Alphapharm's Response to the Productivity Commission's Draft Report into Australia's Intellectual Property Arrangements

Executive Summary

Alphapharm welcomes the Commission's finding that

> Australia's patent system grants protection too easily, allowing a proliferation of low-quality patents, frustrating the efforts of follow-on innovators, stymieing competition and raising costs to the community.

That has certainly been our experience. We therefore welcome this opportunity to review the range of changes that have, over recent decades, tipped the playing field against the interests of generic companies and increased the cost to Australia. We present evidence about this in Section 2A of our submission.

In Section 2B we discuss a number of issues where reform is urgently needed. An issue that we consider has not yet been fully investigated by the Commission is the incentives and penalties that operate on the system as a whole. At present these are very one-sided and this is an important reason for the current imbalance between the rights of creators and users of new technology that Australia at present suffers from. We make recommendations for improving the incentives and penalties so as to encourage a more balanced system – one that will contribute to, rather than detract from, innovation in Australia (page 7).

Other important issues addressed in Section 2B are poor quality patents. The low height of the inventive step requirement and the extension of patentable subject matter in the form of method of medical treatment patents have both contributed to the failure of springboarding policies to offset the limitations on competition caused by overly generous patent term extensions. The consequent evergreening pharmaceutical patents come at a significant cost to Australian taxpayers and have a damaging effect on the health of the generics industry. In this regard, we welcome the Commission's draft recommendations on patent term extensions, the inventive step and patentable subject matter. But we think these recommendations do not go far enough. We need more than the modest proposals for change if we are to achieve a level playing field between brand-generating and generics companies.

We note that one part of the US Hatch-Waxman system was imported to Australia through the Australia United States Free Trade Agreement (AUSFTA). But the Hatch-Waxman system had three important elements. Australia urgently needs to develop policies for the missing two elements – a market-based incentive to encourage generic companies to challenge weak pharmaceutical patents and a transparency register to make brand-creating companies accountable for their multiple patents. We make recommendations to address these two elements on pages 11-12.

In Section 3 we make recommendations to improve the patent system so that it is better able to deliver quality, safe, efficacious and affordable medicines to the Australian population. These recommendations cover patentability standards and eligibility, data exclusivity, biologics, infringement and contributory infringement, injunctions, innovation patents, patent term extensions and 'ceased' patents.

We would welcome the opportunity to discuss these matters further with the Commission during the hearings scheduled for Sydney on Tuesday 21 June.

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1. Introduction

A. About Alphapharm

Alphapharm was established in **1982** and so has thirty-four years of direct experience, not only of Australia's patent system administered by IP Australia, but also of Australia's medicines-regulatory system administered by the Therapeutic Goods Administration (TGA). Today Alphapharm is a fully owned subsidiary of Mylan, a global pharmaceutical company.

Mylan is a global pharmaceutical company committed to setting new standards in health care. Working together around the world to provide 7 billion people access to high quality medicine, we innovate to satisfy unmet needs; make reliability and service a habit, do what's right, not what's easy and impact the future through passionate global leadership. We offer a growing portfolio of more than 1,400 generic pharmaceuticals and several brand medications. In addition, we offer a wide range of antiretroviral therapies, upon which approximately one-third of HIV/AIDS patients in developing countries depend. We also operate one of the largest active pharmaceutical ingredient manufacturers and currently market products in approximately 165 countries and territories. Our workforce of more than 35,000 people is dedicated to improving the customer experience and increasing pharmaceutical access to consumers around the world.

Alphapharm is Australia's leading supplier by volume of prescription medicines to the Pharmaceutical Benefits Scheme (PBS). It specialises in bringing patent-expired (generic) medicines to market, which contributes to the sustainability of the PBS by providing timely access to *quality, safe, efficacious and affordable medicines.* Its medicines are made to the highest global quality standards, including those of Australia's Therapeutic Goods Administration (TGA), the U.S. Food and Drug Administration, and the European Medicines Agency, and have the same effect on the body as initial brands.

B Summary position in regard to Draft PC Report

Alphapharm fully concurs with the Productivity Commission's overall finding concerning Australia's patent system, specifically, that it is:

> Failing to meet the principles of a well-functioning intellectual property system.

Alphapharm agrees with many of the proposed recommendations but argues that some do not go far enough. The real issue is the lack of balance. The system is too one-sided in favour of brand-creating pharmaceutical companies.

2. Submission regarding Draft PC Report

Section A puts the substantive section of its submission into perspective by explaining the significant changes to Australia's patent system between 1982, when Alphapharm was established as a local company, and 2016, now as a fully-owned subsidiary of Mylan. Section B addresses the wide range of factors that lead to an extremely unbalanced patent system. These substantially delay generic entry, with large negative welfare impacts for Australia. Section C provides a number of recommendations that are designed to rebalance the patent system and provide the generics sector with the ability to deliver *quality, safe, efficacious and affordable medicines* to Australians.

A. Significant changes to Australia's patent system between 1982 and 2016

(i) IPAC Report and the new Patents Act 1990

The first significant change came with the passage of the *Patents Act 1990*. This new legislation, a direct result of a five-year review of Australia's patent system under the *Patents Act 1952*, was conducted by the Industrial Property Advisory Committee (IPAC) between 1979 and 1984. The IPAC Report 1984 was extensive, however, it was not unanimous. The Committee's sole economist, Prof Don Lamberton, forcefully dissented. In his opinion:

> This Report does not live up to its claim to have adopted an economic perspective and to have applied economic criteria. It has not consistently applied economic criteria; it has not made full use of available empirical evidence; and the concept of social cost, so frequently mentioned, has never really been fully grasped. The underlying idea of the process of innovation is little more than faith that more patent protection will ensure more innovation. The sensible objective is rightly declared to be "to modify the Australian patent laws, adjusting the length, strength and breadth of patent rights" to maximize the net benefit. It is unfortunate that the Report soon strays from this path.

Even so, the IPAC Report recommended against extending the patent term beyond 16 years. It also recommended for the complete abolition of patent-term extensions. The IPAC Report stated:

> In the view of the majority, in the absence of contrary empirical evidence, it strains credulity to contemplate that research or innovation investment decisions, made early in the life of the invention, could ever be materially influenced by the prospective availability of an extension after expiration of the initial 16-year term to compensate for inadequate remuneration, particularly when allowance is made for discounting. On the other hand, such extensions would increase social costs.[1]

While the first recommendation was accepted, the second was only partially accepted. Under the 1990 legislation patents for "pharmaceuticals for human use" were eligible for a patent term extension of a period not exceeding four years, to a maximum of 20 years.

Alphapharm agrees with Prof Lamberton. Indeed, the available empirical evidence confirms that: "The underlying idea of the process of innovation is little more than faith that *more patent protection will ensure more innovation*." Alphapharm maintains that there is no empirical evidence available to demonstrate that *more patent protection will ensure more innovation* in Australia.

[1] *Patents, Innovation and Competition*, IPAC, 1984, 39.

(ii) Standard patent term increase from 16 to 20 years

The second significant change came when Australia joined the World Trade Organisation. As a result, within five years of the 1990 legislation and contrary to the IPAC Report, the standard patent term for *any* Australian patent, not just for patents for "pharmaceuticals for human use", was extended by a period of four years to 20 years. The patent term extension for "pharmaceuticals for human use" was repealed by the *Patents (World Trade Organization Amendments) Act 1994*. There was no empirical data to support this change in the standard patent term, which was made only because it became a condition of Australia's continued membership of the General Agreement on Tariffs and Trade (GATT).[2]

(iii) Five-year patent term extension for pharmaceuticals

The third significant change came with the passage of the *Intellectual Property Laws Amendment Act 1998*.[3] As a result, "pharmaceutical patents" became eligible for a <u>further</u> period of up to five years to a maximum of 25 years. Once again, there was no empirical data to support this change to Australia's patent system, which was made only "in recognition of the exceptionally long development time and regulatory requirements involved in developing and commercialising a new drug."[4]

(iv) Data exclusivity (pharmaceuticals)

The fourth significant change also came with the passage of the *Therapeutic Goods Legislation Amendment Act 1998*.[5] The amendment provided for a data exclusivity period of five years over "protected information". Under s25(2) *Therapeutic Goods Act 1989 any* 'protected information' provided to the TGA as part of an application for marketing approval of a pharmaceutical cannot be disclosed to unauthorised third parties. It applies regardless of whether the 'protected information' relates to a patented pharmaceutical invention.

In 2004, by effect of the Australia-United States of America Free Trade Agreement (AUSFTA) data exclusivity became an entrenched part of Australia's IP system.[6]

(v) Innovation patents

The fifth significant change came with the passage of the *Patent Amendments (Innovation Patents) Act 2000*. The primary rationale for the reformulation of the petty patent system into the innovation patent system was to assist small business enterprises obtain protection for lower order innovations that would not qualify for a standard patent. The innovation patent term is limited to eight years. The principle difference between an innovation and standard patents is that the 'invention' involves an "innovative step" as distinct from an "inventive step".

(vi) Patent certificates (TGA)

The sixth significant change came with the passage of the *US Free Trade Agreement Implementation Act 2004*. The *US Free Trade Agreement Implementation Act 2004*, consisting of 175 pages, transposed Australian law in accordance with the terms of AUSFTA. This legislation amended the *Therapeutic Goods Act 1989* by inserting s26B, thereby mandating any application lodged with the TGA for marketing approval of "therapeutic goods" to be accompanied by a patent certificate. The patent certificate "must be signed by, or on behalf of, the applicant", usually a generic company.

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[2] Agreement on Related Aspects of Intellectual Property Rights (TRIPS) Art 33.
[3] *Patents Act 1990* (Chapter 6, Part 3, ss.70-79A).
[4] Intellectual Property Laws Amendment Bill, 1997 Explanatory memorandum.
[5] *Inserted s25A into the Therapeutic Goods Act 1989.*
[6] AUSFTA Art 17.10.01

Moreover, it is a *criminal offence* for a person, usually the managing director, to "give a certificate" that "is false or misleading in a material particular."

The provision contemplates two types of patent certificate. The first type (under s26B(1)(a)) certifies that the applicant "believes on reasonable grounds that it is not marketing, and does not propose to market, the therapeutic goods in a manner, or in circumstances, that would infringe a *valid claim of a patent* that has been granted in relation to the therapeutic goods."

The second type of certificate (under s26B(1)(b)) certifies that the applicant, being aware that a "*patent has been granted* in relation to the therapeutic goods", intends to "market the therapeutic goods before the end of the term of the patent" and "has given the patentee notice of the application".

The second kind of patent certificate usually triggers patent infringement litigation. This normally commences with the grant of an interim injunction enjoining the applicant (usually a generic company) from marketing the generic pharmaceutical until the patent litigation is finalised.

