



Unitaid's approach to intellectual property

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1 Context

Unitaid is engaged in finding new ways to prevent, treat and diagnose HIV/AIDS, tuberculosis (TB) and malaria more quickly, more cheaply and more effectively. It takes game-changing ideas and helps to turn them into practical solutions that can help accelerate the end of the three diseases. By helping to fast-track access and reduce costs of new, more effective medicines and diagnostics, Unitaid aims to maximize the impact of every dollar spent to overcome these diseases.

Unitaid recognizes that there can be many determinants of access; intellectual property rights (IPR) – notably patents – are one of them.

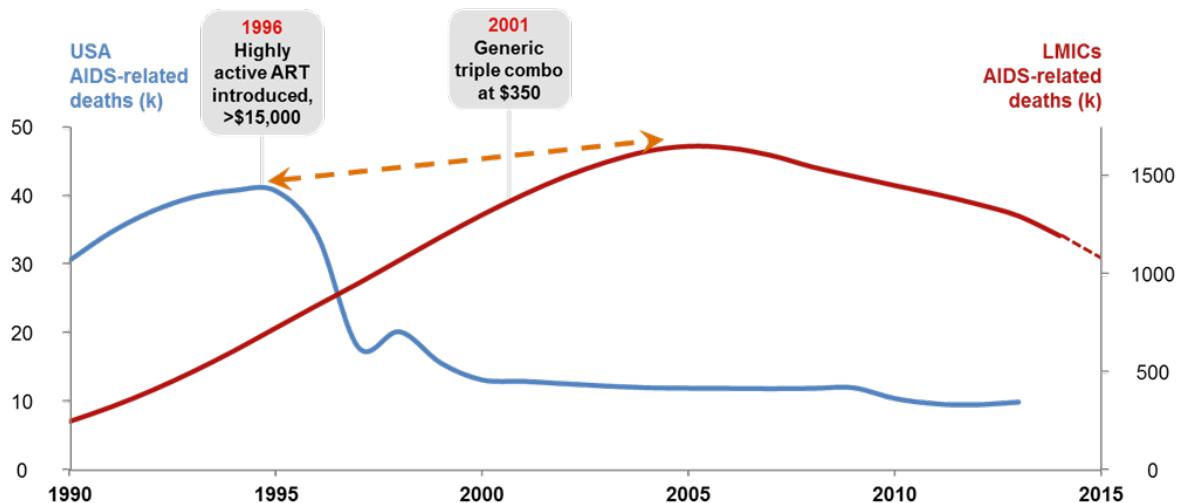
The patent system is designed to support innovation, and has been effective in stimulating and rewarding innovation in several of the disease areas that Unitaid works on. But while patents can incentivize innovation, they also limit competition that could stabilize supply and/or reduce prices.

The purpose of this paper is to set out Unitaid's approach to intellectual property rights (IPR) and the rationale for it. It builds on the disease narratives, which reflect Unitaid's systematic approach of identifying challenges in HIV, TB and malaria, and prioritizing those challenges that Unitaid is best positioned to address. Starting with the challenges identified in the disease narratives, this paper focuses on those challenges that are or may be caused by IPR, and identifies tools that Unitaid can use to address them. In doing so, to the extent possible, this paper follows the approach used in the disease narratives.

1.1 Accelerating the response

The history of HIV illustrates the importance of access to innovative products. In 1996, the introduction of highly-active antiretroviral therapy (HAART) in the US triggered a 75% drop in AIDS-related mortality over three years. During the same period, AIDS-related mortality continued to soar in low-and middle-income countries due to the lack of affordable treatment. Only after 2001, when more affordable generic fixed-dose combinations became available in low-and middle-income countries, did mortality start to decline in these countries (see Figure 1). [1].

Figure 1: Large time lag between the introduction of antiretroviral therapy and mortality in the USA and in low-and middle-income countries [1]



The ambitious goals that the international community has set itself – ending the epidemics of AIDS, tuberculosis and malaria by 2030 – will require a paradigm shift in the global response to these diseases in the coming years. It is imperative to move away from a “business-as-usual” approach to an accelerated response, underpinned by the accelerated use of innovative medicines, diagnostics and approaches in countries where the majority of the disease burden is occurring.

1.2 Intellectual property rights and access to medicines

The patent system is designed to support innovation and, at the same time, offer a mechanism to ensure that such innovations are accessible to society.[2] For more details on patents, innovation and access, see Annex 1.

Patents have been effective in stimulating and rewarding innovation in several of the disease areas that Unitaid works on. For example, antiretroviral medicines have been instrumental in reducing the number of deaths from HIV (as shown in Figure 1), and since their initial introduction in the late 1990s, a number of new and better medicines have been developed and entered the market – and innovation is continuing.[3,4]

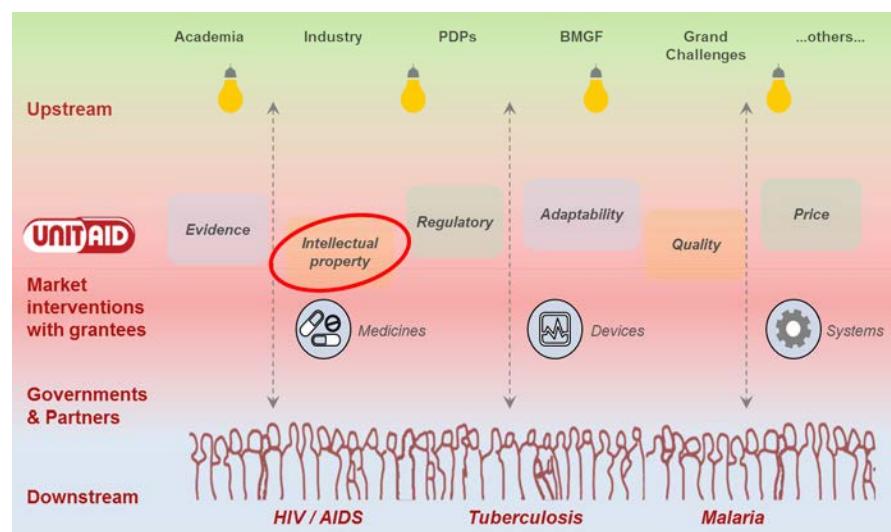
Furthermore, nine new medicines (direct acting antivirals) for the treatment of hepatitis C have been launched in late 2013 and 2014. Three other hepatitis C medicines have received their first marketing approval in the first half of 2016, and more hepatitis C medicines are in the pipeline.[5-7] Combinations of these medicines are able to cure the vast majority of patients within 12 weeks, and are revolutionizing hepatitis C treatment and care.

But while patents can stimulate innovation, they can also limit competition; as a result of the latter, prices of patented medicines may remain a barrier to broad access.

1.3 Intellectual property rights are one of several potential barriers

Efforts to facilitate and speed up access to better medicines and diagnostics can be hampered by several barriers (see Figure 2); intellectual property barriers can be the cause of some of these barriers to access.

Figure 2. Barriers between upstream innovation and downstream access



These various potential barriers are important, as all can delay and hamper access to medical products. Thus, all of them need to be addressed, and need to be addressed in a timely manner, in order to accelerate the global response.¹ Unitaid has both the ability and the mandate to do this; Unitaid's Constitution states "Where intellectual property barriers hamper competition and price reductions, it will support the use by countries of compulsory licensing or other flexibilities under the framework of the Doha declaration on the Trade-Related Aspects on Intellectual Property Rights (TRIPS) Agreement and Public Health, when applicable."²

Moreover, several of these barriers are common across the diseases Unitaid works on – and the approaches and tools to overcome them, too, are not specific to one disease or disease area. A common approach can therefore be used across several diseases.

This paper focuses on intellectual property related barriers to access and sets out Unitaid's approach to resolving them.

NOTE: Readers who are less familiar with intellectual property rights (IPR) and their implications for public health and access to medicines/medical products may wish to read Annex 1 – which briefly sets out the main issues – before continuing reading the subsequent sections of this paper.

1.4 Global goals and rules

In the area of intellectual property, there are no goals that are directly comparable with the global goals in the diseases Unitaid works on. There are, however, "global rules" for intellectual property rights, notably the TRIPS Agreement (see Annex 1, section A.1.5).³

The stated objective of the TRIPS Agreement is that "The protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations." [8]

There are global goals and targets in the diseases that Unitaid works on: HIV, TB and malaria. In May 2016, the World Health Assembly has, for the first time, adopted global goals for viral hepatitis, including hepatitis C. These goals, and the challenges to reaching them, are described in Unitaid's disease narratives.⁴ For several of these diseases, progress toward achieving the global goals is affected by intellectual property barriers (see section 3).

¹ For more details on the various barriers and the fact that they all need to be addressed, see the submission to the United Nations Secretary-General's High-Level Panel on Access to Medicines, entitled "Accelerating access to innovation: lessons learned by Unitaid". Available:

<http://www.unsgaccessmeds.org/inbox/2016/2/26/unitaidb>

² Unitaid Constitution, paragraph 1.2.

³ The TRIPS Agreement is not a "global" agreement in the sense that it does not apply to all countries; it applies only to WTO Members. However, as of March 2016, 162 countries and territories are WTO members, and another 21 are in the process of seeking WTO membership. Thus, the TRIPS Agreement does or will apply to the majority of countries.

⁴ The disease narratives are available at: <http://www.unitaid.eu/en/resources/publications/disease-narratives>

2 Partner landscape

2.1 Partners working upstream

Key partners support upstream innovation, with R&D carried out by academia, industry, research institutes and product development partnerships (PDPs), among others. Some of these upstream innovators are supported by donors/funders (such as the Bill and Melinda Gates Foundation) or by Governments.

