Author's response to reviews

Title: A review of the health and economic implications of patent protection, with a specific focus on Thailand

Authors:

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Author's response to reviews: see over
Dear Editors-in-Chief,

Thank you for your consideration of our manuscript and request for a revised version. We thank the reviewers for their comments. Most comments are addressed in the revised version of the paper. Here we highlight the changes we made. The reviewer comments are in bold, our replies in normal case, and revised text in italics.

Reviewer 1: Rachel K Kiddell-Monroe

1. As a review of literature, it is fairly hands off and there is little expression of authors leanings. In fact, it is a little too bland and I think could do with a bit more analysis.

Authors:

Thank you for your useful comment. We have done more analysis and they were highlighted in below sections and main article. In conclusion, we provide more on discussing results, limitations of methods and suggestions to future research.

2. As a review of literature it seems balanced with a clear and relatively simple methodology. Since it is a review of literature, the gaps in methodology are acceptable since the conclusion is simply to raise the fact that there are not many empirical studies and that the answers to their (very important) questions cannot be deduced from the studies as such – they only give indications. I think this point needs to be made clearer in the abstract and the conclusion.

Authors:

We agree with the point and have inserted this point in the abstract and the conclusion. In the conclusion part of abstract, it now reads...
“Empirical studies in Thailand, and other similar countries, are rare, compromising the robustness and generalizability of conclusions. However, evidence does suggest that patenting presents a significant inter-temporal challenge in balancing aspects of current versus future access to technologies. This underlines the urgent need to prioritise health research resources to assess the wider implications of patent protection.”

In the conclusion part, it now reads

The empirical literature provides answers to some important questions related to the impact of patents, although evidence remains largely inconclusive. With respect to patent impact on price, both Thai and international evidence confirm that patenting shifts prices up and has an effect on the price of the new registration of medicines. In terms of present access, international empirical evidence demonstrates that patent protection does not always impede access, whereas a Thai study suggested that implementing a limited patent life may actually increase access. As for future access, evidence suggests that strengthening patent policy in a given nation may speed up the time required for entry into the pharmaceutical market. Empirical models estimate that higher profits, from patents, would increase the number of new medicines to market through higher R&D budgets, enabling patients to benefit from access to new medicines in the future. Conversely, one observational study revealed that withdrawing exclusive rights by compulsory licensing might not have an effect on innovation in the future.

The review revealed that little empirical research has been undertaken on the extent to which patent rights affect health and economic factors. With respect to health, the settings of the studies are very mixed across therapeutic areas and medicines. The literature generally shows that the size of impact varies wildly, depending on which methods are employed in the studies. Current evidence therefore makes it difficult for a country, such as Thailand, to come to a conclusion on advice to national policy makers who are to make decisions which trade off health or access impacts with wider economic issues. The high price of medicines may not be related to patent rights. Furthermore, price may not be related to access, either.

Minor revisions

Language check - grammar particularly and phrasing of sentences.

Authors:

We have sent the revised manuscript to native English speaker to closely edit the quality of English.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
1. I feel a lot of info is in the tables but little reference is made to them in the articles (BTW, the figures are missing in my version…) – would be be possible to link tables and article together better?

Authors:

We revised the format of the table. We linked the number of reference in the article with the first column in the table. If readers would like to know more in any study, they can see brief details of that study from table. We understand that putting all studies in one table is hard to read so we splitted the table to present each topic of patent impact so it is more convenience for readers to see both text and table in the same area.

2. Very few studies are mentioned by name in the article and it would be good to mention groups of authors/articles under each category of, for instance, type of methodology on prices. These kinds of indicators would help readers/researchers how want to continue on this work.

Authors:

We added the authors' details in the article and put authors' names in the table.

3. While this is a literature review, I would have liked to see a little more analysis. Or if analysis is not relevant, then at least raise some new questions from the literature survey – why is FDI from US/EU inversely proportional to IPR protection? What are exceptions in some of the conclusions and how indicative of the situation are they? Is Attaran right? The conclusions are a little in substantive and I think calling for more empirical studies is a good idea but it would be great to give some guidance on what empirical analysis needs to be done.

Authors:

Thank you reviewer for this suggestion. After description of each group of study, we discussed the limitations of methods employed and different setting affecting study's results. Also, we gave the guidance on the future research in the conclusion part.

