents on a single medicine are relatively common. Forty-four percent of the 419 medicines on the Patent Register are covered by more than one patent.

Among other things, PhRMA claims that Health Canada has been inconsistent in its policies and practices relating to the listing and delisting of brand name companies' patents and in requiring generic companies to send a NOA; that Health Canada is continually and systematically limiting further the types of patents that can be listed

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[66] Rx&D. *S-17: a necessary first step to bring Canada's patent act to internationally competitive standards. A brief to the House of Commons Standing Committee on Industry, Science and Technology*. Rx&D, Ottawa, May 29, 2001.

[67] Rx&D. *S-17: a necessary first step to bring Canada's patent act to internationally competitive standards. A brief to the House of Commons Standing Committee on Industry, Science and Technology*. Rx&D, Ottawa, May 29, 2001.

[68] Canadian Generic Pharmaceutical Association. *The patented medicines (notice of compliance) regulations*. http://www.cdma-acfpp.org/en/issues_federal/noc_regulations.html. Accessed 15 January 2003

on the Patent Register; that Canadian courts fail to provide effective recourse in cases where an NOC is issued for an infringing generic medicine; and that ultimately Canadian courts are not applying standards required of them under NAFTA and TRIPS. PhRMA's ultimate conclusion is that the "USTR should attach high priority to remedying this situation." A 2006 report from the US Trade Representative echoed PhRMA's concerns about enforcement of Canadian patent laws. "Canada's compliance with its TRIPS and NAFTA obligations remains a matter of concern. Although Canada has instituted statutory data protection, several judicial rulings have cast doubt on how well these protections are being enforced, as required by TRIPS Article 39.3 and NAFTA Article1711."[69]

The NOC regulations that Canada adopted are an ongoing source of controversy not only domestically in Canada between the generic and brand name sectors of the pharmaceutical industry but also between the US pharmaceutical industry and the Canadian government. In financial terms, if the generic industry is to believed, these regulations have probably added hundreds of millions of dollars to the Canadian drug bill since 1993 when they were first put into place. Furthermore, if the dispute around their enforcement between Canada and the US continues to escalate there is the potential lead for the US to impose trade sanctions against Canada.

Quality and Safety-Patent Linkage: Article 17.10.4 AUSFTA

Of chief "evergreening" concern is that the so-called "linkage" article (of quality and safety approval and patent status) in the AUSFTA (17.10.4) appears to be far broader than the US or Canadian

[69] Office of the United States Trade Representative. 2006 national trade estimate report on foreign trade barriers. Available at http://www.ustr.gov/Document_Library/Reports_Publications/2006/2006_NTE_Report/Section_Index.html?ht=. Accessed 20 June 2006

versions.[70] For the first time in Australia it potentially links the approval of a drug safety and efficacy regulator (the TGA) with the supervision patent law. It requires that TGA drug marketing approval be "prevented" indefinitely (not for the 30 month and 24 month periods as in the US and Canada) whenever any type of patent (including a speculative "evergreening" patent) is merely "claimed." "Claimed" is not defined in the AUSFTA.

The Generic Medicines Industry Association of Australia (GMiA) in its submission to the Senate inquiry on the AUSFTA stated that this "evergreening" provision (if its terms were incorporated in Australian legislation) could lead to "long delays or generic equivalents not reaching the market."[71] Pharmacoeconomists have predicted that if this strategy succeeds in substantially delaying generic drug market entry by multiple products (at levels of generic competition seen in 2003) for as little as 24 months, the Federal cost for just the first few highest expenditure PBS drugs could be substantial. Public Hospital drug expenditures will increase 12%.[72] The provision's main effect, however, is likely to be seen as inhibiting the development of a strong and independent generic industry in Australia.

The so-called "evergreening" or "linkage" article in the AUSFTA (17.10.4) appears to be far broader than the US or Canadian versions.[73] For the first time in Australia it potentially links the approval of a drug safety and efficacy regulator (the TGA) with the supervision of patent law. It requires that TGA drug marketing approval be "prevented" indefinitely (not for the 30 month and 24 month periods as in the US and Canada, respectively) whenever any

[70] C Arup 'The United States-Australia free Trade Agreement – the intellectual property chapter' (2004) 15 *Australian Intellectual Property Journal* 205
[71] Generic Medicines Industry Association (GMiA)
[72] B Lokuge, TA Faunce, R Denniss, A Backdoor to Higher Medicine Prices?" Intellectual Property and the Australia-US Free Trade Agreement (2003)
[73] C Arup 'The United States-Australia free Trade Agreement – the intellectual property chapter' (2004) 15 *Australian Intellectual Property Journal* 205

type of patent (including a speculative Some researchers have anticipated little change on the ability to evergreen in Australia as a result of the AUSFTA and its implementing legislation. They consider that existing patent examination, opposition and revocation systems are adequate to stifle 'dodgy' patents, but consider that other impacts are possible on the frequency of litigation of pharmaceutical patents.[74]

US and PhRMA Views Regarding the Australian Anti-evergreening Amendments

U.S. Trade Representative Robert Zoellick in his exchange of letters with Trade Minister Vaile expressly reserved the right of the U.S. to call into question the evergreening amendments. In some ways this concern confirms the validity of the amendments in tackling an agenda by the multinational brand name pharmaceutical industry to raise its rent from patents in Australia.

> [i]f Australia's law is not sufficient to prevent the marketing of a product, or a product for an approved use, where the product or use is covered by a patent, Australia will have acted inconsistently with the Agreement. We will be monitoring this matter closely, and reserve all rights and remedies as discussed below.
>
> We also remain concerned about recent amendments to sections 26B(1)(a) 26C and 26D of the Therapeutic Goods Act of 1989. Under these amendments, pharmaceutical patent owners risk incurring significant penalties when they seek to enforce their patent rights. These provisions impose a potentially significant, unjustifiable and discriminatory burden on the enjoyment of patent rights, specifically on owners of pharmaceutical patents. I urge the Australian Government to review this matter, particular in the light of Australia's international legal obligations. The US reserves its rights to challenge the consistency of these amendments with such obligations.[75]

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[74] Karin Innes, above n 18.