It is estimated that 60% of health R&D is funded by the private sector, 30-35% is funded by the public sector, and the remainder is coming from other sources, including private non-profit organizations.[9,10] In 2009, total investment in health R&D was estimated at US\$ 240 billion.[9] It has been estimated that roughly 8-15% of global turnover on pharmaceuticals is reinvested into R&D by the private sector⁵. Traditionally, universities and public research institutes have focused on basic research, with industry doing most of the development; this is however changing.[11]

These upstream partners use IPR, but do so primarily in order to protect their commercial interests or to obtain/share in the financial benefits from their inventions.

Exceptions exist, notably the PDPs. PDPs focus on the development of products for which there is a limited market (due to small numbers of patients or patients generally living in poverty); there are PDPs that focus on the development of products for malaria and TB (as well as neglected diseases). There are no PDPs that focus exclusively on the development of HIV or HCV medicines, though the Drugs for Neglected Diseases Initiative (DNDi) does work on the development of 'missing' products for HIV and HCV, such as certain needed HIV paediatric formulations. While PDPs also use IPRs and may file for patents, they manage their intellectual property portfolio in manner that favours access; however, their leverage varies on a case-by-case basis, and they can only influence or manage IPR of products they substantially help develop.

2.2 Partners working downstream

Downstream, the delivery of commodities to patients who need them is generally undertaken by countries and implementers supported through funding partners such as the Global Fund, multilateral and bilateral partners.

These downstream partners may be affected by IPR; for example, patents may prevent them from purchasing an affordable generic medicine. When this happens, they may try to overcome patent barriers, for instance via a compulsory license⁶ or by opposing patents or patent applications⁶. However, these remedies are used relatively infrequently as their use requires significant legal and technical expertise and the process tends to be lengthy. Instead, downstream actors usually decide to purchase the more expensive originator product, opt for a clinically inferior alternative product, or forego the purchase altogether.

Valuable perspectives on availability and delivery, allowing Unitaid to anticipate and respond to country needs, are provided by WHO as well as non-governmental organizations (NGOs) and civil society – including representatives of communities living with the diseases. A number of NGOs and civil society organizations have developed significant expertise and

⁵ According industry estimates (or estimates based on industry data), around 15% of global turnover on pharmaceuticals is reinvested into R&D by the private sector.[12,13] Industry estimates have been criticized [14-17]; according to some, half of this (i.e. 7-8%) would be more accurate [18,19].

⁶ For a brief explanation of compulsory licensing, patent oppositions and other TRIPS flexibilities, see Table 3 in Annex 1.

know-how with regard to IPR and public health, and play an active role in safeguarding access to medicines. Most, however, have insufficient human and financial resources to work on a large scale. Moreover, in many low- and middle-income countries, there is limited legal and technical expertise on IPR.

In addition, organizations that work on intellectual property rights include national, and sometimes regional, intellectual property offices. At the international level, the World Intellectual Property Organization (WIPO) and the World Trade Organization (which administers the TRIPS Agreement) are primarily concerned with the functioning and implementation of IPRs.

A number of multilateral organizations (notably UNAIDS, UNCTAD, UNDP, WHO, WIPO and WTO) undertake analysis and/or provide guidance on intellectual property issues that interface with their area(s) of work; this may include medical innovation and/or access to medicines. Nevertheless, these organizations do not normally identify intellectual property barriers for specific medical products, nor do they implement solutions to overcome specific IPR barriers at a large scale, in order to ensure that people in low- and middle-income countries will have timely access to innovative products; Unitaid is unique in playing this role.

Unitaid's Constitution refers explicitly to addressing intellectual property barriers, where necessary. Key partners rely on Unitaid to address IPR barriers⁷. For a summary of Unitaid-funded projects that focus on addressing intellectual property barriers, see Annex 2.

3 IPR challenges threatening progress towards global disease goals

Each of Unitaid's disease narratives contains a comprehensive overview of the challenges that threaten progress towards achieving the global goals for each disease. The disease narratives furthermore identify, through a standardized process, those challenges where Unitaid's interventions would be most relevant. This process involved a prioritization based on four criteria:

1. Unitaid's expertise: focus on challenges that are inherently commodity access issues;
2. Potential public health impact: focus on challenges for which there is strong evidence of high potential public health impact;
3. Feasibility: focus on challenges for which the necessary technology already exists or can be available in the relevant timeframe;
4. Optimized use of resources: focus on challenges for which critical gaps exist in the global response and where scale up is possible.[21]

Following this prioritization exercise, each disease narrative contains a more focused set of disease-specific challenges that Unitaid potentially seeks to address.

For the purpose this paper, these focused, disease-specific challenges identified in the disease narratives have been reviewed with a view of identifying those challenges that may be caused, in whole or in part, by intellectual property barriers.

It was found that several disease narratives have identified multiple challenges where IPR may be a contributing factor, or have identified IPR as a root cause.[22-24] An overview of these disease-specific challenges is presented in Table 1.

⁷ The Global Fund's Market Shaping Strategy states: "The Global Fund will work closely with technical and development partners that focus further 'upstream' ... For example, Unitaid provides expertise on new product introduction, demand generation and intellectual property." [20]

Table 1. Challenges identified in disease narratives that relate to IPR

Disease	Challenge (from disease narrative)	Link with IPR
HIV	Lack of children formulations	Patent holders may lack incentives to develop paediatric formulations of HIV or TB medicines, as there is a limited market (there are few paediatric HIV or TB patients in high-income countries). Generic manufacturers may be interested in developing such formulations but patents, or other IPR barriers ^a , may prevent them from doing so.
TB	Children treated with suboptimal medicines	
HIV	High cost of 2nd and 3rd line medicines	
TB	Out-of-pocket costs of medicines	Patents, or other IPR barriers ^a , prevent generic competition. In the absence of competition, prices may be so high that people or health care systems cannot afford them.
HCV	New treatments not affordable	
HIV	Increased patent coverage of medicines	Root cause.
TB	Standard drug development not optimal for TB	Patents do not provide sufficient incentives for R&D for new TB medicines, as there is a limited market.
HCV	Companies develop "own" not "best" FDCs	Patent holders may lack incentives to develop and market combination tablets containing medicines from different patent holders (they may prefer to develop combinations of their own medicines, even if clinically inferior). Generic manufacturers may be interested in developing such formulations but patents, or other IPR barriers ^a , may prevent them from doing so.
HCV	Voluntary licences and access programmes exclude certain MICs	Voluntary mechanisms to overcome patent and other IPR barriers ^a on some HCV medicines are in place, but do not include all MICs.

^a For example data exclusivity (see Annex 1, section A.1.12).

To summarize, the disease narratives have identified three types of challenges where IPR (in particular patents) may play a role:

- patents/IPR can result in or contribute to a **lack of affordability** of innovative products;
- patents/IPR can **block or hamper the development of appropriate formulations** (such as fixed-dose combinations (FDCs) and paediatric formulations);
- patents do **not always provide sufficient incentive to stimulate R&D**, notably when the market is small, uncertain or concentrated in low income countries.

Box 1. Another challenge: patents and supply risk

Patented products are normally available only from a single supplier. This may increase the risk of supply shortages, in case demand exceeds production volumes or in markets that are not prioritized by the supplier. For example, in 2015, South Africa experienced difficulties in obtaining sufficient supplies of the HIV medicine lopinavir/ritonavir (LPV/r). Generic

versions were available elsewhere, but not in South Africa because this product is patented in South Africa.[25,26]

Subsequently, a voluntary license with the MPP sought to remedy this situation.[27,28]

4 Tools to address intellectual property challenges

As mentioned above, the disease narratives start with an overview of all challenges, and then select the relevant ones where Unitaid could consider intervening. Unlike the diseases, Unitaid is not working on IPR issues in order to resolve challenges in the intellectual property system per se or to contribute to the achievement of a specific “IPR goal”.⁸ Unitaid is interested in resolving situations where IPR create a barrier to access or fail to incentivize the development of needed medical products. Thus, the priority IPR-related challenges that Unitaid will work on are informed by the disease narratives and are listed in Table 1 above.

4.1 Tools to address intellectual property barriers to affordability and to appropriate formulations

There is a vast body of literature on IPR and access to medicines. It includes, but is not limited to, reports and papers prepared in the context of the various international processes summarized in Annex 1 (section A.1.9). Solutions (or tools) to overcome IP barriers are described with varying degree of detail in this body of literature.

Essentially, within the intellectual property system, tools to overcome IP barriers that contribute to the lack of affordability and appropriate formulations exist. The number of available tools is however limited; these tools can be grouped into three broad categories:

- Voluntary or collaborative approaches: notably the use of voluntary licenses⁹;
- Approaches based on the use of TRIPS flexibilities¹⁰;
- Approaches based on challenging the validity of a patent in Court.

Section 4.4 will further assess whether Unitaid should pursue or support the use of these tools to address the challenges identified in the disease narratives.

4.2 Tools to address the fact that patents do not always provide sufficient incentive to stimulate R&D

The patent system is designed to support innovation and, at the same time, offer a mechanism to ensure that such innovations are accessible to society.[2] Patents aim to foster innovation in the private sector by allowing inventors to profit from their inventions.[29]

⁸ Unitaid however does and should support projects that are mainly or exclusively dedicated to addressing IP challenges pertaining to access to medical products or to medical innovation. IPR is a highly specialized field; thus, supporting dedicated IP-related projects, undertaken by organizations with appropriate technical and legal expertise, is the most effective approach. Attempts to include activities aimed at overcoming IPR barriers in projects with a broader aim have been unsuccessful, except where the grantee had significant in-house IP expertise.

⁹ For a brief explanation of voluntary licensing and other voluntary approaches, see Annex 1, section A.1.4.

¹⁰ The term “TRIPS flexibilities” is used here broadly to include all safeguards and flexibilities allowed under the TRIPS Agreement, irrespective of whether they are explicitly mentioned in TRIPS. For an overview and brief explanation of the main TRIPS flexibilities, see Table 3 in Annex 1.

This, however, presupposes that there is a market. It has been widely recognized that patents and other IPR do not provide an effective incentive for innovation “where the potential paying market is small or uncertain”.[30] See also Annex 1, section A.1.8.

