The Promise to the Public: Generic Competition
Submission to the Pharmaceutical Patents Review
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Introduction
This submission takes a public policy perspective, focusing on the public return from the patent system through competition based on the new technology after the 20-year patent monopoly period expires. The government has agreed time-limited monopolies to encourage domestic invention (the patent system). At the end of the agreed period, the patented invention should be reproducible by skilled persons without undue experimentation and the new knowledge embodied in the invention should be freely available and useable by all.

This submission presents evidence on delays to generic entry in Australia then considers (briefly) the arguments put by "big pharma" in support of a range of regulatory interventions that contribute to these delays. It then considers the key patent and health policy issues delaying competition. The regulatory environment is then assessed from the perspective of achieving a supportive policy environment for timely entry of competition at the expiry of the agreed patent monopoly period.

Evidence on evergreening
The public benefit side of the patent bargain is that at the end of the 20-year patent period others will be able to enter the market, using the knowledge disclosed in that invention. Prices should fall dramatically. There is a serious question as to whether this happens in respect of pharmaceuticals. In 2009 the European Commission (EC) reported on an inquiry motivated by concerns about "observed delays in the entry of generic medicines to the market and the apparent decline in innovation as measured by the number of new medicines coming to the market." The inquiry found delays in generic entry had substantial budgetary impacts. It also found a range of tactics used to prolong the life cycle of patented medicines, including substantial patent thickets and a high level of patent and market authorisation disputation.

To what extent are similar tactics evident in Australia? When the AUSFTA was debated in parliament the then Minister for Trade advised that evergreening was a US phenomenon and did not occur in Australia. Here evidence on evergreening is presented for four pharmaceutical products. Two are products where generic entry was delayed though disputes over patent later found to be invalid (venlafaxine and clopidogrel); one involves delayed entry where a disputed patent was found to be valid (omeprazole); and the fourth is a product group (statins) which involves "me too" research by large global companies.

Venlafaxine/desvenlafaxine
Venlafaxine is a serotonin-norepinephrine reuptake inhibitor (SNRI) and is a major treatment for depression. The original Australian patent (567524) was filed on 6 Dec 1983 and expired on 6 Dec 2008, having been granted a 5-year term extension. It is surrounded by a modest number of associated ("evergreen") patents. Two are method of treatment patents (744990 and 2003204077) both expiring in mid 2014; two are extended release (XR) patents, starting on 20 March 1997. The first XR patent, 727653, will expire on 20 March 2017. A divisional

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2 Hansard, House of Representatives, 5 August 2004, 32319.
child (2000065442) and divisional grandchild (2003259586) were filed on 10 October 2000 – the child lapsed before grant but the grandchild was sealed on 11 May 2007. In preparing for launch of its generic product, Sigma had not found this grandchild patent.

Venlafaxine is interesting, both because of disputed patent 2003259586 and because patents were also granted for its major metabolite desvenlafaxine. The European Medicines Agency (EMA) concluded that "relative to the mother compound venlafaxine, des-venlafaxine appears less effective with a similar safety and tolerability profile. The clinical value of such a product is questioned." Three desvenlafaxine patents complete the set of evergreen patents. With the original patent for venlafaxine commencing on 6 Dec 1983 and the final desvenlafaxine patent expiring on 18 August 2023, patent "protection" for what is effectively the same product has been sought and granted for a period covering almost 40 years.

The dispute about generic entry of venlafaxine prevented generic competition during the months immediately after desvenlafaxine entered the market in February 2009. During this period it appears that effective representations by Pfizer's sales force led to a massive shift in prescribing to what is effectively the same drug (Figure 1). The injunction (imposed in December 2008) was finally lifted in November 2011 when the key evergreen patent was held to be invalid. By this time desvenlafaxine had achieved a 37% market share.

**Figure 1: Prescribing shift: venlafaxine to desvenlafaxine**


While the EMA effectively refused desvenlafaxine, the PBAC accepted it because it "would provide a further treatment option for major depressive disorders" despite the fact that "no evidence was presented to suggest that desvenlafaxine would offer an advantage for any

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3 Which itself has a child – 2007201828 (lapsed before grant) and a grandchild (2010214740 – one of the rare instances where the Australian Patent Office refused a patent application). As of 23 January 2013 AusPat shows 244 refusals and 123,305 sealed patents.


