

Medicines Patent Pool licence strengthens Merck's market control and undermines the Pool's core principles

The announcement of a Merck Sharp & Dohme Corp (MSD) and Medicines Patent Pool (MPP) voluntary licensing agreement on 27 October 2021 led to euphoric media headlines that MSD was sharing its recipe for its COVID-19 pill, molnupiravir (MOL), with poor countries.

However, a close examination of the MSD-MPP deal reveals limited country coverage, unjustified royalties and anti-competitive provisions amidst a weak patent portfolio held by MSD. It is a perfect example of using a voluntary licence (VL) for rent-seeking purposes.

Civil society organizations have also echoed similar concerns. Sergey Kondratuk from the International Treatment Preparedness Coalition (ITPC) referred to the VL as “a market-guarding wolf dressed as an access-expanding lamb”.

In early October, Merck issued a press release revealing an interim analysis of its Phase 3 study, that molnupiravir reduced the risk of hospitalization or death by approximately 50% for patients with mild to moderate COVID-19.

While the full data on MOL has yet to be released, this announcement raised hopes that MOL would provide outpatient antiviral therapy for newly diagnosed cases of COVID-19 early in the infection stage. If proven effective, MOL could provide governments with the possibility of deploying a “test and treat” strategy to contain COVID-19.

For this to happen, the challenge of sufficient supply and affordable price would have to be addressed. Merck's contract price to the United States is \$700 per course of treatment. However, the estimated generic price could be as low as \$20 per 5-day regimen including 10% profit margin and taxes.

MOL was invented by Emory University's Drug Innovation Ventures at Emory (DRIVE) with the support of substantial public funding (approx. \$35 million between 2013 and 2020) and subsequently licensed to Ridgeback Biotherapeutics. It is currently being assessed by the US Food and Drug Administration (USFDA) as well as the European Medicines Agency (EMA) for emergency use authorization.

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Prior to the MSD-MPP announcement, MSD had entered into bilateral agreements with eight Indian generic companies for manufacture and supply to 104 countries.

However, experts say that several other Indian generic manufacturers were ready to launch at risk in view of the weak patent portfolio held by MSD in India and beyond. In India, home to many generic manufacturers, the pending patent applications are heavily opposed. Several other manufacturers in developing countries are also ready to manufacture. Moreover, there are currently no patents in many of the countries covered by the VL.

The limited patent holding of MSD and the terms of the MSD-MPP agreement raise the question of whether the agreement brings any added value to the cause of equitable access.

Scope of MSD-MPP Agreement

The MSD-MPP licence (main Agreement) allows MPP the ability to grant royalty-bearing sub-licences to certain manufacturers of active pharmaceutical ingredient (API) and finished product (sub-licensees) for purposes of supplying API or the finished product into the Territory for use in the treatment of COVID-19. “Territory” refers to the 105 countries covered by the Agreement.

The licence uses a broad definition of “patents”:

Patents shall mean any unexpired letters patent or any patent applications as set forth in Exhibit A hereto, that are granted or pending, relating to the Substance and/or Product and made a part of this Agreement, including divisionals, continuations, continuations-in-part, reissues, renewals, substitutions, registrations, re-examinations, revalidations, extensions, supplementary protection certificates, pediatric exclusivity, and the like of any such patents and patent applications, and international (e.g. WIPO), regional (e.g., EPO, EA), and foreign national equivalents of the foregoing.

Arguably this broad definition of patents provides cover for the existing weak patent holding of MOL and payment of royalties to MSD.

Apart from the listed patent applications annexed to the Agreement (discussed below), there is a new international patent application PCT/US2021/016984 titled “N4-hydroxycytidine and derivatives and anti-viral uses related thereto”. It claims molnupiravir (EIDD-2801) and its active ingredient EIDD-1931 could be used to treat SARS-CoV-2. EIDD-1931 and its efficacy against SAR coronaviruses is well known since 2004 while EIDD-2801 is an obvious modification, i.e., a prodrug, of EIDD-1931. It is well known that a prodrug is an inactive form of a drug and breaks down in the body forming metabolites, one of which transforms into an active ingredient with therapeutic effect. **This patent application filed by Emory University is frivolous for the claims are neither inventive nor novel, hence not patentable.**

In addition, although included in the scope, unpublished patent applications for the 18-month window from the respective filing dates are redacted in the Agreement available on MPP’s website, despite MPP’s commitment to transparency.

