Submission on
the impact of patent and data protection policy on access to affordable medicines

to the

United Nations Secretary-General's High-Level Panel on Access to Medicines

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The views presented in this submission are my own and should not be taken to represent the views of any institution with which I am affiliated.

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Author information

I have an honours degree in economics from Cambridge University (1969) and a PhD from Brown University (USA) where I specialised in demography and development economics (1975). My early working experience included market research, private health insurance and development assistance (working for The Population Council). During my 19 years' service in the Australian Public Service, I spent over 5 years in the Bureau of Industry Economics, where I undertook a major study of the pharmaceutical industry. In 2004 I embarked on a second PhD, in public policy at the ANU. The subject of my dissertation was an economic assessment of the patent system, using data on granted patents to assess the height of the inventive step and identify the principal rules which caused such a very low standard for the inventiveness test. Since then I have explored a number of aspects of patent policy, including secondary pharmaceutical patents, patent policy in trade agreements and the norms that would be required to implement Article 7 of TRIPS – the Article which calls for balance in patent policy. In addition to academic papers I have made submissions to a number of government and parliamentary enquiries. I hold the position of Adjunct Associate Professor at the Centre for European Studies, College of the Arts & Social Sciences, Australian National University, where I do research on patents, data protection, geographical indications and trade agreements.

The impact of patent and data protection policy on access to affordable medicines

1. Introduction

This submission focuses on two issues:

- the aspects of current patent policy which delay the entry of generic medicines; and
- the role of data protection policies in delayed access to affordable medicines.

In the time available – I only heard about this panel on 22 February – my comments are necessarily brief. I refer to a range of empirical studies.

Before starting, a few comments on data availability are necessary. The global pharmaceutical industry – particularly large originator companies – has systematically refused to share data on costs and profits. They do however fund some research centres, particularly in the USA, and researchers at these institutes have produced various estimates showing very high costs for clinical trials. These estimates have major methodological flaws and are highly disputed (Light and Warburton, 2011b, 2011a). The panel will need to check conflict of interest issues for much of the research submitted to it.

2. The role of patents in developing new medicines

There is general acceptance that patents are needed to allow pharmaceutical companies to recoup the high costs of developing genuinely new medicines. The points I make in this submission do not challenge this, but rather are directed to demonstrating the flaws in patent systems which allow pharmaceutical companies to patent a range of subsequent – often very minor – variations on the original new compound invention, thus delaying generic entry.

I do, however, note recent research which demonstrates that granting patents for pharmaceutical products has the same effect as tariff barriers (Chaudhuri *et al.*, 2010; Branstetter *et al.*, 2011; Dutta, 2011). The cost to consumers is extremely high – 6 to 7 times higher than the benefit to producing companies. It would therefore be far more efficient to cease granting pharmaceutical product patents and simply provide a direct subsidy to pharmaceutical companies. Further, such an approach to funding new medicines would not have the negative effects on access to medicines created by the higher prices implicit in patent policy.

3. Low patent standards

It is generally assumed that patents are only granted for genuinely inventive things. This is simply not true. The inventive step (non-obviousness) requirement involves myriad detailed rules that aggregate to creating a very low standard for patent grant. As the US Federal Trade Commission (FTC) said "A plethora of presumptions and procedures tip the scales in favor of the ultimate issuance of a patent, once an application has been filed" (FTC, 2003: 8).

My own work has focussed on investigating the inventive step standard and identifying the doctrines which create and reinforce the very low standards (Moir, 2013a, 2013b, 2013c, Moir, 2013d). While my initial research was in a different IPC group, I have since been investigating the inventiveness standard for pharmaceutical patents (Moir and Palombi, 2013).[1]

[1] And am currently in the final stages of writing another paper on this (due for completion early March). I would also draw the panel's attention to the 2012-13 Australian Pharmaceutical Patent Review (Harris *et al.*, 2013). The submissions to this review contain some very useful data (at http://web.archive.org/web/20130425142849/https://pharmapatentsreview.govspace.gov.au/submissions/).

