MSF review of the July 2011 Gilead licences to the Medicines Patent Pool

- On 12 July 2011 the Medicines Patent Pool (MPP) and US pharmaceutical company Gilead Science announced that they had reached an agreement under which Gilead would license patent rights for several HIV treatments for use in certain developing countries. This is the second MPP licence since the agency was created in 2010, and the first licence it has concluded with a pharmaceutical company. The MSF Access Campaign responded to the MPP/Gilead announcement, highlighting what was positive about the announcement, but also expressing concern about several serious limitations.[1]

- This MSF review seeks to look at voluntary licence practices, both within the broader context of access to medicines and generic competition, and in the particular case of the Gilead licences to the Medicines Patent Pool. It also provides the current MSF position on the MPP and suggests next steps to ensure public health interests drive the practice of voluntary licensing.

PART 1 - BACKGROUND AND CONTEXT

- **Unrestrained competition is the key factor in reducing drug prices:** MSF has consistently taken the view that the most effective route to lowering the price of medicines is through unrestrained competition between different manufacturers. The evidence has long been documented in MSF's annual review of antiretroviral (ARV) prices *"Untangling the Web"* – in the absence of intellectual property rights (IPR), or where these have been opposed or expired, the price of first-generation ARVs has fallen from over $10,000 in 2000 to under $70 today.[2] This effect also takes place whether at the raw material level (competition between different suppliers of active pharmaceutical ingredients or API) or at finished medicines level.

- **Patents are now a major barrier for newer medicines:** With the TRIPS Agreement coming into force in more countries, including from 2005 in India (where MSF sources around 80% of the ARVs we use in developing countries), many developing countries, have now introduced a product patent regime for pharmaceuticals. This poses a threat to affordability of newer medicines as the granting of product patents allow patent holders to exclude competition, since the absence of generic competition keeps prices high. Due to patent barriers including in India, there are no generic sources for etravirine (ETV) or raltegravir (RAL), for example, two drugs that are used to treat people who have failed on first and second line treatments.
- **Company price discounts are insufficient:** Company price discounts are insufficient to make these drugs affordable for developing countries. Without generic competition to bring prices down, a potential third-line regimen (RAL+DRV+r+ETV) could be available for the poorest countries for the prohibitive price of $2,766 ppy at best. This price applies to Africa and least-developed countries only, with middle-income countries paying substantially more (around $6000 for RAL in Brazil, for example). More generally, companies are increasingly excluding lower middle and middle-income countries from offers of discounted prices. ViiV

[1] Gilead Licence Expands Access, But Several Countries Left Out. MSF press release. 12 July 2011. See http://www.msfaccess.org/resources/press-releases/1092

[2] See Untangling the Web 14th edition online at utw.msfaccess.org (archives of former editions also available)

considers Global Fund-financed programmes in middle-income countries to be ineligible for standardised discounted prices, so these countries have to negotiate prices on a case-by-case basis. Merck has ceased to offer standardised price discounts to all lower middle- and upper middle-income countries. Abbott specifically excludes lower middle-income and low-income countries outside of Africa from standardised price discounts for the heat-stable ritonavir 100mg tablet. Tibotec/Johnson & Johnson are also excluding all middle-income countries from standardised price discounts for all their ARVs.[3]

- **Use of TRIPS flexibilities to allow for competition:** Some developing countries' patent laws, including the amended Indian patent act (2005), allow for a pre-grant opposition process to patent applications, compulsory licenses and other flexibilities or legal tools to allow competition. It is important to oppose those patent applications which are critical for generic production of key medicines and to use compulsory licensing as well as other flexibilities available where needed. Access to the ARV medicine tenofovir disoproxil fumarate (TDF) provides a good example of how these flexibilities have been successfully utilized to expand access. Tenofovir was the subject of several patent applications by Gilead which were successfully opposed by patient groups.

"*Untangling the Web*" found a noteworthy downward trend in the prices of improved tenofovir-based first-line combinations. In countries where the drugs are not under patent or patent owners permit generic competition, the one-pill-once-a-day generic triple combination containing tenofovir/lamivudine/efavirenz (TDF/3TC/EFV) is now available for $173 ppy. For a co-pack of TDF/3TC+EFV the price is even lower at $143, since there are more producers. However for some lower middle-income countries, patents prevent access to the generic products, meaning that countries have to rely on the 'discounted' price offered by originator companies – $1,033 ppy for tenofovir/emtricitabine/efavirenz (TDF/FTC/EFV), nearly six times the cost of the alternative equivalent generic version which is available for $219 ppy.

- **When IP barriers exist, generic competition will only be possible by some form of licensing – be it compulsory or voluntary:** Compulsory licences issued by Thailand, Brazil and other countries have illustrated the positive effects these have on price. Voluntary licences[4] granted by patent-owning companies have also been increasing in recent years. Countries are free to determine when and where they want to issue compulsory licences, which is a matter governed under domestic patent laws. While compulsory licences are dependent on the political will of governments, voluntary licences (VL) rely on pharmaceutical company goodwill – recent VLs have been driven at least in part by the pursuit of commercial objectives in developing countries as well as a response to pressure to make treatments more affordable.

- **MSF has long been involved in applying the concept of a patent pool to medicines:** As supporters of the concept of a patent pool to boost access to medicines, MSF co-submitted a proposal to the UNITAID Board to create a Medicines Patent Pool for HIV medicines in 2006. The compulsory nature of the Pool – and its proposed link to a compulsory licensing mechanism - was rejected by the UNITAID board for a variety of legal, practical and political reasons. The Pool was required to be a voluntary mechanism and as such can only rely on non-legal methods - and particularly public pressure – to encourage participation by the patent-owning companies. MSF supported the principles under which the voluntary

[3] Companies shut down drug discount prices. MSF press release. 18 July 2011. http://www.msfaccess.org/resources/press-releases/1329

[4] The term voluntary licences is used broadly here to refer also to other practices very similar to VLs, such as non-assert declarations or covenants-not-to-sue.

