Report of the Medicines Patent Pool Expert Advisory Group on the Proposed Licence Agreement with BMS

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 (Board) on the proposed License and Technology Transfer Agreement (the Agreement) collaboration between MPP and Bristol-Myers Squibb (BMS) for daclatasvir (DCV).

Given that this is the first proposed licence agreement that the MPP has negotiated on a treatment for Hepatitis C (HCV), the EAG benefitted from four *ad hoc* experts in HCV that were invited to help the EAG assess the agreement. The four individuals were: Isabelle Andrieux-Meyer, of MSF, Ludmila Maistat of the International HIV/AIDS Alliance, Ukraine, Raquel Peck of the World Hepatitis Alliance, and Ellen 't Hoen, of Medicines Law and Policy.

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 the requirements set out in the Statutes and the Memorandum of Understanding (MoU) between the MPP and UNITAID, and (ii) do the negotiation results offer sufficient added value over the *status quo*?

Having reviewed the draft Agreement and having received a briefing from the MPP on the proposed collaboration between the MPP and BMS, the majority of the EAG and the *ad hoc* experts answer both questions in the affirmative and recommend that the Board request the Executive Director of the MPP to finalise and execute the necessary documents with BMS. Three members of the EAG, however, voiced their reservations regarding the geographical scope of the proposed licence, and requested that this concern be noted in the report.

Background, Overview of the Proposed Agreement

The MPP and BMS signed in December 2013 a licence agreement over atazanavir (ATV), a product of significant medical interest for HIV. The ATV agreement covered a territory of 110 countries comprising 88.5% of people living with HIV in low- and middle-income countries (LMICs), and contained a number of key public health-oriented terms and conditions that were viewed favourably by this EAG.

In November 2014, BMS had announced its intention to provide voluntary licensing agreements for DCV that would enable manufacturing and sale in 90 countries. Further details were unknown and to date no licences appear to have been issued. Immediately following the MPP's expansion of its mandate to cover HCV and tuberculosis in November 2015, BMS entered into negotiations with MPP for DCV.

Negotiations have progressed rapidly, as BMS has indicated willingness to license DCV on essentially identical terms and conditions as ATV, with an expanded territory comprising 112 countries (including 80 MICs).

The proposed Agreement on DCV consists of a main Agreement between MPP and BMS that grants MPP the right to sublicense in the form of the Sublicense Agreement attached as a schedule to the Agreement.

The Sublicense Agreement is royalty free and allows for the manufacture and sale of both active pharmaceutical ingredient (API) and finished product anywhere in the world for use within the Territory, defined as 112 countries, covering, according to MPP's estimates, 67.3% of people living with HCV in the developing world.[1] Even more people outside the 112 countries can potentially benefit, as the proposed Agreement provides that MPP licensees may engage in any activity outside the Territory where a licensee's "Commercialization" activities do not infringe a granted patent, and where the licensed know-how is not relied upon. The EAG understands from the MPP that most potential licensees will most likely not need to rely on the licensed know-how, thus allowing them to take advantage of this important flexibility.

The proposed License Agreement contains a number of other important public health-oriented terms and conditions. BMS agrees to waive any data exclusivity rights it may have within the Territory, provide documentation to assist in local registration, allows licensee to combine DCV with other drugs to make, e.g., fixed-dose combinations, and requires Licensed Products to receive Stringent Regulatory Authority approval or WHO pre-qualification. Importantly, the proposed Agreement steers clear of imposing any specialised anti-diversion programmes on other HCV medicines that have been the cause of many stakeholders' concern.

Assessment of the Proposed Collaboration 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 and the *ad hoc* group of experts find that the proposed collaboration meets the requirements in both the Statutes and MoU with UNITAID, as summarised in the tables below.

[1] The full list of countries included in the Territory is available in Schedule D of the Agreement.

Relevant Considerations in the Statutes of the Medicines Patent Pool

Statutes	Terms in Proposed Licence
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	• Agreement to waive data exclusivity rights • Allows for sale outside the Territory where Commercialization do not (i) infringe Licensed Patent Rights and Non-Territory Patents; and (ii) rely on the Licensed Manufacturing Know-How. For the purposes of this provision, "to infringe" will mean the infringement of a patent in force, or any other activities that are prohibited under applicable laws in relation to Licensed Patent Rights and Non-Territory Patent Rights. • No restrictions on ability of licensees to challenge the validity of licensed patents
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 has the right to issue non-exclusive sublicences to any qualified entity in the world. BMS to perform due-diligence together with MPP to ensure Sublicensees' compliance with GMP, anti-corruption laws

Relevant Considerations in the MoU between the MPP and UNITAID

MoU	Terms in Proposed Licence
Use all reasonable efforts to define standard terms and conditions of licence agreements	• Terms and conditions of Sublicense standardised across all sublicenses via the form Sublicense Agreement
Define the terms and conditions of the licences and sublicences, respecting the differing patentability criteria across jurisdictions	• Royalty free • No breach of the Agreement if commercialization outside the Territory where there are no infringement of Licensed Patent Rights and Non-Territory Patents • No restrictions on challenging licensed 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 pre-qualification or Stringent Regulatory Authority
Ensure that licence agreements specify an alternative dispute resolution mechanism	• Arbitration in accordance with ICC rules stipulated
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 BMS
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	• Technical transfer package provided to all sublicensees • Sublicensees can be based anywhere in the world

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

The EAG and the *ad hoc* group of experts find that the terms and conditions of the proposed Agreement represent a significant advance over the *status quo*.