(vii) Patentability standards

The seventh significant change came in 2013 with the *Intellectual Property Laws Amendment (Raising the Bar) Act 2012*. The trigger for the 'Raising the Bar' amendments was the 2008 *Venturous Australia* Report. The National Innovation System Review Panel, chaired by economist Dr Terry Cutler recommended that "patent law … be reviewed to ensure that the inventive steps to qualify for patents are considerable …".[7] The Panel noted that "current thresholds of inventiveness are too low."[8] The Rudd-Gillard governments accepted this recommendation and the 'Raising the Bar' explanatory memorandum specifically addressed the Panel's concern. The amendments widened the range of existing knowledge that would be used to assess the patentability threshold of 'inventive step'. First, the geographical boundary was increased from "Australia" to "anywhere in the world". Second, the nature of the information was expanded from that which would be "ascertained, understood and regarded as relevant" to include "all information" publicly available.

Accordingly, the existing knowledge used to assess the inventive step is now consistent with Australia's major trading partners. A further amendment unrelated to inventive step, was also made. This amendment dealt with the utility threshold. It is now a requirement that a patent specification must disclose a "specific, substantial and credible use" of the patented invention. Another important reform was to the disclosure requirements. This reform principally addressed disclosure across the full scope of the claims.[9]

(viii) Range of issues included in the TPPA and foreshadowed in the AUSFTA

Finally, are changes in the Trans-Pacific Partnership Agreement (TPPA), and foreshadowed in the AUSFTA. The TPPA was signed by Australia in December 2015 but has yet to be ratified by the Australian government. While there is no guarantee that the TPPA will be ratified, it is – nevertheless - relevant to take the TPPA into account given that it has the potential to impose further changes to Australia's patent system. If and when the TPPA is ratified, it is likely that the amending legislation will be passed into law shortly thereafter.

First is the mandating of the current approach to assessing the inventive step (TPPA Art 18.37.1, footnote 30). It is this approach that has created a very low inventiveness threshold for patent grant.

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[7] venturousaustralia - *building strength in innovation: Report on the Review of the National Innovation System*, Recommendation 7.2, 86.

[8] Ibid, xii.

[9] Explanatory Memorandum, 9.

This change will ensure large volumes of evergreening patents unless other elements of the test are made far more stringent.

Second, is the increase in scope of patent-eligible subject matter observed by comparing the corresponding clauses in AUSFTA (2004) and the TPPA (2015). Accordingly, "new processes of using a known product"[10] will be prescribed as patent-eligible subject matter once the TPPA is ratified.

Third is a presumption of patent validity. Presently, the *Patents Act 1990* contains an express disclaimer of patent validity: ["Nothing done under this Act or the PCT guarantees the granting of a patent, or that a patent is valid, in Australia or anywhere else"].[11] And while a certificate of validity may be issued by a court, such a certificate is available only in respect of a patent that has had its validity challenged in court proceedings. Even then, a certificate of validity does not rise to the level of a presumption of validity. Any patent, even when a certificate of validity has been issued, can be challenged without a presumption of validity.[12] However, the TPPA mandates that a granted patent must be considered in any "civil or administrative enforcement involving a patent" to "prima facie … satisfy the applicable criteria of patentability …".[13]

Fourth is the provision of two types of patent term extension, both introduced in the AUSFTA and repeated in the TPPA. Term extensions for patent office delays are in AUSFTA Art. 17.9.8(a) and TPPA Art 18.46. Term extensions for delays in marketing approval are mandated in AUSFTA Art. 17.9.8(b) and TPPA Art. 18.48.

Finally, is the revisiting of data exclusivity in 10 years. While the present Australian government, and previous Australian governments since AUSFTA, have steadfastly refused to agree to any changes to the present data exclusivity regime, there is real potential for change in the future. Brand-creating pharmaceutical companies have lobbied hard for extensions to the scope of patents that can be the subject of data exclusivity as well as the duration of data exclusivity. Data exclusivity arrangements vary from country to country and this variation has created a narrative aimed at harmonisation. Despite current government commitments, the pressure for longer and wider data exclusivity will continue, and it cannot be assumed that the present regime in Australia will remain as it is. And it is fair to assume that it will not. The brief history of patent-related law reform since 1982 does not augur well for a balanced approach.

B. The absence of balance – disequilibrium in the pharmaceutical market

It is fair to conclude that these seven significant changes to Australia's patent system, together with the further potential changes in the TPPA, have led to a sizable imbalance in Australia's patent system in favour of patent right-holders. None of these changes has been based on any economic evidence.

With one exception – the 'Raising the Bar' amendments to the *Patents Act* 1990[14] – these changes favour the brand-creating pharmaceutical industry and delay generic entry to the market. The issues discussed here are: the lack of clear objectives that prevent the patent and pharmaceutical systems working effectively, combined with an absence of effective oversight of the patent system; patent term extensions and the failure of springboarding to offset this imbalance; issues of poor patent

[10] TPPA, Art 18.37(2). This is a small additional change compared to the addition of "any new uses or methods of using a known product" in AUSFTA Art. 17.9.1.

[11] s20(1) Patents Act 1990. Cf: *Apple v Samsung* [2011] FCA 1164; *Novartis v Hospira* [2012] FCA 1055.

[12] s19 Patents Act 1990.

[13] Art 18.72(3) TPPA. This approach while consistent with the single Federal Court judge decisions in *Apple v Samsung* [2011] FCA 1164 and *Novartis v Hospira* [2012] FCA 1055 has not been the subject of any appeal decision and is, nevertheless, patently inconsistent with s.20(1) *Patents Act 1990*.

[14] Which can best be described as neutral since the changes purportedly brought Australia into line with major trading partners.

quality, including method of use patents, which allow for evergreening thus delaying generic entry; patent certificates and the lack of incentives to challenge weak patents; data exclusivity; and issues around the new biologic medicines.

The trend in patent and patent-related law reform since 1982 has benefited patent rights-holders (mostly in the pharmaceutical sector). The imbalance that this has generated has not, however, benefited the Australian economy overall. There has been no empirical analysis regarding the impact of any of these changes for Australian taxpayers and the economy. Put bluntly, the policy development behind *all patent and patent-related law* reform has been achieved on nothing more than 'faith' – as Prof Lamberton said in 1984 "that more patent protection will ensure more innovation." If the TPPA is ratified, the imbalance will worsen.

Overall system objectives and accountability

A key omission from the Draft Report is any assessment of the structures and incentives that affect the degree of balance between the interests of creators and users of new technology. Myriad detailed rules favour grant of a patent, regardless of whether the 'invention' is induced or whether there are any net spillover benefits. As a result the entry of competitors to the market is substantially delayed, particularly the entry of generic pharmaceuticals. These dysfunctional rules range from the presumption that an application is inventive unless an examiner can demonstrate that it is not, to IP Australia's willingness to grant extremely retrospective applications.[15] One reason that the inventive step has fallen to such a low level is the lack of proper incentives to challenge invalid patents combined with the lack of any penalties for seeking and holding low-quality patents.

There is an absolute need to protect medical and pharmaceutical expenditure as much as there is to protect taxation revenue. The *Income Tax Assessment Act 1997* and other tax-related legislation provide penalties, both criminal and civil, to ensure taxpayer compliance. The ATO, an independent government-funded, statutory authority, is expressly empowered to administer, protect and enforce tax legislation. However, when it comes to pharmaceutical patents there is no corresponding policy despite the fact that patent pharmaceuticals directly impact upon government expenditure through the PBS. In this respect a granted patent, which is expressly not guaranteed to be valid,[16] gives to the patent owner very powerful economic and legal rights, the misuse of which not only burdens the Australian economy with deadweight costs but directly and unnecessarily increases government expenditure. The point being that while the ATO has the responsibility and obligation to recoup from taxpayers tax revenue that has not been paid (with penalties applying in appropriate cases), there is no corresponding statutory authority that has the responsibility and obligation to recoup from pharmaceutical patent owners the revenue they have earned through the grant of an invalid patent.

The Commission correctly identifies that the goal is to grant patents only for induced inventions which have positive spillover benefits for society. These spillovers offset the losses incurred during the period of patent protection. The Commission has noted the excessively long duration of standard patents. An implicit secondary goal is that competition should commence as soon as possible after the patent ends.

Current rules operate to extend the market exclusivity of medicines well beyond the agreed term of the underlying API patent. The privileges granted by TRIPS (Article 28) are far too extensive and must be a priority for re-negotiation in any leadership Australia takes in respect of international IP policy. In the meantime Alphapharm strongly supports draft recommendations 9.1 and 9.2.

[15] For example IP Australia's grant of an extension of time for an application for a patent term extension to Lundbeck *more than ten years after the deadline for such applications*. Such actions mean that no innovating firm can ever presume that a ceased patent has genuinely ceased.

[16] *Patents Act 1990*, s. 20.

However the tailored patent term extension in recommendation 9.2 should address stockpiling for entry on day one after patent expiry as well as manufacturing for export. Effectively the only privilege granted under a tailored term extension system should be the right to prevent sale in the domestic market.[17]

There are a number of specific aspects of patent policy reforms that have been identified in the draft report and in submissions to the Commission. These are addressed below. But no amount of excellent reform will hold traction unless the limited perspectives and biases of those managing both patent administration and patent policy advice are effectively addressed. One cannot overemphasise the importance of all patent policy decisions being taken in an environment which recognises the centrality of competition for innovation to thrive. Unless patent administration and policy culture changes to one where the focus is on maximising competition and minimising monopoly – unless this is warranted and provides net spillover benefits – the many good reforms proposed by the Commission and those making submissions to it will be of no use.

Alphapharm strongly recommends that the following additional reforms be considered for inclusion in the final report:

Pharmaceutical patent system oversight

1. Establish the Office of the Intellectual Property Regulator being independent and given the responsibility to oversee the overall operation of the system and empower it to intervene and, when necessary, provide appropriate relief through mediation or due process of law.

Integrated policies

2. Develop integrated policies that work to promote a strong and viable generic pharmaceuticals industry, while leaving intact a financial incentive for research and development of new medicines that provide significantly improved health outcomes.

Disincentives to abuse the system

3. Amend the *Patents Act 1990*, the *Therapeutic Goods Act 1989*, the *National Health Act 1953* and the *Competition and Consumer Act 2010* so that each contains an objects clause that brings together a co-ordinated policy framework to create disincentives to behaviour that would unfairly and inappropriately exploit the system.

4. Amend each of these Acts so that, at a minimum, the Commonwealth is able to recoup the cost incurred by the PBS through the grant of a patent that is subsequently revoked.

5. Amend each of these Acts so that unfair and inappropriate exploitation of the system has legal consequences.

[17] And this right should not over-ride the right of parallel import.

Patent term extensions and the failure of 'springboarding' as a calibrating policy

Although term extensions were removed when the standard patent term was extended from 16 to 20 years in 1994, they were re-introduced in 1998. It might have been thought that substantial evidence would be required to provide a further term extension for pharmaceutical patents after the standard patent term had been so generously increased just a few years earlier. There was none.

'Springboarding' was introduced at the same time as the re-instituted term extensions. This was in recognition of the negative impact of term extensions on the local generic pharmaceuticals industry. The government pointed to the existence of such provisions in the USA (where they are known as Bolar provisions), and expressed concern about the risk that an absence of such provisions would pose for Australian-based development work by the $600 million per annum generics industry. Term extensions and springboarding are discussed in more detail in Appendix A.