Medicines Patent Pool was created; namely, to have a public health-focused approach to voluntary licensing; to overcome patent barriers to affordable HIV treatments; and to allow access to intellectual property to facilitate better formulations such as fixed-dose combinations (FDCs) and child friendly medicines.

- **The patent pool is just one of the measures supported by MSF to boost access:** Over the past two years, MSF has been advocating for pharmaceutical companies and other patent holders to license their patents to the MPP[5]. Others strategies actively pursued by MSF include the use of TRIPS flexibilities (e.g. support to patent oppositions and compulsory licence campaigns), and actively pushing against TRIPS-Plus measures (e.g. public campaigns against harmful measures in free trade agreements[6]).

PART 2 - VOLUNTARY LICENCES INSIDE AND OUTSIDE THE POOL

- **The Gilead-MPP voluntary licenses should be seen as part of a growing trend in relation to voluntary licences:** Driven partly by commercial considerations of seeking to increase ties with and leverage over their main competitors, pharmaceutical companies started to actively pursue voluntary licences with generic companies based in India – who had started to pursue patent oppositions- from 2005. Coupled with increased pressure on patent-holding companies to do something about the lack of affordable medicines, this has led to a growing trend towards voluntary licences, usually involving several Indian and one South African generic manufacturer and predominantly, but not exclusively, for ARVs.

- **These voluntary licences have ushered in a form of 'restricted competition':** If negotiated and implemented well, VLs can enable robust generic competition and allow for the sale of generic products in developing countries where patents are in force, improving the affordability and accessibility of medicines. However, with VLs, the devil is in the details: voluntary licenses can but do not necessarily lead to competition and significantly improved access. Many VLs have allowed patent-holding companies to segment the market by determining in which countries the licensee can sell its product. All VLs have differing geographic scopes, reflecting differing 'red lines' for patent-holding companies **There is no company VL that covers all developing countries.** By excluding certain countries, companies can protect their own market access in what they see as key emerging markets. VLs do not address the problem of affordability of medicines in excluded countries. Since these VLs that manage competition affect patients in developing countries it is important to understand the stakes involved.

- **Perhaps the most well-known VL, Gilead's 2006 licence on TDF, provides an illustration of these limitations:** In 2006, Gilead signed voluntary licences with key generic manufacturers in India – with the notable exception of Cipla - allowing them to sell TDF in 95 territories. Under the terms of the VL, Gilead retains control over manufacture and distribution of the API and finished product, and certain countries are excluded.[7] The Gilead licence was a major setback for Indian civil society groups who had filed oppositions to TDF patent applications. Gilead's move was motivated by the fact its prospects for patent protection for TDF were weak, both in India (where the main patent was later rejected on the

[5] See the 2009 'Make it Happen' campaign http://www.msfaccess.org/make-it-happen
[6] See the 2011 'Hands Off our Medicines' campaign http://www.msfaccess.org/hands-off-our-medicine-campaign
[7] A summary of some of the problems with the 2006 TDF licences is available in the Knowledge Ecology International anti-competition complaint to the US Federal Trade Commission available here: http://keionline.org/content/view/23/1

basis of non-obviousness and Section 3(d) of the Patents Act, although other patents are expiring in 2018 and divisional applications are still pending) and elsewhere. The motivation for generic manufacturers was to secure earlier access to the TDF market. Cipla however did not opt for the Gilead licence in 2006 and instead participated in patent oppositions to safeguard its generic production.

- **Since then, several other VLs for ARV's have been signed:** See annex 1.

Objective, credible analysis of voluntary licensing as an access tool is complicated by the fact that nearly all voluntary licenses are currently negotiated between private firms (patent-holders and generics) or in recent times between countries and patent holders (as with the recently announced VL for atazanavir between Bristol-Myers Squibb and Brazil), which keep the key terms and conditions of such licenses confidential. While press releases and the media may report on some terms and conditions (e.g. which drug, for which countries), critical information and analysis of VL terms is not readily available in the public domain. It is therefore difficult to completely evaluate their effect on access to affordable generic medicines.

- **The terms of the 2011 Gilead voluntary licences are even more limited :** In July 2011, on the same day the Gilead-MPP agreement was made public, Gilead also announced it had also signed separate (i.e. not within the MPP) semi-exclusive licensing agreements with four "preferred Indian generic partners"[8]. These licences include semi-exclusive rights for five years to market three drugs - elvitegravir (EVG), cobicistat (COBI), and a combination pill termed 'the Quad' (TDF/FTC/COBI/EVG) - to a list of countries, including nine countries that are excluded from the terms of the licences signed on the same day by Gilead with the MPP. The terms of this agreement have not been made public but MSF has learned more about the terms of the agreement from meetings with Gilead. The terms of these separate licences set higher royalty rates and include no termination clause, and the licences carve up the nine countries between the suppliers, so that each of the four companies has semi exclusivity in particular territories[9]. The strategy seems to be to divide countries amongst generic companies with semi-exclusive licences to manufacture and distribute products in exchange for higher royalty rates. In this it is more limited than the 2006 licences, where the idea of competition between manufacturers, though managed by Gilead, remains, as the generic licensees can compete with each other in all covered territories. The 2011 licences sets a disturbing trend as the lack of competition in the semi exclusive territories will act as a strong disincentive for the licensees to lower prices. Gilead has indicated these semi-exclusive agreements could be the future Gilead "access model" for middle-income economies.