At the international level, efforts are ongoing to identify new ways to pay for or encourage R&D for some of the situations where IPR do not provide sufficient or effective incentives for the development of new health products – including for the so-called “neglected diseases” but also, for example, for new antibiotics.[31,32] In this context, ‘delinkage’ may be a relevant concept. Delinkage refers to delinking the price of the product from the cost of R&D in order to ensure access to the product.

Unitaid has not supported upstream research or development, to date, and support for early stage R&D is not consistent with Unitaid’s positioning. However, in line with its positioning, Unitaid has provided some support for late stage development/market entry of innovative products. For this type of projects, Unitaid already has Guidelines on Access & Intellectual Property for Market Entry Projects (discussed and endorsed at PSC11 and presented at EB20 in 2014) that aim to ensure access.¹¹

Unitaid could nevertheless contribute to efforts to identify possible sources or ‘delinked’ mechanisms for funding R&D, and could help analyze the potential impact on market dynamics and downstream access. Unitaid could also explore the potential role and modalities of implementing “delinkage” in the context of late stage development/market entry projects, if any.

4.3 Supporting actions

Promoting and protecting TRIPS flexibilities. The potential impact of using TRIPS flexibilities can be significant (see Table 5 in Annex 3). Moreover, in countries that are not included in voluntary licenses, the use of TRIPS flexibilities is the only option if patent barriers cause medical products to be unaffordable or unavailable. It is therefore important that countries include, in their national legislation, TRIPS flexibilities that will allow them to protect public health and access to medicines, and that they do not give up or limit their ability to use these flexibilities. The latter can happen for example in the context of bilateral or regional trade negotiations (through the inclusion of “TRIPS-plus” provisions in such agreements). Unitaid can support the promotion and protection of TRIPS flexibilities through the provision of information and analysis. It can also do this by engaging in and supporting policy dialogues with policymakers and lawmakers as well as by raising awareness of patients and the general public.

Finally, **the availability of data and information** on patents and patent status is crucial to identify when and where patents create or contribute to barriers to access. It is also required to determine whether generic versions of a medicine can be used in a given country. Information contained in patents is, and is intended to be, publicly available. Nevertheless, obtaining and interpreting patent information can be time consuming and requires technical and legal expertise. Access to patent data and information is also necessary for Unitaid to identify barriers and opportunities, to assess the potential value for money of proposed interventions and to evaluate impact.¹² Unitaid expects its projects to make patent

¹¹ These Guidelines contain requirements that fall in two broad categories:

- Requirements that aim to ensure access to the product(s) whose market entry Unitaid supports; they focus on availability (registration, launch and supply) and affordability (price).
- Requirements related to IPR pertaining to such product(s), including requirements that will enable Unitaid to intervene in the event that the developer breaches agreed terms related to availability and affordability of the products in question and fails to remedy this in a timely manner.

¹² Thus, the Secretariat at times commissions papers or studies on IPRs, innovation and/or access.

information, collected in order to execute the project activities, available; this would certainly apply to projects that focus on addressing intellectual property issues.

4.4 Selection of tools

Tools to address intellectual property challenges are inherently related to commodity access, and there is a gap in the global response with regard to intellectual property challenges (see section 2).

This section focuses on feasibility and impact in order to select tools and approaches that Unitaid will use to address intellectual property barriers (i.e. it focuses on the tools mentioned in section 4.1: i) voluntary approaches/voluntary licensing, ii) TRIPS flexibilities and iii) challenging patents in Court).

4.4.1 Feasibility: focus on pragmatic solutions

The TRIPS Agreement allows countries to maintain some flexibility in implementing their intellectual property regimes and contains several clauses (“safeguards”) that can be used to protect public health. The freedom to implement TRIPS in accordance with national needs allows countries to, for instance, have stringent patentability criteria in order to ensure that only significant innovations are patented. It also allows countries to have simple procedures for the use of compulsory licensing and government use, and to have a patent opposition system open to the public.

These flexibilities and safeguards are also in line with other multilateral intellectual property treaties, and most national patent laws or intellectual property laws contain one or more safeguards and/or flexibilities.

Thus, there are mechanisms, within the patent system, that can be used to overcome patent barriers or to prevent misuse of patent rights, notably:

- i. *Voluntary or collaborative approaches*: notably the use of voluntary licenses.
- ii. *Approaches based on the use of “TRIPS flexibilities”*: notably compulsory licensing, parallel importation, stringent patentability criteria and opposition procedures.
- iii. *Lawsuits*: patents can be challenged in Court.

Voluntary licenses are regularly used between companies. A patent holder can grant a voluntary license to enable another manufacturer to produce and sell generic versions of a medicine, even where patents exist. The license establishes in which countries the generic company can sell its product, and usually contains other conditions. Normally the patent holder receives royalties from the sales of licensed generics.

Similarly, it is not uncommon for pharmaceutical companies to challenge competitor’s patents and patent applications through opposition procedures or through the courts.

Compulsory licenses, like voluntary licenses, allow generic manufacture and supply even where a patent is in force. Compulsory licenses, however, are not granted by the patent holder; instead, the government steps in and grants the license, normally in order to achieve an overriding public interest. There have also been instances where courts have ordered a patent holder to issue a license to a competitor, for example to prevent or remedy anti-competitive behaviour by the patent holder.[33]

When companies use these mechanisms, they do so to achieve their commercial objectives. However, the same mechanisms can also be used to achieve public health objectives – in fact, Unitaid already supports projects that use some of these mechanisms:

- *The Medicines Patent Pool* (MPP) is an innovative solution created and supported by Unitaid. The Medicines Patent Pool negotiates “public-health oriented” voluntary licenses for medicines, and functions as a “pool” for such licenses – i.e. a one-stop-shop where licenses for multiple products are available for interested generic manufacturers.
- *The Lawyers Collective and the International Treatment Preparedness Coalition* projects aim to facilitate access to selected medicines in five middle-income countries through the use of TRIPS flexibilities.

Both voluntary and non-voluntary approaches can play an important role in facilitating access to medicines. The pooled voluntary approach of the MPP has the advantage of being a collaborative approach, and of covering multiple countries simultaneously. Nevertheless, because they involve agreement by the patent holder, voluntary licenses do not include all middle-income countries; in countries excluded from voluntary licenses, the use of TRIPS flexibilities is the only remaining option. In this sense, the two approaches complement each other.

There are other ways in which voluntary licensing and TRIPS flexibilities may be able to complement or reinforce each other. For example, it may be possible to use the “threat” of a compulsory license to increase the likelihood that a country will be included in a voluntary license. Indeed, the fact that Indonesia has issued several compulsory licenses may have been a factor in its inclusion in HCV voluntary licenses¹³.

Box 2. Voluntary licensing and TRIPS flexibilities working in tandem (example)

MPP licenses contain provisions that enable sub-licensees to supply to countries not included in the license when there is no patent. The latter can be due to various reasons, including use of TRIPS flexibilities (e.g. a successful patent opposition or issuing of a compulsory license). In that situation, the benefit of the MPP license would be that there is a source of supply, which otherwise might not be the case. Another example is summarized below:

- In 1998, Gilead filed a patent application for an HIV medicine, tenofovir disoproxil fumarate (TDF), in several countries, including India.
- In January 2006, WHO recommended that TDF be used as part of the first line regimen for the treatment of HIV.
- In May 2006, oppositions were filed to the TDF patent application in India. Shortly thereafter, Gilead signed voluntary licenses for TDF with the major Indian generic manufacturers. This enabled those companies to start producing generic TDF and supplying it to the 95 countries in the license.
- In September 2009, the patent application was rejected (i.e. the TDF patent was not granted in India). The generic manufacturers that had signed Gilead’s license, however, still could supply only to 95 countries, as they were bound by the license.
- In July 2011, the MPP signed a license with Gilead for four HIV medicines, including TDF. This license covers 17 additional countries (in addition to the 95 countries in the earlier Gilead licenses). It also has provisions that allow generic licensees to terminate the license for one or more of the included medicines.
- Several generic manufacturers then switched from their original TDF license with Gilead to the MPP license. Some of those subsequently terminated the MPP license with regard to TDF; this enabled them to supply TDF to additional countries – outside the licenses – where

¹³ Indonesia has issued compulsory licenses for various HIV medicines in 2004, 2007 and 2012; it is included in the HCV voluntary license by Gilead as well as the BMS-MPP HCV voluntary license. Compulsory licensing was also used to increase leverage in price negotiations, e.g. in Brazil.[34,35]

TDF is not patented, such as El Salvador, Georgia, Paraguay and Tunisia.

- Savings, due to lower or no royalties, began to be realized in 2012¹⁴.

Within the patent system, mechanisms exist to overcome patent barriers. Some of these are already being used by Unitaid:

- i. Voluntary approaches/voluntary licenses;
- ii. TRIPS flexibilities.

4.4.2 Potential public health impact

The impact of the MPP/voluntary licensing approach, as of 31 December 2015:

- more than 3 billion tablets – equivalent to 9.1 million treatment years – have been supplied by MPP sub-licensees to people living with HIV in 121 countries.
- due to lower prices, budgets for procuring these treatments were US\$ 194 million lower than they would have been at the original price (see Figure 3).

These results are essentially¹⁵ due to one license (signed in July 2011)/one molecule: TDF.

Impact from all subsequent MPP licenses is yet to be realized; the MPP expects that several of its sub-licensees will complete the development of new generic products and start applying for regulatory approvals in the second half of 2016 or early 2017.

The impact of the MPP's licenses consists of two components: savings (reduced budget for treatment of people who already were on treatment before the MPP's intervention) and increased coverage (due to lower prices). The MPP has built a model that estimates the impact of its work (savings as well as increased coverage) in terms of the lowering of treatment cost due to the MPP's intervention; these estimates are summarized in Annex 3.