5 These cover the period from 21 November 2000 to 18 August 2003. While patent 767835 has ceased, under current procedures the owner (now Pfizer) can restore this patent simply by the late payment of renewal fees.
particular patient group over the parent drug venlafaxine."6 Despite essentially similar chemistry and equivalent therapeutic effect, the drugs are in different PBS formularies. As a result the tax-payer pays between $5.60 and $6.32 more each time a doctor chooses to prescribe desvenlafaxine. As at June 2012 over 250,000 scrips were written monthly for the two drugs. The additional impost on the taxpayer from desvenlafaxine is $0.57m each month.

**Clopidogrel**

The interesting feature of this case is that generic entry was delayed from the original patent expiry date of 7 July 2003 to 12 March 2010 when the injunction in respect of disputed patent 597784 was lifted and that patent revoked.7 Patent 597784 (a process and compound patent) had been granted a 5-year patent extension. The monopoly for the five years from 7 July 2003 disappeared when the patent was revoked. The combination of a 5-year term extension on an evergreen patent with its subsequent revocation meant that for nearly 7 years the PBS was paying higher prices for this blood thinning product than it should have. In fact another evergreen patent – 715655 combining clopidogrel and aspirin – effectively addressed major medical uses and limited the ability of generic companies to succeed in the market. This so-called invention combined two well-known substances where it was clear (from the treatment indications for clopidogrel)8 that the combination was well-known and therefore not inventive. Nonetheless the patent office granted a patent. This was eventually challenged and was revoked on 29 May 2012, clearing the way for more substantial generic competition more almost nine years after such competition should have commenced.

Patent systems do not currently include any clear mechanisms for seeking reimbursement from patent owners where they have profited from an invalid patent monopoly. The terms of the injunction on the 597784 patent provided for those adversely affected to seek compensation for the injunction period (September 2007 to March 2010)9 but not for the term extension period. There are no clear mechanisms for recouping losses for either the term extension period or the period between March 2010 and May 2012 when the (subsequently revoked) 715655 patent limited generic competition. Sanofi-Aventis benefitted considerably from the high prices paid by the PBS from July 2003 through May 2012. During this period 20.5 million scripts for clopidogrel were funded through the PBS.10 In July 2003 the approved price to pharmacists was $72.16. Now that generic entry has occurred the price has fallen to $50.15 and should fall further. This is a very substantial transfer of funds from Australian taxpayers to Sanofi-Aventis.

Patentees use a wide range of strategies to maximise their returns from the patent system. There should also be substantial penalties to deter abuses and invalid earning such as those that occurred in this case. At a minimum losers (the PBS) should be fully compensated.

**Omeprazole / esomeprazole**

Omeprazole (LOSEC) is effective in the treatment of dyspepsia, peptic ulcers and reflux. The Australian patent (529654) has been surrounded by a further 53 patents which extend the expiry date from 11 April 1999 to 7 May 2027 – an additional 28 years beyond the original 20 approved with the grant of the patent for the NCE. Three of these patents have expired, and a further 24 are ceased. These 24 could probably be re-instated by the late payment of renewal

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6 This very strange "logic" is presented in "Your questions to the PBAC: patent expiry and 'new' drug approval", Australian Prescriber, 32:3, June 2009, p.63.
7 *Apotex Pty Ltd v Sanofi-Aventis* [2009] FCAFC 134 (29 September 2009)
8 Clopidogrel is marketed with two treatment indications, one of which is its combination with aspirin to treat acute coronary syndrome.
9 This does not mean that the process for achieving compensation is clear, straightforward and cost-effective.
fees, though there is a right to appeal against this. This leaves 26 evergreen patents which have kept generic competition from the large omeprazole market until very recently.

Alphapharm attempted to enter the market in 1999 when the original patent expired, challenging the 601974 patent which extended the patent period to April 2007. The Full Federal Court held the patent to be obvious, but the High Court overturned this decision in a judgement which Lawson has referred indicating the quantum of inventiveness required for a patent was "almost a per se rule so that the quality of obviousness will almost never be relevant in assessing patentability." While this decision was made in respect of the Patent Act 1952, subsequent decisions, such as Lockwood, confirm a very low inventiveness requirement. The decision was an expensive one for the Australian taxpayer.

The statin group (LIPITOR et al)

Because of the "powerful exclusive right" of a patent, there is a strong incentive for competitors to develop products which are sufficiently different to meet the patent system requirements for novelty and inventiveness yet which provide the same therapeutic effect, thus allowing the competitor to gain a share in a break-through drug market. Statins (HMG-CoA reductase inhibitors) are a set of drugs used to lower cholesterol levels. Reduced cholesterol levels are thought to reduce the incidence of cardiovascular disease. Atorvastatin (LIPITOR) is reported as the best-selling pharmaceutical in history and Pfizer reported global sales of $12.4 billion in 2008.

