

The Medicines Patent Pool/Gilead Licences: Questions and Answers

1. Which products do the licences cover?

The licences cover: tenofovir (TDF), cobicistat (COBI), elvitegravir (EVG), and the Quad, a fixed-dose combination of TDF-COBI-EVG-emtricitabine. There is also a covenant not to enforce emtricitabine (FTC) patents, and the ability to make other fixed-dose combinations involving these compounds.

Tenofovir, cobicistat, and elvitegravir are three of the 19 drugs prioritised as especially critical to public health by the Medicines Patent Pool in cooperation with the World Health Organization HIV/AIDS Department and innovative financing mechanism UNITAID.

2. What is tenofovir? Why is it important?

Tenofovir is a reverse transcriptase inhibitor - an antiretroviral drug that prevents viruses from reproducing by blocking an enzyme that makes it possible for them to do so. It is used in combination with other ARVs in first-line and second-line regimens for HIV as well as for hepatitis B. The TDF licence in the Pool allows for it to be supplied as either an HIV or hepatitis B treatment.

In March 2010 it was also approved for use in children over the age of 12, and is in clinical trials for younger children. It has been recommended by the World Health Organization to replace stavudine, a widely-used HIV treatment in the developing world that is less preferred due to adverse side effects.

3. What is cobicistat? Why is it important?

Cobicistat is a medical product in the development stage. It helps improve the efficacy of other antiretroviral medicines by boosting their availability in the blood. This means that those ARVs would be more effective at lower doses, decreasing their negative side effects without losing treatment benefits.

4. What is elvitegravir? Why is it important?

Elvitegravir is a medical product in the development stage. It is an integrase inhibitor - antiretroviral that works by preventing a step in the AIDS virus' replication cycle. EVG is under exclusive licence to Gilead from Japan Tobacco.

5. What is emtricitabine? Why is it important?

Emtricitabine is an antiretroviral drug that works by blocking an enzyme needed in viral replication. It is used in first and second line treatment for adults.

6. Why are these licences significant?

These licences are a proof of concept that the Pool can negotiate constructive, public-health oriented licences with pharmaceutical companies that represent an improvement on the status quo. These licences have improved on existing voluntary agreements with the inclusion of more countries and new molecules.

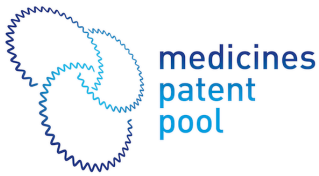
The Pool is now ready to grant licences to generic companies.

7. What is the public health benefit of these licences?

These licences are a critical step forward in changing norms on voluntary licensing – turning access initiatives in the direction of greater transparency and greater public health focus.

These licences improve on existing agreements in several ways:

- ❖ **Transparency:** The terms and conditions of most privately negotiated licences are not known. In a move unprecedented in the pharmaceutical field, the Pool has published the entire text of the voluntary licences on its website. This allows for generic companies and product development partnerships to understand exactly what rights and obligations are contained in Pool licences. It also allows key stakeholders in the public health community to provide feedback on the licences and suggestions for improvement to ensure that subsequent licences negotiated by the Pool represent an improvement on what has come before.
- ❖ **Public health focus:** The Pool has negotiated the licence so that critical flexibilities in intellectual property law are not compromised. For instance, the agreement expressly ensures that licensees are able to supply to countries outside the licensed territory where compulsory licences are issued. (See further detail below.)
- ❖ **Any applicable data or regulatory exclusivity rights are explicitly waived,** removing a key non-patent barrier to access to medicines.
- ❖ **Pipeline products:** the licensing of products still in clinical development by a commercial, research-based company to generic companies for use in resource-poor settings is rare. These licences on products still in development will help speed the arrival of newer, potentially more effective drugs for people who need them most.
- ❖ **Special provisions for paediatric formulations:** Royalties will be waived for any new paediatric formulations, and there are provisions for medicines for children under 12 to be made available outside the licence territory.
- ❖ **Expansion of geographical scope:** the number of countries in the licenced territory is greater than in any previous Gilead licence or any other company's voluntary licence.
- ❖ **Use of TDF for hepatitis B:** previous voluntary licences have only allowed the use of tenofovir in the treatment and prevention of HIV. The Pool's licences also allow for its use in the treatment of Hepatitis B, which is a significant



health problem in developing countries that the World Health Organization estimates kills 600,000 people a year.