The impact from projects using TRIPS flexibilities is mostly yet to materialize, as the final decision (whether the opposed patents will be granted or not) is still pending. This relatively long time to impact is not unusual for opposition procedures¹⁶; for example, in India, it took more than 3 years from the filing of oppositions to the final decision on the TDF patent application. Thereafter, it took another 2.5 years before savings due to the use of generics began to be realized (see Box 2).

Nevertheless, one Unitaid funded project using TRIPS flexibilities (the ITPC project, see Annex 2) already reported an early impact: one of its pre-grant oppositions already resulted in savings in the first year. These savings amount to US\$ 10 million for one HIV medicine in one country in one year.

Projections regarding potential savings and budget difference¹⁷ due to the use of TRIPS flexibilities have been developed and are summarized in Annex 3. While these projections

¹⁴ Royalties are 3% in the MPP license, versus 5% in the earlier Gilead licenses. No royalties apply when there is no license (as there is no patent in India).

¹⁵ 1% of impact (in terms of the number of treatments supplied) relates to other medicines.

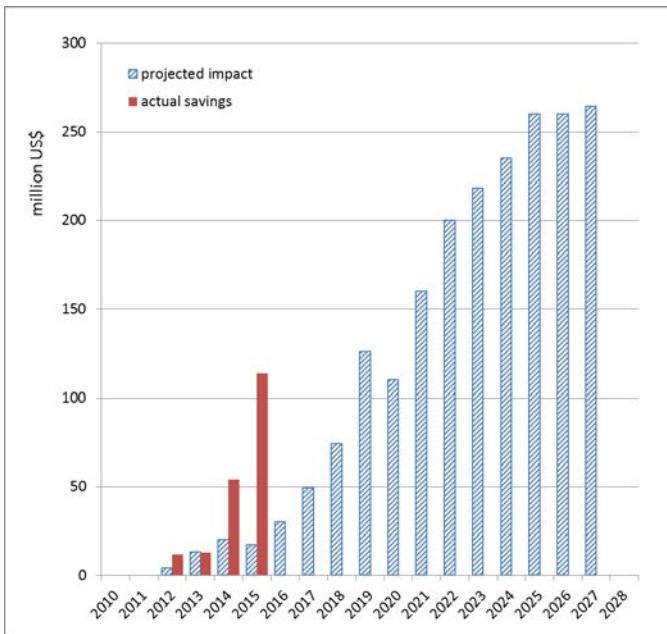
¹⁶ There also is a relatively long time to impact for other intellectual property interventions, such as voluntary licensing (see Annex 2).

¹⁷ For people who are on treatment already, price reductions result in savings. Lower prices may also enable treatment of a larger number of people. Thus, total expenditures on treatment may increase.

obviously are estimates, they enable comparison of the potential impact of the use of voluntary approaches with the potential impact of using TRIPS flexibilities.

The potential impact (see Annex 3) can be substantial, in particular for HIV and HCV. As these are estimates, the numbers can be questioned. To put this into perspective, it may be noted (as mentioned above) that actual data are already available for pooled voluntary licensing for HIV medicines through the Medicines Patent Pool. These data show that the actual impact over the period 2012-2015 was more than three times the estimated amount (see Figure 3).

Figure 3. Projected impact and actual savings from MPP HIV licenses, in million US\$ (2012-2028)



Source: Medicines Patent Pool. Notes: For the period 2016-2028, the most recent/high end estimates are represented in Figure 3. Projections for 2012-2015 were made – using the same methodology – before the actual data became available.

In addition, there may be other, indirect effects related to the use of voluntary licensing and TRIPS flexibilities, for example the fact that some originator companies are no longer applying for or enforcing patents in least-developed countries¹⁸ or that a pre-grant opposition in one country can be the basis for similar pre-grant oppositions in other countries. Similarly, the use of flexibilities to protect public health and access to medicines in one country may encourage other countries to do the same.¹⁹ Indirect effects can expand to diseases beyond those that Unitaid is working on.¹⁸

Both voluntary licensing and the use of TRIPS flexibilities can potentially have a significant impact/result in significant savings, which – if reinvested in health – substantially increase the number of people that can be treated.

¹⁸ For a recent example, that goes beyond HIV, TB and malaria, see the announcement by GSK.[36]

¹⁹ During the Consultation on Intellectual Property Approach at Unitaid on 25 May 2016, the use of a pre-grant opposition to a patent application pertaining to the hepatitis C medicine sofosbuvir at the European Patent Office was cited by various experts as an example.

5 Summary of identified needs and next steps

5.1 Summary of identified needs

Starting with the intellectual property-related challenges that have been identified through the disease narratives, this document has identified tools that exist to address these challenges, and has assessed the relevance and potential usefulness of those tools. This assessment, which has also been informed by Unitaid's experience to date in addressing intellectual property barriers finds that **there is a need for continued support to both voluntary licensing**, notably pooled voluntary licensing through the Medicines Patent Pool, as well as **the use of TRIPS flexibilities** as a way to accelerate access to affordable, innovative medical products. These two approaches can be – and often are – complementary (see section 4.4.1), and either strategy has the potential to achieve significant impact (see Tables 5 and 6 in Annex 3) and value for money.

Addressing intellectual property barriers can be undertaken through “stand-alone” grants (investment in projects that aim to work exclusively or mostly on IPR). In addition, at times activities to overcome intellectual property barriers can be incorporated in other projects.

Moreover, there is a need to highlight the importance of TRIPS flexibilities for public health, and a need to protect them – including by drawing attention to the negative implications of “TRIPS-plus” provisions on access to medicines.

Finally, data and information on the patent status of key products is essential in order to set priorities and assess the (potential) impact of interventions. This information is also very useful for others, notably procurement agencies.

Table 2. Relevance of various tools to address IPR challenges to Unitaid's model.

Tools	Challenges	Lack of affordability (high price)	Lack of appropriate formulations	Late stage development/ market entry	Insufficient incentives for R&D
Support the use of voluntary licensing, notably pooled voluntary licensing	+++	+++	+-	-	
Support the use of TRIPS flexibilities	+++	+++	+-	-	
Support challenging the validity of patents in Courts	+/-	+/-	+-	-	
Apply Unitaid Guidelines on Access & Intellectual Property for Market Entry Projects	N/A	N/A	++	N/A	
Explore new ways to fund R&D, incl. delinking R&D costs and price	+/- ²⁰	+/- ²⁰	+/- ²⁰	+/- ²⁰	
Supporting actions					
Support the promotion and protection of TRIPS	++	++	N/A	-	

²⁰ Not directly relevant in view of Unitaid's current mandate; however, Unitaid could play a role in assessing potential impact and could contribute to the debate on new/delinkage mechanisms.

flexibilities				
Support the availability of information and data on patents and patent status	++	++	+	-

+ to +++ = relevant to highly relevant; - = not relevant or not in scope; N/A = not applicable.

5.2 Recommendations for Unitaid's approach

5.2.1 Suggestions from consultations

On 25 May 2016, Unitaid held a first consultation on its future intellectual property approach. Experts participating in the consultation **confirmed the approach** proposed by the Secretariat and described above.

During the consultation, a number of issues were highlighted and several recommendations were made:

- **Intellectual property related challenges** to access to medicines **are likely to increase** as more patents are granted in more countries, and as demands and pressures on countries to enact and implement “TRIPS-plus” legislation increase.
- **Unitaid should continue to address intellectual property barriers.** Addressing IPR barriers is in line with Unitaid’s mandate – and represents a **major challenge** in the global response.
- **TRIPS flexibilities** and pooled voluntary licensing through the **Medicines Patent Pool** are **complementary**, and **Unitaid should continue to support both**. Unitaid’s funding enables the MPP to implement high standards and to focus on maximizing public health benefits. TRIPS flexibilities are crucial to ensure access in countries or among populations that are not included in voluntary licenses. They can also be used to encourage voluntary licensing. Implementation target 3.b of the SDGs makes explicit reference to using TRIPS flexibilities to provide access to affordable essential medicines.²¹
- **In many countries there is a lack of expertise**, including on how to implement and use TRIPS flexibilities. Thus, there is a **need for sustained knowledge and action** on IPR and access to medicines/medical products. Specific activities could include support for :
 - effective implementation of TRIPS flexibilities, for example the LDC pharmaceutical patent waiver;
 - law reform and “pro-public health” implementation of patent laws;

²¹ Target 3b of the Sustainable Development Goals reads: “Support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all.”[37]

- initiatives that will allow countries that are negotiating trade agreements to understand the potential consequences of TRIPS-plus measures on access to medical products.
- Unitaid should **engage with ongoing processes** such as the WHO's Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) and the UN Secretary General's High Level Panel on Access to Medicines (UN HLP), and should seek to **support the implementation of the recommendations** of these processes, when relevant and with partners.
- Unitaid could contribute to the debate on **new mechanisms** (e.g. a prize for innovation, implementing "delinkage"²²) **to incentivize innovation**, where relevant for its business model.

Further consultations have been held with relevant experts. Their comments have been used to update the IP Approach where relevant.

5.2.2 Next steps

The following **next steps** are proposed:

- **Medicines Patent Pool:** The Executive Board already agreed to fund the Medicines Patent Pool for the period 2016-2020 (Unitaid/EB21/2014/R13), and to expand the scope of the grant to the Medicines Patent Pool to include HCV and TB (Unitaid/EB23/2015/R6/Rev.1).
- **TRIPS flexibilities:** The Secretariat will continue to evaluate the results and impact of ongoing projects using TRIPS flexibilities, and will assess future opportunities in this area.
- **Engagement with ongoing processes:** The Secretariat is already engaging with and following the UN HLP and CEWG processes, and will consider the outcomes of these processes in its work. In order to identify opportunities for investment, the Secretariat has conducted an on-line consultation (from 25 August to 15 September 2016). A total of 36 submissions, containing over 90 suggestions, were received. For more information on the submissions, suggestions and opportunities identified, see *Update on intellectual property approach and potential opportunities*.
- Unitaid could **contribute to the debate on the potential impact of 'delinkage'** on market dynamics and downstream access. Unitaid could also explore the potential role and modalities of implementing 'delinkage' in the context of late stage development/market entry projects, as relevant for Unitaid's business model and positioning.