The EAG is pleased to note that many concerns previously expressed by some civil society organisations concerning Gilead HCV licence had been taken into account in the proposed License Agreement. The EAG views this as a significant improvement over the *status quo* in terms of promoting public health-oriented

terms and conditions in voluntary licences. These include: (i) the ability for MPP licensees to be located anywhere in the world for purposes of supplying within the Territory; (ii) freedom to manufacture and sell API and finished product anywhere in the world for purposes of supplying within the Territory; (iii) the absence of any problematic anti-diversion programmes to be implemented, and (iv) the quality assurance provisions require approval by a Stringent Regulatory Authority or WHO pre-qualification.

The EAG and the *ad hoc* group of experts also stressed the need for rapid registration of this product throughout the Territory, and are pleased that the proposed Agreement sets timelines for registration, provides for BMS's documentation assistance in pursuing these registrations, and requires MPP licensees to respond to MPP's reasonable requests for registration in a country within the Territory. The group also stressed the need for the availability of DCV in combination with other HCV drugs – in particular sofosbuvir, and note that the proposed Agreement provides for the freedom of MPP licensees to make such combinations, including fixed-dose combinations.

The EAG and the *ad hoc* group of experts also understand that the requirement that the MPP licensees not rely on the licensed know-how most likely will not practically form an impediment to the MPP Licensees' ability to utilize the important flexibility of being able to supply outside the 112 countries where no granted patents are being infringed. The EAG and the *ad hoc* group of experts understands that most, if not all, MPP licensees will not need to rely on the licensed know-how, and thus the "effective" coverage of the proposed Agreement will be greater than 112 countries, as the group has been advised that there are no patents in some of the countries that have been excluded from the Territory. Although the MPP relied upon publicly-available sources of HCV patent data (e.g., the WHO landscapes, IMS patent data) in performing its analysis, one EAG member indicated that it would have been preferable had a comprehensive landscape be conducted. The EAG and the *ad hoc* group of experts look forward to receiving a more detailed analysis from the MPP regarding the effective coverage of the Agreement as it obtains more detailed patent information on DCV from BMS and other sources.

The EAG and the *ad hoc* group of experts recommended to the MPP to continue to work with BMS to seek to improve geographical scope of the Agreement. However, the majority of the EAG and the *ad hoc* group of experts felt that the number of people who could immediately begin to benefit from the licence outweighed the delay that would be caused by seeking to include more countries prior to signing the Agreement. However, three EAG members voiced concern regarding the geographical scope as it relates to the exclusion from the territory of certain LMICs with significant populations of people living with HCV, and requested that these concerns be noted in the final report of the EAG. One member indicated a desire to obtain a clearer understanding from BMS regarding the basis upon which the Territory had been defined.

One of the HCV *ad hoc* members wished it highlighted in this report that at present there is no other generic source of DCV and that this agreement opens the door for generic production barely six months after the WHO added DCV to the WHO Model List of Essential Medicines, which sets an important precedent in assuring availability of generic versions of new essential medicines. This same expert wished it highlighted that the agreement will accelerate the availability of a key pangenotypic WHO recommended HCV treatment (DCV in combination with another direct acting antiviral such as SOF).

Recommendation

The EAG and the *ad hoc* group of experts conclude that the proposed Agreement with BMS is consistent with MPP's mandate as defined in its Statutes and MoU with UNITAID, and represents a significant improvement over the *status quo* in terms of the public health-oriented nature of the licensing terms and conditions. The majority of the EAG and the *ad hoc* group of experts further conclude that the proposed Agreement represents a significant improvement over the *status quo* in terms of geographical scope, although they strongly recommend that the MPP continues to work with BMS to further expand the geographical scope after execution of the Agreement. Three members of the EAG felt differently, and noted their reservations on the geographical scope of the proposed Agreement, and two of them would recommend that MPP seek to expand the geographical scope prior to execution. Therefore, the majority of the EAG and the *ad hoc* group of experts recommend that the Medicines Patent Pool Governance Board request the Executive Director to sign the proposed Agreement between BMS and MPP. The EAG also recommends that MPP actively continue discussions with BMS seeking to incorporate countries currently excluded from the Territory.

Signed,

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Chair, Expert Advisory Group