- ❖ Termination clauses: previous TDF licences did not allow for the licensee to terminate without cause. The Pool licences allow for licensees to terminate for any reason and on a drug-by-drug basis. That is, licensees can terminate the licence for one medicine, while retaining the licence to produce the others (known as “unbundling” - see further detail below).

The Pool is working to deliver even greater public health benefits – such as the development of new fixed-dose combinations – by concluding licences for additional medicines.

8. How will these licences impact medicines prices?

The Pool licences will facilitate increased competition in the markets for these medicines. Competition has proven to be the most effective, reliable and predictable way to decrease HIV medicines prices. For example, generic competition in the tenofovir market contributed to an 80 per cent decrease in its price over the past few years. The Pool licences are non-exclusive (within India), which means that any company that meets the eligibility criteria may receive a licence from the Pool. As HIV treatment scale-up continues and demand for HIV medicines continues to grow, it will be critical to ensure sufficient production capacity and robust competition in markets, while taking into account the need for economies of scale.

For products already on the market (tenofovir, emtricitabine, and some FDCs containing these medicines), the Pool licences will clear the path for additional competition and production capacity.

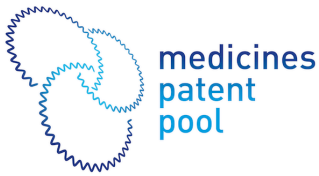
For the pipeline products (cobicistat, elvitegravir, the Quad and other FDCs containing these medicines), the Pool licences will allow multiple licensees to prepare to market these new medicines as soon as Gilead receives regulatory approval, thereby facilitating early generic competition for these products.

9. Do these licences prevent the use of flexibilities in the World Trade Organization’s Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) or the Doha Declaration on TRIPS and Public Health?

No. The ability of licensees to supply medicines to countries that have used TRIPS flexibilities and/or to countries where the government of India has issued a compulsory licence for export is expressly guarded in sections 7.3(c) and 10.3(d).

10. Are there any provisions such as bundling or “no patent challenge” clauses in these licences?

No. Bundling is a practice in which the licences on several products are tied together so that, for example, a company cannot take a licence to use cobicistat without also taking



the licence on tenofovir. A “no challenge” clause can prevent a licensee from challenging the licensed patents. Such provisions can have a negative effect on competition and affordability. The Pool has therefore negotiated so that no such provisions appear. A licensee can terminate the licence on a drug-by-drug basis, at any time. The licence also explicitly acknowledges that where a patent is no longer valid in India and in the country of sale, the licensee no longer has any obligation to pay royalties.

11. Do the licences include know-how transfer?

Yes, the licences include a “one-time technology transfer of know-how” to the licensee. The know-how “shall be sufficient to enable Licensee to manufacture TDF and TDF Product, EVG and COBI, EVG Product, COBI Product and Quad, at commercial-scale quantities.” This is a significant improvement over existing licences. The Pool did not want the transfer of know-how to result in onerous obligations, and this is reflected in the text of the agreement.

The know-how transfer in the licences does not come with any additional royalty obligations. A licensee may terminate the licensing agreement for any reason with a 30-day notice.

12. Are there any provisions related to data exclusivity?

The licences require Gilead to waive any data exclusivity rights that might apply, and prevents the licensee from applying for any such exclusivity.

