TECHNICAL BRIEFING

PUBLIC HEALTH CONCERNS ON PAT-INFORMED DATABASE

Prepared for the WIPO Standing Committee of Patents (Agenda Item 7: Patents and Health)

2 December 2019

In September 2018, the World Intellectual Property Organization (WIPO) together with the International Federation of Pharmaceutical Manufactures Associations (IFPMA) launched a partnership called Pat-INFORMED – a database of drug patent information based on voluntary sharing by the patent-holding originator pharmaceutical companies. Since its launch, Pat-INFORMED has triggered controversy given the apparent conflicts of interest and the potential to mislead national and international procurement agencies due to its current operational structure and information sources. This brief note outlines key concerns with respect to Pat-INFORMED in the context of access to medicines and patent information transparency.

We hope these concerns will be raised at the 31st session of Standing Committee of Patents meeting in Geneva 2-5 December 2019 and especially under Agenda item 7 concerning Patents and Health.

Conflict of interests

WIPO's partnership with IFPMA raises serious concerns about conflicts of interest.

The initiative was launched without consultation nor authorisation by WIPO's Member States. It also twists the recommendation set forth by the United Nations Secretary-General's High-Level Panel (UNHLP) Access to Medicines Report regarding the need for transparency on medicines patents. During a recent meeting held between the WIPO Director General and non-governmental organisations (NGOs), WIPO also wrongly claimed that the construction of Pat-INFORMED was at the request of Médecins Sans Frontières (MSF), which was never the case. To the contrary, the UNHLP report recommends that governments and WIPO work out the transparency issues with WIPO consolidating data and release it in a user-friendly manner.[1] None of the UNHLP report recommendations requested WIPO to bypass its Member States and rely on the patent-holding IFPMA member companies to fulfil its mandates. Neither MSF nor any other civil society organisations

[1] UN Secretary General's High Level Panel on Access to Medicines, Final report: http://www.unsgaccessmeds.org/final-report , Page 37.

advocating for transparency on pharmaceutical patents have requested WIPO to form such a controversial partnership with IFPMA.

Pat-INFORMED claims that its objective is to "[provide] a service to the global health community, particularly those involved in procurement of medicines, by facilitating easy access to medicine patent information".[2] We question the need to specifically target procurement entities.

Further, as shown below, patent information uploaded to Pat-INFORMED is very selective, incomplete and oftentimes erroneous. It also contains a number of irrelevant patents that in practice should not block procurement agencies from acquiring more affordable generic or biosimilar alternatives. Procurement agencies may be intimidated by the existence of multiple patents and may choose to be cautious and avoid procuring generic medicines that may not even infringe the patents listed.

It is apparent (see examples below) that the patent information provided in Pat-INFORMED is in favour of the commercial interests of the patent-holding originator pharmaceutical companies. This conclusion is further reinforced by Pat-INFORMED facilitating contact between procurement agencies and patent-holding companies. Instead of providing independent and verified information directly, this approach is biased in favour of the patent holder. The biased information and approach may further the commercial interest of the patent-holding companies by facilitating price negotiations for patented originator products instead of facilitating options to procure generic medicines at more competitive prices. Hence we reiterate concerns that the platform is mainly targeted at procurement agencies.

There is no mechanism to verify the information provided by the patent-holding companies or to monitor their actions. The companies can also omit information that is not in their favour. And they have done so, as highlighted in the examples mentioned below. As a result, the accountability of the patent-holding companies and Pat-INFORMED in ensuring the accuracy and independency of data is entirely missing.

In its current form, Pat-INFORMED is a huge disservice to public health. WIPO Member States should be very concerned that this initiative is targeted at procurement agencies and other national health actors and that they will be provided with incomplete, inaccurate, biased and misleading patent information. See the examples below.

While the WIPO Secretariat may partner with industry, the partnership must consider the context and in particular whether the partnership results in conflicts of interest. In providing information about the patent status of medicines, it is unacceptable that WIPO partners with IFPMA and patent-holding companies that can benefit commercially from the type of information and features that are provided by Pat-INFORMED.

[2] https://www.wipo.int/pat-informed/en/

For example, Pat-INFORMED provides the opportunity for a procurement agency to open an account and ask further questions to the patent-holding companies with respect to the data published. However, any information provided by the patent-holding companies to the procurement agency is not publicly available. As shown below, the lack of clarity of the provided patent data appears to be deliberate to compel the procurement agencies to contact the concerned companies with respect to a procurement-related inquiry.