²² See Annex 1, section A.1.10.

Annex 1. IPR and access to medicines: a brief summary

Intellectual property rights (IPR) are legal rights that apply to creations of the mind.[38,39] Intellectual property is divided into two categories:

- *Industrial property*, which includes patents for inventions, and trademarks.
- *Copyright*, which covers literary works, films, music, artistic works (e.g. drawings, paintings, photographs and sculptures) and architectural design.[38,39]

In the context of debates on IPR and access to medicines/medical products, patents are the most important form of intellectual property protection. Thus, this paper, like most discussions on IPR and public health, mainly focuses on patents and contains less detail about other relevant IPR (such as data exclusivity, see section A.1.12).

A.1.1. Patents

The patent system is designed to support innovation and, at the same time, offer a mechanism to ensure that such innovations are accessible to society.[2]

A patent provides the patent holder with a *negative right*: the right to prevent others from making, using, importing, or selling his/her invention for a certain period of time. A patent does not give the inventor the right to sell a patented medicine; in order to be allowed to sell a medicine in a given jurisdiction, it has to be registered by the relevant regulatory authority²³.

Because a patent may result in market exclusivity, patents provide the inventor the opportunity to recoup investments by charging higher prices than would be possible in a competitive environment.

The patent system is intended to strike a balance between incentivising innovation (by rewarding innovators), and ensuring the public can benefit from innovations. In practice this balance is not always achieved. Patents have incentivized the development and marketing of many new medicines, but patents on medicines also can create hurdles to access by excluding competitors from the market. Generic medicines cannot be produced and offered for sale during the time of the patent term; thus, the originator can keep prices high.

A.1.2. Obtaining a patent

To obtain a patent, an innovator (e.g. a pharmaceutical company or research organization) must file a patent application at the national patent office of each country in which it would like to obtain exclusivity. Each patent office is then responsible for examining the application and deciding whether the invention described in the application fulfils the criteria for patentability, i.e. the invention must be i) new, ii) exhibit an inventive step and iii) be industrially applicable.

The patent examination process generally takes several years and during that period the patent application is considered to be pending. If the invention is considered to meet the patentability criteria, the patent office grants a patent which confers exclusive rights on the patent holder, thus enabling the patent holder to prevent others (i.e. generic companies) from making, selling, importing or using the patented product or process in the country for

²³ E.g. in order to be able to produce or sell a medicine in the USA, it needs to be registered with the US Food and Drug Administration.

which the patent was granted. Some patent offices provide opportunities for third parties to submit patent oppositions during a specified period of time.

A.1.3. Patents on medicines²⁴

Patents may be granted for new products such as new medicines, or for processes for manufacturing those medicines. Product patents may be granted on new molecules (often referred to as “base” patents or “compound” patents), or on specific forms or formulations of medicines (often referred to as “secondary” patents). The former may relate to finished pharmaceutical products or to the active pharmaceutical ingredient. The latter could include, for example, a particular salt form, an oral solution or tablet formulation of a given medicine, or a fixed-dose combination that combines more than one compound into a single tablet. Some secondary patents are relevant to paediatric formulations of a medicine but do not cover formulations for adults (or vice versa). In practice, new medicines are generally covered by more than one patent or patent application.

Patents are territorial rights, which means that they have effect only in the specific territory for which they were granted. Usually the territory is a country, but there are also some regional patent offices that grant patents for a group of countries. As a result of the territorial nature of patents, a product may be patented in some countries but not in others.

Despite the territorial nature of patents, it is important to note that the existence of patents in the countries where most medicines are currently manufactured (notably India) may be sufficient to ensure exclusivity across developing countries to the patent holders. This is because patents in manufacturing countries could be used to prevent the production – and therefore prevent export – of the patented medicine to other countries. Thus, in order to understand whether there are patents that may have an impact on market competition in a country that imports medicines, it is often necessary to review the patent status in countries that are likely to manufacture the medicines as well as in the importing country.

A.1.4. Voluntary licenses and other voluntary approaches

During the life of the patent, the patent holder may exercise the right to block others from manufacturing, selling, importing or using the patented product. However, the patent holder may also choose to allow other (generic) manufacturers to make or sell the product. This is generally done through a “voluntary licence”. In the voluntary license, the patent holder states the conditions that the licensee (the recipient of the license) has to comply with.

Licensing terms and conditions generally specify the countries in which a medicine may be made or sold by the licensee, whether the licensee is allowed to develop fixed-dose combinations, whether royalties are payable to the patent holder, and a wide range of other provisions that indicate what the licensee may and may not do. Voluntary licensing between companies is not uncommon; however, the full terms and conditions of such licences are usually confidential.

Apart from voluntary licensing, there are other voluntary approaches (or mechanisms whereby the patent holder voluntarily allows others to produce or sell the product); notably, the patent holder may announce a commitment not to enforce its patents in certain countries. This may be done through a non-assert declaration, a commitment not to enforce, an immunity-from-suit agreement or similar mechanism. The practical effect of these

²⁴ This section focuses on medicines as there are clear examples of patent barriers affecting access to innovative and appropriately formulated medicines, and because the IPR-related challenges identified in the disease narratives related to medicines (rather than other health products), see Table 1 in section 3.

approaches is often similar to that of licences. Nevertheless, the scope and certainty of these mechanisms varies.

A.1.5. The TRIPS Agreement

Countries used to have considerable freedom to design their patent system to fit with their priorities and needs – for example, countries could determine the duration of the patent term. However, the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (or TRIPS Agreement) has to a large extent harmonised patent systems.

For instance, TRIPS makes it mandatory for countries to ensure that patent protection is available in all fields of technology. As a result, it is no longer possible for countries to exempt pharmaceuticals from patent protection – as a number of countries did, before TRIPS came into force. Because of the TRIPS Agreement, India had to start granting product patents for pharmaceuticals in 2005. Even though TRIPS contains a number of safeguards and flexibilities (see section A.1.6), this led to concerns over access to affordable medicines (see section A.1.7).

A.1.6. TRIPS flexibilities

Table 3 provides an overview and short description of the main TRIPS flexibilities. It also indicates how they can affect public health.

Table 3. Overview main TRIPS flexibilities

Flexibility	Description	Impact on public health
Bolar provision (also called “early working exception” or “regulatory review exception”)	A clause that can be incorporated into patent law which allows testing and regulatory approval of generic versions of a medicine before its patent expires.	Since generic manufacturers are able to develop their product and submit for/obtain registration during the patent term, they can start production and sale immediately after patent expiry. This accelerates availability of generic versions after expiry of the relevant patents.
Compulsory license	A compulsory license is a license granted by a government to allow the use of a patented invention without the permission of the patent holder. Compulsory licenses can be issued for various purposes, including to protect public health or to promote access to medicines.	Allows generic production, importation and use, during the patent term.
Least-developed country (LDC) transition period	LDCs do not have to implement or enforce TRIPS provisions related to patents and test data protection (data exclusivity) for pharmaceutical products, until 1 January 2033.[40]	In LDCs that make use of this transition period, production, importation, and use of generics is allowed (regardless of patent status or data exclusivity).
Parallel importation	Parallel imports refer to purchasing patented products in another country and importing them through a channel	Allows importation of a patented product from a country where the patent holder sells it

	parallel to the one authorized by the patent holder (and without the patent holder's consent).	at a lower price (during the patent term). Thus, parallel importation can enhance the affordability and availability of medicines.
Patent opposition (called "observation" in some jurisdictions)	Provision that allows third parties to submit information regarding a patent or patent application to the patent office. For example, an opponent may submit evidence that the key features of an invention have already been publicly disclosed. Opposition procedures are thus a tool that can contribute to higher quality of patents and legal certainty.	Opposition procedures can help prevent the granting of unwarranted patents/patents that do not meet the patentability standards. As a result, fewer patents may be granted; this can facilitate/accelerate generic competition.
Standards for patentability	In order to be patentable, an invention needs to meet 3 criteria: i) it should be new, ii) it should be inventive (i.e. it should not be obvious), and iii) it should have industrial applicability. However, countries have the freedom to apply stringent or lenient standards for novelty, inventiveness and industrial applicability.	Stringent or high standards generally lead to fewer patents being granted; this can facilitate/accelerate generic competition.

Notes: Adapted from [2] and [41]. This is not an exhaustive list.

A.1.7. Affordability and the role of India

Before 2005, India did not grant product patents for pharmaceuticals²⁵. As a result, Indian companies could legally produce generic versions of medicines that were still under patent elsewhere. As India was (and still is) a major supplier of affordable generic medicines to many low-income countries, the introduction of product patents in India led to considerable concern, both within and outside India, regarding access to affordable versions of medicines, in particular medicines developed after 2005.

The inclusion of robust safeguards in India's patent law has helped to alleviate those concerns. Due to these safeguard-mechanisms, and to the presence of actors (including civil society groups) using them, it has to some extent been possible to mitigate the anticipated negative implications of stronger patent protection on the supply of affordable generic medicines from India.

A.1.8. Patents and innovation

At the same time, it has become increasingly clear that the incentives to innovate, provided by the patent system, have limitations. In May 2003, the World Health Assembly noted that "... available data indicates that of some 1400 new products developed by the pharmaceutical industry between 1975 and 1999, only 13 were for tropical diseases and three were for tuberculosis." [42]

²⁵ India did grant process patents for pharmaceuticals; however, process patents offer less protection to innovators than product patents.