The statins provide another example of the pricing impact when drugs with similar health outcomes are not grouped together in the PBS. Atorvastatin came off patent on 18 May 2012. Rosuvastatin is still covered by a patent. There is generic competition for simvastatin and pravastatin. The items in Table 1 are equivalent doses to achieve a 40-45% reduction in LDL-C. Doctors are free to prescribe any of these options, although atorvastatin costs 78% more than the equivalent dose of simvastatin. Where a patient has a concession card the additional cost falls on the taxpayer. Where they do not, a large part of the additional cost falls on the patient, though in the case of atorvastatin some of this cost is shared with the taxpayer.

Table 1: Statins: price relativities and "me-too" drugs

<table>
<thead>
<tr>
<th>Product (all 30 tablets)</th>
<th>PBS item number</th>
<th>Price at Jan 2013</th>
<th>Relative price</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 mg simvastatin</td>
<td>8173E</td>
<td>$22.78</td>
<td>100%</td>
</tr>
<tr>
<td>5 mg rosuvastatin</td>
<td>3402C</td>
<td>$32.20</td>
<td>141%</td>
</tr>
<tr>
<td>80mg pravastatin</td>
<td>8829Q</td>
<td>$33.91</td>
<td>149%</td>
</tr>
<tr>
<td>20 mg atorvastatin</td>
<td>8214H</td>
<td>$40.50</td>
<td>178%</td>
</tr>
</tbody>
</table>


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13 The fact that a similar therapeutic effect can be achieved while meeting patent standards of novelty and inventiveness is yet further evidence on how low these patent standards are.
14 Though there is some dispute as to whether lowering cholesterol actually does reduce cardiac disease – see for example Daniel Steinberg, The Cholesterol Wars: The Skeptics vs. The Preponderance of Evidence, Academic Press, 2007, pp. 6–9 and Reginald Marsh, "Cholesterol levels have negligible correlations with cardiovascular incidents", The New Zealand Medical Journal, 125: 1364, 2012.
The public policy question is why the government policy allows for the payment of different prices for the same outcome. For any other procurement issue this would be a matter of public scandal. For some reason asking Australian taxpayers to fund the profits of overseas "big pharma" does not generate the same concern.

The original patent expired on 18 May 2012 after a 5-year extension. The term extension grant was despite LIPTOR being the best-selling drug in pharmaceutical history. Pfizer has earned in excess of $130 billion worldwide for this one drug, $7 billion of that from Australia. There was no requirement for Pfizer to show that the term extension was needed to fund the relevant R&D. LIPTOR is surrounded by 7 evergreen patents, one of which has been revoked after being challenged by Ranbaxy. Pfizer also settled out of court with Ranbaxy over a US patent dispute related to LIPTOR.

The settlement has given Ranbaxy early access to the atorvastatin market allowing it a head-start on its rivals. Not satisfied with this Ranbaxy has offered pharmacists nearly $15,000 of free stock, a guaranteed price discount of 90% and a "lowest price guarantee". This behaviour would seem on its face to be anti-competitive and has certainly deprived rivals of an anticipated share of the atorvastatin market. The situation is further complicated by Pfizer's launch of its own "generic" brand and its full-page "information" direct to the public about the continued availability of LIPTOR. Such games playing goes well beyond ordinary rivalrous competition, raising concerns about sustainability in the generics industry if no action is taken to enforce standards.

The remaining 6 atorvastatin patents extend the patent period to 18 December 2020. One of these is for the combination of atorvastatin and amlodipine thus treating high cholesterol and high blood pressure simultaneously. While neither atorvastatin nor amlodipine are still in patent, the obvious combination is patent protected until 20 July 2020. Australia has a particularly low standard for the grant of combination patents – well below the "significant advance over what is known" standard. In this case there cannot be generic competition for this obvious combination for nearly a decade. Yet again the low inventiveness standards of the patent system undermine the sustainability of the generics medicines industry at considerable cost to the Australian taxpayer.

**Arguments by "big pharma"**

Large pharmaceutical companies which focus on the development of new chemical entities (NCEs) providing useful and genuinely new treatments are motivated by the high returns the patent system provides. As *The Economist* has pointed out "most big pharmaceutical companies are hugely profitable: operating margins are more than 25%". The policy perspective is that such very high returns provide the incentive for the risk and cost of developing significant new health treatments.

