Medicines Patent Pool has potential for wider scope

In just over five years, the Medicines Patent Pool (MPP) has achieved several notable successes. But far more is to come, executive director Greg Perry tells Aidan Fry.

Greg Perry

Reflecting on his three years at the helm of the Medicines Patent Pool (MPP), executive director Greg Perry has good reason to be proud. By negotiating voluntary licences with all the major originators and intellectual-property (IP) holders in the antiretrovirals sector, the MPP has already saved healthcare authorities around the world well over US$100 million, and savings of around US$1.5 billion are anticipated up to 2028. And with a remit recently broadened to cover hepatitis C and tuberculosis treatments, the organisation is in prime position to fulfil a major public-health role.

In an exclusive interview with **Generics *bulletin***, Perry – who joined the MPP at the start of 2013, having previously served as director-general of the European Generic and Biosimilar medicines Association (EGA) – points out that the US$120 million savings achieved to date through making treatments more affordable and reducing royalties paid by generics manufacturers are "equivalent to one year of first-line treatment for approximately 950,000 people".

Based on voluntary licensing and free-market competition, the MPP operates within the existing international trade and intellectual-property frameworks, recognises the rights of inventors and intellectual-property holders and offers generics companies a simple and viable path to market whilst promoting public health considerations.

Now into its sixth year after it was established in July 2010 by global health financing mechanism UNITAID and at the request of the international community, the MPP spent most of that time negotiating licensing deals that improved access to antiretroviral HIV/AIDS treatments in developing countries. But towards the end of last year, the organisation – which is funded through a memorandum of understanding with UNITAID – obtained a mandate to broaden its remit to negotiate licences for hepatitis C and tuberculosis treatments.

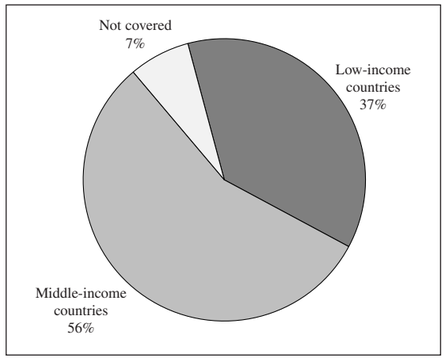

Figure 2: Dolutegravir (DTG) adult licence effective coverage in low- and middle-income countries, measured by people living with HIV/AIDS (Source – MPP)

Within weeks of being established in 2010, the MPP had enlisted its first licensing partner for intellectual-property rights, the US National Institutes of Health (NIH), which granted a royalty-free licence to use patents covering the protease-inhibitor HIV medicine darunavir. A wide-ranging agreement with the MPP's first corporate partner, Gilead, followed in July 2011, before the first generics company, Aurobindo, signed up three months later in October 2011.

By its fifth anniversary midway through last year, the MPP had signed voluntary licences with seven patent holders for 12 antiretrovirals, as well as for one direct-acting antiviral hepatitis C treatment and an agreement for a nano-formulations technology. Accountancy firm KPMG has verified that the MPP's 12 generics partners have already supplied more than 7 million patient-years of HIV medicines to 117 low- to middle-income countries.

Taking the example of tenofovir disoproxil fumarate (TDF) and combinations containing the antiretroviral drug, prices have tumbled since the MPP agreed voluntary licences to facilitate generic competition in developing countries, with price falls in certain countries exceeding 90% (see Figure 1).

"The terms and conditions of our licences provide generics companies with significant business flexibilities," Perry points out. For example, he says, MPP sub-licensees can combine antiretroviral agents to develop novel fixed-dose combinations (FDCs) and, under certain circumstances, can sell outside of the licensed territories, such as to countries that have issued compulsory licences that are in accordance with the World Trade Organization's (WTO's) agreement on trade-related aspects on IP rights (TRIPS). "There are waivers for data exclusivity and, in some cases, technology-transfer packages," he highlights.

Country	Product	Lowest price before agreement 2010-2011 (US$)	Lowest price from MPP partners after agreement 2011-2012 (US$)	Lowest price from MPP partners 2013-2014 (US$)
Azerbaijan	TDF/FTC	582	80	–
Belarus	TDF/FTC	577	77	67
Egypt	TDF/FTC	384	85	76
El Salvador	TDF/FTC	553	72	61
Georgia	TDF/FTC	657	88	–
Iran	TDF	577	48	48
Iraq	TDF	440	55	55
Paraguay	TDF/FTC	536*	–	86
Tunisia	TDF/FTC	358	118	95

TDF: tenofovir disoproxil fumarate. TDF/FTC: tenofovir disoproxil fumarate/emtricitabine

* 2012 price

Figure 1: Prices for tenofovir disoproxil fumarate (TDF) and TDF combinations following MPP agreement in an illustrative list of countries. Prices displayed in US$ per patient per year (Source – MPP)

Perry is keen to point out that collaborating with the MPP is "not just a question of corporate social responsibility". The antiretroviral drugs covered by its licences are, he says, "crucial first- and second-line HIV medicines and there are strong markets for them". While generics partners help the MPP to fulfil its goal of broadening access to modern medicines in the developing world, originators can draw confidence from working with a UN-backed organisation.