These low standards are found in all countries.[2] The standards appear to be somewhat lower in Australia and the USA than in Europe as the synergy doctrine has been abandoned in both Australia and the USA. This doctrine still applies in Europe – combinations of known things are deemed obvious unless the new combination has an unexpected result or a result greater than the sum of its parts. Absent the synergy test, patent examiners are forced to deem combinations of known (and patented) compounds with known release mechanisms (delayed, immediate, etc) sufficiently inventive to warrant a further patent. Such release mechanism patents are important in delaying generic entry. In Australia they delayed generic venlafaxine by 2½ years and omeprazole by 7 years. Delayed entry of venlafaxine cost Australian taxpayers $A85 million, while delayed omeprazole entry cost taxpayers $A1.1 billion.

Another type of secondary (evergreening) patent is for variations on the original formulation. An example is seeking a patent for both a racemate and an isomer. Isomers, chiral centres and racemic mixes were discovered by Louis Pasteur in 1848. These compounds have a chiral centre made up of two forms (called isomers, or enantiomers). These are mirror images of each other, as one's left and right hands are mirror images of each other. The racemate contains equal quantities of both isomers. It has long been understood that isomers behave differently biologically and that one isomer will usually be more pharmaceutically efficacious than the other, often with one isomer having all of the activity and the other isomer being inactive. The most globally famous case of isomer patenting is the racemate omeprazole and its isomer esomeprazole – better known as LOSEC and NEXIUM. In Australia the grant of a second patent (for esomeprazole) has cost taxpayers $A1.8 billion so far.

While these cost data are for a country which has an effective program for ensuring all residents can afford medicines, similar processes in other countries can mean that people who need these medicines simply cannot afford them. While investigating the potential impact of the proposed patent regime in the draft Trans-Pacific Partnership Agreement (TPPA), I came across an interesting example of a low quality evergreening anti-retroviral (ARV) patent granted by the United States Patent and Trademark Office (USPTO) (Moir *et al.*, 2014: 19-20). This patent, for an extended release formulation of nevirapine has been filed in Vietnam using the PCT route (WO2008154234). It is based on a 2009 US application (12/523226, priority 8 June 2007) which had a difficult passage through the USPTO. It was rejected in November 2011 as unclear and obvious. The applicant then deleted 23 of the 24 claims, but it was again rejected as obvious. The applicant then withdrew the single remaining claim and substituted a marginally different single claim (see Box 1). As can be seen from the changes made to the single claim the major difference was a change from a patent for *a composition* to a patent for *the use of the composition to treat HIV*.[3] By 2009 the use of nevirapine for treatment of HIV was well known.[4] Nothing about the extended release composition was inventive. So how could its *use* for a well-known purpose suddenly create sufficient inventiveness for grant of yet another nevirapine patent? Clearly, in the normal meaning of the term obvious, no patent should have been granted. But it was.

While the application has not yet been granted in Vietnam, national phase entry occurred in January 2009. As Drahos has demonstrated, technical assistance from organisations such as the European Patent Office (EPO) ensures that many lower income countries use the standards and norms of the EPO in assessing patent applications. Indeed, given resource

[2] Most work has been done in respect of the USA where many analysts point to very low standards of grant (see, for example Dreyfuss, 1989; Harris, 1989; Lunney, 2001; Jaffe and Lerner, 2004; Lunney, 2004; Quillen Jr., 2006).

[3] The specification of the hypromellose component was also changed, but only by deleting the trademark name.

[4] Indeed Nevirapine was added to the World Health Organization's List of Essential Medicines in 2000, 7 years before the priority date for this patent application (*World Health Organization, Comparative table of medicines on the WHO Essential Medicines Lists from 1977-2011,* worksheet "additions to EML", available at www.who.int/medicines/publications/essentialmedicines/EMLsChanges1977_2011.xls).

constraints for examiners, grant is often simply based on whether grant has already occurred in a major patent office (Drahos, 2008, 2009).

