Meeting minutes between Eastern European and Central Asian Community Advisory Board (EECA CAB) and Medicines Patent Pool (MPP)

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Kiev, Ukraine

Participants:

From MPP:
Chan Park, Medicines Patent Pool General Counsel

EECA CAB Participants:

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Facilitator: Alexandra Volgina

Patent Pool Presentation

Chan Park

Thank you for the opportunity to participate in this meeting. Basic information about patents: a patent is the authorisation granted by the government to the owner of an invention for a limited period of time, usually 20 years. In exchange for the disclosure of information about the invention, the right is obtained for its exclusive use. It is assumed that patents provide an incentive for innovation.

There are no international patents, despite the existence of international agreements in the area of patent law. A patent is issued on the territory of a particular country.

Previously, many countries did not recognize patent protection for pharmaceutical products. Indian companies hold 90% of the world market for generic anti-retroviral drugs and have played a key role in increasing access to ARV drugs.

In 1995, the TRIPS agreement was signed within the framework of WHO. In accordance with this agreement, developing countries should ensure patent protection, including that for pharmaceutical goods. In 2005, new legislation was passed in India that recognized patent protection for medicines. Inasmuch as generics often cannot enter the market because of patents, this can hamper competition and result in high prices for drugs.

Several patents can be obtained for one drug. For example, nevirapine. The patent on the nevirapine molecule has expired, but up until now there is a patent for the children's version of nevirapine in several countries as well as for the version that is taken once per day.

The patent status is important in those countries where drugs are needed and also in those countries where they are manufactured. Especially important are the patents that have been issued in India where most of the generic ARV drugs are produced.

Patents on drugs with fixed dose combinations poses a serious problem. The advantage of these drugs is increased adherence, simplified prescription and administration of the drug, as well as simplified logistics. But a patent on one of the drug's components can have an impact on the sale of the combination drug.

Comment: In Russia, separate components are being purchased instead of fixed dose combinations because they are cheaper and because it is difficult to prove the latter's therapeutic superiority. But one of the obvious advantages is the simplified prescription process, as it is difficult for doctors to make a mistake with fixed dose combination drugs. National guidelines (except for Russia) prescribe that drugs with fixed dose combinations are preferable from the point of view of increasing adherence to treatment. However, there aren't that many studies that prove this.

Comment: In Ukraine it was hard to prove that the fixed dose combination drugs should be purchased, as they cost more than the individual components. In the end, the Ministry announced a tender for the combined drug, but it was only possible to achieve this necessary result when the company reduced pricing on the combined drug by 50%, and when it could be proven that the prices on individual components were overstated.

Question: If the patent holders on monotherapies are different companies, then who will hold the patent on the combination drug?
Response: It all depends upon which countries and which drugs have patents. For example, in Russia, the patents for atazanavir and ritonavir are held by different companies and it is not possible to make a combination drug without a license. In India, there aren't any patents on these drugs, and Indian generic companies are making a combination drug, and as far as I know, not patenting it.

Comment: Brand companies that have the right to mono-components of a combination drug often share among themselves the markets of various countries. One company gets the rights for a combination drug in several countries, the other companies get other countries.

Question: If you could find a way of combining drugs, for which other companies have the patent, would it be possible to patent the combination process itself?
Response: In theory, generic companies in India could patent the combination process, for example, on atazanavir and ritonavir, in countries where it is patentable. The company Cipla was the first company to create a combination drug (stavudine / lamivudine / nevirapine). The company submitted an application for the combination process, but hasn't ever actively defended its rights and the patent hasn't posed an obstacle to access to treatment.

Question: If there is a patent on both the method of production and on the product itself, do these pose an equal barrier to treatment access?
Response: There is an important difference. If the patent is on the product itself, then no one can manufacture it. If the method of production is patented, then it may possible to find another method of production for the same product.

Three main problems:

- Ever more PLWH live in middle income countries which are excluded from access programmes provided by manufacturers.
- Ever more people require second and third line treatment, the price of which is much higher than of first line treatment, even for generics.
- Ever more patents are being issued to companies in middle income countries.

Key question: will the trends of decreasing prices for ARV and increasing numbers of people on treatment continue, given the fact that ever more countries are moving up into the category of middle income countries and ever more people are requiring second and third line treatment?

Comment: The problem is that in our country, in the majority of cases, agreements were signed that don't make use of the mechanisms listed above. For example, the Eurasian Patent Convention. Even when the law stipulates that in the case of an epidemic, these types of measures are possible, the fact that there is an epidemic is simply not recognized. The legislation of Russia, Kazakhstan, Belarus, Tajikistan and Uzbekistan states that a compulsory license can be granted by a court decision provided that over the course of a certain amount of time, the patent holder does not make sufficient use of the invention. The legislation of some countries specifies that a compulsory license is granted only when compensation is made to the patent holder.

