



Report of the Medicines Patent Pool Expert Advisory Group on the Proposed Licence Agreement with Merck Sharp & Dohme (MSD) on Molnupiravir

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 Agreement (the Agreement) between MPP and MSD for molnupiravir (MOL) for treatment of mild to moderate COVID-19.

This report reflects the outcome of consultations with the EAG on 7 June 2021 (chaired by Peter Beyer and joined by EAG members Zeba Aziz, Akthem Fourati, Manuel Gonçalves, Giten Khwairakpam, Gugu Mahlangu, Deus Mubangizi, Valérie Paris, Fatima Suleman and Ellen 't Hoen, as well as François Venter from the Scientific Advisory Panel (SAP)) and on 21st of October 2021 (chaired by Peter Beyer and joined by EAG members - Alexandra Calmy, Akthem Fourati, Jan Gheuens, Manuel Gonçalves, Martha Gyansa-Lutterodt, Jordan Jarvis, Giten Khwairakpam, Gugu Mahlangu, Deus Mubangizi, Valérie Paris, Fatima Suleman and Ellen 't Hoen, as well as Nathan Ford from the SAP). François Venter from the SAP endorsed the conclusions of this report.

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 (ii) do the negotiation results offer sufficient added value over the *status quo*?

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

Background, Overview of the Proposed Agreement

In March 2020, as the severity of the Covid-19 pandemic became increasingly clear to the global community, MPP's Governance Board announced the temporary expansion of MPP's mandate to include any health technology that could contribute to the global response to Covid-19 and where licensing could facilitate innovation and access. The proposed Agreement would represent the first MPP licence on a Covid-19 technology following the mandate expansion.

MOL is a key target of the Access to Covid-19 Tools Accelerator (ACT-A) therapeutics pillar, noted as a promising small molecule Covid-19 treatment in late-stage development for non-hospitalized patients with mild to moderate symptoms. MSD's Phase 3 trials showed promising results (reduction of hospitalization by 50%, according to MSD's press release) in at risk, non-hospitalized adult patients with mild-to-moderate COVID-19. WHO will make a recommendation based on these Phase 3 results. Currently MOL is not included in WHO COVID-19 treatment guidelines.

With the support of Unitaid and other key members of ACT-A, MPP entered into negotiations with MSD for MOL in February 2021. The EAG was initially consulted in March 2021 and in June 2021 at earlier stages in the negotiations, and at that time stressed the need to expand the proposed Territory, and to ensure that the Agreement would be compatible with TRIPS flexibilities. In October 2021 MSD updated MPP about the encouraging Phase 3 outcome and its request for emergency use authorization by the US Food and Drug Administration (FDA).

Key aspects of the proposed Agreement are as follows:

Scope of Grant of Licence. The proposed Agreement would grant MPP a nonexclusive licence to the MSD patents and documentary know-how with the ability to grant nonexclusive, royalty-bearing sublicences to eligible API and finished product manufacturers anywhere in the world for purposes of supplying API or finished product into the Territory for use in the treatment of Covid-19.

Patent Status. Many patent applications have been filed in different jurisdictions and the patents have started to be granted in several countries. Some unpublished patent applications that are not yet in the public domain as they are still within the 18-month window from filing date will not be listed in Appendix 2 in the proposed Agreement. The EAG notes that this is MSD's statutory right and a legitimate exception to MPP's commitment to transparency as noted in the organisation's Transparency Policy.

Royalties. Royalties are set at 5% of net sales for governments and other public purchasers (including NGOs) in the Territory, and at 10% of net sales to commercial entities in the Territory. Royalties are payable regardless of patent status in the country of manufacture or sale. The Agreement is royalty-free until the World Health Organization (WHO) declares the end of the Public Health Emergency of International Concern regarding COVID-19 (PHEIC).

Territory. The Territory of the proposed Agreement consists of 105 countries.

Other key public health-oriented terms and conditions. The proposed Agreement contains other important public health-oriented terms and conditions, such as the requirement that MSD provides regulatory waivers. Anti-diversion restrictions are limited to those countries outside the Territory where there is a Non-Territory Patent.