Box 1 Extended release nevirapine: granted patent claim and differences from previously rejected obvious claim

Nevirapine, extended release formulation. US patent application 12/523226

Rejected claim 15 and accepted claim 24

Claim ~~15~~24

A method for treating HIV-1 infection which comprises once daily administration to a human infected by HIV-1 a ~~A~~ tablet pharmaceutical dosage from wherein each tablet comprises:

(a) 400 mg of anhydrous nevirapine;

(b) 270 mg of hypromellose 2208

~~(Methocel™ K4M Premium CR)~~

(c) 400 mg of lactose monohydrate; and

(d) 10 mg of Magnesium stearate

Wherein each tablet is compressed by a force of 10-25 kN.

Note: the editing shows the differences between the granted patent (in blue and black) and the rejected obvious claim (in black and red).

Kingston has drawn attention to the risks of harmonising patent policy. As he demonstrates, US patent policy was redesigned in the early 1950s by the US pharmaceutical industry (Kingston, 2004). The story of how the pharmaceutical industry played the leading role in achieving the passage of the Agreement on Trade Related Intellectual Property Rights (TRIPS) has been well told (Drahos and Braithwaite, 2002; Sell, 2003). There are impediments in TRIPS to the design of balanced patent policy – indeed TRIPS is internally inconsistent in that some of the patent articles directly oppose the Article 7 objective on balance (Moir, 2014).[5] Subsequent bilateral and plurilateral trade agreements have increased the imbalances as these all shift norms further towards the interests of originator pharmaceutical companies (Moir, 2015). They have a consequent negative impact on access to affordable medicines.

4. Other policies which impede access to medicines

While low patentability standards are a major cause of delayed access to affordable medicines, there are also other elements at play. Allowing new medicines to be sold under a trademark name rather than the International Non-proprietary Name (INN) allows originator companies to increase their post-patent market share beyond what would otherwise be the case. Machlup advised the US Congress that allowing the use of trademarks to create consumer loyalty after the end of the patent period was an abuse of the system (Machlup, 1958: 10-11).[6]

[5] See also my submission to Australia's current Productivity Commission Inquiry into Intellectual Property Arrangements, p.9 and 19-20. Available at http://www.pc.gov.au/inquiries/current/intellectual-property/submissions, submission 130.

[6] In contrast, charging high prices for patented products is not an abuse of the patent system, even though it means some people will die earlier than would otherwise be the case.

In many countries governments have accepted patents for pharmaceutical products but have also intervened in the market with a variety of policies to ensure that medicines are affordable for all. In the proposed TPPA this has been under attack (Gleeson *et al.*, 2013). Limiting the right of national governments to ensure affordable medicines substantially endangers access to affordable medicines.

Data protection / data exclusivity

Data protection deserves special mention here. This policy was introduced in the USA in 1984 as part of a package of measures designed to over-ride a Court of Appeals for the Federal Circuit (CAFC) decision[7] and ensure that generic companies could enter the market as soon as possible after the key patent expired. It appears that it was part of Congressional bargaining.

But the ethics of data protection are highly questionable. These clinical trial data are required by regulatory authorities to ensure that medicines are safe and effective. A generic medicine is identical to the original medicine in terms of the active ingredients. In terms of both ethics and economics it is therefore highly questionable why clinical trials would ever be undertaken (replicated) for generic medicines. Ethically it would be wrong to give a proportion of patients a placebo when it is known that the approved medicine has demonstrated efficacy.[8]

The World Medical Association Declaration of Helsinki sets out ethical principles for medical research involving humans. In the 2008 version, this included the statement:

> "Physicians may not participate in a research study involving human subjects unless ... *Physicians must immediately stop a study when* the risks are found to outweigh the potential benefits or when t*here is conclusive proof of positive and beneficial results*"
> (2008 Declaration of Helsinki, Article 20, emphasis added).

Interestingly this was watered down in 2013, with physicians now required only to "*assess whether to continue, modify or immediately stop* the study" (2013 Declaration of Helsinki, Article 18, emphasis added).