Comment: In Russia, legislation provides enough opportunity to grant compulsory licensing.

Comment: In Georgia, legislation provides broad opportunities for challenging patents, in particular, any public organisation can challenge a patent. It is also worth focusing on strengthening the criteria for patentability with regard to pharmaceutical drugs.

Resources where it is possible to receive information about drug patents in a variety of countries:

- Patent Pool data base (emphasis is on ARV in developing countries, the most complete data base, 25 drugs in 80 countries, including countries from the Eurasian patent organisation)
- Eurasian Patent Organisation's website
- European Patent Organisation's website
- FDA Orange Book

Comment: As of today, it was not possible to find Kazakhstan or Belarus in the data base, although Uzbekistan was there (data was for the year 2011). Although the base is helpful, and the data is updated, for some countries the information is out of date.
Response: There is a significant problem with data transparency on patents at the level of national patent offices. The data in our base is built on data from the national patent offices. Unfortunately, the majority of developing countries don't have an electronic data base on the internet.

Comment: I'm in partial agreement regarding Uzbekistan, but in Kazakhstan and Belarus there are data bases with open access and it isn't really clear why information is not available for these countries. If necessary, we can provide the link.
Answer: As has already been mentioned, the Patent Pool is not a patent office, and we created the data base in way that it could be supplemented with information from third parties. We would be grateful for such data.

Important point: According to the rules of the Eurasian Patent Organisation, the patent holder has to pay a fee each year in order to renew the patent on the territory of each country. If he is not interested in extending the patent on the territory of any particular country, then he doesn't have to pay the fee, and in that case, the patent ceases to exist on the territory of that country.

Comment: In addition to patents from the Eurasian Patent Organisation, some countries might have national patents which don't need to be extended.

Question: Nelfinavir is not in the data base. Will this drug be added?
Response: I think the patent for nelfinavir has expired, but we can clarify this.

Information in Patent Pool's data base might not be complete. If you are interested in a patent, for example, from the Eurasian Patent Organisation, you need to search for information on its website as well.

Information about the Patent Pool: founded in 2010, a UNITAID project, it is now an independent organisation with headquarters in Geneva. The Pool's main objective is to conduct negotiations with patent holders about obtaining voluntary licenses for the benefit of public health. The Pool then offers the licenses obtained to those generic companies who apply for them. Under the terms of the agreement, compensation is paid to the patent holders. The three main objectives: 1) promote fixed dose combination drugs 2) promote special versions – children's and heat-resistant versions, with special attention to children's anti-retroviral drugs given the high demand for such drugs in developing countries 3) increase availability of ARV drugs by stimulating competition with the participation of generic companies.

Patent Pool's negotiation principles: 1) emphasis is placed on the benefit of public health 2) licenses are not exclusive; the goal is to grant licenses to as many manufacturers as possible 3) all licenses are transparent and upon signing are immediately posted on the Pool's website 4) The Pool seeks to include in the scope of license coverage all countries with lower and middle income levels.

Question: How do you select the the drugs for licensing and what are the criteria for including countries in the license's coverage – income level, the need for the drug?
Answer: 1) clinical significance of the drug (for example, tenofovir is more important than nelfinavir) 2) patent status (for example, dolutegravir is more important than lamivudine, because it has more patents in different countries).
With regard to countries: we try to include all countries with low and medium income levels. But we try to emphasise countries with a high disease burden and poorer countries. Negotiations are voluntary, and the patent holder can refuse to include one or the other country within the license's coverage. Once we achieve intermediary results in the negotiation process, we approach a specialist from a group of experts, who makes recommendations as to whether it is worth continuing the negotiations in order to get better conditions, or whether the obtained license offers sufficient additional benefit to public health.

Question: Russia is a country with a high income level. What are the chances that it will be included in licenses given its high burden of disease?
Answer: The main focus, according to UNITAID requirements, are countries with low and middle income levels. Therefore, it is extremely difficult for us to include Russia in licenses.

