Report of the Medicines Patent Pool Expert Advisory Group
on the Proposed Amendments to the MPP-Gilead Agreement to Incorporate TAF

Introduction

The Expert Advisory Group (EAG) of the Medicines Patent Pool (MPP) submits the following report to the Governance Board of the Medicines Patent Pool on the proposed amendments to the Licence Agreement between MPP and Gilead Sciences to incorporate tenofovir alafenamide (TAF).[1]

The Terms of Reference for the EAG pose two questions that the EAG must address in assessing the results of final negotiations: (i) do the results sufficiently meet requirements set out in the Statutes and the Memorandum of Understanding between the Patent Pool and UNITAID, and (ii) do the negotiation results offer sufficient added value over the *status quo*?

Having reviewed the proposed amendments, and having received a briefing from MPP on the proposed revised agreement between MPP and Gilead, the EAG answers both questions in the affirmative and recommends that the Board request the Executive Director of the MPP to finalise and execute the necessary documents with Gilead.

Background, Overview of the Proposed Agreement

MPP and Gilead signed a licence agreement in 2011 covering four Gilead compounds: tenofovir disoproxil fumarate (TDF), elvitegravir (EVG), cobicistat (COBI) and emtricitabine (FTC). In early 2013, TAF entered phase III clinical trials, at which point the EAG understands that the two parties began discussing the inclusion of TAF into the existing licensing framework.

TAF is an alternate pro-drug of tenofovir that is currently in phase III clinical trials for the treatment of HIV and hepatitis-B viral infection (HBV). This new pro-drug allows TAF to be dosed at much lower levels than TDF; it is being investigated at less than one-tenth of the 300mg recommended daily dosage for TDF. Because of the lower dosage, TAF can potentially be manufactured at a much lower cost than TDF, while also potentially offering significant clinical benefits, such as reduced side effects and toxicity, and easier formulation into fixed-dose combinations.

The MPP informed the EAG that the TAF patent has been granted in several key jurisdictions, including India, China, ARIPO, OAPI and South Africa.

[1] Alexandra Calmy was unable to take part in this Report.

For these reasons, the MPP informed the EAG that TAF was identified as a high priority in the MPP's latest edition of *ARV Priority List for the Medicines Patent Pool*.[2]

The proposed amendment to the MPP-Gilead agreement comprises four agreements: (1) an amended and restated agreement between MPP and Gilead that replaces in its entirety the existing licence agreement, as well as three form sublicence agreements attached as exhibits: (2) a form sublicence agreement for existing Indian licensees; (3) a form sublicence agreement for new Indian licensees; and (4) a form sublicence agreement for new Chinese licensees.

The proposed amendment includes TAF as a licensed compound, and allows entities in India or China to manufacture both API and finished product for sale in 112 countries, which, according to MPP estimates, covers 92.2% of PLHIV in the developing world. The licence for TAF is royalty-bearing, charged at 5% of net sales of finished product in the licensed territory. As TAF is currently being investigated as a treatment for both HIV and HBV, the field expressly indicates that the field of use is for whatever label the US FDA approves for TAF, including for HBV.

The China form agreement differs in three important ways from the form Indian agreements: (1) the scope of the China licences do not cover EVG, which the EAG understands is a Japan Tobacco compound that has been sublicensed to Gilead; (2) there is no technology transfer in the China licence; and (3) Gilead expressly reserves the right to certain remedies (injunctive relief, damages) in the event of diversion, but only if Gilead has a valid patent in force in either China or the country of diversion. Nevertheless, the EAG agrees with the MPP's assessment that the inclusion of China for manufacture, a country with significant low-cost API manufacturing capacity, is a step forward.

The proposed amendments retain all of the key flexibilities that were contained in the original MPP-Gilead agreement, including the sublicensee right of unilateral termination, either of the entire agreement or on a compound-by-compound basis. The proposed amendments also contain a number of other changes that the EAG views as improvements to the existing framework. These include improvements to the diversion and royalty term language, as well as an expansion of the covenant-not-to-sue on FTC to include key combination patents covering TDF and FTC.[3] Finally, the EAG understands that, upon MPP's request, Gilead agreed to include various provisions that allow MPP to better monitor, manage and enforce the sublicence agreements as against its sublicensees. The MPP informed the the EAG that this was an important amendment that would significantly strengthen MPP's ability to ensure that

[2] http://www.medicinespatentpool.org/wp-content/uploads/Priority-Antiretrovirals-for-the-Medicines-Patent-Pool-Unabridged-Third-Edition-Final-Web.pdf

[3] The EAG understands that MPP requested, and Gilead agreed, in principle, to also include the combination patent covering TDF/FTC/EFV within the covenant-not-to-sue, but that because this patent is co-owned by Gilead and BMS, Gilead is still in the process of obtaining the requisite consent from BMS. The EAG understands that the agreement will further be amended to include this patent if and when the consent from BMS is obtained.

licensees develop, register and make broadly available the licensed products as soon as possible.

Assessment of the Proposed Amendments in Light of MPP's Statutes and MoU

MPP's Statutes and MoU with UNITAID contain guiding principles against which the results of negotiations are assessed. The EAG finds that the proposed amendments meet the requirements in both the Statutes and MoU with UNITAID, as summarised in the tables below.