Compatibility with TRIPS flexibilities. The proposed Agreement contains language that provides that nothing in the Agreement shall be interpreted as preventing activities that would not infringe upon MSD's patents and/or know-how.

Termination-for-challenge provision. For the first time, an MPP licence includes a termination-for-challenge provision, which provides

- MSD the right to terminate the head licence in the event that MPP or any of the sublicensees with the support of MPP challenges any of the licensed patents, and
- MPP the right (but not the obligation) to terminate a sublicense in the event that a sublicensee challenges any of the licensed patents.

The provision states that these clauses were included only as a result of a requirement of MSD's upstream licensors, namely, DRIVE (a fully-owned subsidiary of Emory University) and Ridgeback Therapeutics and expressly states that this provision is severable from the rest of the Agreement in the event that the clause is declared invalid or unenforceable.

The EAG's interpretation of this language is discussed further below.

Assessment of the Proposed Agreement in Light of MPP's Statutes

MPP's Statutes contain guiding principles against which the results of negotiations are assessed. The EAG finds that the proposed licence agreement meets the requirements in the Statutes, as summarised in the table below.

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); WTO Doha Declaration	Provisions ensuring that sales inside or outside the Territory are not a breach of the Agreement if the sales do not infringe MSD intellectual property (as, for example, if a compulsory licence has been granted) and/or misappropriate MSD know-how.
Entering into licence agreements with patent holding entities, and sublicense agreements with generic manufacturers and other appropriate sublicensees on a non-exclusive and non-discriminatory basis	MPP to enter into non-exclusive licences with licensees chosen through MPP's Expression of Interest Portal.
As and when necessary, enforcing terms and conditions of licence agreements, with appropriate dispute resolution mechanisms	MPP takes on significant obligations to monitor and enforce terms of agreements; specifies mediation at WIPO in case of dispute.
Requiring stringent quality criteria for licensed products	Requires all licensed products to be made in accordance with WHO PQ or Stringent Regulatory Authority standards, or through any provisional or emergency use authorizations available from WHO or an SRA.
Including anti-diversion and traceability mechanisms	Licensees required to implement a system of batch control as a means of tracing of product to monitor potential diversion.

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

The EAG finds that the terms and conditions of the proposed Agreement represent a significant added value over the *status quo*. The added value consists of the potential medical significance of enabling affordable access to MOL in 105 countries around the world, as well as the strategic and norm-setting significance of demonstrating MPP's viability in meaningfully engaging in the fight against Covid-19.

From a medical standpoint, in the event that it proves to be safe and effective, the EAG believes that MOL can form an important component of the Covid-19 response, as it will be an all-oral treatment available to high-risk patients outside the hospital setting that appears to significantly reduce the risk of hospitalisation and death. The need for such interventions for Covid-19 treatments is all the more apparent in light of the ongoing disparities of access to vaccines against the virus.

The EAG notes that the Agreement marks the first transparent, public health-oriented MPP licence on a Covid-19 technology. This accomplishment represents an important step both for MPP as well as the global community, as this Agreement may encourage other innovators to step forward and engage with MPP on other important Covid-19 technologies.

In the earlier EAG consultation on MOL, the EAG stressed the importance of ensuring that the Agreement would be compatible with TRIPS flexibilities. The EAG notes that the critical element of compatibility with TRIPS flexibilities has been preserved through Section 2.6:

For the avoidance of doubt, nothing in this Agreement shall be construed to prevent the Licensee from engaging in activities inside or outside the Territory where such activities would not (1) infringe the Patents and/or any other intellectual property rights; and/or (2) misappropriate MSD Know-How. Licensee acknowledges that MSD has expressly reserved all its rights under the Patents, except as expressly set forth in the MSD-MPP Agreement, and under any additional patents and/or patent applications owned or controlled by MSD. Licensee also acknowledges that MSD does not waive any applicable statutory and/or regulatory exclusivities owned or controlled by MSD, except as expressly set forth in the MSD-MPP Agreement. Nothing in this Agreement shall provide a right to commercialize outside the Territory.