Included Territory

Under the MSD-MPP VL, sub-licensees can only supply 105 low- and middle-income countries (LMICs), i.e., only one more country than in MSD’s previous bilateral agreements. Of these countries, MSD has only filed patent applications in India, South Africa, Indonesia, the Philippines, Jamaica, Pakistan and Venezuela.

Of the 105 countries, 46 are classified by the United Nations as least developed countries (LDCs), and irrespective of any patent status, these LDCs enjoy full exemption from having to provide any kind of intellectual property protection. In many of the other countries included in the Territory, pharmaceutical companies rarely file patent applications (based on information available on medspal.org).

Strikingly, the VL Territory predominantly covers low-income countries. But experts say that for MOL to be effective, it has to be administered very early on, which requires robust testing capability. Ironically, such testing is extremely limited in those countries. According to the Geneva-based Foundation for Innovative New Diagnostics (FIND), there are about 10 tests per 100,000 of population in low-income countries.

India is also included in the VL Territory. There are two pending patent applications, the grant of which has been opposed. Application No. 201717025098 claims N4-hydroxycytidine nucleoside derivatives, compositions and methods related thereto and relates to treatment and prophylaxis of viral infections. This application claims a Markush structure/a general formula and host of compounds that may encompass in it, and only impliedly discloses MOL. The Indian patent office does not generally entertain such patent applications. There are three to four pre-grant oppositions pending before the Indian patent office.

The other patent application, No. 202017019418, expressly claims MOL and other derivatives of β -D-N4-hydroxycytidine which have been in existence for more than 50 years. Since 2004, it was found that β -D-N4-hydroxycytidine or EIDD-1931, the active ingredient in MOL, was active against a range of RNA viruses including the hepatitis C virus, seasonal and pandemic flu viruses and coronaviruses such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). However, EIDD-1931 was not well absorbed orally and hence it was converted to a prodrug (an inactive drug that is converted into an active drug after absorption) which is molnupiravir. Thus the patent application is unlikely to meet India's patentability requirements. This application is also opposed in India.

In the case of South Africa, only the public sector may be supplied under the VL. In Indonesia, the only patent application filed has also been opposed.

Excluded Territory

Supply to a large number of developing countries is excluded from the licence, in particular supply to upper-middle-income countries including in Latin America, although middle-income countries excluded from the licence had 30 million infections in the first half of 2021, and 50% of all infections in LMICs.

According to paragraph 2.6 of the sub-licence agreement, licensees may only supply countries in the excluded Territory if the activity would not “(1) *infringe the Patents and/or any other intellectual property rights; and/or (2) misappropriate MSD know-how*”.

It also adds that the “*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*” and 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*”.

The same paragraph then reinforces that “*Nothing in this Agreement shall provide a right to commercialize outside the Territory*”.

This paragraph combined with the broad definitions of “patents” as well as “MSD know-how” is likely to create legal uncertainty and hesitancy among licensees with respect to supplying the excluded Territory.

Royalties

Royalties are set at 5% of net sales to government entities and public purchasers in the Territory, and at 10% of net sales to commercial entities in the Territory. These royalties do not apply until the World Health Organization (WHO) declares the end of the Public Health Emergency of International Concern (PHEIC) regarding COVID19.

In comparison to previous MPP licences (several of which have been royalty-free), the proposed royalties are extremely high and divide the market into public and private sectors. This especially compromises access in developing countries where the majority of people depend on the private sector for their healthcare needs, with increasing out-of-pocket expenses as healthcare costs rise.

These royalties are especially concerning because the MSD-MPP Agreement recognizes **MSD's right to royalties in the absence of any patents in most of the included Territory**. It establishes MSD's rights when no such rights exist in the first place.