- **Separate voluntary licences are now being used to side-step the MPP:** Gilead's 2011 licences show a deliberate attempt to side-step the Pool by directly signing separate VLs with four of the major ARV producers in India. 3 of which also supply API to other generic manufacturers of TDF and therefore have a large role in determining prices. (Note that although approached by Gilead to enter this semi-exclusive agreement, Aurobindo chose instead to sign the MPP sub-licensee agreement.)

- **The MPP's involvement in voluntary licences is a welcome step:** Existing VL's have inherent limitations. For MSF the involvement of the Pool is a welcome step as the Pool is an

[8] Gilead's press release on the voluntary licences is available from: http://www.gilead.com/pr_1584101
[9] Matrix has semi exclusivity in Sri Lanka and Thailand;Ranbaxy Laborateries Ltd and Hetero Drugs Ltd have smei- exclusivity in Botswana and Namibia; and Strides Aroclab LTD has semi exclusivity in El Salvador, Ecuador, Indonesia, Kazakhstan and Turkmenistan.)

independent organisation free from commercial interests, focusing on public health objectives and with a clear mandate to address intellectual property barriers in developing countries to increase access to ARVs. The MPP aims to progressively involve and negotiate with originator companies on the terms and conditions of the VLs. As such, the MPP is well placed to ensure VLs are made with public health interests, and not commercial imperatives in mind. The MPP also intends to make these licences available to public scrutiny, which can help provide objective, credible analysis of voluntary licensing as a tool to stimulate access to medicines

- **The effectiveness of the Pool as a mechanism cannot not be judged on the basis of the Gilead licence alone:** The July 2011 agreement between the MPP and Gilead was the first time a licence agreement with a pharmaceutical company was made available in the public domain through its publication on the MPP website.. With the creation of the MPP, the first MPP licence with the National Institutes of Health (NIH) on darunavir and now the first licence signed by the new entity with a pharmaceutical company, VL's are attracting increased political attention and scrutiny.

- **However, lessons must be drawn from this licence and the context in which the Pool operates in order to guide the Pool's future work.**

PART 3 – ANALYSIS OF THE TERMS OF THE GILEAD-MPP LICENCE

The Basics

- **There are three documents in the MPP-Gilead licences:** The first is the primary licensing agreement signed by the Pool and Gilead[10]. This agreement states that the MPP will use two forms in its sub-licensing to generic companies. The second is an 'amended and restated' sub-licence agreement for generic companies that had already participated in Gilead's 2006 voluntary licence[11]. It is therefore not a totally new licence but one that builds on the terms of the 2006 licence. The third is a form sub-licence agreement for new sub-licensees[12]. The licences have been amended twice since they were signed. First to add South Sudan to the list of licences territories when the Republic was created in July 2011[13] and second in November 2011 to clarify two issued raised in civil society feedback on the agreement. [14] When reviewing the licences it is important to be aware that the MPP was required to include some conditions in the licence on the basis of a MOU it signed with UNITAID. Where this is the case it is noted below.

[10] Main licensing agreement between the Pool and Gilead signed on July 11, 2011. Full text available at http://www.medicinespatentpool.org/content/download/480/2847/version/1/file/Gilead-MPPF+Non-Excl+License+Agmt+%28FINAL%29+08JUL11%5B2%5D.pdf

[11] Amended and Restated License Agreement. Full text available at http://www.medicinespatentpool.org/content/download/481/2851/version/1/file/Form+3-way+Amend+and+Rest+Generic+License+%28FINAL%29+08JUL11.pdf

[12] Form Sublisensee Agreement. Full text available at http://www.medicinespatentpool.org/content/download/482/2855/version/1/file/Form+3-way+Generic+License+%28FINAL%29+08JUL11.pdf

[13] Amendment adding South Sudan in July 2011 (July 15, 2011) at http://www.medicinespatentpool.org/content/download/505/2987/version/1/file/Signed+amendment+adding+South+Sudan.pdf

[14] Second Amedment to License Agreement (November 14, 2011) at http://www.medicinespatentpool.org/content/download/597/3420/version/1/file/MPP+Second+Amendment+%28fully+executed%29.pdf

- **The MPP-Gilead licences covers a number of ARVs, including some in development:** It allows for the production in India and distribution in certain developing countries of generic versions of TDF, emtricitabine (FTC) and three new products currently under development - cobicistat (COBI), an investigational antiretroviral boosting agent, elvitegravir (EVG) an investigational integrase inhibitor, and a combination of these four products in a once-daily, single-table regime, known as the 'Quad'. Indian generic producers are offered non-exclusive, non-transferable, non-sub-licensable and royalty-bearing licences subject to conditions laid out in the agreement. The products are important from a medical point of view. A joint February 2011 submission of the Medicines Patent Pool, UNITAID, and WHO HIV/AIDS Department to the WHO Expert Committee on the Selection and Use of Essential Medicines (endorsed by MSF and many other organisations) lists the priority missing essential medicines, including relevant products in late stage development[15]. COBI, EVG and the "Quad" were part of this list. The inclusion of products under development answers to one of the key lessons from the last decade, namely that the time delay between drug approval in rich countries and access in developing countries needs to be shortened[16].

- **Manufacturing limitations: Only Indian generic companies are eligible for licences – whether for the finished product or the API:** This India-centric approach in the Gilead-MPP licences is problematic and discriminatory. Any generic company based outside of India, such as the Government Pharmaceutical Organization (a publicly-owned Thai generic manufacturer) is simply ineligible to apply for a VL. India's role as 'pharmacy of the developing world' is well-documented - Indian companies currently produce more than 80% of the ARVs used by MSF and more than 87% of the ARVs purchased using funds from international donors[17]. This situation is likely to change in the future. Efforts to increase the capacity of developing countries to increase local production should be encouraged in licences. A number of countries already rely on local manufacturers for access to low-cost medications. Uganda, Brazil and Thailand have strong manufacturing capacity and countries like the Philippines, Argentina, Pakistan and China could potentially play an important role if national patent barriers are overcome and technical support on quality assurance is provided to generic manufacturers in these countries.