More recently it was noted that only 4 (1%) of 336 new medicines (new chemical entities) developed during the period 2000-2011 were for neglected diseases²⁶. During the same period, additionally, 514 new formulations or new indications of existing products were developed, but only 33 (6%) of those were for neglected diseases²⁶.[43]

These data underpin and confirm existing analysis that that the incentive provided by IPR “does not meet the need for the development of new products to fight diseases where the potential paying market is small or uncertain.”[30]

A.1.9. Multilateral discussions

Concerns regarding innovation and availability of affordable medicines have led to significant discussion in multiple international fora. At the World Trade Organization, concerns over prices of patented medicines this resulted in the adoption, in 2001, of the Doha Declaration on the TRIPS Agreement and Public Health, which re-affirms that the TRIPS Agreement contains safeguard mechanisms which can be used to protect public health. The Doha Declaration also states that TRIPS “can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all.”[44]

At the World Health Organization, these concerns resulted in the creation, in 2004, of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH). This was followed by the negotiation of a Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (adopted by the World Health Assembly in 2008), and subsequently by the creation of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG), mandated to examine the financing and coordination of research and development (R&D), as well as proposals for new and innovative sources of funding to stimulate R&D for diseases that disproportionately affect developing countries. This was followed by the implementation of a number of health R&D demonstration projects (ongoing), and further work on effective financing mechanisms for health R&D.[31]

In November 2015, the United Nations Secretary-General created a High Level Panel on Access to Medicines, to “review and assess proposals and recommend solutions for remedying the policy incoherence between the justifiable rights of inventors, international human rights law, trade rules and public health in the context of health technologies.”[45] Its creation highlights that concerns and unresolved challenges remain.

Through these and other multilateral processes, extensive analysis on IPR, innovation and access has been conducted – including by civil society organizations and academics.

A.1.10. Delinkage

In the context of these debates on stimulating innovation for diseases that predominantly affect developing countries, the need to ‘de-link’ the funding for R&D from the price of the product is increasingly being raised. The CEWG already noted:

“Delinkage is a powerful principle. The intellectual property system encourages a business model that allows developers of products to recoup the costs of R&D and to make profits through charging consumers on the basis of the exclusivity conferred by intellectual property rights. Depending on the pricing policies of the originator in developing countries, this can result in the patient, or those purchasing

²⁶ Neglected diseases were defined as: neglected tropical diseases (WHO definition), malaria, TB, diarrhoeal diseases plus 19 other diseases of poverty.[43]

on behalf of a patient such as a government or a health insurer, being unable to afford a life-saving treatment. Delinking, which can happen in a number of different ways, is a means of divorcing the funding of R&D from product pricing. Once a patent has expired, delinking occurs naturally because generic competition should bring the price down to levels determined by market conditions and the cost of production rather than by R&D costs.”[46]

The CEWG used delinkage as one of the criteria for assessing proposals for new and innovative sources of funding to stimulate R&D for diseases that disproportionately affect developing countries. Delinkage also was a recurrent theme in contributions to the High Level Panel on Access to Medicines (see section A.1.9).

A.1.11. “TRIPS-plus” provisions

In parallel with discussions on innovation and access, countries continued negotiating trade agreements. These often include so-called “TRIPS-plus” provisions.

“TRIPS-plus” is a widely used but informal term. It refers to a variety of provisions that i) impose a higher level of protection for IPR than is required under TRIPS, or ii) that limit countries’ options for legislating and using TRIPS flexibilities and safeguards. An example of a “TRIPS-plus” provision is data exclusivity (see section A.1.12).

The common feature of “TRIPS-plus” provisions is that they delay the marketing of generic products and competition. As such, they run counter to efforts to increase the affordability of, and access to, medicines and other medical products.

“TRIPS-plus” requirements are often found in bilateral or regional trade agreements (for example the Trans-Pacific Partnership Agreement²⁷).

A.1.12. Data exclusivity

While discussions on IPR and access to medicines are dominated by patents, patents are not the only form of IPR that can affect generic competition. Another important barrier is data exclusivity. Data exclusivity is a legal provision that provides originator companies exclusive rights over the data submitted to obtain regulatory approval²⁸. The effect of data exclusivity can be to delay the registration, and thus the use, of generic medicines.

Data exclusivity operates independently of patents. In the countries that provide data exclusivity, it can block generic competition for a certain period of time, even when there is no patent, by de facto delaying the registration of generics.

The TRIPS Agreement requires countries to protect undisclosed registration data, but does not require data exclusivity; thus, data exclusivity is “TRIPS-plus”.

²⁷ One example of a free trade agreement that contains “TRIPS-plus” provisions, including – but not limited to – data exclusivity, is the Trans-Pacific Partnership Agreement. Unitaid has conducted an extensive analysis of this Agreement.[47]

²⁸ During the data exclusivity period, the regulatory authority is not allowed to refer to or rely on the clinical test data submitted by the originator, for the purpose of registration of a generic product. As regulators in many countries indirectly rely on originator data when approving generics based on bio-equivalence data, generics cannot be registered during the data exclusivity period.

Annex 2. Current Unitaid funded intellectual property projects

An overview of current, Unitaid-funded intellectual property projects is provided in Table 4. These projects will be discussed in more detail below.

Table 4. Unitaid-funded intellectual property projects

Organization	Start date	Approved budget	Approach
Medicines Patent Pool	July 2010	US\$ 56.5 million (phase 1 and 2)	voluntary / collaborative approach
Lawyers Collective	August 2013	US\$ 677,100	use of “TRIPS flexibilities”
International Treatment Preparedness Coalition	November 2014	US\$ 6 million	use of “TRIPS flexibilities”

As new medicines, including pipeline medicines, appear to be increasingly widely patented (see Figure 4), the relevance of IP-related barriers to access may be increasing.

Timing, approach and impact of intellectual property projects

IPR are applied for relatively early in the product development chain²⁹; thus, interventions related to IPR may also have to take place relatively early in the value chain. This is, by definition, the case for pre-grant oppositions; however the MPP also has the experience that can be easier to obtain voluntary licenses when a product of interest is still in development.³⁰

This has two important consequences:

- *it is likely to take relatively long before impact materializes*: normally, generic manufacturers would start to develop their product only once a patent barrier has successfully been removed (i.e. after they obtained a voluntary sub-license or after the patent office rejected the patent application(s)³¹). Subsequently, the generic product may need to be prequalified and registered; only thereafter will it be purchased and used, and can start to generate savings. Generic development alone can take 2-3 years.
- *the potential impact can be very substantial*: because removing IP barriers and enabling competition may take place relatively early in the value chain, savings can accumulate over multiple years. In addition, all stakeholders that purchase the concerned medicine can benefit from more affordable prices, adding to the magnitude of the impact (savings).

Two projects (MPP and Lawyers Collective) also had a relatively long start-up time, see Figure 5.

All projects have, as an inevitable “by-product”, generated data on the patent status of medicines, and are making these data publicly available. This is important as patent

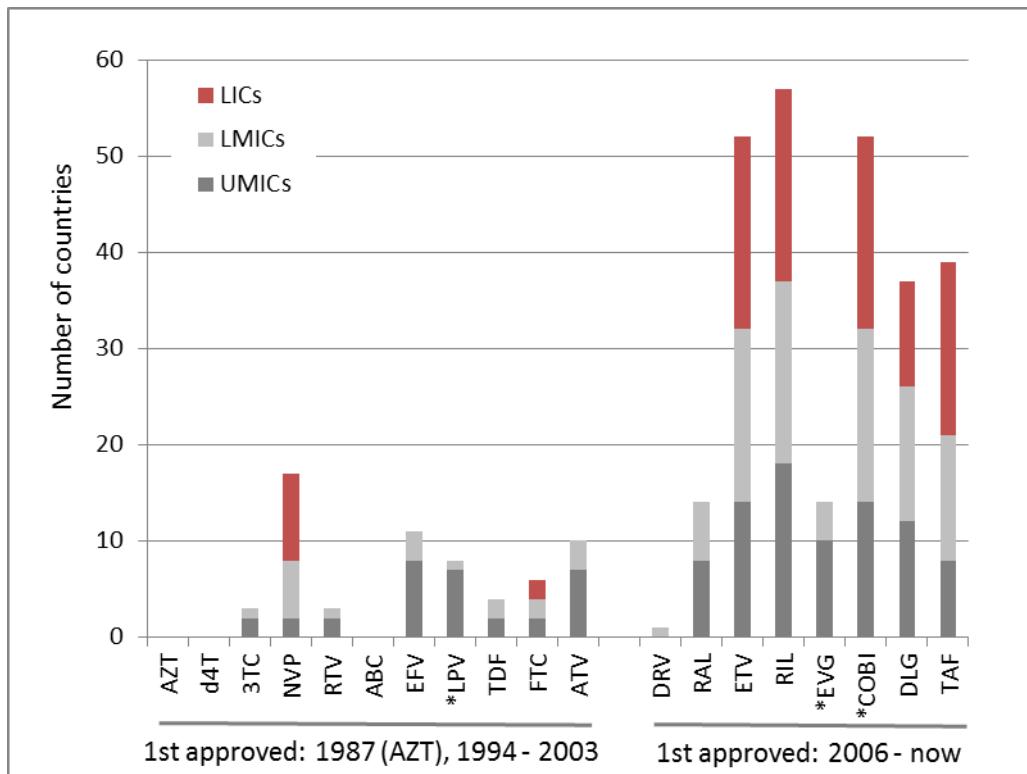
²⁹ The key patent (compound patent) is normally applied for when the product is still in clinical development.

³⁰ Though there is variation among different originator companies.

³¹ The decision of the patent office may be significantly later than the date of submitting the opposition; for example, in the case of TDF in India, it took more than 3 years (see Box 2).

information – though theoretically in the public domain – requires specialized expertise to find and is in practice hard to obtain or interpret for many stakeholders.

Figure 4. Number of countries where the main patent of selected ARVs has been granted or is pending



Notes: Based on information available for 80 countries in MPP database (Dec. 2013); “1st approved” refers to year of first approval in the USA [48]; * approved as part of an FDC.