Unfortunately, springboarding has proven to be completely ineffective as a calibrating instrument. A principal cause is evergreening, a major example of patent system failure. Weak or very low patentability standards, broadening patentability to include methods of medical treatment without evidence of potential health outcome benefits, poor patent quality, lack of financial incentives to challenge dubious pharma patents, the readiness of courts to enjoin pharma patent challengers through preliminary injunctions, poorly drafted contributory infringement provisions, too much emphasis on the courts to vet the system and the complete absence of criminal and effective civil sanctions against the misuse of the system, all contribute to a lack of balance in the pharmaceutical patent system.

If the system was operating as intended, then generic pharmaceutical companies would be able to use springboarding, without excessive risk or cost, to help them enter the pharmaceutical market near the end of or after patent protection has ceased. However, the patent system has been gamed and is burdened by a plethora of evergreening patents. These surround the relevant ARTG-listed medicine and are used to delay generic entry. This negative effect neutralises any positive benefits that springboarding would have otherwise provided. The objective of evergreening as a lifecycle management strategy is to delay the move of medicines from the F1 formulary to the F2 formulary under the PBS, a move that generates an immediate price fall, and a loss of revenue to the brand-creating company.

Detailed information on the use of innovation patents for evergreening is provided in Appendix B. This information shows how innovation patents are used strategically to delay generic entry. Although designed to meet the needs of smaller Australian innovators, data presented in the Pharmaceutical Patents Report shows that the innovation patent system has been heavily used by overseas pharmaceutical companies. As the standard of examination is lower, innovation patents can be granted quickly and used to fend off generic entry. In the example of citalopram and escitalopram discussed in Appendix B (and shown in Figure 1), eight of the 39 evergreening patents are innovation patents. The primary function of these innovation patents is to fill a legal void while the longer examination process for standard patents is taking place.[18]

The data in Appendix B also show the extent to which standard and innovation patent specifications overlap. Examination standards and inventiveness standards differ between the two systems, reflecting their different objectives, yet divisionals from standard patent applications become innovation patent applications. This ability to use effectively the same application across the two quite different systems is problematic for potential competitors.

[18] A standard patent cannot be enforced until it is sealed.

Beyond innovation patents the evergreening data on es/citalopram also shows the range of types of patents which show evergreening features. Examples analysed in Appendix B include methods and processes for preparing citalopram, formulations and alternative structures in the basic compound.

The ambition of using springboarding to ensure early generic entry and a healthy generics industry is commendable. But, combined as it is with a system that strongly favours brand-creating companies, can it lead to a "strong local pharmaceutical industry" and the benefits this brings? Alphapharm submits it does not. Indeed, the local pharmaceutical industry is weaker in 2016 than it was in 1982, when Alphapharm was first established.[19]

The way in which the patent system operates – such that companies are not allowed to take most actions to prepare for market entry until after a patent has expired – operates to make an already long patent term even longer. The patent privileges granted by TRIPS, and extended in Australia to cover stockpiling, have been interpreted so that they operate to extend the standard patent term beyond 20 years. Further, the way in which data exclusivity operates is that the TGA is not allowed to ***commence*** evaluating a market approval application for a generic product until ***after*** the 5 years 'protection' has expired. While the former is beyond Australia's capacity to reform, due to TRIPS Article 28, the latter could and should be reformed.

Poor patent quality

Poor patent quality has serious negative ramifications for the Australian economy. Poor quality patents produce market distortions, driving up costs without providing any countervailing benefits to society. High patent quality is, therefore, not only desirable but essential if the Australian economy and Australians are to benefit from the patent system. It is particularly important for achieving balance between creators and users of new medicines.

Patents are legally enforceable monopolies which, while not monopolies in the context of competition law, do nonetheless, provide patentees with the ability to control the supply and price of a patented product. That kind of control may, depending on the elasticity of substitution of the relevant good and how control is exercised, have serious implications for the Australian economy. Low-quality pharmaceutical patents substantially increase the cost of Australia's healthcare system. Poor pharmaceutical patent quality means that the cost of the PBS is higher than it should be as it delays the transfer of medicines from the F1 to the F2 formulary.

The draft report recognises the "compelling evidence" that the inventive step is too low and recommends a small change to increase it. But the recommendation falls far short of what is needed to restore balance between the generic and brand-creating segments of the pharmaceutical industry. An example of evergreening is shown in Appendix B. For high-volume medicines, evergreening patents are the rule not the exception. Unless the inventive step is increased to the "significant advance in what is known" standard promised to the industry in 2011,[20] then Australia will continue to experience a significant net welfare loss through large payments for medicines which are shielded for far too long from generic competition.

Methods of medical treatment

Section 2A presented historical data on statutory and treaty-based changes making the patent system more unbalanced. But there were also a range of judicial decisions that had similar effects. In particular the 1994 Federal Court decision[21] to remove the traditional exclusion for patentability of methods of medical treatment has substantially enlarged the scope of evergreening patents and

[19] Heffernan, M. (2013) 'Drug companies target overseas growth', *Sydney Morning Herald* (4 January 2013).
[20] Explanatory Memorandum, Raising the Bar Bill, p.42.
[21] *Anaesthetic Supplies Pty Ltd v Rescare Ltd* (Rescare) [1994] 50 FCR 1.

given rise to problems on contributory infringement for the pharmaceutical industry. In 2013 the High Court confirmed that a method of medical treatment was patentable subject matter.[22]

But there has never been any evidence-based analysis of whether patents are needed to ensure that existing medicines are appropriately tested for new indications (uses). The Federal Court decision was based on the fact that, when the Harradine amendments were introduced in the *Patents Act 1990*, traditional exclusions were not also written into the Act. Clearly at the time of passage there was no parliamentary intent to remove the traditional exclusion of methods of medical treatment.

The new judicially-determined policy of providing patents for methods of medical treatment effectively means that second, third and fourth patents can be granted for the same compound – albeit narrowed in scope to the new use. But providing 20 years protection for a new use is an excessive reward. As data protection for new uses (indications) is provided in the major markets of the USA and the EU, relevant clinical trials will already have been completed. The TPPA proposes requiring three years of data protection for new indications (Article 18.50.2). This is more than adequate reward for re-submitting those clinical trial data to the TGA.

Methods of medical treatment patents are problematic for generic manufacturers and distributors because of contributory infringement. The High Court has recently held that a method of treatment patent is not infringed by the mere marketing of a generic medicine that contains the active ingredient of a medicine that could be, if so prescribed by a doctor to a patient, used as part of a medical treatment for a condition that is the subject of a valid method of treatment patent.[23] Even so, it may be possible to foresee a situation where an attempted carve-out of indirect patent infringement by excluding a specific indication from marketing-regulatory approval cannot be so easily and neatly made by a generic company.[24]

Patent Certificates; Lack of a Market-Based Incentive to challenge poor quality

The idea of a patent certificate, to be provided to a pharmaceutical patent owner at the time that a generic pharmaceutical producer seeks marketing-regulatory approval for a generic version of a patented pharmaceutical, comes from the United States.[25] A very important related aspect of the US 'patent linkage' system is patent transparency. This is achieved through a register of pharmaceutical patents identified by the patent owners as being relevant to the protection of each medicine approved for marketing.[26]

The purpose and objectives of the U.S. Hatch-Waxman Act was to provide a set of incentives and disincentives aimed, in the context of the U.S. legislative and regulatory framework, at promoting both the development of new medicines and the production and marketing of generic medicines at the same time.[27] There has been considerable debate in the United States over whether it has achieved its multiple objectives for health, innovation and competition systems.[28] Despite this, the law has stood the test of time.

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[22] *Apotex v Sanofi-Aventis* [2013] HC 50.
[23] Ibid.
[24] *Otsuka v Generic Health* [2015] FCA 634
[25] Specifically, it was the *Drug Price Competition and Patent Term Restoration Act 1984*, commonly referred to as the Hatch-Waxman Act, that created the need for such a document as *one part* of a legislative scheme that included a whole range of other important and relevant measures – the most important of which was an incentive to generic companies challenge pharmaceutical patents in the United States.
[26] Known as the 'Orange Book'; see Holovac, M.A., 2004, "A balancing act in the United States Drug Industry: pioneer and generic drugs, the Orange Book, marketing protection and the US consumer" *World Patent Information* 26(2):123–129.
[27] Filardi, E.V. (1999) 'Patent Issues That Both Regulatory Affairs Personnel and Patent Attorneys Should Understand', *Food and Drug Law Journal, 54*, 215-221; Holovac, M.A. (2004) 'A balancing act in the United States Drug Industry: pioneer and generic drugs, the Orange Book, marketing protection and the US consumer', *World Patent Information*, 26, 123-129.
[28] Grobowski, H.G., Kyle, M., Mortimer, R., Long, G. and Kiron, N.(2011) 'Evolving Brand-Name and Generic Drug

As is typical in patent changes mandated by trade treaties, only part of the US system was imported, with the balancing provisions required to meet user-needs ignored. So what is notably absent in the Australian context is a counterbalancing incentive encouraging generic companies to challenge weak pharmaceutical-related patents that extend market exclusivity for the first patented medicine. Accordingly, AUSFTA provided a distinctly sloping playing field in the pharmaceutical patent system in Australia. By cherry picking only one aspect of the Hatch-Waxman scheme it created a distortion that favoured one segment of the pharmaceutical industry and to the express disadvantage of the generics segment.

The imported patent certificate system,[29] imposes onerous obligations on generics companies (with criminal offences) and requires them to provide brand-creating pharmaceutical companies with an advance warning of the impending market launch of a new generic medicine. There is, however, no obligation on brand-creating companies to identify all patents relevant to the medicine.

Given the industry influences on US trade and IP policy, it is unsurprising that only one part of the US system was required from Australia. But there was nothing in AUSFTA – except inattention by the relevant parts of government – to prevent simultaneous importation of a transparent patent register and incentives to challenge weak patents. The recalibration of the patent-pharmaceutical regulatory systems must now be a priority for Australia, just as it was for the United States in 1984.

Given Australia's much smaller market, the incentive used in the USA – a 180-day, market-exclusivity period – would simply not work here. However an alternative system could easily be developed, based on sharing the PBS outlays saved through earlier generic entry. Alphapharm recommended such a system to the Pharmaceutical Patent Review.

Alphapharm recommends reforms to provide a market-based incentive for generic firms to challenge weak patents, thus achieving savings in the PBS and a more balanced patent system.

The reforms would contain the following elements:

1. Immediately amend the *Patents Act 1990* so that a remedy is available to any party that is the first to initiate revocation proceedings in the Federal Court, or another prescribed court, leading directly to the revocation of a patent or any claims, that would, but for that patent or its claims, prevent a therapeutic good being marketed in Australia (a pharmaceutical patent revocation award).

2. Immediately amend the *Patents Act 1990* so that a pharmaceutical patent revocation award, as damages, is an amount equal to the cost to the PBS attributable to that patent, compared with the cost to the PBS as if that patent had never been granted as determined by a legislated formula.

3. Immediately amend the *Patents Act 1990* so that on the payment of a pharmaceutical patent revocation award the recipient must pay one half of the amount so received to the Commonwealth within thirty days.

Further, to balance out the onerous certification obligations imposed on generic companies and to improve transparency in Australia's patent system, a register of relevant patents should be required.