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17 All this information is from Ken Harvey, "Companies tussle over market share for anti-cholesterol drug Lipitor® and its generic equal", *The Conversation*, 18 May 2012.
18 Yet the PBS still pays a much higher price – this action by Ranbaxy provides a very large windfall gain to pharmacists and no benefit to the taxpayers who fund the PBS. While the price review mechanism will over the longer term achieve good savings, the delays built into the system are overly generous to pharmacists and a poor bargain for taxpayers.
Despite these high returns big global pharmaceutical companies invest substantially in lobbying for further regulatory rules to limit competition. The TRIPS agenda was driven largely by "big pharma" and achieved: a 4 year extension in the term of standard patents, recognition of the new monopoly "right" of data exclusivity; limitations on exclusions from patentability; the end of local working requirements; and limitations on compulsory licensing. Since then a TRIPS-Plus agenda has been actively pursued. Australia, for example, agreed to formalisation of data exclusivity regulations, appeal rights over PBS pricing decisions, requirements on generic companies to advise of intent to enter the market (AUSFTA). The current agenda – not publically available but evident in leaked versions of the draft Trans Pacific Partnership Agreement (TPPA) includes formalising low standards for patentability – in particular excluding any requirement for enhanced efficacy in determining inventiveness – and extending the new monopoly grant of "data exclusivity". "Big pharma" companies cite extremely high costs for clinical trials in support of their demands for such regulatory impediments to competition as: very low patentability standards, data exclusivity, term extensions, limited rights of crown use of compulsory license and asymmetric notice regarding market competition. But the estimates presented are based on undisclosed sources and do not stand up to scrutiny.

Those lobbying for increased market intervention in respect of innovation and R&D also argue that without "intellectual property" there will be little innovation. There is no empirical support for this mantra. Professor Granstrand has found that "the IPR system in general, and the patent system in particular, has been neither necessary nor sufficient for technical and/or economic progress at country and company level historically." The pharmaceutical industry is the major exception to the substantial empirical evidence that in most industries the patent system is the least useful means of ensuring good returns to innovation investment. But even in pharmaceuticals there are many important products that were developed without patent "protection", and comparison of British, French and German experience suggests that too sweeping a patent system can inhibit rather than encourage innovation in the chemical industries. It is clear, then that patent policy can go too far even in the pharmaceutical industry. Monopoly "protection" for every trifling variation may assist the profit levels of global companies, but actively undermine the vitality of the generic medicines industry.

**Critical issues**

What are the key issues preventing timely entry of generic medicines into the Australian market when the original patent expires? Consideration of the evidence identifies a number of regulatory issues in both the patent and the health systems that encourage behaviour which delays generic competition.

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26 This substantial evidence is well summarised by Andrés López, 2009, "Innovation and appropriability: empirical evidence and research agenda" pp. 1-32 in WIPO (ed.) *The Economics of Intellectual Property: Suggestions for Further Research in Developing Countries and Economies in Transition*.


Inventive step: far too low
Australia has a very very low inventive step threshold – a mere "scintilla" of inventiveness. When one reviews the types of evergreen patents in just the examples listed above these low standards are evident. I canvassed these issues in my original submission to this review and will not repeat this material here.

In 2007 the US Supreme Court (SC) considered the issue of inventiveness (or nonobviousness as it is referred to in the USA). The SC emphasised that its older doctrines remained in place – including the synergy doctrine for combinations; that the person skilled in the art could have normal imagination and that "obvious to try" indeed makes an invention obvious.

In regard to Question 3 in the Issues Paper, I cannot agree that the recent amendments raised the height of the inventive step. All existing case law (specifying that almost no inventiveness is required for patentability) remains on the books. The data on evergreening show that there is a considerable need to raise the height of the inventive step to remove the impediments to timely generic competition at the end of patent life. The Australian parliament has been advised that patents are only granted "for things that are a significant advance over what was known and what was available to the public at the priority date of the patent." This standard should be implemented as a matter of urgency. This standard would eliminate most evergreen patents. This change alone could solve many of the impediments to timely entry of generic pharmaceutical competition. To test this, the Commissioner could be asked to review all evergreen patents against the "significant advance" standard and advise the committee (and the public) of the outcome of this experiment.

**Recommendation 1:** Amend the inventive step standard in the *Patent Act 1990* to "a significant advance over what is known or publicly available at the priority date." The date of effect should be the date this standard was advised to parliament and should apply to all patents regardless of the date of grant. In respect of pharmaceutical substances a significantly improved health outcome compared to other treatment approaches could be reasonable evidence of a significant advance.

**Methods of medical treatment**
This long-standing exception to patentability was overturned by the Federal Court on the spurious grounds that accepting a legislative amendment proposed by Senator Harradine meant that parliament meant all long-standing exceptions to patentability should be abandoned. This judge-made policy contributes to the thickets of minor variations that surround patents for genuinely inventive NCEs. Venlafaxine has three method of treatment patents among the set of evergreen patents, atorvastatin has four and omeprazole has 19.