MPP's Expert Advisory Group itself notes that "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 royalties (once applicable) would terminate "*upon the later of: (a) the expiration, invalidation or abandonment date of the last Patent that includes a Valid Claim that covers such Product in such country in the Territory; (b) ten (10) years from first commercial sale of such Product in such country in the Territory; or (c) expiration of regulatory exclusivity of such Product in such country in the Territory*".

With a broad definition of patents and expected further patent filings by MSD, the duration for the payment of royalties could be further extended.

Manufacturers

An argument being made for this licence is that it will allow more manufacturers to produce the medicine. In reality, however, in the absence of patents any manufacturer is free to produce. LDCs in any case are exempt from implementing, applying or enforcing pharmaceutical patent protection. And in the event there is a patent application/grant in developing countries (there are but very few of them, as discussed above), there are flexibilities available, such as oppositions and compulsory licences, that may be deployed.

Further, under the sub-licence agreement (paragraph 3.3), the manufacture of the substance and product has to be consistent with standards of WHO prequalification or of a stringent regulatory authority (SRA). Sale is possible only if the product has obtained WHO prequalification or SRA approval, or any provisional or emergency use authorizations available through WHO or an SRA.

This requirement itself limits the number of developing-country manufacturers that could be recipients of a sub-licence. To date, the main recipients of the MPP licences have been Indian pharmaceutical companies.

Active Pharmaceutical Ingredient (API)

Sourcing of the substance (API) is from an "authorized supplier" (that has entered into an agreement with MSD regarding the right to supply) or an MPP licensee. A licensee may source from a third party but only with the agreement of MSD. Any agreement between the licensee and the "authorized supplier or MPP licensee" with respect to API has to be with prior notice to MSD through MPP.

Presently API producers are independently making API for several generic companies in developing countries. If they sign the MPP licence, then their API would only be for those who are licensees or authorized suppliers under the MSD-MPP arrangement. Independent supply of API, which is crucial to galvanize production and supply in all developing countries, would be adversely affected.

Undermining TRIPS Flexibilities – the Right to Oppose

In paragraph 10.3(g) of the sub-licensing agreement, MPP has the right to terminate the sub-licence agreement given to a licensed manufacturer where the manufacturer "*challenges the validity, enforceability or scope of any claim within the Patent in a court or other governmental agency of competent jurisdiction, including in*

a re-examination or opposition proceeding, or as a defense to enforcement of this Agreement or the terms of this Agreement, including applicable payment obligations”.

In addition, “[t]o the extent that this Section 10.3(g) is deemed invalid or unenforceable in any jurisdiction, this Section 10.3(g) is intended to be severable without affecting the validity of the rest of this Agreement”.

A similar paragraph is also the basis for MSD terminating the MPP licence, including in a situation where a sub-licensee acting at the instance or with the support of MPP or its affiliates challenges MSD’s patents.

The inclusion of this provision in the licence agreement has been justified on the basis that these clauses were a requirement of MSD’s upstream licensors, namely, DRIVE (a fully owned subsidiary of Emory University) and Ridgeback Biotherapeutics.

MPP’s Expert Advisory Group in its report notes with concern that the “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” and “may raise competition law concerns in many jurisdictions”.

MPP’s Board also concurred with this assessment, stating that “inclusion of a termination-for-challenge provision runs contrary to MPP’s core principles” and that “MPP has the right, but not the obligation, to terminate a sublicense in the event of a challenge”.

While the Board calls on MPP to work with MSD and its upstream licensors to remove this clause, significant damage has been done to access to medicines and MPP’s role in upholding public health.

Worryingly, the sub-licence agreement also recognizes MSD and Emory University’s DRIVE as a “*third party beneficiary*” “*entitled to enforce the terms and provisions of the Agreement on its own behalf to the same extent as MPP*”.

While the effect of this and other provisions remains to be seen, what is crystal clear is that this licence will create a chilling effect on further patent opposition on MOL (despite MSD’s weak patent portfolio) and further strengthen MSD’s market power.

In the case of MPP, the Agreement has sent a strong message to Big Pharma that MPP is willing to compromise on any core principles to obtain a VL.