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Patents and the WHO Model List of Essential Medicines (18th Edition): Clarifying the Debate on IP and Access

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1 minute read: key messages

- Contrary to common belief, 95% of the drugs on the MLEM are off-patent.
- The remaining 5% of medicines (20 drugs) under patent protection are largely for antivirals (especially HIV), but also for non-communicable diseases and others.
- The percentage of developing countries covered by each of the 20 patent portfolios varies widely from less than 1% to 44% with a median of 15%.
- Patents for essential drugs appear more commonly in higher income countries with larger populations where there are relatively more market and manufacturing opportunities.
- Patent transparency is critical to addressing access concerns for essential medicines.

Patent Protection and Access to Essential Medicines

While all lifesaving or life-sustaining medicines may be considered "essential", the World Health Organization (WHO) provides its Model List of Essential Medicines (MLEM) to guide lower-income countries and global health actors to identify those medicines for which access should—as a minimum starting point—be guaranteed. When the WHO adds a new medicine to its MLEM, it encourages individual countries to add it to their own national List of Essential Medicines (LEM) and to internal drug registries. Similarly, several foundations and major charities base the medicines they supply to lower-income countries on the MLEM. The MLEM therefore has influence on the availability of medicines in lower-income countries. Updated biannually, it takes account of changing disease profiles and new medicines that have come onto the market. Medicines are included irrespective of patent status and cost (though cost-effectiveness is a criteria for inclusion when two similar products are considered).

The WHO identifies "affordable prices" as one of four conditions in its "access to medicines framework" for ensuring sustainable access to medicines. As patents may confer market exclusivity on a product, prices could be raised beyond what is affordable for individuals or third-party payers. The extent to which MLEM products are patent-protected in low- and middle-income countries is therefore fundamental to addressing potential essential medicine access barriers. Given the consensus on the global public health importance of MLEM products, it is necessary to update research to identify those instances where essential medicines are (and are not) patent-protected, to more effectively guide policy measures and ensure access.

Identifying Essential Medicines' Patent Status

Information on medicines' patent status is not readily available in most countries, even for essential medicines.

This information is critical because it is only when patents for a given MLEM product exist, either locally or in the manufacturer's country, that patent protection may be one determinant of access. Building upon the methods of previous studies, this brief reports on the results and implications of a patent landscape study of the 2013 MLEM. It documents, to the extent possible, where MLEM products are patent-protected in developing countries and to have this information validated by supplier companies. The fieldwork was undertaken in 2014/15 using the latest available edition of the MLEM (18th edition revised in 2013).

Which Essential Medicines are Patented?

Of the 375 items on the 2013 WHO MLEM, 95% are off-patent, meaning that these medicines patents have expired and that generic equivalents are likely available. This result is consistent with previous studies, as the percentage of off-patent MLEM products has regularly been above 90%. Attaran[1] found that 94% (300 of 319) of the 2003 MLEM items were likely to be off-patent, and Kowalski and Cavicchi[2] found that 95% (333 of 350) were when using the 2009 MLEM. Our preliminary assessment of the recently published 2015 MLEM has this number at 92% (375 of 409).

The present study identified the below 20 drugs as likely to be under some kind of patent protection in certain developing countries (see Box 1). Most are antivirals (especially HIV) (13 of 20), though there are others, including those for non-communicable diseases (cancer and gastroesophageal reflux disease). Generic equivalents to several of these drugs are available on the international market, especially the HIV/AIDS medicines.[3] This is possible because these patents are still old enough to predate the implementation of product patent protection in major medicine-exporting countries, such as India. Further, a number of voluntary licensing agreements exist between brand name and generic manufacturers (i.e., innovator companies license generic medicines to supply certain developing countries with equivalents). This same level of generic availability, however, is unlikely the case for bevacizumab for treating cancer as it a biologic, a type of pharmaceutical that is uniquely difficult and expensive for other manufacturers to produce equivalents of, regardless of patent status.