**Recommendation 2:** Amend the *Patent Act 1990* to re-institute the traditional exceptions to patentability that existed at the time parliament passed the Patent Bill 1990. In particular the prohibitions against patenting methods of medical treatment or use should be re-instituted.

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30 Explanatory Memorandum to the Intellectual Property Laws Amendment (Raising the Bar) Bill 2011, p.42.
The innovation patent system
IP Australia's recent consultation paper on the inventiveness standard for innovation patents shows that this second-tier system – which was designed for local companies – is increasingly being used by international companies, especially in relation to pharmaceuticals. There are no international obligations affecting this second-tier system. Australia is therefore free to redesign it to achieve its policy goals. If the system were renamed so that it was clear it was not part of our international patent obligations – for example the local innovators incentive act – then access could also be restricted to small domestic companies and patentability could exclude all pharmaceuticals and pharmaceutical-related innovations (as well as other traditional exclusions such as software and business methods).

Recommendation 3: Reshape the innovation patent system to limit use to small domestic companies. Exclude all chemical compounds, pharmaceutical patents and methods of medical treatment or use from its ambit.

Data exclusivity
Data exclusivity is a relatively new form of government-granted monopoly. It was first introduced in 1984 in the USA as part of the Hatch-Waxman Act. That act was motivated by the need to overturn a CAFC decision making it unlawful to use data in a patent to prepare for market entry before the patent had expired. This court decision effectively extended the period of patent monopoly beyond 20 years. To offset this the Hatch-Waxman Act introduced a package of reforms to ensure that generic companies could use patent data to prepare for market entry as soon as possible after patent expiry. The act included the first provisions limiting the ability of third parties to use data required by regulatory agencies for market approval. Such use was precluded for 5 years. Use of such data for "unfair commercial use" was then written into the TRIPS Agreement (Article 39)

The rationale for turning data required by governments to ensure the health and safety of their citizens into private property is unclear. Such data are required for good reasons. There is a substantial public interest in such data, both for medical research purposes and for use by generic companies to demonstrate bio-equivalence. Any use of such a dubious monopoly privilege to delay generic entry (thus effectively extending patent terms) should not be agreed in any circumstances. If we must have such an odious form of monopoly, we should ensure that it does not apply during the last 2-3 years of the life of any associated patent. The patent bargain (and the public interest) favours immediate competition on expiry of a patent term and new monopoly grants should not be allowed to interfere with this goal.

Recommendation 4: Ensure that any data exclusivity rights that Australia is forced to agree to as part of trade bargaining do not allow such data to be private during the last three years of the life of a patent.

PBS policy does not offset poor patent policy
The F1/F2 formulary approach seems to have real problems in providing value to the taxpayer. Both the statin example and the (des)venlafaxine example show that taxpayers are paying more than needed to allow doctors a free choice between therapeutically equivalent treatments. Given the extent to which "big pharma" markets direct to doctors – and the evident effectiveness of that marketing (Figure 1) – this seems to be nothing more than a massive and hidden subsidy to overseas pharmaceutical companies.

32 Using a capitalisation or employment number criterion for "small" and an ownership requirement (not more than 25% overseas owned) for "domestic".
Recommendation 5: Ensure that all pharmaceuticals that provide the same therapeutic effect are grouped together in a specific F2 formulary to ensure that taxpayers do not pay unnecessarily high prices for equivalent treatments.

A pro-active policy approach
The overall objective of the interlocking patent and health systems should be to encourage timely entry of generic competition as soon as NCE patents expire. Consideration of what is required to achieve this policy goal allows a clear focus on the range of current impediments. This covers issues relating to the development of patent thickets, uncertainty in planning for generic entry, information disclosure, incentives to act in line with overall policy objectives, price signals, and regulatory efficiency. Because of bio-equivalence issues timely entry needs to be considered separately for traditional pharmaceuticals and for the newer class of products generally referred to as "biologics".

The mainstream entry system
Patent thickets: If evergreen patents could be eliminated this would do much to ensure the timely entry of generic pharmaceutical competition. The most important issue to ensure the patent bargain is delivered to the public is substantially raising the height of the inventive step. The appropriate standard is that advised to parliament in 2011 – "a significant advance". Over-turning the judge-made law that allows patents for methods of medical treatment (or use) would also assist in eliminating patent thickets around NCEs.