Comment: Thank you very much for your detailed report as to how countries are selected and how maximum benefit from licenses is achieved. We are convinced that the benefits will be even greater if the Patent Pool considers the possibility of attracting to negotiations members of community, including those from the region of Eastern Europe and Central Asia.
Question: We have already approached UNITAID about working with drug manufacturers to treat hepatitis C. Will the Pool work with drugs treating hepatitis C?
Answer: UNITAID is a Patent Pool donor and determines how funds will be used. At the moment, a memorandum of mutual understanding states that the Pool is working with ARV drugs for the treatment of HIV.
Question: Are representatives from civil society represented in the Pool's expert commission? Are the negotiations with pharmaceutical companies closed, or can representatives from civil society attend?
Answer: There are 12 people on the expert commission – the list is posted on our site. There are five members on Patent Pool's board. Community representatives are in both structures. One of the board members is Anna Zakowitz. Three members of the expert commission are from the patient community, Wim Vandevelde, Nelson Otwoma, and Gracia Violeta Ross. Negotiations between the Pool and pharmaceutical companies are not open to the public.

<u>The Pool's Licensing Agreements:</u> important aspects of the agreements
1) geographical coverage (in what countries can drugs be delivered)
2) the number of sub-licensees (companies, who could potentially get the license)
3) the right to manufacture the active substance (this can represent up to 70% of the cost of a generic drug)
4) the amount of compensation to the patent owner
5) no restrictions on production of combination drugs

6) the possibility of delivering to countries outside of the license's territory, etc. The Pool's licensing agreements stipulate that in such cases, even if one or the other country is not included in the agreement, it could still be potentially possible to supply drugs using TRIPS flexibilities.

The challenge: including countries with a medium-high income level in the license's territory.

List of drugs for which license agreements have been concluded:
Tenofovir, elvitegravir, emtricitabine, cobicistat, Quad (combination of the four previousl mentioned drugs), and pediatric versions of abacavir, valgancyclovir, and darunavir.

A license for darunavir has been obtained from the U.S. National Institute of Health. Janssen has a number of other patents for darunavir, but at the moment, the company has not entered into negotiations. Valgancyclovir is a drug for treating the cytomegalovirus infection (CMV). The agreement with Roche specifies reduced prices with elements of a voluntary license.

Currently negiotations are under way with BMS about atazanavir, with ViiV about dolutegravir, and with Gilead about a new form of tenofovir, TAF.

Question: There was information that TAF would be issued only as a component of a combination drug. Is there any information about whether it will be available as a separate product?
Response: TAF is currently included in a combination drug together with elvitegravir, cobisistat, and emtricitabine. As far as we know, Gilead is developing TAF as a monodrug for treating hepatitis B.
In negotiations we are trying to ensure that TAF will also be available as a separate drug, and not just in combination.

First agreement – 2011, Gilead.
Drugs: tenofovir, elvitegravir, emtricitabine, cobisistat, Quad (combination of the four previously mentioned drugs).
Tenofovir / emtricitabine – 112 countries.
Cobicistat – 103 countries.
Elvitegravir – 100 countries.
The agreement provides for the transfer of technologies, compensation 3-5% depending upon the product, no compensation for the sale of children's versions. License recipients can decide for themselves what licensed rights they want to receive. It is possible, for instance, to obtain the license for cobicistat and elvitegravir, but not that for tenofovir. A provision is included about the possibility of supplying a country where there is compulsory licensing.

Question: Can you name the countries from the EECA region included in the license?
Response: There is no patent for tenofovir in countries from the EECA region. If tenofovir is registered in a country there, then it can be delivered without any restrictions.

Question: As far as I remember, the Patent Pool has faced criticism from the international community with regard to this agreement. One of the reasons for this was that the majority of countries included in the license were already covered by other licences. Did you contact generic companies for licenses on Gilead's products? Another point of criticism was that the Pool received a percentage from the sale of drugs. Does the Pool still receive remuneration from sales?
Response: The Pool does not receive remuneration from sales. About the first point, Gilead had a licensing programme for 95 countries. The number of countries in the Pool license has increased to 112. There is another significant improvement: the companies can now supply countries where there is no

patent on tenofovir (which includes all countries in the EECA region). There are generic companies, therefore, who supply products to countries not included in these 112 countries. As far as we know, Hetero is currently handling the registration of tenofovir in Ukraine. Altogether, five or six generic companies have received licenses.

Question: Is the Pool continuing to work with Gilead on increasing license territory?
Response: We are now working to include TAF in the agreement, inasmuch as it is a very important drug. We are also trying to include new conditions and new countries into the existing agreement. However, at this stage, we can't say whether we will be successful in the end.

Second agreement, February 2013. ViiV – pediatric version of abacavir.
The pediatric version of abacavir is especially important in relation to both the new WHO guidelines and to the availability of patents for abacavir in many countries.