Figure 5(a). Timeline of Unitaid IP grants, showing acceleration following initial start-up phase

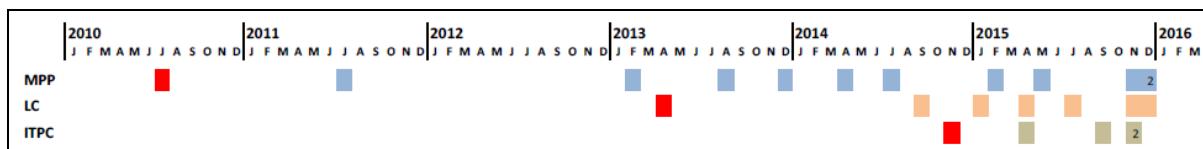
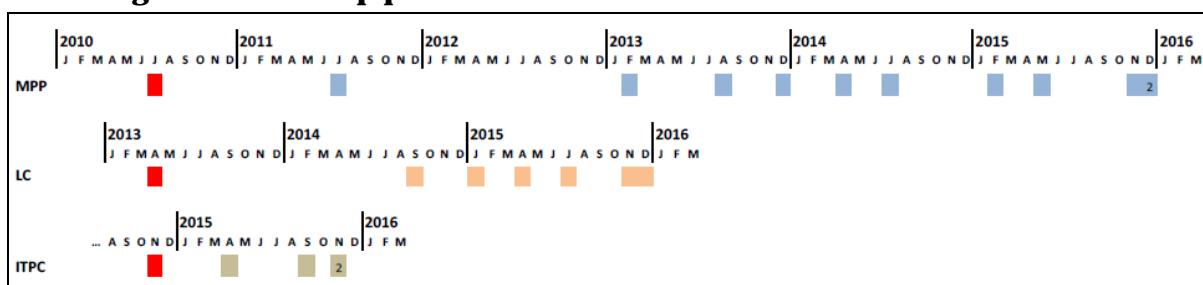


Figure 5(b). Comparative timeline of Unitaid IP grants, showing acceleration following initial start-up phase



Notes: Each coloured block represents a major event (in-license signed or opposition filed); the red block indicates the start date of the grant; 2 indicates two major events in the same month.

Medicines Patent Pool

Approach

The MPP is negotiating voluntary licenses for as many low- and middle-income countries as possible, in order to advance public health. The MPP subsequently signs sub-licenses with generic companies; this enables competition to start before the patents pertaining to a licensed medicine expire. Since the MPP holds licenses for different medicines from different companies, it also facilitates the development of fixed-dose combinations.

MPP licenses contain provisions that ensure compatibility with the use of TRIPS flexibilities; for example, MPP licenses allow sub-licensees to supply to a country outside the license in case a compulsory license is issued. Most commercial voluntary licenses, in as far as known, do not allow this (which leaves countries that do not have domestic manufacturing capacity potentially without a supplier, even if they would issue a compulsory license).

The sub-licensing process is based on a transparent and impartial process of selection among interested generic companies. The number of sub-licensees is determined based on forecasts of the market size, thus ensuring that there is competition but also enabling sub-licensees to obtain a viable market share.

Main results (as of 31 December 2015)

- Licenses for 13 HIV medicines and 1 medicine for HCV;
- Sublicenses have been signed for 11 HIV medicines and 1 HCV medicine;
- Licenses signed with 5 originator companies, the US National Institute of Health, 14 generic companies and 1 university. Other collaborations with 2 other originator companies;
- Data base with information on the patent status of 25 HIV medicines in 88 countries is available on the MPP's website³².

Note: During most of the period 2010-2015, the MPP's area of work related to HIV medicines only. In November 2015, the scope was expanded to include HCV and TB.

Impact (as of 31 December 2015)

- savings generated by the MPP's work amount to US\$ 194 million (see Figure 3).
- more than 3 billion tablets – equivalent to 9.1 million treatment years – have been supplied by MPP sub-licensees to people living with HIV in 121 countries.

These results, which have been calculated based on actual sales data of MPP sub-licensees, are essentially³³ due to one license (signed in July 2011)/one molecule: TDF.

Savings from all subsequent MPP licenses are yet to be realized; the MPP expects that several sub-licensees will finish to develop various products and start applying for regulatory approvals in the second half of 2016 or early 2017. Once these products enter the market³⁴, impact of the MPP's work could increase significantly, see projections in Annex 3 and Figure 3 in section 4.4.2.

³² See: <http://www.medicinespatentpool.org/patent-data/patent-status-of-arvs/>

³³ 1% of impact (in terms of the number of treatments supplied) relates to other medicines.

³⁴ Time for regulatory approval varies significantly among countries; WHO prequalification – though also variable – generally takes about a year. Only after regulatory approval can products be used and will they start to generate savings/have impact.

Lawyers Collective

Approach

The Lawyers Collective project seeks to prevent patent barriers on HIV, TB or HCV medicines in India, by making use of TRIPS flexibilities. The focus is on preventing the grant of patents that do not meet India's stringent criteria for patentability, through pre-grant oppositions. In some cases, the project may also seek to remove existing patent barriers through post-grant opposition.

In the absence of patent barriers, companies in India will be able to manufacture more affordable, generic versions of such medicines. This is crucial to ensure affordability of medicines within India, but also in many other low- and middle-income countries that import their medicines from India.

Main results (as of 31 December 2015)

- Six pre-grant oppositions have been filed; all cases are still pending at the Patent Office (i.e. the final decision on granting the patent has yet to be made);
- One reply to the applicant's response to the opposition has been submitted;
- Drafting of several oppositions is ongoing;
- Data base with patent information on 27 medicines in India is available on the Lawyers Collective website.³⁵

Impact

As the Patent Office in India has not yet made a final decision on whether or not to grant the patents that have been subject to any of the pre-grant oppositions under this project, there is no impact yet. This is not unusual; time between action and impact tends to be relatively long for work on IPR. This can be due to the time lag between the filing of an opposition and the decision whether the patent will be granted (e.g. for TDF this took more than 3 years, see Box 2) as well as because of other patents pertaining to the same medicine (see Box 3).

Efforts to quantify potential impact of the oppositions filed to date are currently ongoing.

The impact of several previous oppositions³⁶ in India has been quantified:

- A patent opposition on lamivudine/zidovudine in India resulted in withdrawal of the patent application. This led to savings of around US\$ 304 million, globally, during 2006-2011.³⁷
- Following an opposition, the Patent Office in India rejected, in 2008, a patent application for a paediatric formulation of nevirapine. This resulted in savings, globally, of more than US\$ 33 million during 2008-2011.^{37, 38}
- Around 60% of the MPP savings on TDF (as of 30 June 2015) are due to the combined effect of patent oppositions and the MPP's license (as described in Box 2).

³⁵ See: <http://www.lawyerscollective.org/drugs-list>

³⁶ These oppositions were filed in 2006, i.e. well before the Unitaid project.

³⁷ Savings are global savings as Indian suppliers provide most of the ARVs to L&MICs.

³⁸ The opposition was filed in May 2006. The decision by the patent office followed after 2 years (in June 2008).

International Treatment Preparedness Initiative (ITPC)

Approach

ITPC and partners are seeking to prevent or remove patent barriers on HIV medicines in 4 countries (Argentina, Brazil, Thailand and Ukraine) by using or encouraging the use of TRIPS flexibilities (patent oppositions, but also other flexibilities, e.g. the project advocates for stringent patentability criteria).

In the absence of patent barriers, the countries will be able to manufacture or import more affordable, generic HIV medicines that are already on the market and that are used in many other low- and middle-income countries.

Where necessary, the project will support law reform with the aim of ensuring that flexibilities, necessary to protect access to medicines, are included in national legislation. In addition, it aims to increase awareness of the importance of TRIPS flexibilities and the risks of TRIPS-plus provisions for access to medicines.

Main results (as of 31 December 2015)

- Four pre-grant oppositions were filed;
- Policy dialogues and actions to defend currently existing TRIPS flexibilities (e.g. ANVISA's involvement in pharmaceutical patent examination in Brazil), to prevent "TRIPS-plus" and to use other strategies to reduce prices;
- Data collection and research are ongoing to prepare for further oppositions and other use/defence of TRIPS flexibilities. Data will be on the website later in 2016.

Impact (as of 31 December 2015)

- Savings of US\$ 10-17 million have already been generated, because of pre-grant oppositions that have already catalysed procurement of generic products in one of the countries.³⁹ This is an early impact; impact from the use of pre-grant oppositions usually would take several years to materialize, see Box 3.
- Savings amounting to US\$ 55 million were realized in two other countries as a result of price negotiations (probably helped by the implicit "threat" of compulsory licensing).

Box 3. Acting now for future impact: example of a pre-grant opposition [49,50]

The combination product LPV/r is an important, WHO recommended HIV medicine. In Argentina, patents on LPV/r are currently in force. These patents will expire in 2018; thus, after 2018, generic LPV/r can be used in Argentina.

Abbott however has filed another patent application for LPV/r; if granted, it would expand Abbott's exclusive rights (and delay the use of more affordable generics) until 2025.

Under the Unitaid project, an opposition to this new patent application has been filed. If successful, the impact of this opposition will still start to materialize in 2018 (when the current patents expire).

That impact could be substantial: in 2015, over 5,500 patients were treated with LPV/r, at a

³⁹ Savings of US\$ 10 million are due to an opposition filed during the project. Dialogues and follow-up of an earlier opposition led to savings of another US\$ 14 million (50% of which was allocated to the grant).

price of US\$ 1,975 per person per year. Generic versions cost US\$ 300 per person per year. The use of generics could therefore result in savings of more than US\$ 9 million per year.

Yet, to realize these savings in/after 2018, it was necessary to oppose the patent application in 2015.

Annex 3. Estimated budget savings

As mentioned in section 4.4.2, the MPP has built a model that estimates the impact of its work in HIV (savings as well as increased coverage) in terms of lowering of treatment cost due to the MPP's intervention. The MPP has also commissioned reports that estimate the potential impact of voluntary licenses for TB and HCV medicines. These estimates are summarized in Table 5. With regard to HIV, the actual impact of the MPP's work over the period 2012-2015 was more than three times the estimated amount (see Figure 3 in section 4.4.2).