Competition May Warrant a Revision of the Hatch-Waxman Act', *Health Affairs*, 30 (11), 2157-2166; Branstetter, L.G., C. Chatterjee, and M. Higgins, 2011, *Regulation and Welfare: Evidence from Paragraph IV Generic Entry in the Pharmaceutical Industry*, National Bureau of Economic Research Working Paper no. 17188.

[29] s26A(1)(b)(i) and s26B, *Therapeutic Goods Act 1989*.

Alphapharm recommends a transparency register of medicine-related patents, as follows:

1. Immediately require the entry onto the Register of Australian Patents (the Patents Register) the international non-proprietary name (INN), trade name and ARTG registration number, and if not available at the time then within seven days of ARTG registration, of any therapeutic good (as defined in s3 *Therapeutic Goods Act 1989*) in respect to which a patent or patent application pertains, relates or is relevant to.

2. Immediately amend the *Patents Act 1990* so as to enable an ordinary person to freely, instantly, easily, accurately and electronically obtain from the Patents Register at any time:
    a) An exhaustive list itemising each and every patent and patent application by reference to the international non-proprietary name (INN), the trade name or registration number of a therapeutic good (a pharmaceutical patent list);
    b) a pharmaceutical patent list printed with a certified date and time stamp;
    c) the identity and Australian address for service of the owner, including the beneficial owner, of a patent and patent application; and,
    d) the identity and Australian address for service of any party that has an interest in a patent or any part thereof and including the following information:
        i) the nature of such interest;
        ii) the date and description of the document, if any, creating such interest;
        iii) the commencing and ending dates of such interest;
        iv) the geographical area encompassed by such interest; and
        v) if the interest is a licence to exploit the patent, the international non-proprietary name (INN), the trade name and ARTG registration number of the licensee's therapeutic good, and if not available at the time then within seven days of ARTG registration.

3. Immediately amend the *Therapeutic Goods Act 1989* so that a person providing a certificate pursuant to s.26B(1) of the Act (a patent certificate) need not take into account any patent, or patent application, not included on a pharmaceutical patent list relating to a therapeutic good.

4. Immediately amend the *Therapeutic Goods Act 1989* so that a person providing a patent certificate and relying on a pharmaceutical patent list in relation to a specific therapeutic good is not guilty of an offence under s.26B(2) of the Act; and,

5. Immediately amend the *Patents Act 1990* so that it is not an infringement of a patent to market a therapeutic good if its international non-proprietary name (INN), trade or pharmaceutical name is not entered on the Patents Register.

Data Exclusivity

Phase III clinical trial data are produced to meet the needs of regulatory authorities, for example the TGA, charged with protecting the health of their citizens. Although these data are required for public good reasons, brand pharmaceutical companies have succeeded in persuading governments that they should have private property rights over these data.

In Australia data exclusivity is provided for five years for pharmaceutical products that contain a new active substance. Data exclusivity provisions are a condition of participating in the international free

trade community. The requirement is to "protect such data from unfair commercial use".[30] Much, of course, hangs on one's understanding of what commercial uses are fair and what are unfair.

We take the view that allowing for market entry by generic companies as soon as the agreed period of 20 years of patent protection is finished constitutes fair competition. After all, this is what the Australian Parliament has agreed. We also consider it would be unethical to repeat clinical trials where the outcome is already known, as would be the case for generics.

Quillen considers that:

> If data exclusivity provides all of the monopoly incentive needed to induce pharmaceutical innovation, then higher standards for patentability, which are decidedly in the interest of other innovators, will not diminish pharmaceutical innovation.[31]

This is an interesting suggestion – that data exclusivity provides such a strong barrier to competition that the patent system could effectively be re-designed with the needs of other industries in mind, thus substantially raising the height of the inventive step.

Certainly the Competition Directorate of the European Commission found that data exclusivity was part of the arsenal used by brand pharmaceutical companies to delay generic entry.[32]

Citing from the preliminary report Adamini found:[33]

> Data exclusivity appears to be one of several strategies by the research-based industry to delay generic price competition. A recent study by DG Competition of the European Commission has found that "in many instances originator companies use two or more instruments from the 'tool box' in parallel and/or successively in order to prolong the life cycle of their medicines".[34] These instruments notably include secondary patenting, patent-related contacts and disputes, litigation, settlements, and interventions. From 2000 to 2007, the research-based industry initiated nearly seven hundred lawsuits covering patents and data exclusivity, even though "the claims of the originator companies were upheld in only 2% of the cases".[35] DG Competition of the European Commission concluded that these tactics "significantly increase legal uncertainty to the detriment of generic entry and can cost public health budgets and ultimately consumers significant amounts of money".[36]

As with patent term extensions, objective data showing the costs and benefits of providing periods of exclusivity for these safety and efficacy data have never been published. Indeed it appears that brand pharmaceutical companies use the same argument – the cost of Phase III clinical trials – to argue for high prices during the patent period and extensions of patent term as well as for this new form of monopoly privilege (data exclusivity).

On the other side of the coin, it is generally accepted that people should not be subjected to repeated trials for the same drugs. When the US Congress considered the matter in 1984 – following the new CAFC court finding that preparations for generic entry infringed patent rights – a package

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[30] They are enshrined in TRIPS Article 39(3).
[31] Quillen C.D., (20080, 'Commentary on Bessen and Meurer's Patent Failure: an industry perspective', *Journal of Intellectual Property Law* 16, 57-81, 61.
[32] European Commission, 2009, Final Report Competition Inquiry into the Pharmaceutical Sector, Brussels: EC.
[33] S. Adamini et al, (2009) 'Policy making on data exclusivity in the European Union: from industrial interests to legal realities', *Journal of Health Politics, Policy and Law*, 34(6), 979-1010, 1003.
[34] European Commission, Pharmaceutical Sector Inquiry: Preliminary Report of DG Competition, Staff Working Paper, November 28. Brussels, 294.
[35] Ibid, 294.
[36] Ibid, 13.

of reforms was introduced. These were aimed at easing generic market entry (the Bolar exception to patent rights and procedures for abbreviated processes for gaining FDA approval for market entry). To counter-balance these improved processes for generic drug companies, Congress also provided for a period of data exclusivity for brand companies.

Australia's data exclusivity provisions were introduced as a result of TRIPS[37] and re-stated in AUSFTA[38] – though it is hard to understand how a new monopoly privilege properly fits within a free trade agreement. In respect of enantiomers, the Federal Court held that the first registration on the ARTG constitutes the start date for data exclusivity. That is, when a mirror image drug is registered it takes its start date from the earliest version.

The economic benefits of providing monopoly privileges for safety trial data are unclear. These data are important sources of information as to how to effectively prescribe and administer the medicine for health professionals and are required by regulatory authorities for public purposes. Companies providing these data are compensated for their cost in the higher prices they achieve during the patent period. When the AUSFTA or the TPPA (should it be ratified) is reviewed, the government should consider winding back these provisions.

Biologic medicines

Biologics provide a particular policy challenge in ensuring that competition occurs following patent expiry. There are issues both in relation to regulatory approval and to patent disclosure, and these are intertwined. In the context of the Commission's brief, the regulatory problems are outside the scope of the inquiry. Alphapharm simply notes that the costs are high, and provides some information on this in Appendix C. Alphapharm does, however, wish to draw to the Commission's attention the need to resolve these issues if the generics and biosimilars industry in Australia are to thrive and health expenditure be contained. One of the issues identified – the adequacy of disclosure for biologics - does, however, lie firmly within the scope of this inquiry.

Regulatory approval for most biologics is not a straightforward process, as it is for small molecule drugs. There appears to be substantial regulatory uncertainty in the face of a strong line being pushed by brand-creating pharmaceutical companies that it is challenging to demonstrate bioequivalence for biologics. Much of this research is written by experts who have close ties with brand-generating pharmaceutical companies, and there is an emphasis on the variability of production processes and the structural complexity of biological molecules, and hence problems in quality control and health outcomes.[39] Yet if variability in production is a problem, it is one the brand companies must have overcome to achieve regulatory approval.[40] Why then is it that when patents expire generics companies are unable to use the information in the patent to develop exactly equivalent processes and thus generic approval?

The lack of a clear and consistent pathway for regulatory approval prevents the development of a significant biosimilars industry in Australia. Given the widespread agreement that biologics will be a

[37] Though the provisions introduced in Australia went much beyond what was required by TRIPS.

[38] Art 17.10.1(a) – see Faunce et al., 'New forms of evergreening in Australia: misleading advertising, enantiomers and data exclusivity: Apotex v Servier and Alphapharm v Lundbeck', *Journal of Law and Medicine*, 16:2, 2008, pp 220-232 at 229.

[39] Papers arguing such a series of problems started to appear in the 2000s, after brand generics had been on the market for some years. Simon D. Roger, 2006, 'Biosimilars: how similar or dissimilar are they?' *Nephrology*, 11, pp. 341-346, discloses strong funding ties to Roche, Amgen and Janssen-Cilag (a Johnson &Johnson company) in this article. No such ties are disclosed in a subsequent article: Simon D. Roger and Ashraf Mikhail, 'Biosimilars: opportunity or cause for concern?' *Journal of Pharmacy and Pharmaceutical Science*, 10:3, pp. 406-410. Both articles raise a range of 'concerns' regarding generic products, including reliability and quality. However the only example provided of such problems is of a quality problem in a brand biologic – Johnson & Johnson's epoetin alfa, licensed from Amgen, the original patenters of erythropoietin.

[40] Amgen obtained TGA approval for erythropoietin within 8 years of the earliest priority date (within 7 years of the patent filing date in Australia).

growing share of the pharmaceutical market over the years to come, this apparent regulatory impasse is concerning. Both from a health expenditure and an industry development perspective, a well-functioning process is needed for generics companies to gain regulatory and PBS approval for biosimilars as they do for other generics.

The arguments that brand-generating pharmaceutical companies put forward against biosimilar marketing approval have implications for biologic patents and the patent disclosure requirement. If it is not possible to adequately define the process to ensure a consistent high-quality outcome, then how can the patented invention be clearly described so that a person skilled in the art (PSA) can re-produce it?

Appendix C provides more detailed data on biologic patents and biologic medicines. One example addressed in some detail is EPREX (epoetin alfa). If a condition for the grant of a patent is the disclosure to a person of ordinary skill (PSA) of how to make the invention without undue experimentation, how is it that IP Australia agreed to grant Amgen a patent which included claims such as claims 51[41], 52[42] or 53[43] some 10 months prior to EPREX being approved by the TGA and listed on the ARTG? How is it that the disclosure appears insufficient to permit the development and registration of a bioequivalent epoetin alfa immediately after patent expiry?[44]

The obvious answer is that the thresholds of patentability for a medicine and the marketing approval of that medicine are not the same. A patent is the product of a policy that has a different purpose and objective to that regulating the marketing of medicines. The social and economic consequences of the lack of disclosure in the patent, as this example shows, are serious. Moreover, the methodologies used to manufacture epoetin alfa to a consistent quality standard are not sufficiently detailed in the patent disclosure to allow others to reproduce the biological equivalent therapeutic outcomes.

If this is not a problem, and the invention can be disclosed to the standards required by the *Patents Act 1990*, why is approval of biosimilars a problem?