Licences from a single source

In contrast to the "costly and time-consuming process" of obtaining compulsory licences for individual products in individual countries, Perry outlines, generics suppliers can use the MPP's non-exclusive licences to access large territories – often comprising more than 100 low- and middle-income countries – through straightforward licences available from a single source.

"Most of our current licensees appreciate the MPP's hands-on approach to supporting their development plans, from providing HIV medicines forecasts developed with the World Health Organization (WHO) to advice on regulatory pathways," Perry maintains. "Moreover, the MPP's ability to license new, often breakthrough antiretrovirals – such as dolutegravir and tenofovir alafenamide (TAF) – is giving generics firms a head-start in bringing new medicines to the market."

Two dolutegravir licences agreed with ViiV Healthcare in April 2014, covering adult and paediatric formulations respectively, marked a novel approach to licences under the MPP's framework. A sliding scale of royalties, based on per capita income, helped to secure a geographically broad licence that included six large middle-income countries – Egypt, India, Indonesia, the Philippines, Turkmenistan and Vietnam. As can be seen from Figure 2, middle-income countries predominate in terms of the number of people living with HIV/AIDS who could benefit.

Recognising that such flexibilities on royalties could prove a useful way to ensure more affluent middle-income countries were covered by voluntary licences, Perry points out that the dolutegravir deal was concluded just eight months after the novel antiretroviral was approved in the US, and two months after it was authorised in the European Union (EU). This, he says, is an example of the MPP's commitment to "work today for tomorrow's treatments" and to plan for public-health requirements over the next five to 10 years. "A licence for TAF was agreed immediately after regulatory approval," he observes.

As Figure 3 shows, several generics companies have to date obtained sub-licences to supply dolutegravir and TAF. "The vast majority of our agreements allow manufacturers based anywhere in the world to sub-license through the MPP, provided they meet certain criteria," Perry notes. Such criteria, he outlines, include sufficient capacity, capability and experience to develop, register, manufacture and distribute quality active pharmaceutical ingredients (APIs) and finished-dose formulations widely in the territory of the licence.

A royalty-free licensing agreement struck with AbbVie late last year fulfilled one of the MPP's key priorities in "addressing future demands for lopinavir/ritonavir in South Africa and across [the rest of] Africa". The deal covering adult formulations – which followed an agreement for paediatric formulations that had been concluded a year earlier – allows sub-licensees to make and market not only generic versions of lopinavir/ritonavir, but also combinations of ritonavir with other antiretrovirals, such as atazanavir and darunavir (**Generics *bulletin***, 8 January 2016, page 13).

Aurobindo became the first generics sub-licensee for lopinavir/ritonavir in February this year. "Other manufacturers have expressed interest in the licence and their requests are being processed," the MPP reveals.

Lopinavir and ritonavir were each listed as being of high clinical and market/IP priority in a working paper on antiretroviral priorities that the MPP published in March last year. Perry tells **Generics *bulletin*** that now the MPP has concluded agreements for the vast majority of marketed antiretrovirals, the organisation is reviewing its priorities to reflect the considerable pipeline of HIV/AIDS treatments that are in development. "We are discussions with companies and other stakeholders, such as the WHO and national authorities, to formulate new priorities," he says.

Encouraging novel paediatric formulations and

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	Abacavir (paediatric)	Atazanavir	Cobicistat	Dolutegravir	Elvitegravir	Emtricitabine	Lopinavir (paediatric)	Ritonavir (paediatric)	TAF	TDF	Quad
Aurobindo	X	X	X		X	X			X		X
Cipla		X	X	X	X	X			X		X
Desano		X	X	X	X	X			X	X	X
Emcure		X	X	X	X	X			X		X
Hetero			X	X	X	X	X	X	X		X
Huahai			X			X			X	X	
Laurus			X	X	X	X			X	X	X
Lupin			X	X		X			X		X
Micro Labs				X		X			X		X
Mylan				X							
Strides				X							

Figure 3: The Medicines Patent Pool's 11 current generics sub-licensees for antiretroviral active ingredients, with X' marking substances for which each generics supplier has agreed a licensing deal (Source – Generics *bulletin*)

fixed-dose combinations will continue to be a priority for the MPP, Perry pledges. "We would like to work with more local producers," he states.

Commenting on the predominance of Indian companies among the MPP's generics sub-licensees, Perry maintains this reflects companies' portfolio and pipeline focus, rather than any geographic bias. "Indian firms are leaders in antiretrovirals," he points out, stressing that partnerships with Chinese companies such as Desano and Huahai could be "important to help improve cost efficiencies for generic antiretrovirals".