Unbundling and termination clauses

- **Although there are not separate licences for the different products, an approach preferred by MSF, Gilead agreed to allow the licences to be unbundled from each other: The MPP licence also includes a termination clause:** Licensees therefore have the flexibility to choose the drugs for which they want a licence and the drugs they want to produce and sell without a licence – assuming patents do not stand in the way of this production. In many territories, TDF is not patented. Out of the 112 licences territories, TDF patents are filed or granted in only two countries: India and Indonesia. The main

[15] Medicines Patent Pool, UNITAID and the WHO HIV/AIDS Department, 'Updated List of Missing Drug Formulations for HIV Treatment to be Reviewed by the WHO 18th Expert Committee on the Selection and Use of Essential Medicines' (18 February 2011) at http://www.who.int/selection_medicines/committees/expert/18/policy/Missing_HIV_formulations.pdf

[16] Ford N, Calmy A, von Schoen-Angerer T. Treating HIV in the developing world: getting ahead of the drug development curve. Drug Discovery Today. 2007; 12(1-2):1-3. Available from: http://www.msfaccess.org/content/treating-hiv-developing-world-getting-ahead-drug-development-curve

[17] Brenda Waning, Ellen Diedrichsen and Suerie Moon 'A lifeline to treatment: the role of Indian generic manufacturers in supplying antiretroviral medicines to developing countries' Journal of the International AIDS Society (2010) Volume 13, Number 1, 35 at http://www.aids-kampagne.de/fileadmin/Downloads/Pharmaindustrie/2010_JIAS_Role_of_Indian_Generics_in_Supply_to_Dev._Countires.pdf

blocking patent is in Indonesia. In India TDF's main patent was rejected on the basis of non – obviousness and section 3(d) of the Indian Patents Act 1970.[18] But with Gilead holding patents or having filed patent applications on COBI[19], EVG[20] and the Quad in several countries, including India, it is assumed that generic manufacturers will sign up to the licences covering these medicines. However it should be noted that for COBI the option of pre- grant oppositions could also be exercised by the Indian generic companies or civil society.

- Generic licensees can terminate the licences unilaterally at any point for any reason. Such a feature was not in the 2006 TDF licence and had meant that the original licensees were locked into the 2006 agreement. Indian generic companies that signed the 2006 VL now have an option of switching to the Gilead-MPP licences by signing the "amended and restated" sub-licence agreement for existing Gilead sub-licensees. Given the unbundling feature of the Gilead-MPP licence, it is possible for generic companies to terminate the TDF component of the licence and retain the licence for the remaining products. Aurobindo did exactly this when it recently signed the 'amended and restated' sub-licence agreement from the MPP and made use of this unbundling provision to terminate their previous TDF licence with Gilead, whilst licensing EVG, COBI and the Quad. This shows the benefit of the unbundling feature. Other generic companies that signed the 2006 VL are unlikely to follow suit, as they have signed July 2011 voluntary licences with Gilead on the very same products but outside of the Pool - and this licence does not appear to include a termination clause so it is unlikely that they will be able to terminate this licence.

- **The MPP licence contains a covenant not to enforce FTC patents, and allows for the production of other fixed-dose combinations involving the licensed compounds:** There is no patent on FTC in India but Gilead has patent rights on FTC in 45 other developing countries. There were concerns raised by a number of civil society groups that the wording on this clause in the pool licence was ambiguous and Gilead would therefore enforce its covenant to stop production if the licence was unbundled. In response this was clarified through an amending provision to the licence negotiated by the MPP with Gilead. The amendment to the licence with Gilead makes it clear that the non-assert will continue to apply if the licence is unbundled. After unbundling the licence, Aurobindo will be able to use the non-assert on FTC to supply the 45 countries in which FTC is patented. An alternative option for the 45 countries that do have patents on FTC is to opt for the TDF/3TC fixed dose combination as lamivudine (3TC) is off-patent and an equally acceptable drug in place of FTC according to WHO treatment guidelines for resource poor countries. It is also cheaper to produce. The current lowest price for a FDC of TDF/3TC is $91, whereas the lowest generic price for a FDC of TDF/FTC is $116.

New Indications

- **The MPP licences include broader indications:** According to the terms reached with Gilead, TDF can be produced under licence from the MPP for treatment of HIV but also hepatitis B – unlike in 2006 where the sale of generic TDF was restricted to HIV by the terms of the VLs. Sales of EVG and COBI are authorised for treatment of HIV and any indications that are subsequently approved. The broader coverage is good news from an access point of view as the medicines produced can be made and sold for a broader uses as well. There has been a concern amongst some civil society groups that this will lead to a situation where the

[18] One process patent is granted expiring in 2018 and a couple of divisional applications are still pending.
[19] Three patent applications on COBI are pending in India, with no pre- grant oppositions reportedly filed to date.
[20] One EVG patent is already granted in India, while two applications are pending.

payment of royalties will be justified for the new use of known products. For MSF these are two separate issues. New indications, labels approved by the FDA or other regulatory authorities, do not give rise to a royalty payment. Royalties are only payable on the patents that Gilead has licensed to the Pool. These patents do not include patents for new uses. In relation to the general issue of patents for new uses, MSF clearly recommends that countries including India should not allow for such patents. MSF will continue its technical support in India on such patent oppositions