In fact there seems to be a process of continual development in biologic medicines, so that by the time a biologic patent expires, the medicine based on the expired patent is different from that produced earlier in the patent life. Disclosure can thus become outdated for biologic patents.

As disclosure is a requirement for the grant of the patent, is it reasonable then to allow the patent to be renewed? If the disclosure becomes so outdated that it cannot be used by the PSA when the patent expires, does this not then breach the patent contract?

[41] Claim 51. A pharmaceutical composition comprising an effective amount of a polypeptide according to any one of claims 1, 16, 38 or 39, and a pharmaceutically acceptable diluent, adjuvant or carrier.

[42] Claim 52. A method for providing erythropoietin therapy to a mammal comprising administering an effective amount of a polypeptide according to any one of claims 1, 16, 38 or 39.

[43] Claim 53. A method according to claim 52 wherein the therapy comprises enhancing hematocrit levels.

[44] It is particularly curious that Amgen would in 2016 suggest there is no bioequivalency given that in 1989 Amgen provided data in U.S. court proceedings to prove, so the court held by "overwhelming evidence", that natural erythropoietin and Amgen's recombinant erythropoietin were "the same product". The same court concluded on the basis of "Amgen's own admissions" that natural erythropoietin "preparation had an equivalent biological activity" to Amgen's recombinant erythropoietin. *Amgen, Inc v Chugai Pharmaceutical Co and Genetics Institute, Inc* (1989) 13 U.S.P.Q.2D 1737.

3. Rebalancing the system to deliver quality affordable medicines

Patentability: standards and eligibility

1. Immediately amend, with retrospective effect, the *Patents Act 1990* so that a standard patent cannot be granted unless the specification discloses an invention that constitutes a significant advance over what was known and what was available to the public at the priority date of the patent.
2. Introduce into the *Patents Act 1990* an objects clause that the objective of granting patents is to enhance the wellbeing of Australians by providing patent protection to socially valuable innovations that would not have otherwise occurred.
3. In addition to excluding business methods and software from patentability, amend the *Patents Act 1990* such that diagnostic, therapeutic and surgical methods for the treatment of humans or animals are excluded from patentability and clarify that this includes specific uses of pharmaceuticals.
4. Amend the Patents Act 1990 to exclude from patentability any substance, whether isolated or purified in whole or in part and howsoever made, that is not markedly different to anything found in nature.

Data exclusivity

5. Amend data exclusivity regulations such that TGA approval processes can proceed during the period of data exclusivity, but that a draft regulatory approval will not take effect until after the data exclusivity period ceases.

Biologics

6. Immediately amend the *Patents Act 1990* so that any patent concerning or relating, including but not limited to uses, methods or process, to any substance derived from nature, whether in whole or in part and howsoever made, must not be renewed without the full and complete public disclosure, including the making available to the public of any biological materials relating to that disclosure, sufficient to enable the substance to be made in Australia and be therapeutically substitutable with any therapeutic good registered on the Australian Register of Therapeutic Goods.

Limiting infringement of patents relating to therapeutic goods

7. Immediately amend the *Patents Act 1990* so that a patent cannot be used to interfere, hinder or prevent the marketing of a therapeutic good if:
   a) the authorised therapeutic good is not shown to provide a health outcome that is significantly better than that provided by another therapeutic good within the same therapeutic group; or
   b) but for a use or methods of treatment claim in a patent the marketing of that good would not infringe that patent, unless the invention to which the claim relates is a significant advance over what was known and what was available to the public at the priority date of the patent.
8. Immediately amend the *Patents Act 1990* so that proceedings claiming infringement of a pharmaceutical patent must commence one year from the date on which the first infringing act occurred.

Interim injunctions

9. Immediately amended the *Patents Act 1990*, so as to reinforce s.20(1) that no patent should ever be presumed valid even if it has survived an infringement challenge and expressly

overrule recent single-judge decisions[45] to the contrary.

10. Immediately amend the *Patents Act 1990* so that an interim injunction is unavailable as a remedy for patent infringement of a patent unless and until the patentee or, if applicable, the exclusive licensee, has posted a cash bond with the Federal Court, or other prescribed courts, of an amount equal to the value of the price reductions that would otherwise be applicable pursuant to Division 3A, National Health Act 1953 during the period of time that the interim injunction would apply (the bond).
11. Immediately amend the *Patents Act 1990* so that if the bond has been posted and an interim injunction granted and the patent is ordered to be revoked, the bond becomes immediately payable to the Commonwealth on the entry of the revocation of the patent on the Patents Register.

Contributory infringement

12. Immediately amend the *Patents Act 1990* so that the supply or marketing of a therapeutic good or a component thereof cannot constitute an act of contributory infringement.

Innovation patents

13. In preference, abolish the innovation patent system. If it is retained, immediately amend the *Patents Act 1990*, with retrospective effect, so that an innovation patent cannot contain a claim relating, concerning or associated with a therapeutic good.

Patent term extensions

14. Implement recommendation 9.1 to reform patent term extensions.
15. Implement recommendation 9.2, but limit the special privileges to prevention of domestic sale (not including preventing parallel importation).
16. Immediately amend the *Patents Act 1990* to clarify the meaning of 'pharmaceutical substance' so as to limit eligibility of patent term extension to the earliest patent to claim that substance in a pharmaceutical composition contained in a therapeutic good (the first pharmaceutical patent).

Ceased patents - clearing the patents register of superfluous patents

17. Immediately amend the Patents Act 1990 to ensure that a patent that has ceased for a period of six months cannot ever be revived.

As well as the reforms listed here, Alphapharm has also made recommendations for reforms to address overall system focus and accountability (page 7), introduction of incentives for challenging weak pharmaceutical patents (page 13) and introduction of a transparency register to hold brand-creating companies accountable for their patents and ensure no capacity to ambush generic entrants (pages 11-12).

With the potential advent of even more unbalanced policy through the TPPA, the time has come for Australia to introduce a more effective and efficient patent system. And it must do this if there is to be a viable and local generic pharmaceutical industry in Australia. Without such an industry, not only will Australia lose its capability in the manufacture of locally-made Australian medicines, it will seriously impede its ability to regulate the prices of medicines on the PBS. This loss will produce very poor economic and social outcomes for Australia and Australians and make it difficult, if not impossible, for any Australian government to provide timely access for Australians to quality, safe, efficacious and affordable medicines at a cost the PBS and taxpayers can afford.

[45] *Apple v Samsung* [2011] FCA 1164 and *Novartis v Hospira* [2012] FCA 1055

Appendix A: Patent term extensions and the failure of springboarding

What then Minister John Moore overlooked in 1998 when he re-introduced term extensions for pharmaceuticals is that when a limited four-year patent term extension was provided in 1990, the standard patent term was only 16 years. This meant that the maximum extended term for pharmaceutical patents could not exceed 20 years. But by 1998 the standard patent term had been extended to 20 years because of TRIPS. While the idea of a 20-year term was not new, as the IPAC Report shows, IPAC had already considered and rejected any standard patent term beyond 16 years.[46]

Referring to the Industry Commission's *Pharmaceutical Industry Report*[47] Minister Moore glossed over the significant changes to patent law ushered in by Australia's membership to the WTO. The increase from 16 years to 20 years in the standard patent term already achieved the government's objective of providing "15 year effective patent life for pharmaceuticals". The re-introduction of a patent term extension, increasing from four years for "pharmaceuticals for human use" to five years for "pharmaceutical patents", provided no net social gain for Australia.

There was no empirical evidence to support this extension. Just as it "strained credulity" in 1984 to expect, "without contrary empirical evidence", that "research or innovation investment decisions, made early in the life of the invention, could ever be materially influenced by the prospective availability of an extension after expiration", so it does today, 32 years later.

The decision to provide 'springboarding'[48] at the same time as patent term extensions for pharmaceuticals, continued the recognition of the inherent threat that its absence posed to the local generic pharmaceuticals industry. Minister Moore acknowledged the risk of losing a viable, local generic pharmaceuticals industry:

> A patents regime which lacks the flexibility to allow springboarding would also put at risk generic development and manufacturing in Australia. This is because of the significant advantage which derives from being first in the market with a generic product. A lack of springboarding provisions in Australia will encourage generic drug importers to undertake development work offshore, in countries like the United States, which allows springboarding throughout the patent term, or in countries with weak patent protection and access the Australian market immediately the patent expires.[49]

Springboarding was supposed to provide a check against the potential imbalance created within the pharmaceutical industry in Australia by patent term extensions. The Minister explained its supposed benefits:

> Allowing springboarding … would place Australian companies on a more equal footing with their international competitors. It would do so without reducing the period during which the originator company retains an exclusive right to sell its product on the Australian market. [It] also reduces the risk of pushing development work on generic drugs offshore, either to the United States where springboarding is allowed, or to countries providing weak patent protection. It also gives the industry more flexibility in preparing to access the Australian market. As such, [it] would be of particular benefit to

[46] *Patents, Innovation and Competition*, IPAC, 1984, 39.
[47] The Pharmaceutical Industry (Volume 1), Industry Commission, Report No 51 (3 May 1996)
[48] Springboarding provisions are also known as Bolar provisions and are understood to be allowed by TRIPS Article 30.
[49] *Intellectual Property Laws Amendment Bill, 1997* Explanatory memorandum, 7 (emphasis added).

> Australia's fledgling pharmaceutical active ingredient manufacturers as well as to Australian producers of 'innovative' generic drugs.[50]

The Minister also acknowledged the potential downside:

> At risk is a generic drug sector currently worth approximately $600 million per annum to Australia, plus spillovers into employment and collaborative development work.[51]

His colleague, the Minister for Health and Family Services, Michael Wooldridge said:

> A strong local pharmaceutical industry is important to ensure access to high quality drugs for all Australians.[52]

This may have been a worthy ambition but, nearly two decades later, does Australia have a "strong local pharmaceutical industry"?

Springboarding alone is not effective as an instrument to balance patent policy. The principle causes are (a) the evergreening of pharma patents, (b) data exclusivity and (c) a lack of transparency leading to the inadequate disclosure of relevant clinical or production data near or at the end of patent protection. Factors (b) and (c) are particularly relevant to biologic drugs and are discussed on p 14. Here we present detailed evidence on evergreening.

The phenomenon called evergreening is a major example of a system failure. Weak or very low patentability standards, broadening patentability to include methods of medical treatment without evidence of potential health outcome benefits, poor patent quality, lack of financial incentives to challenge dubious pharma patents, the readiness of courts to enjoin pharma patent challengers through preliminary injunctions, poorly drafted contributory infringement provisions, too much emphasis on the courts to vet the system and the complete absence of criminal and effective civil sanctions against the misuse of the system, have all contributed to an apparent absence of balance in the pharmaceutical patent system.

If springboarding worked effectively, it would be relatively straightforward and inexpensive for generic pharmaceutical companies to use it to enter the market as soon as possible after patent protection has ceased. However, the 'system' is burdened by a plethora of evergreening patents surrounding the ARTG-listed medicine, neutralising the benefits that springboarding should have provided.