In practice, to mitigate the potential legal risk of patent infringement, procurement decision making needs to be guided by information from independent, unbiased and verifiable sources. Presently, as shown below, the current form of Pat-INFORMED is neither an independent nor a reliable source of information that can be used to guide procurement practices.

Providing selective and incomplete information about patent status

The legal status of a patent and patent application can change over time after its initial filing or the grant. Applications for a patent could be rejected, withdrawn or opposed. The granted patents could also be revoked, invalidated or lapsed in different jurisdictions. For primary patents concerning pharmaceutical products, a major change of the legal status could effectively open up the opportunity to procure from multiple generic or biosimilar producers. Therefore, a timely, accurate and complete update of the legal status is crucial in patent information transparency. However, Pat-INFORMED contains several problems in this regard as shown below in the examples.

As presented in its current state, data uploaded in Pat-INFORMED often contain incomplete legal status information. For instance, the pharmaceutical company Bristol-Myers Squibb (BMS) has widely withdrawn its primary compound patent on daclatasvir, a medicine used to treat hepatitis C infection, in low- and middle-income countries (LMICs).[3] This means that countries that are not covered by the Medicines Patent Pool (MPP)-BMS voluntary licenses and no longer have a valid patent could have the opportunity to source generic versions of the medicine from generic producers in the future. However, the patent data on daclatasvir as uploaded in Pat-INFORMED selectively presents only countries where BMS has been granted and maintained its patent, but no further information is available about the withdrawal of patents in LMICs. For instance, according to MedsPal, for daclatasvir 30mg and 60mg tablets, all patents have been withdrawn for Armenia, Belarus, Kyrgyzstan, Kazakhstan, Moldova and Tajikistan. None of these countries are included in the MPP-BMS voluntary licences. As there are no blocking patents in these aforementioned countries, procurement agencies have the possibility of procuring affordable generic daclatasvir in the future. The Pat-INFORMED database does not provide any information pertaining to daclatasvir in the aforementioned countries.

[3] This trend has been captured by MedsPal, the database of patent information of selected medicines managed by the Medicines Patent Pool. See. https://www.medspal.org/?product_standardized_name%5B%5D=Daclatasvir+30+mg&page=1

Similarly, the Pat-INFORMED database does not provide patent information on daclatasvir for countries where patents have not been filed and that are excluded from the MPP-BMS voluntary license. One such example is Thailand.

In Pat-INFORMED, the absence of information cannot be taken as there being no patents in those countries, as in other cases, despite existing patents, patent information is also missing.

Another clear example of providing selective patent information is that of Malaysia. For 30mg and 60mg daclatasvir tablets there are no blocking patents. And yet, entry of the same International Nonproprietary Names (INN) on Pat-INFORMED will reveal a patent has been granted in Malaysia.

Further examples are that of Indonesia and Uganda. In both of these countries, patents related to 30mg and 60mg daclatasvir tablets have not been filed. An Indonesian procurement agency looking for information on Pat-INFORMED would find that for daclatasvir, a patent has been granted in Indonesia and may consider this to be a blocking patent. No information is provided for Uganda. However, in this scenario, both Indonesia and Uganda are included in MPP-BMS voluntary licence which enable the countries to procure generic versions of daclatasvir in the future. Yet this fact that would guide procurement agencies to obtain affordable medicines is absent.

Daclastasvir, recommended on the World Health Organization's (WHO's) Essential Medicines List (EML), is a crucial direct-acting antiviral medicine to treat hepatitis C. As of 2017, BMS's originator version of daclatasvir 60mg tablets was priced up to US$11,800 per bottle[4] while generic versions of daclatasvir 60mg tablets were priced between $7-13 per bottle.[5] The opportunity for countries to source more affordable generic versions of daclatasvir is important to scale up the accessibility of the medicines for all patients who need it. The selective and incomplete information provided by BMS to Pat-INFORMED does not work in favour of such a need.

Key patent information is missing

No information on licensing

As mentioned, Pat-INFORMED does not include information about whether there are voluntary licences that exist with respect to a particular INN, be it bilaterally negotiated between companies or through the MPP. The existence of voluntary licences is relevant information for all public health actors including procurement agencies.

Similarly, Pat-INFORMED does not provide information on whether a compulsory licence or government use licence is available with respect to a particular INN, although this would be especially relevant information to anyone using the database. It should be noted that WIPO's Development

[4] The price of $11,800 per bottle was for Jordan as of 2017. See. https://www.msfaccess.org/hepatitis-c-not-even-close , Page 3.
[5] Generic prices for India and Egypt as of 2017. See. https://www.msfaccess.org/hepatitis-c-not-even-close , Page 3.