Uncertainty: There are further issues affecting the certainty of the environment within which generic companies prepare for market entry. A particularly invidious source of uncertainty is the grant of applications for changes in patent status, claims etc at almost any time. Lundbeck applied for a term extension on patent 623144 one day prior to the expiry of the 20 year patent term and the patent office granted this. The Act provides details on processes for late application for status changes, and in some cases – such as patent term extensions – allows wide scope in when an application must be made. The current system makes for considerable uncertainty for potential competitors in planning to enter the market once a patent has expired.

A particularly invidious retrospective action is the potential for the revival of ceased patents. In theory renewal fees must be paid within the due date, but in practice there are processes for paying after this time. The grace period of six months is more than adequate time to ensure fees are paid. After this ceased should mean ceased, and it is unfair to innovative companies for knowledge that has been placed in the public domain to then be withdrawn.

Recommendation 6: Amend the Patent Act 1990 to clarify that all late applications for changes to patents, whether of status or to claims, must be refused. Applicants must be advised that all deadlines are firm. All scope for late actions beyond limited grace periods should be removed from the act.

Another major source of uncertainty is the courts. There are two aspects to this. The first is that it is the courts which have developed an inventiveness standard far below the "significant advance" level. Changes to that aspect of the law should assist in rectifying this problem. So too would a proper objectives statement in the Act, reminding judges of the economic goals of

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33 As indeed is implied on IP Australia's website where it states "If you don't pay your fee by the end of this grace period [6 months] your patent will no longer be in force.” [http://www.ipaustralia.gov.au/get-the-right-ip/patents/manage-your-patent](http://www.ipaustralia.gov.au/get-the-right-ip/patents/manage-your-patent), as at 25 January 2013.
the patent system. The other issue is the readiness of courts to grant injunctions, even where this seems to be substantially against the public interest. The decision granting an injunction against Sigma (the venlafaxine case) is an astonishing read for an economist. After finding that the patent at issue was probably invalid – surely grounds for refusing an injunction – the judge went on to determine that payment of lost royalties would be difficult to estimate so might not adequately compensate Wyeth if the patent turned out to be valid. In considering the balance of convenience the judge made no mention of the costs to the PBS and the public of delaying generic entry but he did place considerable weight on evidence from a pharmacist that older people would be confused if the packaging changed and then changed again. Tyacke has presented summary data on relevant injunctions issued in Australia suggesting that Australia's courts are too willing to grant such injunctions. The problem with injunctions could be short-circuited if a fast-track process were introduced for resolving the validity issue where a prima facie case is found. There is a strong public interest in such cases being resolved within a few months (say three) rather than years.

Recommendation 7: Introduce a fast-track system to resolve disputed patents which have the potential to delay generic entry within 3 months

Information disclosure: Under the "free" trade umbrella US pharmaceutical companies sought and won the right to require generic companies to provide formal certification that no patent would be contravened prior to market entry of a new generic product. There are severe penalties for failing to meet this new regulatory requirement. This is unsymmetrical and so unfair. If generic companies are required to advise of market entry, then companies owning patents should be required to advise of which patent monopolies relate to which registered pharmaceuticals. Sigma was criticised by Sundberg J for not finding the relevant evergreen patent when it searched for venlafaxine patents prior to its planned market entry. But the criticism should more appropriately be directed at the systems which fail to require clear and easily accessed information about which patents relate to which products. Such a requirement would also enhance the information disclosure role to the patent system.

Recommendation 8: Require companies listing products on the ARTG to identify all patents associated, relevant or concerning such ARTG-registered products on a Patents Register. If a patent is not listed on this Register it cannot be used to challenge market entry of a generic version of the registered product.

Incentive structures: There are considerable imbalances in incentive structures when it comes to the willingness of patent holders to game the system and of generic companies to challenge invalid patents. Given the vast sums to be made from NCEs, it is unsurprising that patent-holders attempt to extend the scope of the monopoly privilege they have been granted. What is concerning is that governments have been naïve about limiting and controlling this behaviour. Useful policy lessons can be imported from other systems where there are

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34 This is not the place to comment on the very self-serving objectives statement offered by ACIP in its report on patentable subject matter. In summary ACIP's suggested objective is "balance competing interests".
36 This raises the issue of allowing trade marks on patented goods. Machlup was of the view that this unfairly extended the market dominance period of a patented invention (Fritz Machlup, 1958, An Economic Review of the Patent System, Washington, D.C.: US Government Printing Office at p.11 citing a Supreme Court case). Certainly allowing drugs to be marketed under trade marked names impedes the easy shift to generics once these are allowed. There is a strong public policy case for introducing plain packaging for all pharmaceuticals, requiring their name only under their proper name and with the company logo restarined to a small part of the package.
substantial incentives for gaming and for creating complexity to hide the games from public scrutiny. The TGA has moved quickly to change the relevant regulations once companies started removing products from ARTG listing so that they could not be used to prove bio-equivalence. Similar active oversight is needed in all other parts of the system. In particular there should be substantial penalties for undermining the overall goals of the system – fines of $20,000 or $50,000 are small change against the profits made from the PBS.