Where are Essential Medicines Patented?

Patent filings for each of the 20 medicines are present in some countries, but not in all, as patents are granted on a country-by-country (or region-by-region) basis. There is wide variability amongst the 20 products' patent portfolios in the number of developing countries covered, ranging from less than 1% to 44% with a median of 15%. Besides each company's unique patenting strategies, this variability reflects the diverse nature and age of the filings contained in each portfolio.

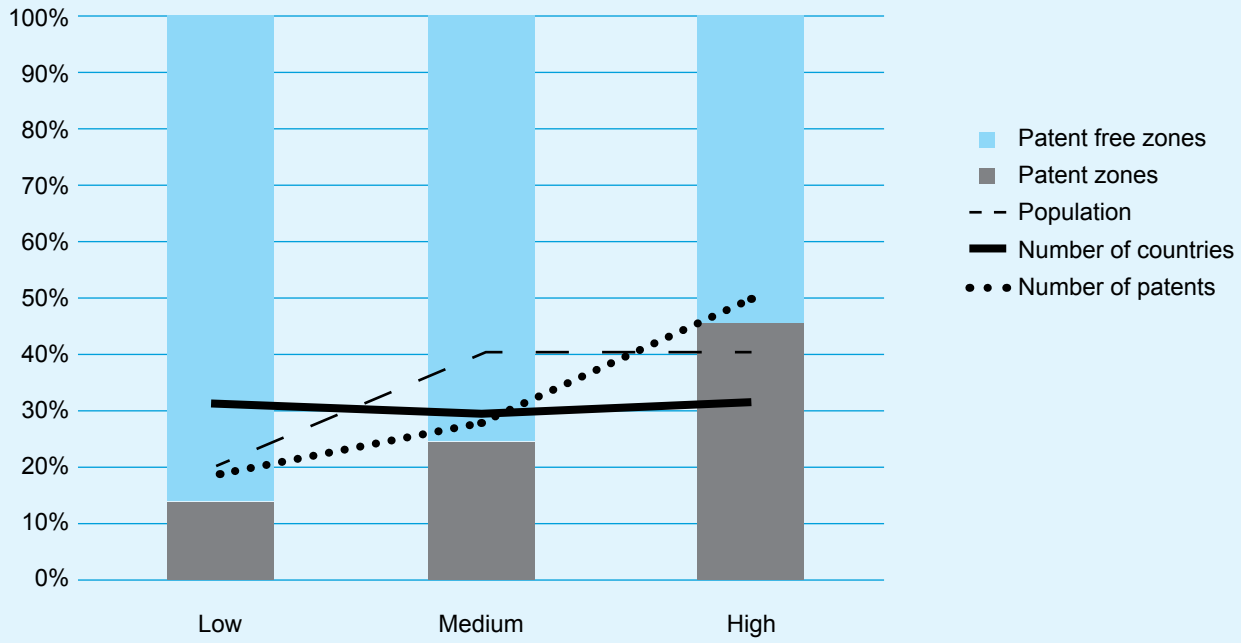
When we consider the geographic coverage of the 20 patent portfolios collectively, patterns emerge. Generally speaking, filings are relatively uncommon in developing countries—over half of the developing countries (n=137) had less than three relevant patent filings in their respective jurisdictions. In fact, 44 of those countries had no filings whatsoever for any of the medicines. A concern for these countries, therefore, is essential medicine patent protection in major medicine-exporting countries, like India, not necessarily patent protection in their own jurisdictions.

Where there were patent filings, they appeared to follow market and manufacturing opportunities, being more common in countries with relatively higher incomes, larger populations, pharmaceutical production capacity, and/or membership in a regional patent organization (see Figure 1). In this sample of 137 developing countries, patents appeared more frequently in Brazil, Bulgaria, China, India, Indonesia, Mexico, the Philippines, Romania, South Africa, and Turkey. The percentage of active patent coverage across the 375 MLEM items and the 137 developing countries is 0.95%; when restricting this calculation to the 20 patented drugs, the active patent coverage is 17%.