4. The 3 questions the authors ask are not touched on again clearly in the article – I would like to see them picked up again in the conclusions and tied to questions which need to be answered before we can get to those questions.

Authors:

We revised as suggested. It now reads

*The empirical literature provides answers to some important questions related to the impact of patents, although evidence remains largely inconclusive. With respect to patent impact on price, both*
Thai and international evidence confirm that patenting shifts prices up and has an effect on the price of the new registration of medicines. In terms of present access, international empirical evidence demonstrates that patent protection does not always impede access, whereas a Thai study suggested that implementing a limited patent life may actually increase access. As for future access, evidence suggests that strengthening patent policy in a given nation may speed up the time required for entry into the pharmaceutical market. Empirical models estimate that higher profits, from patents, would increase the number of new medicines to market through higher R&D budgets, enabling patients to benefit from access to new medicines in the future. Conversely, one observational study revealed that withdrawing exclusive rights by compulsory licensing might not have an effect on innovation in the future.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:** No competing interests

**Reviewer number 2: Kannikar Kijtiwatchakul**

**Major Compulsory Revisions**

On Conceptual framework and Methodology

1. As we know that the two main concepts of patent system are, first, to award an inventor exclusive rights on his/her new invention for a specified period of time (ie; not more than 20 years) to encourage the research and development of new innovations and, second, to allow technological transfer for augmentation into other new inventions, which strike a balance between monopolization and the benefit to public health. However, this study’s framework did not consider the technological transfer derived from patenting system, so, it seems that there is not balance between health and economics.

**Authors:**

We understand and concern that patent system was established to encourage technology transfer as shown in page 3 that we would like to know what impact patent has on innovation in national and international setting. In our framework, we did consider the patent effect on technology transfer. However, since technology transfer can be obtained from either formal means through imports of high-technology products, adoption of foreign technology and acquisition of human capital, licensing,
and personnel movements, or from informal means through imitation, reverse engineering, and spillover[1], choosing activity to reveal patent impact on technology transfer is always difficult.

For the formal means, inward foreign direct investment (FDI) was claimed as the most important channel for technology transfer[2, 3]. Multinational firms not only invest in technology and personnel training, they also hold unique capabilities and transfer their capabilities across national boundaries to their foreign subsidiaries. Therefore, inwards FDI can represent both formal and informal means of technology transfer. This is the reason why we designed the effect of patent on technology transfer using FDI as a proxy. We added this issue in the introduction part. It now reads

“The justification to amend the Thai patent law was to interest multinational companies to invest in Thailand. The other expected benefit of strengthening patent protection in medicines is that this could increase domestic capability and strengthen the local pharmaceutical industry by the transfer of new technologies into the country[4], as the aim of patent is to encourage technology transfer. Although technology diffusion can take place through a variety of channels that involve the transmission of ideas and new technologies, such as imports of high-technology products, adoption of foreign technology and acquisition of human capital through various means, FDI was claimed as the most important channel for technology transfer[2, 3].”

2. The assumption from the framework (Fig.1) revealed that patent has a direct association with price while having indirect effects on both present and future access to medicine, with some influences of price factor. Similarly, patenting has indirect relation with international trade and investment with a more considerable impact of price. However, access to medicine can be affected by other factors beyond price. The authors should not explain the association of patent and access to medicine and also international trade and investment in terms of causal-relation due to the reason mentioned above.

Authors:

We set the research question to find if there are studies that estimated patent impact on two dimensions: access to medicine and international trade and investment dimensions. We agree with the reviewer that there are many factors affecting price and patent is just only one factor of them. We added two paragraphs in page 6 to highlight the limitations of method employed in each type of study.

‘This approach would be useful if the price elasticity of demand is known and correct. For the pharmaceutical market, the consumption decision commonly involves participation by a physician and a third party payer (government or hospital committee). The consumer may or may not play some part in the price payment, depending on a country’s specific regulatory and reimbursement regimes. The pharmaceutical market’s demand function is thus often distorted, and a model based on price elasticity of demand might not present a real world situation of the complexity of the pharmaceutical market.’
However, the effect in each country will differ since each nation has a different health system in terms of medical tradition, policy for financing and supporting generic entry, and brand royalty of physicians, pharmacists and customers. The marketing strategy also differs among pharmaceutical companies, who often spend more heavily on the intensity of advertising once the patent has expired, which could explain at least some of the post-patent price increase. It appears that medicine prices, in general, depend on several supply and demand factors. For example, therapeutic advantage and number of substitutes are both significant price determinants; as the number of substitutes increased in one study from one to two, there was an average 38% decline in the ratio of the new drug price to the average existing market price[5]. Kanavos and Vandoros (2011) also found that product age has a significant and negative effect on prices[6].