Geographical coverage – 118 countries, 98,7% children with HIV in developing countries. The agreement contains the clause stating that it is possible to sell the product in countries not covered by licenses, including those where a compulsory license has been issued.
The agreement doesn't provide for remuneration to ViiV.
Negotiations are currently under way about the pediatric version of dolutergravir. ViiV has given preliminary consent to granting the license for the children's version of dolutegravir to at least these 118 countries. ViiV's company share holders have so far given consent to only 67 countries – those of sub-Saharan Africa and the poorest countries.
Question: 7 countries from the EECA region were excluded from this agreement, including Ukraine and Belarus. EECA CAB made an open appeal in this regard. Can you provide us with any new information?
Answer: We are trying to include these countries in the license for dolutegravir. Ukraine is always a difficult country to include in the license's territory. The country has a lower-middle income level and a high epidemic burden. In all of negotiations we always put emphasis on including Ukraine. Unfortunately, the country is next to Russia and the EU. Companies point out that Ukraine is a referential country for Russia. If the Ukraine becomes a member of the EU, then parallel imports would be possible.

Last agreement – August 2013, Roche, valgancyclovir, a drug for treating CMV.

Prerequisites:
Low level of CMV screening;
There is a widespread belief that due to the broad coverage of ARV treatment in developing countries, CMV and other opportunistic infections are not a problem;
The very high cost of valgancyclovir (alternative – gancyclovir – requires an injection in the eye);
Valgancyclovir is chiefly used in treating CMV in patients who have had transplants and should take immunosuppressants (a market much better equipped to pay for treatment compared to the market for treating opportunistic diseases among HIV positive patients).
There was not enough demand In terms of treatment for CMV among HIV positive patients.

Agreement between Roche and the Pool:

1) Discounts on valgancyclovir of up to 90% of the market price were obtained from Roche
2) Motivation for screening programs and CMV treatment
3) Create interest among generic manufacturers
4) In one year, hold negotiations with Roche about offering licenses to generic companies

Territory: 138 countries, almost all countries with middle-low income levels. It may be possible to expand the license's territory if demand is demonstrated.

How the Pool determines priorities when selecting drugs: each year the Pool publishes a revised document with work priorities. The first version was released in 2011. Now an updated document is being prepared in accordance with the new WHO guidelines. **The documents are available on the Pool's website.**

The two main factors:

1) Clinical importance
2) Importance in terms of existing patent restrictions (how long will the patent be valid, in what countries was the patent granted). Special emphasis is placed on India.

Possible future alterations to the WHO guidelines are also taken into account because the Pool closely follows new developments.

Comment: BMS left the Ukraine in 2008-2009 complaining about corruption in the Ukrainian government. The company AbbVie comprises half of the budget with its drug Aluvia. They actively defend their rights. It is possible that there is an agreement between BMS and Abbvie about selling drugs in different markets.

Comment: Lopinavir / ritonavir – key price setting drug in the region. In many countries, it comprises 50% of the budget. If it is possible to expand accessibility to lopinavir / ritonavir, then it would significantly change the picture in the region. The same applies to atazanavir. For our region it is critically important to drastically reduce pricing on protease inhibitors.

Answer: I agree about reducing prices for second line drugs. BMS has agreed to conduct negotiations. AbbVie has as yet not agreed. The Pool is only one mechanism that can be used to improve access.

Comment: In the Ukraine a project is under way on compulsory licensing. At the last minute, the Association of Innovative Manufacturers got involved, and they tried to ensure that compulsory licensing was only granted in only the most extreme situations (such as war). It is obvious that they are greatly concerned about compulsory licensing.

Comment: Patients who change to generic drugs experience psychosomatic symptoms. Exit from therapy can be as high as 40%. The government now has the task of reducing prices. For us and for the patients, the most important objective is the quality of the drugs, not how cheap they are.
Response: There are a number of aspects regarding access to treatment that are not related to intellectual property: procurements, supply management, etc. The Pool does not have any mechanisms to influence these factors. However, we nonetheless try to ensure that there is not simply access to generics, but rather, access to quality generics. We require prequalification with WHO or the approval of stringent regulatory agencies for generic companies

Question: Does the Pool have a work plan for the EECA region?
Response: The main difficulty for the Pool is countries with middle to middle-high levels of income (the countries of EECA, Southeast Asia and Latin America).

Comment/suggestion: Conduct a joint campaign with one of the main players, for example WHO, with the goal of informing governments about the Pool's activities.

Comment: There have been meetings between the Pool and the Ukraine Ministry of Health. Currently a meeting is being planned with the government service for HIV / AIDS. There is a proposal about organising a meeting at the ministerial level to approve the Pool's activities.

Comment: please pay more attention to the EECA region when conducting negotiations with patent holders given that this region is one of the most problematic in the world in terms of the epidemic's growth. CAB EECA will draft a general position on the region and give it to the Pool.

End of meeting