[50] Ibid (emphasis added).
[51] Ibid.
[52] Press release issued by Mr John Moore, Minister for Industry, Science and Tourism, Dr Michael Wooldridge, Minister for Health and Family Services, and Mr Peter Costello, Treasurer (10 September 1996).

Appendix B: Innovation patents: their strategic use to evergreen medicines

According to IP Australia, the primary function of an innovation patent is to provide patent protection for "functional or incremental innovations [that] were not sufficiently inventive to be granted a standard or petty patent, yet they could not be protected under the designs system… ."[53]

Unfortunately, Figure 1 shows this is not their only function. Innovation patents are also used to evergreen patent monopoly protection around existing medicines. For the medicine es/citalopram, there are 39 evergreening patents, of which 8 are innovation patents. The innovation patents are indicated by shorter bars. This is because their period of operation is only eight years. The standard patent term is 20 years.

Escitalopram (LEXAPRO) is an isomer of citalopram (CIPRAMIL) – that is they are very closely related compounds. Citalopram, the racemic mix of its two isomers, was patented first (patent granted in 1980). Although the presence of escitalopram was disclosed by citalopram, nonetheless a second patent was granted in 1992. Following two Full Federal Court isomer-related decisions,[54] IP Australia introduced changes to its Patent Manual of Practice & Procedure to state that if an "isomer is prepared by routine separation techniques, the single isomer will be an obvious solution. This is true even if it was not obvious beforehand which of the isomers would be more active."[55] This confirms that isomer patents have very little new knowledge (social spillovers) and simply form a particular type of evergreening patent.

That innovation patents are problematic has been acknowledged. In 2012 the Australian Government undertook a review of innovation patents.[56] The Issues Paper to that Review noted that innovation patents are being misused in two principle ways. First, they are being granted "for enhancements which are obvious".[57] Although operating for only eight years, an innovation patent is stronger than a standard patent because one of the key patentability thresholds, namely, an 'innovative' step is virtually meaningless. This means that, in the absence of an objectively measurable 'innovation' test, an innovation patent becomes almost unchallengeable. So one of the strengths of an innovation patent is its ability to withstand a challenge to its validity.[58] Second, they are being used to "inappropriately extend the life of pharmaceutical patents and delay the introduction of less expensive generic medicines, leading to increased costs to consumers and an increase in government expenditure through the Pharmaceutical Benefits Scheme."[59] The process of examination and certification used for to an innovation patent is less rigorous than the examination of a standard patent. It is therefore much easier, simpler, quicker and cheaper to obtain an innovation patent. And while this is precisely what was intended, an unintended consequence is their use in evergreening.

Referring to Figure 1 it is apparent that the primary function of these eight innovation patents is to contribute to a patent thicket. The thicket then fills a legal void around a series of related standard patent applications that are, at the time, being examined but which are not yet granted and, therefore, unenforceable.

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[53] Innovation Patents - Raising The Step, IP Australia Consultation Paper (July 2012) (emphasis added).

[54] *Alphapharm v Lundbeck* [2009] FCAFC 70 (11 June 2009); and *Apotex v Sanofi-Aventis* [2009] FCAFC 134 (29 September 2009).

[55] http://www.ipaustralia.gov.au/pdfs/patentsmanual/WebHelp/Patent_Examiners_Manual.htm (Section 2.5.4.1.3 on optical isomers) (7 October 2013).

[56] Ibid.

[57] "The Delnorth decision showed that the 'innovative step' test permits the grant of an Innovation Patent for enhancements which are obvious, giving the owner of the Innovation Patent exclusive rights to exploit an obvious innovation for up to 8 years. In the Government's view, this is uncompetitive and unacceptable."

[58] *Delnorth v Dura-Post* [2008] FCA 1225.

[59] Innovation Patents - Raising The Step, IP Australia Consultation Paper (July 2012).

A standard patent cannot be enforced until it is sealed. This often takes up to 7 years. However, the certification of an innovation patent, subject to a simpler abbreviated examination, occurs more quickly, allowing the patentee to commence patent infringement proceedings immediately. The owner can proceed with an infringement action regardless of the merits of an equivalent standard patent application, which may or may not be granted. This is very useful to rights-holders because the available remedies for their infringement are identical to those for infringement of a standard patent. As the key objective is to prevent the transitioning of a pharmaceutical compound and related medicines from the F1 formulary to the F2 formulary under the PBS, an interlocutory injunction granted on the basis of an allegation of patent infringement is extremely valuable to a patent evergreener.

In Figure 1, the innovation patents are designated by a specific number sequence made up of the year of application, followed by the number '100' and then a three digit number. An example is AU 2001100440. They are clustered between two standard patents, AU 574819 and AU 738526. A third standard evergreening patent, AU 623144, lies in the middle of the patent thicket, but only because its expiry date is 13 June 2009. The two key standard patents in this gaming of the pharmaceutical patent system are AU 574819 and AU 623144. The first is critically important because it provides marketing exclusivity to CIPRAMIL (between 1997 and 2004) and LEXAPRO (from 2003). The second is just as important because it provides marketing exclusivity to LEXAPRO (from 2003 to 2009, and until December 2012).

All three standard evergreening patents were granted before any of the evergreening innovation patents. This indicates that the innovation patents were not directed to provide cover for these early standard evergreening patents, both of which were granted before any of the innovation patents. Rather, they provided cover to a number of subsequently granted standard patent applications.

The first of these is AU 746664. Indeed, innovation patent AU 2001100197 is a divisional child of standard patent AU 746664, both entitled 'Crystalline case of citalopram'. While AU 746664 was sealed 26 June 2005, AU 2001100197 was certified on 12 June 2001, nearly four years earlier. Having the innovation patent in force earlier provides the patentee with the ability to seek an injunction during the period between the filing of the standard patent application and its grant and sealing.

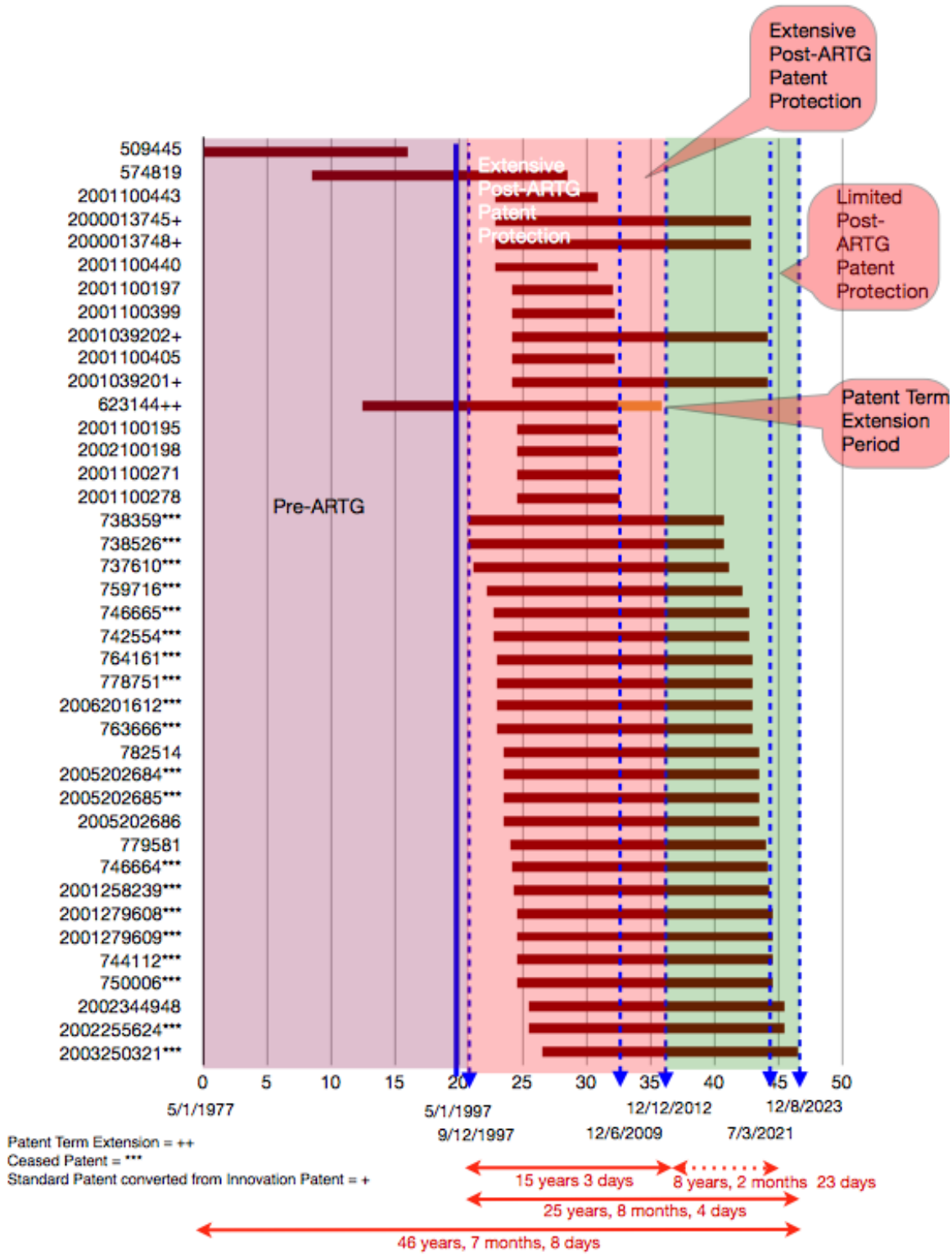
As well as sharing identical titles, these two patents have closely similar specifications. In fact the only difference between them, apart from their respective start and end dates, is the number of patent claims. This is only because an innovation patent is limited to five claims.[60] Claims one to five are also identical.

The high degree of similarity between these documents exposes a serious flaw in the Australian patent system particularly when the objective and purpose of innovation patents is very different to that of standard patents. The different kinds of patents are supposed to be directed to different kinds of inventions, yet the invention defined in claim one[61] is identical; one, apparently, the result of an 'innovative step', while the other, an 'inventive step'. That IP Australia granted two separate and different kinds of patents over the very same 'invention' also undermines the justification for the innovation patent system. It also exposes another flaw.

[60] s.40(2)(c) *Patents Act 1990*.

[61] Claim 1: "A process for the manufacture of a salt of citalopram characterised in that the base of citalopram is set free and precipitated in crystalline form, optionally recrystallised one or more times, and then converted into a salt thereof."

Figure 1. Citalopram/Escitalopram: an example of evergreening



- Divisional patents -

Divisional patent applications are described as 'parent' and 'child' and must be closely associated; the child being derived from the parent. This is also understandable within the context of the 'standard' patent system. It is not, however, acceptable when the parent and child patent applications belong in 'different' systems and serve 'different' purposes for different 'inventions'. Indeed, it is inappropriate for an innovation patent to be a divisional of a standard patent because an innovation patent is about a different kind of invention, examined under a different process, and the product of a policy designed to achieve a different outcome. The intermingling of these different kinds of patents, as the above chart shows, serves to assist in the evergreening of pharma patent protections around existing medicines.

- The other innovation patents-

The data in Figure 1 show a number of features of evergreening. The following discussion focuses on the content of a number of these evergreening patents.