Relevant Considerations in the Statues of the Medicines Patent Pool

Statutes	Terms in Proposed Licences
Negotiating terms and conditions of licence agreements with aim to maximize public health benefits, taking into account the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property of the WHO (GSPOA); Doha Declaration	• No restrictions on ability of Sublicensees to challenge patents. • Agreements to waive data exclusivity rights; prevention of further data exclusivity rights. • Allows for sale outside the Territory where compulsory licence is issued. • Allows for sale outside the Territory where there are no patents in force or patent has been held invalid or unenforceable beyond the possibility of any further appeal in India/China and the country of sale. • Allows licensees to unilaterally terminate entire agreement, or on an API-by-API basis.
Entering into licence agreements with patent holding entities, and sublicence agreements with generic manufacturers and other appropriate sublicensees on a non-exclusive and no-discriminatory basis	• MPP retains the right to issue non-exclusive sublicences to any qualified entity in India and China on a non-discriminatory basis

Relevant Considerations in the MoU between the MPP and UNITAID

MPP-UNITAID MoU	Terms in Proposed Licences
Use all reasonable efforts to define standard terms and conditions of licence agreements	• Terms and conditions of Sublicence standardized across all sublicences via the form Sublicence Agreements
Define the terms and conditions of the licences and sublicences, respecting the differing patentability criteria across jurisdictions	• Royalty payable only until expiration of patent "containing a valid claim" in country of manufacture or sale • Licensee right to terminate without cause, with 30 days notice. • Unbundling provisions remain, allowing licensees to terminate on a product-by-product basis in response to changed circumstances (i.e., invalidated patents) • No restrictions on challenging patents.
Ensure contracts with sublicensees specify that products must obtain approval from a stringent drug regulatory authority or WHO prequalification or temporary arrangements under WHO Expert Review Panel	• Quality provisions require approval by WHO Prequalification or FDA tentative approval or European Medicines Agency approval.
Ensure that licence agreements specify an alternative dispute resolution mechanism	• Arbitration in accordance with ICC Rules of Arbitration.
Define the terms and conditions under which the sublicensees must make insurance arrangements to cover liability risks linked to products produced under sublicence from MPP	• Product liability insurance obligation specified
Safeguard against the diversion and ensuring the traceability of products…by specifying terms and conditions in accordance with WTO [30 Aug Decision] guidelines	• Obligation to bear mark and packaging distinctive from Gilead
Facilitate activities promoting transfer of technology, capacity building and local manufacturing of medicines in developing countries, consistent with the Purpose of the Foundation, and in consultation with other international partners	• Technology transfer to Indian Sublicensees. • No restrictions on the development of combinations. • No restrictions on the development of paediatric formulations.

Assessment of the Proposed Collaboration in Light of the *Status Quo*

The EAG finds that the proposed amendments of the MPP-Gilead agreement represent a significant improvement over the *status quo*, both in terms of geographic scope and in terms of promoting transparent, public health-oriented licensing terms and conditions. The EAG agrees with MPP's assessment that TAF is potentially a very promising compound that, if approved, could improve the quality of treatment for millions of PLHIV in the developing world, as well as generate significant cost savings as a key part of the preferred first-line regimen for adults.

The EAG finds that the coverage of the proposed TAF territory, covering 112 countries representing 92.2% of people living with HIV in developing countries, represents a significant advance over the *status quo* and compares favourably with the nominal percentage coverage of other MPP-negotiated licences (e.g., BMS, with 110 countries, 88.3% coverage; ViiV, with 73 countries, 89.4% coverage) as well as their effective coverage (90.7% and 93.4% respectively).

The EAG notes that in addition to incorporating a very promising compound into the existing licensing framework with Gilead, MPP has also been able to achieve some significant improvements to the terms and conditions of the existing licensing framework that is applicable across the entire agreement, including: (1) the inclusion of China as a country of manufacture; (2) improvement in the terms relating to diversion and royalty term; (3) the expansion of the covenant not to sue to include some key combinations with TDF/FTC; and (4) strengthened ability of MPP to monitor, manage and enforce the licence agreements vis-a-vis its licensees. The EAG is pleased to observe that the MPP has been able to address some issues that were subject to criticism in the original agreement, and encourages the MPP to continue to work with Gilead and other licensors in continually seeking to improve all aspects of its licensing agreements.

The EAG also notes that the proposed licence will be made public on MPP's website, contributing to the goal of injecting greater transparency in the field of HIV licensing, a core mission of the MPP.

Recommendation

The EAG concludes that the proposed amendment to the MPP-Gilead agreement is consistent with MPP's mandate as defined in its Statutes and MoU with UNITAID, and represents a significant improvement over the *status quo*, both in terms of geographical scope and the public health-oriented nature of the licensing terms and conditions. Therefore, the EAG recommends that the Medicines Patent Pool Governance Board request the Executive Director to sign the proposed amendments between Gilead and MPP.

Signed,

Maximiliano Santa Cruz
Chair, Expert Advisory Group