Limited geographical scope

- **The geographical scope of the Gilead-MPP licence is an improvement over any other voluntary licences granted by originator companies but limits to effect.** The geographical scope of the VLs from other companies is even more limited. Note that licences are for the different products cover different geographical territories. For TDF, where the 2006 licences included 95 territories, the MPP licence includes 112. It is unlikely TDF is patented in any of the additional territories[21] so the significance of this license extension is minimal. The COBI licences cover 103 territories, and the EVG and Quad licences include 100 territories.[22] The 2011 licenses signed outside of the scope of the MPP give access to more countries which have been excluded from the MPP licence: Nine of the countries[23] included in the TDF geographical scope in the MPP licences are excluded from both the COBI and the EVG & Quad licences - this is because Gilead has granted outside of the MPP semi-exclusive rights to four generic manufacturers to supply such medicines to these countries (see above). In that sense the four licensees that have signed an agreement with Gilead outside the MPP benefit from a wider geographical scope, as compared to both the 2006 licence and the licence obtained by the Pool. However competition in these countries is limited as noted above.

- **The Gilead-MPP licence still excludes countries from the licence:** Access to the new products will remain difficult for patients in countries that have been excluded from the licences and where the new products are likely to be patented. The exclusion of some lower middle- and middle-income countries (including China, Thailand, Argentina, Peru, Egypt, and Ukraine) disappointed patient groups in these countries, who were hopeful that these VL negotiations would bring an end to their struggle to increase access to Gilead's products (both in terms of access to better regimens and scaling up of treatment) in the face of IP barriers and government inaction.. Several of the countries that are excluded under the Gilead licences are among the first in which MSF provided HIV treatment ten years ago. We do not take their exclusion lightly. We raised our concerns when the licences were announced[24] and will continue to do so. Going forward, MSF urges Gilead and other originator companies to withdraw their restrictions on lower and middle-income developing countries receiving affordable ARVs from India, and looks forward to working with different civil society organisations about the best strategies for achieving this.

Options for excluded countries

- **In the face of VL restrictions on supply from India, excluded countries must plan to**

[21] The 17 additional territories are Anguilla, Armenia, Aruba, British Virgin Islands, Ecuador, El Salvador, Fiji, Georgia, Kazakhstan, Montserrat, Nauru, Palau, South Sudan, Sri Lanka, Tonga, Turkmenistan and Turks & Caicos.
[22] The same list as for COBI, but without Aruba, Dominican Republic and Montserrat.
[23] Botswana, Ecuador, El Salvador, Indonesia, Kazakhstan, Namibia, Sri Lanka, Thailand, and Turkmenistan
[24] Gilead Licence Expands Access, But Several Countries Left Out. MSF press release. 12 July 2011. See http://www.msfaccess.org/resources/press-releases/1092

open up sources of affordable generic ARVs: Strategies to be adopted vary from country to country:

- For excluded countries that have no patents on TDF: For those with manufacturing capacity, the option of local production appears relatively straightforward. However, access to the API may be a problem for manufacturers that do not have a licence with Gilead as the Gilead - MPP licence also restricts the sale of API's to unlicensed manufacturers and many of the licensed Indian generics are key API suppliers. Another option is to source TDF from Cipla or now Aurobindo as they are not Gilead sub-licensees but independent generic producers that face no patent barriers in India. These countries will still face barriers to accessing newer drugs like EVG, however, as these are patented in India, and no independent generic producer maybe available (all future generic producers may have signed up to a VL with Gilead).

- For excluded countries that have or will have patents on TDF, COBI and/or EVG: The options for these countries are limited to issuing a compulsory licence, either to enable local production or to allow generic importation. The issuance of a compulsory licence is governed by national patent laws and the TRIPS Agreement 1994. Countries are free to determine when and where they want to issue compulsory licences.

- **The Gilead-MPP licence allows excluded countries to import under compulsory licence the medicines produced under the terms of licences. It also allows Indian companies to export under a compulsory licence issued in India:** This is an important safeguard, and the licence agreement expressly allows licensees to supply outside the list of agreed territories in this event. The specific language used in the Gilead-MPP licence agreements raised concerns that Gilead would have to agree before any compulsory licence could impact the terms of the licence[25]. The MPP subsequently negotiated an amendment to the licence to remove this wording, so it is clear that there is no requirement for agreement from Gilead. Making use of this clause however maybe a challenge Indeed, it remains to be seen whether any manufacturer that has signed the VL would accept to apply for a compulsory licence (CL) to export, or whether it would agree to honour an order placed under CL for fear of damaging its commercial relationship with Gilead. Nevertheless the terms of the Gilead-MPP licence removes one of the important concerns that may affect this decision – that it would lead to direct retaliation by Gilead by the termination of the licence, by making it clear that responding to a CL request or applying for a CL does not constitute a breach of the licence and will not lead to its termination.