(a) Method for the preparation of citalopram

The title 'Method for the preparation of citalopram' covers a series of standard and innovation patents. The standard patents are: AU 737610, AU 738526, AU 742554, AU 746665, AU 759716, AU 778751 and AU 2001258239. The innovation patents are: AU 2001100195, AU 2001100271, AU 2001100278, AU 2001100433 and AU 2001100440. In total there are 12 patents, seven standard patents and five innovation patents. This is an example of a classic patent thicket. At the centre of this thicket is citalopram-related medicines.

The earliest of the standard patents to have been filed is AU 738526 (10/11/97). The earliest of the innovation patents is AU 2001100433 (19/11/99).

Pages 1, 2 (lines 1 to 14) of both patents are completely identical. Differences begin to emerge after page 2 line 15, but not entirely. There continue to be entire sections that correspond word-for-word. For example page 5 line 20 to page 6 line 13 in AU 2001100433 is identical to page 6 line 21 to page 7 line 24 in AU 738526. Aspects of the claims are also identical. For example, in regard to claim one, both inventions are about 'citalopram' and "a compound of Formula IV". The principle difference between these two, otherwise identical claims, is that in AU 2001100433 the method comprises "reacting a compound of Formula IV", whereas in AU 738526 it comprises "the steps (a) reduction of a compound of Formula IV and (b) effecting ring closure of the resulting compound of Formula V". To be sure, the two claims do define different inventions but this is because the true essence of the 'invention', as described in the respective patent specifications, is buried underneath a linguistic distinction of the patentees choosing.

There are other patents with very close similarities. For example AU 759716 and AU 2001100278. Page 1 of these two patents is identical, word-for-word, with one exception; the words "methods for the preparation of intermediates used in the preparation of citalopram, and methods for conversion of said intermediates into citalopram" are missing from AU 759716. Page 2 to page 3 line 9 are similarly identical. Thereafter, the pagination and content varies, except that the text at page 9 line 27 to page 10 line 27 in AU 2001100278 is identical to page 7 line 9 to page 8 line 2 in AU 759716. And while the claims are different, both claims relate to citalopram.

AU 2001100440 is even more closely identical to AU 759716. The wording from page 1 to page 3 line 3 is identical. The formula, being Formula IV, on page 3 is also identical. Thereafter, the pagination and content varies, except that the text at page 5 line 20 to page 6 line 20 in AU 2001100440 is identical to page 7 line 8 to page 8 line 2 in AU 759716. And again, while the claims are different, both claims relate to citalopram.

Importantly, AU 759716, AU 2001100278 and AU 2001100440 are each, as are all of the other nine evergreening patents using the same title, about citalopram.

AU 2001100195 is a typical example of evergreening – it is simply another form of citalopram – the use of a capsule containing citalopram in a specified "unit dosage". This begs the question: how is this an 'innovation' of sufficient merit to warrant the certification of an innovation patent?

This case study demonstrates that the most incremental of 'innovations' can currently be used to justify a new patent under the Australian Patent System. In the context of the innovation patent system virtually anything qualifies. The question is: is this optimal in encouraging high quality patents?

(b) Process for the preparation of pure citalopram

Using the title 'Process for the preparation of pure citalopram' is a series of four standard and innovation patents. The standard patents are AU 744112 and AU 750006. The innovation patents are AU 2001100399 and AU 2001100405. At the centre of this set are four patents for citalopram-related medicines.

AU 2001100399 and AU 744112 are linked. So are AU 2001100405 and AU 750006. However, all four patents are obviously related to the same substance, 'pure citalopram'. The variations are in the process used to remove chemical impurities.

(c) Crystalline base of citalopram

Using the title 'Crystalline base of citalopram' are two patents, standard patent AU 746664 and innovation patent AU 2001100197. Both patents concern a process for the production of a hydrobromide salt of citalopram. In the "Summary of the Invention" the respective opening paragraphs are as follows:

> AU 2001100405 (Innovation patent)
> The present invention provides a process for the manufacture of the hydrobromide salt of citalopram, in which the free base of citalopram is precipitated in crystalline form, optionally re-crystallised one or more times and then transferred to a hydrobromide salt of citalopram.
>
> AU 746664 (Standard patent)
> The invention provides a process for the manufacture of a salt of citalopram, preferably the hydrobromide or hydrochloride, in which the free base of citalopram is precipitated in crystalline form, optionally re-crystallised one or more times, and then converted into a pharmaceutically acceptable salt of citalopram.

The different coloured text demonstrates how the use of language is employed to obscure an invention's true form. By observing the duplication of key elements in both paragraphs it is clear, that the substance of these so-called separate 'inventions' is, in fact the same.

The more relevant question is: what is the true invention?

- Distinguishing between an innovative and inventive step -

The Australian Government has recognised the problem of the misuse of innovation patents and is proposing to amend the *Patents Act 1990* so that the inventive step threshold will also apply to innovation patents.[62] While this proposal may eliminate the meaningless distinction, it does nothing

[62] The Australian Government argues that "[t]his would align the Innovation Patent requirements with the well-known and legally-settled test for inventiveness that applies to Standard Patents. Raising the inventiveness requirement for

to address the underlying problem: how is the inventive step threshold to be assessed by IP Australia for the purpose of innovation patent's certification?

Adding some difficulty are two recent decisions of the Federal Court[63] that have qualified an express provision in the *Patents Act 1990* to the effect that no granted patent is guaranteed validity.[64] The qualification being that "[r]egistration of the patent is, of itself, prima facie evidence of validity."[65]

This obiter directly contradicts an express provision of the statute. It suggests that an innovation patent, once certified, even if granted under the proposed inventive step threshold, will be presumed to be valid unless revoked. Revocation is not possible at the time a court entertains an application for an interim injunction. This means that a certified innovation patent can be used, just as a standard patent can be used once it is granted, to seek an interim injunction.

The problem is that certification does not involve a review of the innovation patent application to the same standard as occurs with a standard patent application. And there is reason to doubt that the examination of a standard patent application is sufficiently rigorous to give credibility to the position the Federal Court has adopted. This has had serious consequences. For example, interim injunctions were used to delay generic market entry in the cases of clopidogrel and venlafaxine, and while the respective evergreening patents were ultimately invalidated after years of litigation and the expenditure of approximately $10 million in legal fees, this occurrence improperly undermined the operation of the PBS and created a deficit in the Commonwealth's consolidated revenue. The Commonwealth has had to go to court to seek recovery of this loss. The amount does not take into account the cost of the generic industry sector, nor the legal and business costs absorbed by the generic companies directly involved in the relevant litigation.

With no disincentive for them not to, regardless of the proposed 'higher' inventive step threshold, it is reasonably foreseeable that patentees will continue to use innovation patents in evergreening strategies.

Innovation Patents will address community concerns that the Innovation Patent system is being abused, particularly in the information technology industry."

[63] *Apple v Samsung* [2011] FCA 1164; *Novartis v Hospira* [2012] FCA 1055.

[64] s.20(1) *Patents Act 1990*: "Nothing done under this Act or the PCT guarantees the granting of a patent, or that a patent is valid, in Australia or anywhere else."

[65] *Novartis v Hospira* [2012] FCA 1055 per Yates J, paras 51, 91-94.

Appendix C: Biologic medicines: costs and regulatory challenges

Biologics provide a particular policy challenge in ensuring that competition occurs following patent expiry. There are issues both in relation to regulatory approval and to patent disclosure, and these are intertwined. This appendix presents information on a number of biologic medicines to demonstrate the lack of consistent successful competition following patent expiry. Data on the consequent cost in health expenditure are also provided.

Traditional small molecule medicines are chemically derived and copying is relatively easy. In contrast the biologic new medicines are composed of biologically derived molecules such as amino acid chains, large proteins and carbohydrate based compounds which have a biological activity in humans, are far more difficult to manufacture. They are manufactured by biological, not synthetic chemical, processes. They are also extremely expensive (per prescription) in comparison to traditional chemical medicines. The cost to prepare a biosimilar is "is approximately 15 – 200 times the cost of development of small molecule generic medicines".[66]

Some of the world's first approved biologics were human insulin, approved by the FDA in 1982, human interferon alpha-2a and human growth hormone, approved by the FDA in 1986, and human tissue-plasminogen activator, approved by the FDA in 1987, all human proteins and all patented by Genentech.[67] Another early biologic, human erythropoietin, approved by the FDA in 1989, turned Amgen into the world's largest biotechnology company.[68]

Biologics, therefore, are not new. They have been commercially available since the early 1920s, with the introduction of the original porcine insulins used to treat type I diabetes, but their significance is growing. Among the biologics currently on the PBS is LUCENTIS (ranibizumab).[69] In 2011 it cost the PBS $249m for 117,000 prescriptions. Each prescription cost $2,125, it was ranked 3, behind LIPITOR and CRESTOR respectively, in terms of total cost. Another biologic, HUMIRA (adalimumab)[70], cost the PBS $168m for 94,000 prescriptions. Each prescription cost $1,798 it was ranked 5. Yet another biologic, ENBREL (etanercept)[71], cost $118m for 66,000 prescriptions. Each prescription cost $1,780, it was ranked 10. At $4,087 per prescription, GLIVEC (imatinib)[72], ranked 15, was the most expensive per prescription medicine on the PBS. Its total cost was $90m.

One of the earliest biologic medicines was erythropoietin, marketed as EPREX by Janssen-Cilag, under license from Amgen. Amgen's patent expired in 2006. But, ten years later, there has been no generic entry. As a consequence an erythropoiesis stimulating protein,[73] currently marketed as EPREX (epoetin alpha), remains in the F1 formulary

EPREX was first listed on the ARTG on 24 April 1991, just four years after patent examination was requested. Within 18 months of that first action the patent application was formally accepted. While the patent application was opposed, the opposition was eventually dismissed by IP Australia.[74] After

[66] Generic Medicines Industry Association, *Guide to Biosimilars*, 2015: 6.

[67] Palombi, L (2009), Gene Cartels Biotech Patents in the Age of Free Trade (Edward Elgar: Cheltenham, UK and Northampton, MA, USA) at 250-274.

[68] Ibid. Since first approved by the FDA for the treatment of anaemia patients undergoing kidney dialysis in 1989, U.S. sales alone have earned Amgen USD 37 billion. It is used to treat anaemia associated with kidney disease and in the treatment of cancer.

[69] Used in the treatment of wet age related macular degeneration.

[70] Used in the treatment of rheumatoid arthritis.

[71] Used in the treatment of rheumatoid arthritis.

[72] Used in the treatment of leukaemias.

[73] Erythropoietin is erythropoiesis stimulating protein which naturally occurs in the human body. Epoetin alfa is human erythropoietin made using a biological process. It is therefore a synthetic form of human erythropoietin.

[74] Kiren-Amgen, Inc v Board of Regents of University of Washington and Genetics Institute, Inc (1995) 33 IPR 557. The title contains a typographical error. 'Kiren' should have been spelt 'Kirin'. Kirin-Amgen, Inc was formed as a consequence of an international patent rights-sharing agreement between Kirin and Amgen.

an appeal from that decision to the Federal Court[75] and a subsequent appeal to the Full Federal Court[76], the patent[77] as amended by court order was granted in its final form on 24 June 1999.