[7575] See item 6 (Pharmaceutical Patents) of Letter from Robert Zoellick to Mark Vaile, 18 May 2004 *Department of Foreign Affairs and Trade* <http://www.dfat.gov.au/trade/negotiations/us_fta/final-text/letters/ip_zoellick_vaile.pdf> accessed July 2005.

In the concluding paragraphs of the letter the U.S. Trade Representative stated:

> bringing the Agreement into effect is without prejudice to any future action the US Government may take regarding compliance of Australia's laws and other measures with the Agreement … [i]f subsequent practice reveals problems with the full exercise of US rights I have discussed above, Australia should expect that we will take appropriate remedial action[76]

Indeed late in 2005 the US Ambassador flagged that if a practical problem did emerge in the operation of these anti-evergreening provisions, which the countries had temporarily 'agreed to disagree' on, then the U.S. would first approach Australia for a bilateral resolution, but failing that would litigate the matter before the World Trade Organisation.[77] Both the International Federation of Pharmaceutical Manufacturing Associations and the US Pharmaceutical Research and Manufacturers Association (PhRMA) have reportedly commented that their view is that these provisions are inconsistent with obligations under TRIPS.[78] This is more a lobbying claim than an argument based on a clear understanding of TRIPS obligations. Article 27 of TRIPS for example, was clearly stated in the WTO *Canadian generic medicines decision*, to permit specific legislation dealing with a problem that only arose in one industry sector (such as evergreening in relation to the pharmaceutical sector).

It is unlikely that an Australian generic manufacturer will, in the immediate future, use the new 26C and 26D in the *Therapeutic Goods Act* 1989 (Cth) to litigate (most in Australia are subsidiaries of US companies). However of crucial importance might be the capacity of

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[76] Ibid

[77] 'US still watchful on FTA' 22 November 2004 *Pharma in Focus* <http://www.pharmainfocus.com.au/news.asp?newsid=517> accessed 12 September 2005.

[78] 'International pharma crits FTA' 25 October 2004 *Pharma in Focus* <http://www.pharmainfocus.com.au/news.asp?newsid=469> accessed 12 September 2005.

the Commonwealth Attorney-General to join an application for an injunction by a brand name patent holder against a generic medicines manufacturer and to claim damages where the injunction has caused a price rise under the PBS. This mechanism allows Australia under article 32 of the Vienna Convention on the Law of Treaties to claim that its actionable legitimate expectation was that article 17.10.4 would not increase medicines prices under the PBS. The burden of proof required to obtain such an "evergreening" injunction could be set high. Rather than such interlocutory injunctions, however, PhRMA will probably argue that article 17.10.4 requires is a mechanism by which the Australian TGA or its equivalent will itself be able to "prevent" generic approval until all patent concerns are resolved. Such a provision would be contrary to the legitimate expectations Australia would have in relation to the meaning of "prevent" and "claimed" in article 17.10.4 as a result of the 26D amendments in particular.

These "anti-evergreening" amendments in the AUSFTA implementing legislation may be interpreted as attempting to reassert the sovereignty of the Australia parliament over this aspect of public health. They are likely to be challenged by PhRMA should they begin to appear effective. Challenges may also come from the U.S. government given its views about the Australian amendments.

It is in the interests of Australia to preserve the so-called anti-evergreening amendments passed by the Australian parliament with the implementing legislation for the AUSFTA. Having studied this area for over two years as Director of an Australian research Council grant we are able to conclusively that there in no evidence supporting the view that these amendments are, or are likely to have, any detrimental effect on the pharmaceutical industry in Australia.

Springboarding and related matters

I support expanding the general thrust of recent amendments to our Patents Act that enhance springboarding protection for intending generic market entrants. This will be a major factor in generic pharmaceutical companies deciding to locate or continue operations in Australia. I would oppose the Medicines Australia amendments here as doing no more than attempting to add unnecessary bureaucratic complexity that they inhibit use of the amendments by smaller generic firms. The value of the amendments to fostering a generic medicines industry in Australia will be greater if they apply retrospectively and to future patents.

I support the inclusion of anti-competitive practises in or patents legislation as a ground for issuing a compulsory license. Annex 2C.1 of the AUSFTA makes clear that the operation of "competitive markets" is one way in which pharmaceutical innovation can be rewarded in the respective countries. This creates a need for much greater involvement of anti-trust and competition regulators in monitoring and shaping the activities of the pharmaceutical industry in Australia.

Australian patent law should carefully circumscribe the data exclusivity monopolistic protections. These, particularly if successive periods of monopolistic protection are piled for subsequent uses on the original five years, can create major problems for access to essential medicines as they may interfere with the capacity to compulsorily license recently patented medicines in national emergencies.

To encourage a generic pharmaceutical industry in Australia it is critical that more legislative encouragement be given to the first generic player willing to take on the patent thicket created by the originator company. At the moment there is a disproportion between

the amount of money required to bring such an action and the amount of rewards likely to be obtain…basically because onec the door is open all the other generic players come in. This cannot be in the long term interest of the Australian health systems as a flourishing generic industry keep drug prices low and provides critical competition. Generic companies have to do a lot of research and development in oder to get around the originator patent thickets. There should be a period of market exclusivity for the first generic market entrant, a reduction of the level of discovery necessary in patent claims (reducing costs and resolution times) and a capacity to have TGA and PBAC fees refunded for the first generic market entrant

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