Even with this less precise advice as to what to do when outcomes are known, it is clear that unnecessary clinical trials are ethically dubious as well as being a simple waste of resources. Why then has there ever been any suggestion that generic companies should not be able to gain marketing approval simply by demonstrating equivalence? Indeed the "use" by generic companies of earlier clinical trial data may merely be a matter of semantics (after all this is the "intellectual property" world). The simple demonstration of equivalence *precludes any need to use any clinical trial data* as the regulatory agency already has the knowledge and proof it needs that that chemical composition is safe and has some degree of efficacy.

From another angle it is questionable whether data provided to demonstrate safety and efficacy should be confidential at all (apart of course from not identifying the participants in the trials). Unfortunately the current regime allows interested parties (the originator companies) to conduct clinical trials. This reduces trust and can lead to medical harm. Ensuring that *all* clinical trial data undertaken on any medicine marketed in any country was available to medical researchers for comparative studies would substantially increase trust in the pharmaceutical development system.

The whole argument for data protection/exclusivity has little economic merit. It is simply a bargaining loss from international trade negotiations, like geographical indications. The

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[7] *Roche Products Inc. v. Bolar Pharmaceuticals Co. Inc*. 733 F.2d 858 (1984).

[8] Though this has not stopped companies doing this for very closely related medicines. See the example of desvenlafaxine, a metabolite of venlafaxine (http://theconversation.com/explainer-evergreening-and-how-big-pharma-keeps-drug-prices-high-33623).

TRIPS Article 39 provision allows substantial room for countries to determine what arrangements best suit their economy and society. In particular data protection only applies where this constitutes 'unfair commercial use', and countries are free to define this. But subsequent trade treaties, particularly where either the USA or the European Union is a partner, include onerous data protection provisions. These delay access to more affordable generics or biosimilars.

When it comes to new-generation biologic medicines there are grave concerns that proposed longer periods of data protection will substantially delay the entry of cheaper biosimilars for these very expensive medicines (Gleeson and Lopert, 2015).

5. Key areas for action

There is considerable incoherence in between patent and data protection policies and the goal of universal access to affordable medicines. Patent policy goes well beyond what is needed to ensure the development of new medicines. The very low inventiveness standard, together with trademarking medicines, increases the cost of medicines to consumers (and taxpayers where there are publicly funded access systems). Elsewhere I have put forward a coherent range of reforms to patent policy (Moir, 2014). If adopted these would achieve the balance in patent policy required by TRIPS Article 7. They would also do a great deal to remove artificial barriers to accessing affordable medicines.

The most important action the panel could recommend to ensure affordable access to medicines for all would be to recommend an amendment to TRIPS making it unlawful to provide patents for pharmaceutical products.

Failing this, a substantial increase in the height of the inventive step is needed. Such action is inhibited by detailed prescriptive regulations in post-TRIPS trade agreements, with the planned TPPA reaching new depths in requiring abysmally low standards for patent grant. The major impediment to achieving this is the lobbying power of the pharmaceutical industry and the unwillingness of democratic governments to stand up for the public interest.

A further important policy change that would reduce conflict between policies supported by originator pharmaceutical companies and human rights and public health policies relates to data protection. The TRIPS provisions are not a problem, but TRIPS-Plus data protection provisions are not only problematic with respect to affordable medicines. They also raise serious ethical issues.

Limitations to government programs supporting affordable medicines imposed by foreign interests are very questionable. Their recent entry into trade treaties (the TPPA) is of serious concern. A means needs to be found to get all countries to agree to take no such actions and to rescind any current provisions limiting the right of sovereign nations to use national buyer (monopsony) power to offset the monopoly power of in-patent medicine producers.

Because originator companies often have many secondary patents surrounding a medicine (es/omeprazole in Australia has 61), it would be useful to require originator companies to list all such patents with the authority which provides marketing approval for medicines. If only listed patents could be used to challenge generic entry, this would remove ambushes on generic companies.

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