Agenda 17 states "[I]n its activities, including norm-setting, WIPO should take into account the flexibilities in international intellectual property agreements, especially those which are of interest to developing countries and LDCs".[6]

A comparison could be made to the MedsPal database, managed by MPP, in which information about voluntary licenses and compulsory licenses is included.

Inconsistent or no information of key status, filing date and expected expiry date of a patent

In addition, Pat-INFORMED does not provide or provides inconsistent information about the filing date and the expected date of expiration of a particular patent. For instance, when searching Pat-INFORMED for lopinavir/ritonavir, an important HIV treatment on WHO's EML, one of the six patents listed on Pat-INFORMED concerns a polymorph of ritonavir with patent grant numbers IDP0030609B, IDP0030607B and ID0021288 for Indonesia. No information about the filing date and the expected expiry date is provided. According to MedsPal, these patents are expected to have expired in Indonesia in July 2019.[7] IFPMA and AbbVie may argue that they are not able to update the database regularly, hence such mistakes are possible. However, had the expiry dates been made available as part of the standard format of information, the update of the database would be a non-issue.

In the case of Brazil, no patent information about lopinavir/ritonavir is available on Pat-INFORMED although most of the patents relating to lopinavir/ritonavir treatment have been rejected and/or are under appeal.[8]

No information of opposition, revocation and other disputes

Pat-INFORMED also does not provide information about granted patents or patent applications that are under opposition, revocation or other dispute procedures. An example can be found with tenofovir disoproxy fumerate/emtricitabine (TDF/FTC) combination, one of the important medicines recommended by WHO for the prevention and treatment of HIV/AIDS. According to information shown on MedsPal, the combination patent of TDF/FTC (WO/2004/064845) has been rejected, withdrawn, not filed or under appeal in multiple countries including India, Brazil, Indonesia, South Africa, Malaysia, Uganda and others.[9] In Brazil, a granted patent BR0112646 covering tenofovir alafenamide fumarate (TAF), a prodrug of tenofovir that is under the company Gilead's development

6 Recommendation 17, Cluster B, https://www.wipo.int/ip-development/en/agenda/recommendations.html#c
WIPO Development Agenda Recommendation. 2007.

7 https://www.medspal.org/?product_standardized_name%5B%5D=Lopinavir%2FRitonavir+100%2F25+mg&country_name%5B%5D=Indonesia&page=1

8 https://www.medspal.org/?product_standardized_name%5B%5D=Lopinavir%2FRitonavir+100%2F25+mg&country_name%5B%5D=Brazil&page=1

9 https://www.medspal.org/?product_standardized_name%5B%5D=Tenofovir%2FEmtricitabine+150%2F100+mg&page=5

and may also be combined with FTC, is listed as opposed in MedsPal.[10] However, this crucial information about Brazil is absent from Pat-INFORMED. The fixed-dose combination of TDF/FTC is available in generic versions due to multiple stimulators including a patent rejection in India and other producing countries, the voluntary licence signed with MPP and the non-enforcement commitment made by the companies for some countries.[11] This is critical information for the global health community, including procurement agencies, to know. However, on Pat-INFORMED, none of this important information related to the TDF/FTC combination patent has been included.

Instead, the company Gilead chooses only information that can reinforce its commercial status to be uploaded on Pat-INFORMED. For instance, on the status of the equivalent patent of emtricitabine/tenofovir disoproxil fumerate combination (TDF/FTC) in the United Kingdom (UK), it includes a 'Grant Number' which, instead of listing the patent number, is actually the number of a Supplementary Protection Certificate (SPC) –SPC/GB05/041,[12] and a link titled 'Open at PATENTSCOPE', which again leads to confusion:

- When clicking the link 'Open at PATENTSCOPE', this supposed TDF/FTC UK patent information leads to a European Patent Office (EPO) patent titled 'Device for Controlling the Line Width Variation Of Characters Produced By A Photographic Composing Apparatus'.
- More critically, this SPC has been invalidated by the High Court of England and Wales in September 2018 in a dispute between generic companies and Gilead[13] following a preliminary ruling of the same by the Court of Justice of European Union in July 2018.[14]

Procurers eyeing the availability of generic TDF/FTC in European markets would appreciate the critical information of the SPC invalidation by the UK court, but Gilead and Pat-INFORMED have not included it.