**Recommendation 9:** (1) introduce a mechanism for requiring reimbursement of all profits from patents subsequently found to be invalid; (2) introduce substantial fines (on both owners and patent attorneys) for attempts to game the patent system or the drug approval system; (3) introduce active oversight arrangements over all parts of the system affecting the delivery of safe and affordable drugs

While there are strong incentives for "big pharma" to game the system, the incentives for generic companies to challenge weak patents are very poor. As is well known this asymmetry in incentives is one reason why judicial review does not ensure high patent system standards. If a patent owner sues for infringement it takes all the risks and receives all the rewards. But if a would-be competitor sues for invalidity it bears all the risks but shares any rewards with other firms. This was recognised in the Hatch-Waxman Act. But the type of incentive provided there – 180 days of market exclusivity on first generic entry – would not work in the much smaller Australian market. Recognising the substantial savings to the PBS from early generic entry a system could be developed to share such savings with the company taking the risk and successfully challenging a blocking patent. The incentive needs to be strong enough to offset the substantial risks of such action.

**Recommendation 10:** Develop an incentive mechanism to encourage weak blocking patents to be challenged through sharing consequent PBS savings.

**Price signals:** Problems in the way in which drugs are grouped in the PBS were discussed above. A major issue in terms of cost-efficiency is the payment of different prices for drugs providing equivalent therapeutic outcomes. Such hidden subsidies to large and extremely profitable overseas companies are a poor use of taxpayer funds and the system should be re-designed to prevent such outcomes. In 2004 the Australian Government took the unprecedented step of signing a "free" trade agreement which allowed overseas entities a role in Australia's domestic health arrangements, particularly the Pharmaceutical Benefits Scheme. One aspect of this gives companies the right to ask for review of PBAC listing decisions. According to Lopert, two reviews had been requested by 2009. While the AUSFTA changes were hailed as increasing transparency, no information about any reviews undertaken is publicly available. This makes it impossible to comment on the impact of this change.

**Regulatory efficiency:** Australia and other countries have developed effective processes for ensuring that drug safety data can be used to demonstrate bio-equivalence and ensure the entry of generic products without the need for unnecessary further experimentation on human populations. Because of the incentives for gaming behaviour an active watch must be kept on such this system. Generic products are approved on the basis of equivalence to drugs registered on the ARTG. Some "big pharma" companies started removing products from the ARTG towards the end of their patent life so that they could not be used for

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40 At least not on the relevant website (http://www.independentreviewpbs.gov.au/).
regulatory approval of generics. The TGA acted quickly to obtain parliamentary approval of an amendment to the Therapeutic Goods Regulations to offset this behaviour and is to be commended for this. Continued active oversight is clearly needed.

**Other strategic games:** There are several other aspects of strategic games playing that have important public policy implications. Ranbaxy's behaviour in respect of generic entry to the atorvastatin market raises concerns about behaviour that goes far beyond normal competition, to the detriment of the market as a whole. Such actions need speedy responses by competition authorities. Another challenge is the shift whereby the original patent-holder now often enters the market with their own "generic brand". This complements the recent spate of purchases of generic companies by "big pharma". Both trends raise competition concerns.

The pharmaceutical market is a strange one involving as it does the government (as regulator of entry and price), medical practitioners (determining what treatments to recommend often without any consultation as to price), consumers (treated as patients and often neither fully informed not paying the cost of the goods they consume), and pharmacists (who can actively manage what products are supplied and who are regarded as a very politically powerful group). The net outcome is that market models are largely inappropriate. Ranbaxy's behaviour over atorvastatin has created massive profits for pharmacists, exposing real deficiencies in the price disclosure mechanism in the PBS. Officials need to actively monitor such behaviour and take swift action to stop such haemorrhaging of the Federal budget.

A further issue which impacts strongly on PBS costs and the affordability of pharmaceuticals is the extent of marketing both to pharmacists and doctors. Comparing the environment between the UK and Australia it seems there may well be a strong pro-proprietary medicines ethos among many of Australia's doctors. There are strong cultural pressures for GPs to meet with drug company representatives and the underlying prescribing databases are provided by "big pharma". As evidenced by the shift from venlafaxine to desvenlafaxine this marketing pays big dividends – dividends funded by the Australian taxpayer.