13. What is the geographical scope of the licences? Is this an improvement on prior licences?

The licences allow for the supply of generic tenofovir (TDF) and emtricitabine in 111 countries, for cobicistat (COBI) in 102 countries, and for elvitegravir (EVG) and the Quad in 99 countries. The list of low- and middle-income countries included and excluded for each medicine is annexed to this document.

This is the first time COBI, EVG and the Quad have been licensed. Previous TDF voluntary licences from Gilead covered 95 countries, representing 93,200 fewer people living with HIV than the Patent Pool licences.

While the number of countries has increased in the Patent Pool licence, there are still developing countries with high HIV burdens that the Pool was unable to negotiate into the licences.

The Pool has been mandated by UNITAID to seek inclusion of all developing countries, and considers the geographical scope to be a key area where these licences could be improved.

14. What about API restrictions, and licensee restrictions?

Licensees must purchase API only from other licensees or directly from Gilead or Gilead distributors. Also, the licence restricts API manufacturers and licensees to Indian manufacturers. These restrictions are not ideal; however, it should be noted that India manufactures a vast majority of ARVs (~90 %) currently used in HIV treatment programmes in developing countries.

The API sourcing and licensee restrictions are another area where the Pool believes the licences could be improved.

15. What are other areas where the licence agreement could have been improved?

In addition to limits on the geographical scope of the licences, and restrictions on API sourcing and eligible licensees, there are a few other areas in which the Pool sought but did not get improvements.

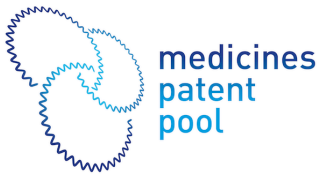
These are:

- ❖ New combination products containing EVG aside from the Quad must be approved in writing by Gilead. EVG is exclusively licensed to Gilead by Japan Tobacco.
- ❖ The EVG geographic scope is smaller than the COBI geographic scope by three countries (Aruba, Dominican Republic, and Montserrat).
- ❖ There are nine countries included in the TDF geographic scope, but excluded from both the COBI and the EVG scope: Botswana, Ecuador, El Salvador, Indonesia, Kazakhstan, Namibia, Sri Lanka, Thailand, and Turkmenistan. Some of these have high HIV burdens. Although the Pool is not privy to the details of the arrangement, the Pool understands that Gilead has entered into "semi-exclusive" voluntary licences covering these countries with a number of Gilead's "Preferred Partners."

16. Do these licences authorise production of other FDC's such as Atripla (tenofovir, emtricitabine, efavirenz) or the in-development FDC containing tenofovir, emtricitabine and rilpivirine?

Only in situations where there are no patent barriers to the use, respectively, of efavirenz or rilpivirine.

Gilead controls the patents on tenofovir and emtricitabine, but another company – Merck – holds the patent on efavirenz, the third component of Atripla. In order to produce fixed-dose combinations, generic manufacturers need to have the legal right to produce all the components in the combination. Merck is not yet in negotiations with the Medicines Patent Pool.



Similarly, other fixed-dose combinations that include products from more than one patent-holder may require additional licences. The fixed dose combination comprising tenofovir, emtricitabine and rilpivirine that is currently under development would require a licence on rilpivirine (where rilpivirine patents exist). Johnson & Johnson holds the patent on rilpivirine, and is not yet in negotiations with the Medicines Patent Pool.

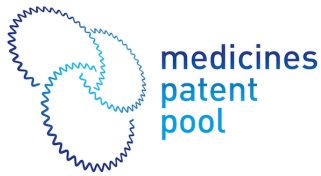
17. What is the decision-making process for the Patent Pool to accept this licence?

The Patent Pool Governance Board is in the process of convening an Expert Advisory Group (EAG) to provide advice as to whether the negotiated licences represent a significant improvement over the status quo. However, because the EAG had not yet been formally convened, an ad hoc group of experts were consulted for these licences. The ad hoc group provided feedback and guidance on on-going negotiations. The ad hoc group's input and suggestions were then shared with the Pool's Governing Board for final decision.