The scope of the claims was very broad. Claim 1 defined the invention as "purified and isolated" human erythropoietin. Claim 17 defined the invention as the "purified and isolated" DNA sequence that coded for "human erythropoietin". And claim 51 defined the invention as a "pharmaceutical composition comprising an effective amount" of human erythropoietin. Effectively Kirin-Amgen controlled, through this patent, the production of human erythropoietin and any pharmaceutical use of human erythropoietin. The patent term was extended from 11 December 2004 to 24 April 2006.

EPREX (epoetin alpha) was and remains today the only epoetin alpha medicine listed on the ARTG and available under the PBS. The other four erythropoietin medicines listed on the ARTG have different Greek suffix in the medicine name (see Table 1). This often signifies a different manufacturer or small change in process, rather than a clinically significant difference in performance. The consequence is that all four erythropoietin medicines remain in the F1 formulary. As a result, none of these are subject to competition and price disclosure. And this remains so more than six years after Kirin-Amgen's patent expired.

Table 1 The PBS cost per prescription: erythropoietin medicines

Erythropoietin Medicine Trade Name (INN)	Code & Prescriber Number	Dispensed Price for Maximum Quantity	Maximum Price for Consumer
EPREX (epoetin alpha) 20,000 international units	5713Q	$3,876	$35.40
NEORECORMON (epoetin beta) 20,000 international units	5370N	$3,876	$35.40
NOVICRIT (epoetin lambda) 10,000 international units	9596C	$1,866.60	$35.40
ARANESP (darbepoetin) 150 micrograms/0.3 mL	6493R	$3,951	$35.40

Source: PBS 2012 Pricing Schedule (as at 11 December 2012).

The longevity of patent protection over biologics is not, however, solely dependent on difficulties in gaining regulatory approval for biosimilars. It is interesting to compare EXPREX (epoetin alfa) and ARANESP (darbepoetin). What are the main differences between these two medicines?

Darbepoetin is simply a modified form of human erythropoietin.[78] This is clear from the patents for the two substances.

The first regulatory approval of ARANESP (darbepoetin) in 2001 towards the end of the patent life of EPREX (epoetin alpha) originally in 2004 is not coincidental. Rather, it is an example of a well applied strategy employed to extend patent protection over medicines, and thereby 'evergreen' the

[75] Genetics Institute v Kirin-Amgen (No 3) [1998] FCA 740.
[76] *Genetics Institute v Kirin-Amgen* [1999] FCA 742.
[77] AU 600650.
[78] Egrie, J.C. and Browne, J. K., (2001), 'Development and characterization of novel erythropoiesis stimulating protein (NESP)', *British Journal of Cancer*, 84 (supp 1), 3-10; Powell, J. and Gurk-Turner, C., (2002), 'Darbepoetin alfa (Aranesp)', *BUMC Proceedings*, 15, 332-335;

monopoly market for erythropoiesis stimulating proteins. The scope of the patent protection is broad enough to provide Amgen with a complete monopoly over darbepoetin alfa in Australia.

In the original patent over epoetin alpha[79] claimed the main invention to be:

> A purified and isolated polypeptide having the primary structural confirmation and possessing a biological property as herein defined of naturally-occurring erythropoietin, and characterised by being the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.

In other words, the invention is defined as an "isolated and purified" substance, defined by the properties of the naturally-occurring substance on which it is based. Any substance that satisfies these two criteria come within the scope of the patent claim. The only qualification in the manner of its production. It must be the product of a specific biological process, "the product of procaryotic or eucaryotic expression of an exogenous DNA sequence."

Does darbepoetin come within the scope of that claim? Yes. While there are a number of patents over darbepoetin, it is clear from the claims that it is an "isolated and purified" substance with the "primary structural confirmation … of naturally occurring erythropoietin". It is also the "product of procaryotic or eucaryotic expression of an exogenous DNA sequence." Without doubt the darbepoetin patents gives Amgen a second patent monopoly over something that comes within the first patent monopoly.

The main claim of the earliest evergreening patent defines darbepoetin as an "analog of human erythropoietin". The analogue has a modified amino acid structure in that there is a defined variation to that structure. Originally expiring on 16 August 2014, the patent term has been extended and will now expire on 13 July 2016.

The process of evergreening is coordinated so that the medical profession also plays a supporting role in the process. In a typical case, there is a noticeable change in prescribing behaviour coinciding with the expiry of the original patent and overlapping with the promotion of the medicine based on the evergreening patent (see Figure 2). This coincides with a period of re-education of medical practitioners in which they are provided with information that is designed to induce this shift, which plays an important role in maximising sales revenue across the two products.

In the period immediately preceding the prescribing shift the total PBS expenditure on erythropoiesis stimulating protein medicines was $42.5m. In the period immediately subsequent to that shift, the total PBS expenditure on erythropoiesis stimulating protein medicines was $75.7m, an increase of 56%. In subsequent periods, the revenue from epoetin alfa sales fell to around $26.5m and revenue from darbepoetin sales rose to around $64m, before sales for each levelled off. The total cost to the PBS, however, rose further to peak at $95m in 2006. This process seems to have doubled the total cost to the PBS of erythropoiesis stimulating protein medicines.

The cost increase coincided with the expiry of original erythropoietin patent.[80] The expiry of this patent should have marked the beginning of generic competition, putting downward pressure on the price of epoetin alfa. That did not happen. Even today there is no generic epoetin alfa approved by the TGA and listed on the ARTG. As a result, as already mentioned, epoetin alfa remains in the F1 formulary and is not subject to either the 16% price reduction that would apply if a generic version

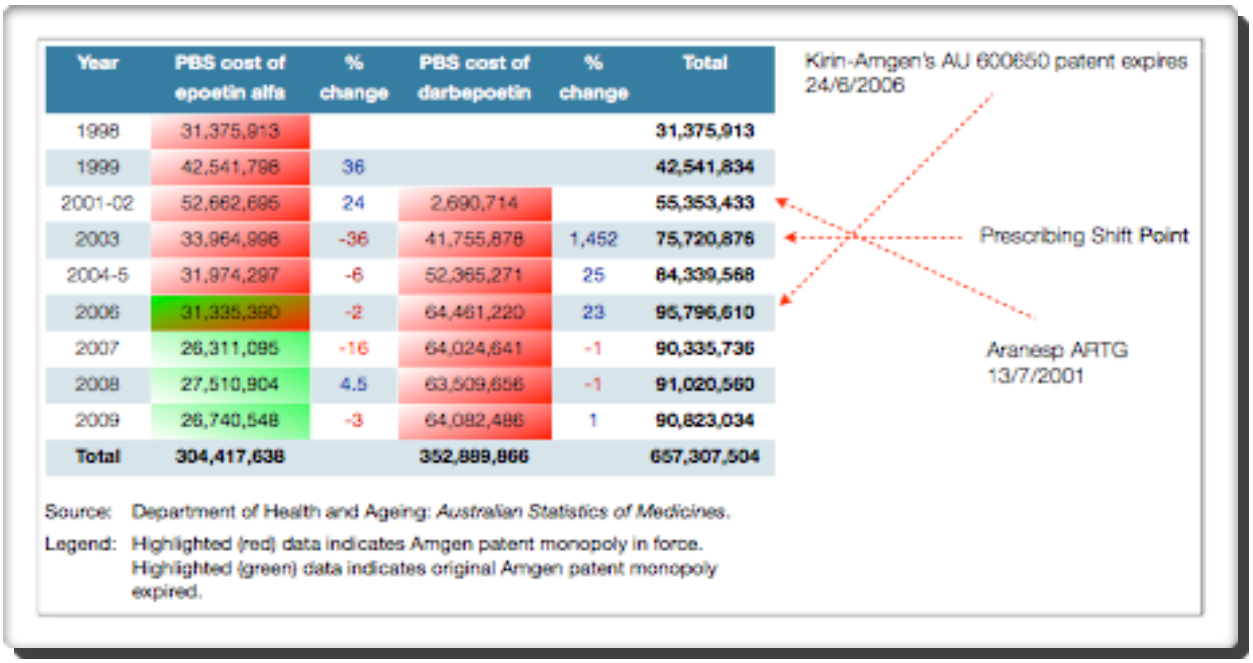
[79] AU 600650 was originally due to expire on 11 December 2004 but was extended to 24 April 2006. There was also an evergreening patent, AU 646822, that expired on 9 October 2010.

[80] In the lead up to the expiry of Amgen's original erythropoietin patent in 2006, some Australian doctors became alarmed at the possibility that generic versions of EPREX (epoetin alfa) would not be substitutable. One doctor expressed the view that the "imminent expiry" of this patent would have "significant implications for nephrology in Australia". Roger, S. D., (2006), 'Biosimilars: How similar or dissimilar are they?', *Nephrology*, 11, 341-346; 341.

was to be listed on the ARTG and made available through the PBS. Nor are sales of EPREX (epoetin alfa) the subject of annual review through the price disclosure process.

There is a pressing need to revisit the F1/F2 PBS formulary to deal with situations such as this. Not only biologics are affected. Another well-known case is venlafaxine and desvenlafaxine.

Figure 2: Epoetin alfa and darbepoetin: prescribing switches



Year	PBS cost of epoetin alfa	% change	PBS cost of darbepoetin	% change	Total
1998	31,375,913				31,375,913
1999	42,541,798	36			42,541,834
2001-02	52,662,695	24	2,690,714		55,353,433
2003	33,964,998	-36	41,755,878	1,452	75,720,876
2004-5	31,974,297	-6	52,365,271	25	84,339,568
2006	31,335,380	-2	64,461,220	23	95,796,610
2007	26,311,095	-16	64,024,641	-1	90,335,736
2008	27,510,904	4.5	63,509,656	-1	91,020,560
2009	26,740,548	-3	64,082,486	1	90,823,034
Total	**304,417,638**		**352,889,866**		**657,307,504**

Source: Department of Health and Ageing: *Australian Statistics of Medicines.*

Legend: Highlighted (red) data indicates Amgen patent monopoly in force. Highlighted (green) data indicates original Amgen patent monopoly expired.

One example of a biologic that has been approved for generic use in Australia illustrates some of the regulatory difficulties. The biosimilar version of filgrastim has been approved as bioequivalent by the TGA. This causes a move of the original brand of filgrastim into the F2 formulary, with a consequent saving to the taxpayer. But the PBS has not approved biosimilar substitution at the pharmacy level as occurs for generic versions of small molecule medicines. Substantial further savings are thus lost. This seems a half-hearted regulatory response. If the TGA is satisfied that there is bioequivalence, why does the PBS not agree? Unless this regulatory gap is addressed, Australian will continue to pay more than necessary for PBS medicines. In New Zealand a biosimilar filgrastim has recently won the national tender from PHARMAC for the sole supply to its health system.

These regulatory problems are, of course, outside the scope of the inquiry. Alphapharm simply notes that the costs are high, and provides some information on this. Alphapharm does, however, wish to draw to the Commission's attention the need to resolve these issues if the generics and biosimilars industry in Australia is to thrive and health expenditure be contained. The issue of adequacy of disclosure for biologics is, of, course, one for this inquiry.