Box 1: Drugs on the MLEM identified as having patents in developing countries

- Abacavir (HIV/AIDS)
- Artemether + lumefantrine (malaria)
- Atazanavir (HIV/AIDS)
- Azithromycin (eye infections)
- Bevacizumab (cancer)
- Didanosine (HIV/AIDS)
- Efavirenz (HIV/AIDS)
- Efavirenz + Emtricitabine + Tenofovir (HIV/AIDS)
- Emtricitabine (HIV/AIDS)
- Emtricitabine + Tenofovir (HIV/AIDS)
- Lamivudine + Nevirapine + Stavudine (HIV/AIDS)
- Lamivudine + Nevirapine + Zidovudine (HIV/AIDS)
- Lopinavir + ritonavir (HIV/AIDS)
- Omeprazole (gastroesophageal reflux disease)
- Oseltamivir (influenza)
- Pegylated interferon alfa 2a (hepatitis)
- Pegylated interferon alfa 2b (hepatitis)
- Ritonavir (HIV/AIDS)
- Saquinavir (HIV/AIDS)
- Tenofovir (HIV/AIDS)

Figure 1: The collective coverage of developing countries for the 20 MLEM products by Human Development Index categorization



Essential Medicine Patent Transparency

A pragmatic approach to improve access to essential medicines is to target interventions, such as licensing agreements authorizing generic manufacturing and/or procurement, squarely upon the specific cases where patenting exists for essential medicines and poses a barrier to access. To take such an approach, the first policy intervention needed is to increase the level of patent transparency on essential medicines. This is most efficiently and effectively done by supplier companies shortly after each update of the MLEM, even when the intellectual property is actually owned by a third party, such as a university.

To illustrate this point, consider that patent landscape reports were generated for each company prior to their validation using commercial-grade international patent databases; after the companies' corrections, it was evident that the reports had misidentified patents in countries where there were no longer ones (30 per cent of the positive results were wrong) and conversely failed to identify patents where there were indeed active filings (11 per cent of the negative results were incorrect). This imprecision in performing the task of merely identifying whether a company had active filings in a particular jurisdiction reflects the difficulty of determining a medicine's patent status in developing countries as a third party. Misinformation on patent status can impact public health by obscuring the actual landscape for policy makers and misdirect actions to evaluate potential access issues.

When information around essential medicine patents is opaque and inaccurate, it may discourage or unnecessarily alter the actions of importers, exporters, manufacturers and other global health actors who fear infringing upon intellectual property rights (e.g., unnecessarily buying brand name over generic). Therefore, initiating a high level of MLEM patent transparency will itself improve access and public health.

Should international consensus be established on this matter, it is feasible that many supplier companies will cooperate. All major companies eventually shared their patent data transparently for our study, with exception to India's Cipla Ltd. Patent transparency by generic companies is especially important when it comes to essential medicines, as we found patent rights held by such companies on products commonly believed to be patent-free. Universities also hold patents on some essential medicines in developing countries. All disclosed patent information could be stored in a centralized database, similar to the Medicine Patent Pool's[4], and/or disclosed on the supplier's websites, similar to Merck's US patent rights page.[5] The disclosed patent information would ideally contain information on which MLEM products are patented (including strength, route, and formulation), the kind of protection (compound, (co-) formulation, method, process, device), in what countries they are patented (including patent numbers and expiration dates), and information on steps the supplier is taking to ensure affordable access.

Targeted Interventions for Patented MLEM Products

Once MLEM products have been identified as patent-protected, then the level of access can be evaluated internationally and interventions can be designed for each context as necessary. The suppliers themselves can immediately implement actions to address access

Key Implications & Considerations for Policy & Policymakers

The following implications and considerations for policy and policymakers are intended as starting points for reflection, to be adapted to specific needs and circumstances:

1. Most MLEM products are off-patent in most lower-income countries. For low-income countries, therefore, patent protection in major medicine-exporting countries is often a more important concern than patent protection domestically.