The Pool also benefited greatly from *pro bono* legal services provided by Wilson Sonsini Goodrich & Rosati, Rajeshwari & Associates, Dechert LLP, and Bird & Bird.

18. When will the licence agreement be made public?

The licence text is available in full from the Patent Pool website [here](#).



ANNEX:

List of countries newly included in the Pool/Gilead licences for TDF and FTC (as compared to old TDF):

- | | |
|---------------------------|--------------------|
| 1. Anguilla | 9. Kazakhstan |
| 2. Armenia | 10. Montserrat |
| 3. Aruba | 11. Nauru |
| 4. British Virgin Islands | 12. Palau |
| 5. Ecuador | 13. Sri Lanka |
| 6. El Salvador | 14. Tonga |
| 7. Fiji | 15. Turkmenistan |
| 8. Georgia | 16. Turks & Caicos |

List of countries excluded from the COBI licence (as compared to new Patent Pool TDF licence):

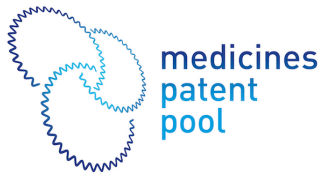
- | | |
|----------------|-----------------|
| 1. Botswana | 6. Namibia |
| 2. Ecuador | 7. Sri Lanka |
| 3. El Salvador | 8. Thailand |
| 4. Indonesia | 9. Turkmenistan |
| 5. Kazakhstan | |

List of countries excluded from the EVG and Quad licences (as compared to new Patent Pool COBI licence):

- | | |
|-----------------------|---------------|
| 1. Aruba | 3. Montserrat |
| 2. Dominican Republic | |

List of countries included in previous TDF voluntary licences:

- | | |
|------------------------|----------------------|
| 1. Afghanistan | 49. Madagascar |
| 2. Angola | 50. Malawi |
| 3. Antigua and Barbuda | 51. Maldives |
| 4. Bahamas | 52. Mali |
| 5. Bangladesh | 53. Mauritania |
| 6. Barbados | 54. Mauritius |
| 7. Belize | 55. Moldova, Rep. of |
| 8. Benin | 56. Mongolia |
| 9. Bhutan | 57. Mozambique |
| 10. Bolivia | 58. Myanmar |
| 11. Botswana | 59. Namibia |
| 12. Burkina Faso | 60. Nepal |
| 13. Burundi | 61. Nicaragua |
| 14. Cambodia | 62. Niger |



15. Cameroon
16. Cape Verde
17. Central African Republic
18. Chad
19. Comoros
20. Congo
21. Congo, Dem. Rep. of the
22. Cote d'Ivoire
23. Cuba
24. Djibouti
25. Dominica
26. Dominican Republic
27. Equatorial Guinea
28. Eritrea
29. Ethiopia
30. Gabon
31. Gambia
32. Ghana
33. Grenada
34. Guatemala
35. Guinea
36. Guinea-Bissau
37. Guyana
38. Haiti
39. Honduras
40. India
41. Indonesia
42. Jamaica
43. Kenya
44. Kiribati
45. Kyrgyzstan
46. Lao, People's Dem. Rep.
47. Lesotho
48. Liberia
63. Nigeria
64. Pakistan
65. Papua New Guinea
66. Rwanda
67. Saint Kitts and Nevis
68. Saint Lucia
69. Saint Vincent & the Grenadines
70. Samoa
71. Sao Tome and Principe
72. Senegal
73. Seychelles
74. Sierra Leone
75. Solomon Islands
76. Somalia
77. South Africa
78. Sudan
79. Surinam
80. Swaziland
81. Syria
82. Tajikistan
83. Tanzania, U. Rep. of
84. Thailand
85. Timor-Leste
86. Togo
87. Trinidad and Tobago
88. Tuvalu
89. Uganda
90. Uzbekistan
91. Vanuatu
92. Vietnam
93. Yemen
94. Zambia
95. Zimbabwe