- **Excluded countries will not likely be able to resort to parallel importation:** Parallel importation is a flexibility allowed under the TRIPS agreement, which enables those countries who have implemented it in their national laws to obtain the best price on the world market for medicines, as it allows imports of a lower cost medicine without the patent owners consent, if that product has been put on the market in another country. Not all countries have parallel importation provisions in their laws, and those that do have them are drafted in different ways, some only apply it to patented medicines, so generic importation would not be allowed, while others also apply it to generic medicines. However, the Gilead-MPP licence (and similarly, Gilead's 2006 licence) forbids generic licensees or their distributors from selling the API or drugs anywhere except where authorised by the licences, and the Gilead MPP licence gives Gilead the right to terminate the agreement (or ask MPP to do so

[25] Articles 7.3 and 10.3 (d) of the original Form sub-licencee agreement. For amedndments see: Second Amedment to License Agreement (November 14, 2011) at http://www.medicinespatentpool.org/content/download/597/3420/version/1/file/MPP+Second+Amendment+%28fully+executed%29.pdf

on its behalf) if the company determines that drugs or the API made or sold by licensees are being diverted to countries outside the scope of the licence. This provision is likely to prevent parallel importation even for countries that allow parallel importation of generic drugs because importing drugs from generic manufactures that are under the MPP-Gilead licence would be a diversion under the terms of the licence. This though, is an additional consequence of the fact that the VL contains limits on the countries that can be supplied. The only limited option that would be available for countries with such laws would be to buy in the retail market in India or other licensed territories, and then parallel import, but this is likely to be a more expensive option than buying directly from a wholesaler or distributor.

Active Pharmaceutical Ingredient

- **The Gilead-MPP licence includes restrictions on the purchase, sale and use of the API:** Under the terms of the agreement, licensees can manufacture the API royalty-free. However, the terms contain important restrictions on the purchase, sale and use of the API in the production of generic products. The API can only be manufactured for a Gilead licensee's own use or to supply other Gilead licensees, and licensees can only purchase the API from other licensees or directly from Gilead or Gilead distributors (in which case Gilead will also be part of the agreement). **The licence restricts API manufacturers and licensees to Indian manufacturers**

- **Restrictions raise anticompetitive concerns:** The terms of the licence prohibit the use of unlicensed API and will therefore affect the market and free competition for API. This will have significant consequences both for Indian and non-Indian manufacturers of API. Indian API producers cannot export API to countries where local manufacturers can lawfully produce the required drugs because Gilead does not have a patent.

- **With these restrictions, few options are left for countries excluded from the Gilead-MPP licences:** In theory, excluded countries where Gilead's products are not patented can produce locally, enter in a separate voluntary licence with Gilead, or issue a compulsory licence. But it is not that simple in reality, as sourcing the API will be difficult. If the API were available from multiple sources, excluded countries would not be affected by the Gilead-MPP licences. However if the API market is restricted to India , the API can only come from those few companies that have not entered into the Gilead-MPP licence The future of a robust and competitive API market is critical to the future of affordability of the finished products. It is important that such restricted licensing terms be avoided in future.

- **These restrictions are not new and were already one of the most negative features in the 2006 TDF Gilead licences:**. The MPP has itself noted that this is a shortcoming but Gilead refused to address these concerns during negotiations.

Quality issues

- **Under the terms of the licence, generic companies will have to meet WHO prequalification or US FDA quality standards:** Within one year of signing the agreement, generic licensees will have to receive WHO prequalification or US FDA condition approval – this applies for TDF, combination for products including TDF, EVG, COBI and Quad formulations the one year time limit runs from the date of the FDA approval of the relevant product. In case generic companies fail to receive the approval within that time, Gilead can suspend licences until they do. Given that the licence is restricted to Indian generics who either have or have the capacity for WHO prequalification or FDA conditional approval, in

practice this quality requirement should not be a restriction.

- **For some, however, this provision could set a negative precedent in some scenarios:** Some civil society organisations have argued that insisting on WHO prequalification or FDA conditional approval could prove prohibitive for some manufacturers. If future licences allow production in Thailand or Brazil, for example, insisting on these quality standards would become a barrier, as these countries have public sector generic manufacturers and rely on their domestic drug regulatory authority (DRA) for registration and quality assurance, rather than external DRAs or WHO prequalification. This issue was debated at some length at the UNITAID Board before the MPP was established. The UNITAID Board eventually decided to include this provision. Language was inserted into the MoU between the MPP and UNITAID (which sets out what the MPP must include in licences), stipulating that in the case generic companies signing a licence with the MPP cannot obtain approval from a stringent DRA or WHO prequalification, the MPP is required to ensure that adequate provision for alternative temporary arrangements through a WHO expert panel.[26] This latter provision was included as an alternative but it is not yet clear how it would apply to such scenarios.

*licence terms and patent oppositions.

- **The Gilead-MPP licences extend the obligation of complying with the licence until all possible patent disputes have been settled:** According to the agreement, a licensee will still have to pay royalties to Gilead, and will still be forbidden from selling the drug in excluded countries, until all patents and patent applications have been held invalid and no further appeals can happen in India.[27] This means that if the Indian patent office rejects a patent application on a drug covered by the licence and generic production were possible for example because it does not meet the strict patentability requirements under Indian patents Act , the generic licensee would still be held liable to pay royalties under the terms of the licence. If this particular clause hadn't been included in the agreement, then as soon as a patent application was rejected - in response to a pre- or post-grant opposition for example- then the generic licensees would be able to export the drug to excluded countries (as long as there were no blocking patents in the importing country). But because the clause is included in the agreement, a generic licensee has to wait until all possible appeals against the patent rejection are exhausted until it can do so. MSF's experience in the imatinib case in India shows that the process of patent applications, rejections, appeals to the High Court, and further appeals to the Supreme Court takes years.[28] This clause therefore acts as a considerable disincentive for generic manufacturers to export drugs to excluded countries. While a generic licensee always has the option to terminate the agreement, this clause unnecessarily puts the burden on them to do so**.** The burden should be on Gilead to file an

[26] Article 6.2 of Memorandum of Understanding between the World Health Organyation acting for UNITAID and the Medicines Patent Pool Foundation (September 14, 2010) at http://www.medicinespatentpool.org/content/download/208/1199/version/3/file/MemorandumOfUnderstanding_MedicinesPatentPoolFoundation_14Sept2010.pdf