2. A pragmatic approach to improve access to essential medicines is to target interventions, such as licensing agreements authorizing generic manufacturing and/or procurement, squarely upon the specific cases where patenting poses a barrier to essential medicine access.

3. Patent transparency on MLEM products is critical for proactively and correctly identifying these specific cases. Accurate patent information on MLEM products is not readily available in most countries, which may act as a deterrent to potential manufacturers and exporters of essential medicines, who may erroneously believe there is patent protection where there is none.

4. The need for patent transparency extends to generic manufacturers, as they sometimes hold patents on products commonly believed to be patent-free.

5. In the long-term, the proportion of patented products on the MLEM will likely increase and therefore there will be more opportunities to design and implement new inventive solutions for the changing essential medicine patent landscape.

gaps. Medicine buyers can negotiate for affordable prices, or can take steps to obtain generics within established legal flexibilities. Responsible and ethical voluntary licensing agreements can provide some of the necessary flexibility, so long as these arrangements have public health as the primary focus and accordingly align incentives and balance powers into a mutually beneficial arrangement for all stakeholders. Getting these arrangements right is easier said than done; as experience accumulates, however, such agreements have good potential for achieving favorable outcomes. Several voluntary licenses have been made on MLEM products already (e.g., licenses by Abbvie, GSK, Merck, Novartis, Roche and others). Compulsory licensing can also provide flexibility in accordance with domestic and international laws, including the World Trade Organization's (WTO's) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and the Doha Declaration. Compulsory licensing is "when a government allows someone else to produce the patented product or process without the consent of the patent owner"[6] though more collaborative approaches may prove more cost-effective depending on circumstances.[7]

The Importance of Future Cooperation

The global demographic transition toward a higher prevalence of non-communicable disease means that more patented products will likely be on the MLEM in the future. This is already apparent in the addition of 4 patented medicines for treating cancers (filgrastim, imatinib, rituximab, and trastuzumab) in the recently published 2015 MLEM. This provides more opportunities to choose new collaborations over conflict (whether that takes the form of licensing agreements or more creative solutions not yet envisaged) and to avoid repeating past frictions between advocates for essential medicines access and advocates for patent protection during the HIV/AIDS crisis. More proactive and pragmatic cooperation could underpin future progress. Patent transparency is critical to that end.

1 Attaran A. 2004. How do Patents and economic policies affect access to essential medicines in developing countries? *Health Affairs* 23(3):155-66.

2 Cavicchi JR and SP Kowalski. 2009. Report of patent literature, search methodology and patent status of medicines on the WHO MLEM. International Technology Transfer Institute, Franklin Pierce Center for Intellectual Property, Concord, NH. www.ow.ly/SdKOJ

3 World Health Organization. 2015. HIV/AIDS: Global price reporting mechanism for HIV, tuberculosis and malaria, 2015. Available at: www.who.int/hiv/amds/gprm/en/

4 Medicines Patent Pool. Licences in the MPP 2015. Available at: www.ow.ly/SdL2u

5 Merck. 2015. Merck US patent rights for products 2015. Available at: www.merck.com/product/patent/home.html

6 World Trade Organization. 2006. Compulsory licensing of pharmaceuticals and TRIPS. Available at www.ow.ly/SOv73

7 Beall RF, R Kuhn and A Attaran. 2015. Compulsory licensing often did not produce lower prices for antiretrovirals compared to international procurement. Health Affairs 34(3):493-501.

This report was prepared by Reed F Beall (reedbeall@gmail.com) and is broadly based on a Global Challenges Report by RF Beall and A Attaran, titled *A patent landscape report on the World Health Organization's Model List of Essential Medicines (18th Edition)*. WIPO, Geneva, 2016.

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