Though - as noted in the last sentence of this Section - the Agreement itself does not confer an explicit right of commercialization outside the Territory, the EAG views an express grant of right unnecessary in light of the first sentence of this Section. Provided that MSD has acknowledged that activities that do not infringe MSD Patents or use MSD Know-How do not constitute a breach of the Agreement, a further right granted by MSD is not needed. The EAG interprets this provision as acknowledging that a licensee is not in breach of the Agreement if it manufactures in a country with no Patents to sell to a country outside the Territory where there are no Patents, as long as it does not rely on the MSD Know-How. It would also acknowledge the same where a licensee sells outside the Territory where a compulsory licence for the patented technology has been issued.

As previously mentioned, an MPP-negotiated licence includes for the first time a termination-for-challenge provision. Such a provision goes against long-established core MPP principles of compatibility with TRIPS flexibilities and complementarity with other access mechanisms, as laid down in MPP's Statutes. Moreover, such a provision may raise competition law concerns in many jurisdictions. MPP recognises this and expressly made clear that the provision was severable from the rest of the agreement in case it is invalid.

In principle, the EAG considers termination-for-challenge provisions as incompatible with the core MPP principles as mentioned above. However, the way in which the provision was drafted allows the EAG to recommend the agreement for adoption:

- First, in the Head licence, MSD is only given the right to terminate if MPP itself challenges any of the licensed patents or actively supports its licensees in challenging the patents – something that MPP does not do.
- Second, in the Form Sublicence, MPP has the right, but not the obligation, to terminate the Sublicence in the event that a Sublicensee challenges any of the licensed patents.

The EAG, however, strongly recommends that the MPP Board clearly state that the inclusion of termination-for-challenge clauses are not compatible with MPP core principles and that the MPP does not intend to exercise this right. The EAG further understands that this provision was included not at MSD's insistence, but of MSD's upstream licensors (DRIVE, a fully-owned subsidiary of Emory University, and Ridgeback). The EAG thus recommends that after execution of the agreement MPP continue to work with MSD and its upstream licensors to delete these provisions.

The EAG further notes that the Territory remains essentially the same as during the previous consultation on MOL in March 2021, and that the Agreement excludes several middle-income countries from the Territory of the licence, particularly in Latin America—one of the regions most impacted by the Covid-19 pandemic. While MSD’s global access plan for MOL states that MSD will make MOL affordable and available worldwide, the plan does not clearly address what level of affordability will be achieved, particularly in those middle-income countries that remain outside of the Territory. The EAG thus recommends that MPP continue to work with MSD to explore options to further expand the Territory in order to ensure access and affordability in all low- and middle-income countries.

The EAG further notes that while the licence is royalty-free for as long as COVID-19 remains the Public Health Emergency of International Concern as per the WHO, the royalty obligations are subsequently payable regardless of patent status in the country of manufacture or sale, marking a departure from MPP’s practice of making royalties payable only where there is a granted patent in force. The EAG understands that this obligation is one that is imposed on MSD from upstream licensors but encourages MPP and MSD to work with such licensors to make appropriate amendments to this provision.

Finally, the EAG notes that MSD has already signed bilateral licence agreements with a number of Indian manufacturers. Given the scope of the pandemic and the dire circumstances in India, however, it is important for there to be a broad base of manufacturers both inside and outside India sufficient to satisfy demand, including in countries where there appear to be no MOL patents. EAG therefore recommends that MPP takes this need into account when identifying and evaluating prospective sublicensees. The EAG strongly recommends that MPP work with MSD in transferring MSD direct licensees into MPP licences, which have important public health-oriented terms that may not exist in the bilateral licences.

Recommendation

The EAG concludes that the proposed Agreement with MSD is consistent with MPP’s mandate as defined in its Statutes and represents a significant improvement over the *status quo* in terms of the public health-oriented nature of the licensing terms and conditions. Therefore, while emphasising the areas for improvement detailed above, the EAG recommends that the Medicines Patent Pool Governance Board request the Executive Director to sign the proposed Agreement between MSD and MPP on the condition that it clearly states that the inclusion of termination-for-challenge clauses are not compatible with MPP core principles and that the MPP does not intend to exercise its right of termination-for-challenge.

Signed,



Peter Beyer
Chair, Expert Advisory Group
Date: 25 October 2021