By the early part of the next decade, the MPP expects to be generating annual savings through its antiretroviral licences of over US$100 million, reaching about US$200 million per year by 2028. Over that period, cumulative savings should exceed US$1.5 billion (see Figure 4).

Exploring nanotech and injectables

Towards the end of last year, the MPP reached an agreement to use the University of Liverpool's solid drug nanoparticle (SDN) technology to develop antiretroviral formulations that overcome challenges such as poor solubility to administer smaller doses of active ingredient, thereby cutting the cost of goods and improving patient compliance (**Generics *bulletin***, 9 December 2015, page 20).

While the project is at a relatively early stage, it reflects the MPP's intent to work on novel technologies that may help achieve its goal of improving access to safer and more cost-effective medicines in low- and middle-income countries.

Discussing the MPP's future plans in the HIV/AIDS space, Perry says the non-profit organisation is exploring opportunities for injectable antiretrovirals that could improve ease of treatment and patient adherence, such as through long-acting formulations.

In the hepatitis C sector, the MPP acted within days of having its mandate extended to secure its first originator partner, Bristol-Myers Squibb, for the direct-acting antiviral daclatasvir. A couple of months later, the MPP unveiled daclatasvir sub-licenses with four generics firms – Cipla, Emcure and Hetero, as well as with a new partner, Natco Pharma (**Generics *bulletin***, 29 January 2016, page 9).

"We will now prioritise other hepatitis C treatments out there," Perry promises, noting that the considerable commercial success of novel treatments that can cure the disease within 12 weeks has attracted several companies to develop their own therapies. "We are in discussions with companies and are identifying the next avenue of products to license," he reveals, insisting that the MPP has provided a viable model for licensing IP rights for such deal.

"The big issue on hepatitis C is who will pay for the treatments, and how?" Perry asserts. "Success in tackling HIV has come from a combination of access agreements and public funding, with huge internal and external funding in countries. That does not currently look likely for hepatitis C."

Given the huge savings to healthcare systems of curing hepatitis C rather than treating it as a chronic condition that can require liver transplants, Perry believes the international community will have to devise a funding solution for the new treatment paradigm. Governments and private insurers may have to step up, including in middle-income countries, he predicts, even with the availability of lower-cost generics through the MPP or other licensing schemes.

By contrast, Perry continues, drug-resistant tuberculosis offers a very different challenge. "Due to the historical concentration of tuberculosis in poorer countries," he notes, "there is less commercial potential for tuberculosis drugs. As a consequence, the lack of economic incentive has caused several pharmaceutical companies to halt their research and development efforts in this area."

Perry outlines that the MPP intends to work with a range of partners, including industry, patient groups and other parties, to explore collaborative models for developing and providing access to new tuberculosis treatments. These, he says, could include grants and prize funds to reward innovation, in line with the '3P' concept of 'push, pull and pool' – push funding to finance research and development upfront; pull funding based on prizes for reaching development milestones; and pooling of data and IP through an open collaborative model.

The 3P tuberculosis proposal is mentioned by the MPP in its recent submission to the UN High-Level Panel on Access to Medicines. "After reviewing the MPP's experience in HIV patent pooling," it suggests in the submission, "the High-Level Panel may like to explore other areas in which such approaches could promote research, development and innovation in the health sector and facilitate access to new products".

Among the MPP's proposals are increasing access to affordable health products in developing countries through non-exclusive voluntary licensing for a wider range of drugs. "The case of medicines included in the WHO's Model List of Essential Medicines may merit attention," it suggests.

Patent-pooling could also contribute to mechanisms for bringing new antibiotics to market, and voluntary licences could also spur follow-on innovation, such as with paediatric formulations of antiretrovirals. And such licensing could provide a way to deal with the 'patent thickets' owned by several different IP holders on products such as vaccines and diagnostics.

Perry maintains that the MPP's "clear, robust and viable model" could be applied successfully in several areas, including oncology. "But first we would discuss its feasibility with relevant stakeholders," he states.

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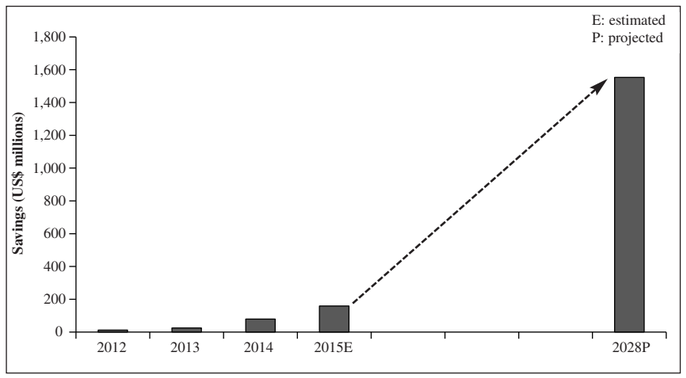

Figure 4: Projected savings from MPP licences for antiretrovirals between 2015 and 2028, the date of the last patent expiry on medicines currently identified as a priority (Source – MPP)