[27] Article 4.9 of the Form Sublicensee Agreement at http://www.medicinespatentpool.org/content/download/482/2855/version/1/file/Form+3-way+Generic+License+%28FINAL%29+08JUL11.pdf

[28] The case of Novartis's challenge against the Indian government & what it could mean for millions of people across the globe (Médecins Sans Frontières Briefing Note – December 2006) at http://www.msfaccess.org/sites/default/files/MSF_assets/Access/Docs/ACCESS_briefing_NovartisCaseAgainstIndia_ENG_2006.pdf. The case was initiated in 2006 after Novartis's patent on Gleevec was rejected by Indian Patent Office. Novarti appealed in Madras High Court and could not succeed there. An appeal was also rejected by Intellectual Property Appellate Board. Novartis then filed an appeal in the Supreme Court of India where matter is pending and the next date of hearing will b in February 2012.

appeal to see if they could overturn the rejection and establish a valid claim. In future licences royalties should be suspended if a patent is successfully opposed pending the outcome of any appeal.

- **Not all patents need to be opposed :** as soon as patents that stand in the way of generic production have been removed in India, a generic licensee could terminate the licence and therefore produce and export to exclude countries and without paying royalties - even if other patents for that product exist. It is important to note therefore that all patents do not have to be opposed - only those that blocks generic production.

Royalty payments

- **The Gilead-MPP licences provide detailed provisions on royalty and payment terms:** For TDF and combinations that include TDF, the licence includes the obligation of payment of 3% royalty to Gilead. If a patent is granted in India on a combination that includes TDF, the royalty rate will increase from 3% to 5%. For EVG, COBI and the Quad, a 5% royalty is payable to Gilead.

- **For the API, the royalty terms are the same as the ones agreed in the 2006 Gilead voluntary licence:** A licensed manufacturer can manufacture the API royalty-free for their own use, or to supply other manufacturers of the finished product – provided they are tied to Gilead through a VL.

- **Gilead will collect royalty payments in India, regardless of the patent status in countries where drugs would actually be marketed:** In practice, this means that Gilead would be earning royalties in countries where it does not have a patent. It's important to note however that this is the reality of the system under the TRIPS agreement, and is similar to the case of compulsory licences issued by India for export purposes- a royalty rate would be payable to Gilead even if there was no patent in the importing country.

Paediatric versions

- **Certain provisions in the licence aim to stimulate innovation for new paediatric formulations:** Royalties are waived on formulations specifically designed for paediatric populations under 12 years old. In addition, there are provisions to allow these products to be made available outside the geographical scope of the licences. This is a welcome addition.

But these provisions are excessively complex: Indeed, they stipulate that Gilead's prior written consent with respect to EVG Product and EVG Combination Product are required.[29] In future agreements, the idea of royalty-free licences with the broadest possible geographic scope should be retained for paediatric formulations - but the option of a simple non-assert (where the patent holder agrees to not assert its intellectual property rights) covering all developing countries for all forms of paediatric versions of an ARV would be more straightforward.

Legal standing and arbitration

- **The MPP is unnecessarily restricting itself by waiving its right to bring legal action:**

[29] Article 6.2 (e) of the Form Sublicensee Agreement.

Two articles of the agreement stipulate that the MPP will not be able to enforce the licences or participate in any dispute between Gilead and a generic licensee,[30] and that the MPP will not be able to undertake legal proceedings against Gilead unless Gilead breaches payment obligations to the MPP[31]. (One other important exception is that the MPP has the right to force Gilead to licence to a generic company if an eligible company is seeking a licence from the MPP). MSF believes the MPP's role should not end at the point where a licence is signed between Gilead and a generic manufacturer. In the case of a dispute between Gilead and a generic licensee, the MPP's role, given its public health-driven mission, could be useful to provide access perspective or pro-access interpretations of the licence terms. It is important to monitor the concrete impact of the licences on access to medicines and the MPP should be in a position to interfere in such a case where parties are not working according to the true spirit of the MPP's objectives.

- **The MPP seems to have accepted closed-door arbitration in the case of a dispute:** The Gilead-MPP licences provide an arbitration clause stating that all disputes shall be settled under the Rules of Arbitration of the International Chamber of Commerce by three arbitrators. This appears to be similar to the arbitration clauses contained in the 2006 original Gilead TDF licence. The MOU signed by the MPP and UNITAID requires that the MPP ensures that its licence agreement specify alternative resolution mechanisms.[32] This form of arbitration is in secret, with no information on the disputes filed and their outcomes. Given that the results of such arbitration may have important effects on the operation of the licence the MPP should explore how such effects can be made public.

PART 4 – CONCLUSIONS AND RECOMMENDATIONS

- **The Medicines Patent Pool is an important tool in the fight for access to affordable medicines:** The best mechanism for ensuring that developing country prices of a new medicine become as affordable as possible is to ensure that there is unrestrained competition amongst a number of suppliers of that medicine. However, while we know that they will only take us so far and are by their very nature limited by their reliance on company goodwill, voluntary mechanisms to help ensure medicines are priced affordably do have a part to play, as one tool in the fight for access, when patent barriers stand in the way of generic competition. MSF will continue to put pressure on companies such as Johnson & Johnson, Abbott and Merck to join negotiations with the MPP and to put pressure on companies that are already negotiating with the MPP to extend licenses to all developing countries.

- **In India, it is important to file oppositions against patent applications for TDF and COBI and other medicines:** If no patent is granted, generic companies can produce affordable versions free from the restrictions in the Gilead licences. Thanks to the termination clauses, should patent oppositions be successful, as in the case of TDF, any company who has already signed the licence can then terminate it and would be free to manufacture their own version of the drug. This could very well be replicated for COBI. Such an outcome would be considerably beneficial for patients in India and in the rest of the developing world.