**An entry system for biologics**

In contrast to the relatively smooth process for approving generic versions of traditional pharmaceuticals for sale, no such processes are evident to the new and growing set of pharmaceuticals referred to as biologics. Here there appears to be insufficient information in patent specifications to allow the invention to be made and approved by the ARTG when the patent expires. There are some biologics whose patents have expired but where there is not yet any generic competition – for example patent 600650 expired in 2006 yet there is still no generic epoetin alfa on the ARTG. Yet there must currently be an effective system for ensuring quality production or the TGA would not have allowed registration of the originator products.

Originator companies have raised concerns about bio-equivalence, and researchers they fund regularly publish material suggesting serious quality concerns about generic biologics. Such quality concerns also, of course, plague the originator companies, as is clear from a careful reading of such papers. Indeed Roger and Mikhail, in raising such problems about generic products, provide only one example of such problems and this in relation to Johnson & Johnson's epoetin alfa, licensed from Amgen, the original patenters of erythropoietin.

So what is the problem? Why is generic entry not taking place? Are the procedures approved by authorities such as the TGA for originator products not transferable to generic products?

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41 Personal communication from a GP with major experience in both countries.
there insufficient disclosure in the patent specification for generics to undertake industrial scale production at end of patent period? If there is not is the patent bargain being met? Should the Patent Act be amended to lift disclosure requirements for biologics? Should this disclosure be continuous? Should there be any additional disclosure requirements at the end of patent life?

**Recommendation 11:** Amend the *Patents Act 1990* so a condition for grant of a biologic patent is that there is sufficient and continuous disclosure to enable industrial scale production of that substance at a bioequivalent standard to the patented product. Penalties for breaching this standard should be substantial (forfeiture of all profits from sales of the patented product plus a substantial fine).

In Australia there appears to be only one example where a biologic has gained TGA approval and therefore ARTG listing. But although the generic version of filgrastim has been deemed bioequivalent by the TGA, the PBS has not approved prescribing this as an equivalent generic to the branded product. This seems odd. If the TGA is satisfied that there is bioequivalence, why does the PBS not agree? After all it is the TGA who deals with safety issues while the PBS deals with price. This regulatory gap needs to be addressed.

**Recommendation 12:** If the TGA determines bioequivalence then the PBS must follow suit and treat such products as generic equivalents.

The overall lack of any effective system for the timely entry of generic competition on the expiry of biologic patents should be of concern to health, competition and industry policy officials. Given the cost of these products, and the general consensus that they will form an increasing part of health treatments, there is an urgent need for an effective system for generic approval and entry. Are the concerns raised by the originator companies real? If so, how have they met them themselves? If the process knowledge cannot be fully disclosed is a patent either necessary or desirable? The recent move in the USA to introduce further monopoly rights for biologics – 12 years of data exclusivity – seems dysfunctional. Governments need to actively address the problems and develop workable solutions. Until such an effective entry approach is developed, patent expiry is unlikely to be followed by generic competition, except in limited circumstances. This is a poor outcome for public policy and for Australians.

**Recommendation 13:** Establish a task force charged with developing system to ensure timely generic entry.

**Overall co-ordination**

It is clear that many parts of government are involved in the overall system affecting the development approval and pricing of pharmaceuticals. These systems intersect, with the low patent inventiveness standard placing pressure on the PBAC to approve equivalent drugs. But health system processes do not operate to offset the deficiencies of the patent system. And strategic anti-competitive behaviour by originator and generic companies alike impede achievement of the goal of rapid entry of generic competition at the end of the approved patent period. It would be useful for there to be an agency with overall responsibility for ensuring that competition succeeds patenting in the agreed manner. This agency should also be charged with ensuring that behaviour during the patent period is not undermining the overall objectives of the patent system. Finally the agency should review whether there are omissions, gaps or inefficiencies in the overall system.

**Recommendation 14:** Establish an agency to provide overall oversight of the system for delivering pharmaceuticals to the market. The principal focus of this agency should be on competition and regulatory efficiency.
One of the challenges of regulating markets is inadvertent outcomes. A well-known inefficiency in the current system is that generic companies are prevented from producing for export to markets where patents have expired if that patent is still in effect in Australia. This probably does not even benefit the patent owner as the overseas market will be supplied by companies which are not impeded in this way. It would be a simple matter to amend the legislation to exclude manufacturing for export to countries where a patent is not in force from the rights granted to a patent holder.

**Recommendation 15:** Amend the *Patent Act 1990* to exclude from the rights granted to patent-holders the right of manufacture for export to a country where the patent is not in force.