3. New medicine registration and new invented medicine may not represent access to medicine in the future directly; therefore, they should be dealt as two separate variables. The study should then seek to explain the relations between the two variables and patenting system.

Authors:

We already separated these two issues into independent issues, as shown in page 8 and 9. On the issue of patent impact on new medicine registration, we showed that we found two empirical studies. On the issue of patent impact on new invented medicine, we showed that there were four studies found.

4. The publishing dates of literature referred to in this study span over 30 years (1980-2009). Some studies may not applicable to current situation or out of date. The author should state the reason for referring to them.

Authors:

We provided empirical evidence from 1980 since it covers the period of requirement of global standard patent protection system. Some countries amended their patent law to cover product patent since late 1970s. It is likely that empirical evidence will be done from that year. We insert the rational. It now reads

"The dates of the published studies (1980-2009) were set so as to ensure the inclusion of all work conducted when the requirement of global standard patent protection was needed as, since the 1980s, intellectual property has became an important business tool, and new internationally-agreed trade rules for intellectual property rights were seen as a way to cope with the international economic tension [7]."
5. The author’s conflict of interest of each studies selected into this study should be elaborated (presented).

Authors:

We checked the included articles and found that many of them did not report conflict of interest. We tried creating a new column in the tables but there are many missing values and we think reader can find more information about authors from the revised table that we included authors’ names.

6. Some studies in the reference cannot be considered as either articles, working papers or reports (references 28 and 29). In addition, some relevant reports on Thailand are not included; for example, Impact on Access to Medicine from TRIPS-Plus: A Case Study of Thai-US FTA, Nusaraporn Kessomboon, Jiraporn Limpanannont, Vidhaya Kulsomboon, Usawadee Maleewong, Achara EkSaengsri and Prinya Paonthong, Southeast Asian Journal Tropical Medicine Public Health, May 2010.

Authors:

We thank the reviewer for pointing out the opportunity to mislead readers. Reference no.28 and 29, which are number 35 and 36 in the revised version, mentioned by the reviewer were not included as empirical evidences in the systematic review. They were citations of general arguments from pharmaceutical companies’ point of view. Therefore, we developed new tables of empirical evidence for each issue. Readers can then see what studies are included. For the study of Nusaraporn et.al. suggested by the reviewer, since we set the scope of work up to 2009 as this study was conducted in 2010, this study was not published yet.

7. The presentation should be adjusted to explain based on the study framework as recommended above.

Authors: We explained the rational of study framework in comment no.1.

8. Presentation on Thailand should be done as a case study to demonstrate the gap of research on patenting system in Thailand, in order to offer information for policymakers.

Authors:

Intentionally we would like to focus on the literature done in Thailand setting. However, as shown in the results part, there were only three Thai studies found. Given the small number of Thai evidence, there is not enough information to recommend to policy makers. Therefore, we extended the scope of study to include empirical evidence done in international setting since we stated that there were lack
of empirical evidence and policy makers can learn from international experience. Also researchers would gain some idea of what research should be done.

9. Verify the relevance of studies used in this research. For instance, there are so many provisions in FTA, not only the chapter of intellectual property rights.

Authors:

From this literature review, there was one study which looked at the implications of FTA on trade. We agree that there are many provisions to negotiate as we stated on page 10 that ‘one of the 23 negotiation issues was TRIPS-Plus, which requires a higher level of intellectual property protection than existed in the TRIPS agreement’.

10. Change (the comparison) “strengthening versus weakening” to “restricted versus unrestricted.”

Authors: We tried with changing to be ‘restricted and unrestricted’. However, readers who are native English speakers get confused. Therefore, we think using ‘strengthening versus weakening’ is suitable with this context and helps readers to understand.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests

Thank you for considering this paper for publication. We look forward to your reply.

Sincerely,

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References