Table 5: Potential (projected) impact of pooled voluntary licensing to address patent-related access challenges

	Period	Countries	Budget difference (US\$)
11 HIV medicines	2015-2028	100-127 countries	1.39-2.04 billion
2 new TB medicines (bedaquiline & delamanid)	2015-2035	116 countries with ± 65% of the global MDR-TB burden	184 million
1 hepatitis C medicine (daclatasvir)	2015-2030	108-114 countries	1.29-1.70 billion

Note: For a summary of methodology and sources, see below.

Projections regarding potential savings and budget difference due to the use of TRIPS flexibilities have also been developed, and are summarized in Table 6.

Table 5: Potential (projected) impact of using TRIPS flexibilities to address patent-related access challenges

	Period	Countries	Budget difference (US\$)
4-6 HIV medicines	2015-2028	4 countries	678-942 million
2 new TB medicines (bedaquiline & delamanid)	2015-2035	22 countries with ± 21% of the global MDR-TB burden	59 million
1 hepatitis C medicine (daclatasvir)	2015-2030	13-19 countries	768 million - 1.17 billion

Note: For a summary of methodology and sources, see below.

At this stage, actual impact data that are directly comparable to the HCV and TB estimates in Table 5 and to the estimates in Table 6 are not available. In addition, in particular for HCV, the size of the actual market (solvent demand) in low- and middle income countries is not clear.⁴⁰

⁴⁰ It may be noted that the projected savings for HCV in Tables 5 and 6 for a period of 15 years are comparable to global sales of another HCV medicine (sofosbuvir) in the last quarter of 2015, or to about 2 months of current global sales of the HCV medicine sofosbuvir/ledipasvir.

Summary of methodology

Methodology for estimate 1: HIV medicines⁴¹

Pooled voluntary licensing: Assessments⁴², undertaken by the Medicines Patent Pool (MPP) for Unitaid, estimate the potential future savings to the international community (donors, national governments and out-of-pocket expenses by patients) due to generic competition for HIV medicines, enabled by the MPP's voluntary licenses. The assessments estimate the impact of generic competition for 11 HIV medicines licensed to the MPP over the timeframe 2015-2028 in 100-127 low- and middle-income countries (the number of countries varies per medicine/license). It is estimated that generic competition enabled by the MPP's voluntary HIV licenses would result in savings of US\$ 1392-2040 million.

The counterfactual scenario assumes that, for each medicine, the situation would essentially remain as it was before the MPP license was signed (including in terms of licenses and originator companies' pricing policies). For several medicines this means that the counterfactual scenario assumes a voluntary license covering a smaller number of countries.

According to the estimates, impact will increase over time (as shown in Figure 3) as generic products are being developed, registered in an increasing number of countries, included in national treatment guidelines, and ultimately used by increasing numbers of people.

Use of TRIPS flexibilities: A proposal submitted to Unitaid in 2014⁴³ estimates the potential savings from enabling generic competition for 4-6 HIV medicines⁴⁴ through the use of TRIPS flexibilities in 4 countries. The proposal estimates the potential savings for each product in each country for one year. Using the data in this proposal as a basis, Unitaid has been able to prepare a multi-year estimate, following the methodology used for the MPP's HIV estimates; potential savings from the use of TRIPS flexibilities in those 4 countries could amount to approximately US\$ 678-942 million over the period 2015-2028.

The counterfactual scenario assumes that no voluntary licenses would be granted (as the concerned countries are not included in such voluntary licenses). It also assumes that originator companies' pricing policies would not change dramatically.

Methodology for estimate 2: two TB medicines (bedaquiline and delamanid)

Pooled voluntary licensing: A study⁴⁵, commissioned by the MPP, has estimated the potential impact of generic availability of two new TB medicines (bedaquiline and delamanid), predominantly in terms of the number of additional people that could be treated if generic versions of these two medicines would be made available. The study, which focuses

⁴¹ The estimates in this section are partly based on unpublished material. Unitaid understands that the MPP is preparing to publish this.

⁴² MPP reports to Unitaid, 2012-2016; [51].

⁴³ ITPC proposal to Unitaid, 2014 and ITPC first project report, 2015.

⁴⁴ The number of medicines varied among the 4 countries.

⁴⁵ Trinity Partners and Elizabeth Gardiner. TB Strategic Expansion Assessment. April 2015. Available: <http://www.medicinespatentpool.org/wp-content/uploads/MPP-Intervention-in-TB-Trinity-Partners-.pdf>

exclusively on people with multi-drug resistant TB (MDR-TB)⁴⁶, estimates the impact of generic availability for the timeframe 2015-2035.

The study assumes that potential licenses would have a geographical coverage similar to some of the MPP's licenses for HIV medicines. Specifically, it is assumed that a voluntary license would include 116 low- and middle income countries that account for approximately 65% of global MDR-TB cases⁴⁷. For such a voluntary license, the study finds that 14,000 additional MDR-TB patients could be cured, 31,700 deaths could be averted and cost saving of US\$ 184 million could be realized.

Use of TRIPS flexibilities: It has been estimated that, of the MDR-TB cases found outside these 116 countries, approximately 14% are in high income countries (mostly Russia), while the remaining (\pm 21% of all MDR-TB cases) would be found in certain middle-income countries that are not included in the MPP's HIV licenses¹⁴. Assuming that those countries with \pm 21% of the MDR-TB burden where to use TRIPS flexibilities in order to enable the availability of generics, and that the impact would be proportionate to that in the 116 countries, this would amount to more than 4,500 additional MDR-TB patients cured, more than 6,800 deaths averted, and potential savings of US\$ 59 million.

For either approach, the counterfactual scenario assumes there would be no voluntary licenses and no use of TRIPS flexibilities (as, traditionally, both have not been used with regard to TB medicines). It also assumes that originator companies' pricing policies would not change dramatically.

Methodology for estimate 3: one hepatitis C medicine (daclatasvir)⁴⁸

Pooled voluntary licensing: An assessment⁴⁹ by the MPP estimates the potential future savings to the international community (donors, national governments and out-of-pocket expenses by patients) if generic competition would be possible for one hepatitis C medicine (daclatasvir). The study estimates the impact of generic competition for daclatasvir over a 15-year timeframe (2015-2030) for 4 scenarios: inclusion of 90, 108, 114 and 127 low- and middle income countries in the license.

Since the study was undertaken, the MPP has signed a voluntary license for daclatasvir, covering 112 countries. Its expected impact therefore would be between that for the 108 and the 114 country scenarios, i.e. this license would result in estimated savings of US\$ 1294 – 1700 million.

The counterfactual scenario assumes a voluntary license covering 90 countries, with a small number of sub-licensees, as per BMS' announced intention before signing the license with

⁴⁶ These are patients with few other options, thus, these new medicines are particularly important for them.

⁴⁷ The percentage of MDR-TB cases has been estimated by Unitaid based on: WHO, Use of high burden country lists for TB by WHO in the post-2015 era: summary. Available: http://www.who.int/tb/publications/global_report/high_tb_burdenCountrylists2016-2020summary.pdf and WHO, MDR-TB burden estimates for 2014. Available: <http://www.who.int/tb/country/data/download/en/>

⁴⁸ The estimates in this section are partly based on unpublished material. Unitaid understands that the MPP is preparing to publish this.

⁴⁹ MPP proposal to Unitaid, 2015 (Annex 14). The assessment is based on the scenarios and methodology in the report: Dalberg. Assessing the feasibility of expanding MPP's mandate into hepatitis C. April 2015. Available: http://www.medicinespatentpool.org/wp-content/uploads/MPP-Intervention-in-Hep-C_Dalberg_CDA.pdf; scenarios in this report have been updated and refined.

the MPP. It also assumes that originator companies' pricing policies would not change dramatically.

Use of TRIPS flexibilities: As the study methodology estimates impact/cost savings based on lower prices due to the availability of generic medicines, the impact estimates do not depend on whether generics are available in countries due to voluntary licenses or due to other mechanisms, such as the use of compulsory licenses or other TRIPS-flexibilities. Therefore, the difference between the 127-country scenario and the other scenarios (pertaining to countries now included in the MPP license) indicates the potential savings for the use of TRIPS flexibilities in an additional 13-19 countries. These savings would range from US\$ 768-1174 million.

The counterfactual scenario assumes that no voluntary licenses would be granted (the concerned countries were not part of the 90 countries for which BMS had announced an intention to license, nor are they included in the MPP's license). It also assumes that originator companies' pricing policies would not change dramatically.

It should be noted that:

- Due to the methodology used in the study, the estimates do not cover all low- and middle income countries; notably Brazil and China are not included in any of the scenarios. Inclusion of one or both these countries (with large populations and relatively large numbers of people with hepatitis C) would significantly increase the potential savings.
- The estimates are comparable, as they are based on the same methodology and assumptions. The methodology is similar to that used for HIV medicines (estimate 1).
- Whether the projected impact will be realized in practice depends on there being an actual market for hepatitis C medicines. This is less certain for hepatitis C medicines (compared to medicines for HIV or TB) as there is virtually no donor funding for hepatitis C treatment, and many low- and middle-income countries have no established treatment programmes for hepatitis C (yet). This caveat applies to both voluntary licensing approaches as well as the use of TRIPS flexibilities.
- Relative to the impact of the voluntary license, the potential impact of the use of TRIPS flexibilities in the additional 13-19 countries is underestimated, as these are the countries where originator prices tend to be higher than in most low-and middle income countries⁵⁰.

⁵⁰ The methodology assumes a low originator price for 90 countries and a higher originator price (of US\$2000/treatment) for the other countries. However, in a number of countries, it is likely that the originator price would be (significantly) above US\$ 2000. These countries are relatively over-represented in the 13-19 countries that are included in the 127-country scenario but not in the other scenarios.

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