[30] Article 5.4 of the Main Licensing Agreement
[31] Article 6.3 of the Main Licensing Agreement
[32] Article 6.2 of Memorandum of Understanding between the World Health Organyation acting for UNITAID and the Medicines Patent Pool Foundation (September 14, 2010) at http://www.medicinespatentpool.org/content/download/208/1199/version/3/file/MemorandumOfUnderstanding_MedicinesPatentPoolFoundation_14Sept2010.pdf

- **Recommendations to the Medicines Patent Pool:** Licensing agreements that the MPP is negotiating with companies can have a direct impact on millions of people's ability to access affordable medicines. In order to ensure it has the best chance of succeeding, the MPP should:
  - Increase transparency in its decision-making process: We welcome and support a more participatory process that fosters broader civil society input. While MSF and other civil society groups have benefited from the MPP's team willingness to respond to meeting requests, as the MPP evolves it is important that renewed efforts are made to have a broader and more transparent engagement of civil society. We welcome the fact that the MPP has said that will create a separate civil society consultation process from the one currently set up for UNITAID and we also welcome commitments to greater transparency of the Board and Expert Advisory Group decisions. These ambitions now need to be fleshed out in greater detail.
  - Use ideal standard terms and conditions rather than former industry licences as the template for future negotiations: Future licences should:
    - Place no restrictions on where medicines can be produced or API sourced (other than those that are required as a part of the MPP's MoU with UNITAID)
    - Include the clause as amended in the Gilead-MPP licence agreements to make explicit that there are no restrictions on a licensee's supplying countries that have been excluded but where a compulsory licence has been issued
    - Set no royalties on paediatric formulations
    - Use different licences for different drugs when an agreement covers multiple products.
  - Seek broader civil society involvement in the MPP's normative work of defining target ARVs: The Medicines Patent Pool does not only have a potential norm-setting role on voluntary licensing and technology transfer, it is also reviewing, with the help of the WHO Expert Committee on the Selection and Use of Essential Medicines, a target list of key ARVs and FDCs that developing countries need or will need in the near future[33]. MSF has submitted comments as a part of this process and many organizations have endorsed the most recent list. It will be useful for an even broader group of civil society, including people living with HIV/AIDS to also contribute with defining the access needs in their countries.

- **Recommendations to UNITAID:** As the founder and funder of the Medicines Patent Pool UNITAID should:
  - Support the use of TRIPS flexibilities: In addition to the support it gives to the MPP, UNITAID (as well as other UN agencies), should advocate for the adoption and use of all TRIPS flexibilities such as strict patentability criteria, patent oppositions and compulsory licences. UNITAID should give practical support to organisations and actions that advocate for intellectual property reform in developing countries, to those filing patent oppositions and seeking compulsory licences. UNITAID should seek a review of which HIV medicines patents are capable of being opposed and in which countries.
  - Pursue strategies to include the excluded countries: Companies are clearly leaving patients living in lower middle- and middle-income countries behind, and the Gilead-MPP licences have not been able to reverse this push. The failure of the MPP to

[33] ARV priority list for the Medicines Patent Pool, September 2011, available from: http://www.medicinespatentpool.org/content/download/560/3237/version/2/file/POOL+ARV+PRIORITIES+WORKING+DOCUMENT+-+Comments+Welcome.pdf

include middle-income countries in its geographical scope should not be seen in isolation from this trend. As a first step, UNITAID could support looking at the different options to expand geographical scope, including the specific use of TRIPS flexibilities.

- Call attention to new dangerous trends in voluntary licences: The terms of most voluntary licences are being negotiated in secret between companies, with no opportunity for government or civil society oversight. The work of the MPP for a public health driven approach to voluntary licences should be seen in the broader context of companies' access policies and voluntary licensing schemes. MSF is especially concerned about recent licences signed by Johnson & Johnson, ViiV and Gilead outside the MPP. UNITAID should make a formal call for the immediate release of such licensing terms and for a review of the effects these have on access and innovation.

Annex: TITLE : Public information about existing Voluntary Licences

Company (Product)	**Eligible Territories**	**Number of countries covered**	**Number of middle-income countries covered (from a total of 101)**	**%age of middle-income countries covered**
Abbott (LPV/r)	None	0	0	0%
Merck (EFV)	11 of 15 SADC countries	11	8	8%
BMS (d4T, ddI, ATV)	Sub-Saharan Africa + India	49	18	18%
ViiV (AZT, 3TC, ABC, MVC + pipeline)	Sub-Saharan Africa + Least-developed countries + Low-income countries	69	25	25%
Roche (SQV, NFV)	Least-developed countries + Sub-Saharan Africa	65	25	25%
J&J (DRV)*	Sub-Saharan Africa + Least-developed countries + India	65	Unknown	Unknown
Boehringer Ingelheim (NVP)	Least-developed countries + Low-income countries + Sub-Saharan Africa	71	26	26%
Gilead (2006) (TDF)	List of 95	95	47	47%
J&J (RIL)**	Countries covered by MPP-Gilead licence	112	58	58%

This table is based on research conducted by the MPP on the scope of existing VLs and presented by Chan Park at Columbia University in November 2010.

* J&J communicated to MSF in a conference call in October 2011 that their licence for DRV now covers 65 countries. MSF has not seen their VL agreements and cannot confirm the details of the licence or whether these agreements have been signed with generics.

** Three months after the Gilead-MPP licence was announced, J&J communicated their intention to expand the scope of their VL for rilpivirine (only) to cover the same 112 territories as the Gilead-MPP licence agreement. MSF has not seen their VL agreements and cannot confirm the details of the licence or whether these agreements have been signed with generics.