In another example, the patent on the sofosbuvir compound (WO/2005/003147, equivalent to EP2604620)[15], another medicine used to treat hepatitis C, is under post-grant opposition procedures before the EPO, launched by several civil society organisations and generic companies.[16] However, the EPO entry on Pat-INFORMED is problematic:

[10] https://www.medspal.org/?product_standardized_name%5B%5D=Tenofovir+alafenamide+25+mg&country_name%5B%5D=Brazil&page=1

[11] See more details on MedsPal, and Patent Opposition Database: https://www.patentoppositions.org/en/drugs/tenofovir-disoproxil-fumarate-slash-emtricitabine

[12] Issued upon the patent EP0915894, which in itself has expired on 24 July, 2017. Reference to UK IPO: https://www.ipo.gov.uk/p-ipsum/Case/PublicationNumber/EP0915894

[13] Teva, Lupin, Accord, Mylan v Gilead, [2018] EWHC 2416 (Pat), https://www.bailii.org/ew/cases/EWHC/Patents/2018/2416.html

[14] Judgment of the Court (Grant Chamber), Case C-121/17, http://curia.europa.eu/juris/document/document.jsf?text=&docid=204388&pageIndex=0&doclang=EN&mode=lst&dir=&occ=first&part=1&cid=740884

[15] WO/2005/003147. The detailed information of the ongoing post grant opposition procedure on sofosubuvir compound patent (EP2604620) is available at European Patent Register : https://register.epo.org/application?number=EP13152340&lng=en&tab=main

[16] See information of oppositions on sofosbuvir as included in Patent Opposition Database: https://www.patentoppositions.org/en/drugs/sofosbuvir;

- Under the EPO entry on the sofosbuvir base compound (modified fluorinated nucleoside analogues), Pat-INFORMED shows patent number 1633766 with a link which says 'Open at PATENTSCOPE'. The link however leads to a United States (US) patent on engine-driven compressor.
- Following the number 1633766 on the EPO Patent Register database, it turns out that this patent has lapsed in some EPO Member States.[17]
- Further looking at the information of 1633766, it is an original application related to EP2604620 – a critical divisional patent that could possibly block generic production and is currently under post-grant opposition procedure.

Pat-INFORMED does not provide information about the lapse of the granted patent 1633766. In addition, why does Pat-INFORMED not include information about EP2604620, which is crucial for generic supply and currently under patent oppositions?

As clearly shown in the above-mentioned examples, the selective approach adopted by the company to only list information that are in favour of its commercial position is utterly problematic.

Including secondary patents that may intimidate procurement agencies

Data as presented in Pat-INFORMED also contains secondary patents that may not prevent the sourcing of generic or biosimilar alternatives that are already available on the market. That information, instead, could have a chilling effect on the procurers.

For instance, in the example of lopinavir/ritonavir combination (LPV/r) as mentioned above, the database shows six patents associated with this formulation held by the company AbbVie, which are all secondary in nature. The primary patent on the lopinavir compound has expired or has not been filed in most countries.[18] The patent on the ritonavir compound has been rejected in Brazil[19] and was not filed in India,[20] and the combination patent itself has been rejected in countries like India and Brazil.[21] This has enabled generic producers in India to make generic versions of LPV/r. However, the information of the rejected combination patent on LPV/r and ritonavir compound are not reflected in Pat-INFORMED, which may be critical for a procurement agency to know. Instead, AbbVie uploaded six secondary patents that do not represent the full picture of patent landscape around LPV/r.

[17] https://register.epo.org/application?number=EP04775900&lng=en&tab=main
[18] WO9721683, reference to the expiry status at MedsPal:
https://www.medspal.org/?product_standardized_name%5B%5D=Lopinavir%2FRitonavir+100%2F25+mg&page=1
[19] https://www.medspal.org/?product_standardized_name%5B%5D=Lopinavir%2FRitonavir+100%2F25+mg&country_name%5B%5D=Brazil&page=1
[20] https://www.medspal.org/?product_standardized_name%5B%5D=Lopinavir%2FRitonavir+100%2F25+mg&country_name%5B%5D=India&page=1
[21] https://www.medspal.org/?product_standardized_name%5B%5D=Lopinavir%2FRitonavir+100%2F25+mg&country_name%5B%5D=Brazil&country_name%5B%5D=India&page=1

Another example concerns stavudine, a first line medicine used to treat HIV/AIDS which has been phasing out following a recommendation by WHO in 2009. As one of the earliest treatments, generic stavudine has long been available as its primary patent on HIV treatment has expired in most countries since 2007.[22] However, the entry of stavudine on Pat-INFORMED contains one secondary patent on the stavudine beadlet form. A procurer might be in doubt when finding this information as to whether the patent might affect the purchase of generic versions. Moreover, this equivalent patent application has been withdrawn or rejected in multiple LMICs[23] and by the EPO.[24] The listing of this weak secondary patent is of no use to the procurement agencies. Instead, procurers who have limited knowledge and experience in patents could be confused or misled by this information.

Misleading presentation of legal status at national level

The actual legal status of a patent in a given country is not clearly presented in Pat-INFORMED. For instance, GlaxoSmithKline (GSK) holds a patent on the hemisulphate salt of abacavir, [25] which was first filed in 1998 and should have started expiring in countries from 2018. However, its legal status in countries as recorded in Pat-INFORMED is confusing. For Brazil, for instance, it only says the patent was filed 22 years ago and granted two years ago, without clarifying the expected expiry date.

For Belarus, Japan and Kazakhstan, Pat-INFORMED data shows that the equivalent patent application was filed only two years ago, and "relates to extended exclusivity".[26] No clarification nor explanation has been given on what this means as GSK should have lost its priority right to apply for an equivalent patent after 10 years from the first filing of its application. It is also entirely unclear what the 'extended exclusivity' refers to in each of these countries.

Abacavir and its combination with other HIV/AIDS medicines such as lamivudine has been produced by Indian generic manufacturers for many years. Given that the secondary patent on the hemisulphate salt should have expired widely as of 2018, countries should have better opportunities to procure generic versions of this medicine. If not carefully clarified, the presentation of the legal status of the abacavir secondary patent may misinform decisions of procurement agencies in forecasting and identifying available sources for procurement.

Pat-INFORMED provides a function for the users to report 'inaccurate' data for correction. However, some of the information as discussed above might be either inaccurate, inappropriate and/or incomplete and thereby providing misleading information for the users. Furthermore, procurement and supply chain specialists who use and depend on data from Pat-INFORMED are not necessarily intellectual property experts, and as such, spotting and reporting inaccurate patent information is not their domain of expertise.

22 https://www.medspal.org/?product_standardized_name%5B%5D=Stavudine+30+mg&page=1
23 https://www.medspal.org/?product_standardized_name%5B%5D=Stavudine+30+mg&page=1
24 https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2001074329&tab=NATIONALPHASE&_cid=P12-K3ETYS-11732-1
25 https://patentscope.wipo.int/search/en/detail.jsf?docId=WO1998052949&_cid=P11-K73DJ9-09412-1
26 Abacavir sulfate: Carbocyclic nucleoside hemisulfate and its use in treating viral infections on https://www.wipo.int/patinformed/, accessed 1 December 2019

Way forward

The issues of the Pat-INFORMED database as a partnership between WIPO and IFPMA raises the critical question of what meaningful transparency of patent data on medicines should be in light of the recommendations made by the UNHLP Access to Medicines Report.[27] The analysis above reveals some examples where the patent data supplied by patent-holding companies is biased, unverified and incomplete, providing inaccurate information to the global public health community. Pat-INFORMED's approach of solely relying on the offline interpretation of this information by the patent-holding originator companies to the procurement agencies is flawed and undermines public health. Given that WIPO can work with patent offices of its Member States and other UN agencies to provide credible patent information, WIPO's endorsement of such initiative is problematic.

In light of the above concerns, and as a way forward, we recommend:

(a) WIPO Member States to address serious concerns about WIPO's partnership with IFPMA, especially the conflict of interests it poses.

(b) WIPO should take over the management of the database, working in collaboration with other UN agencies (WHO, UN Development Programme (UNDP) and UN Conference on Trade and Development (UNCTAD)) and national patent offices to provide reliable and independent patent information that serves the needs of public health. Procurement agencies should not be the main target of the database. WIPO patent information provided through its platform must be complete, unbiased, and independently verified.

(c) A period of public review should be called by WIPO, opening opportunities for Member States and the public to submit commentaries and suggestions to Pat-INFORMED.

(d) Member States of WIPO should also continue working to tackle the issue of low-quality patents that might hinder access to affordable medicines.

[27] UN Secretary General's High Level Panel on Access to Medicines, Final report: http://www.unsgaccessmeds.org/final-report , Page 37.