Meeting minutes

EECA CAB and CIPLA

21 November 2016, Kiev, Ukraine

The Meeting participants:

CIPLA Ltd.:

- Denis Broun - Head of Government Affairs, Cipla Ltd.

EECA CAB:

№	Participant	Organization	Country
1	Igor Chilchevskiy	League of people living with HIV in the Republic of Moldova	Moldova
2	Nofel Sharifov	Public Organization Against AIDS	Azerbaijan
3	Aibar Sultangaziev	Harm reduction programs association "Partner Network"	Kyrgyzstan
4	Igor Pchelin	"Shagi" (Steps) Foundation	Russia
5	Kiromiddin Gulov	NGO "RAVNYYE VOZMOZHNOSTI" (Equal Opportunities)	Tajikistan
6	Paata Sabelashvili	Free consultant, expert	Georgia
7	Sergey Birukov	NGO AGEP'C(ANTIHEPATITIS'C)	Kazakhstan
8	Aleksandr Ladonkin	KROO "Status Plus"	Russia
9	Alexei Mikhailov	ITPCru	Russia
10	Kanat Alseitov	Parents Community	Kazakhstan
11	Samarin Vyacheslav	Positive Movement	Belarus
12	Anatoly Leshenok	Community of People Living with HIV	Belarus
13	Vladimir Zhovtiak	East Europe and Central Asia Union of People Living with HIV	Ukraine
14	Vladimir Mayanovskiy	All-Russian Network of People Living with HIV	Russia
15	Konstantin Fegjajev	Estonian Network of PLWH	Estonia
16	Konstantin Lezhentsev	East Europe and Central Asia Union of People Living with HIV	Ukraine
17	Anahit Harutyunyan	"Positive People Armenian Network" Soc. NGO	Armenia
18	Nikita Trofimenko	All-Ukrainian Network of People Living with HIV	Ukraine

Facilitator – ECUO

Start of the meeting. Introducing participants

HIV

About CIPLA Ltd.: Cipla Ltd. is the oldest pharmaceutical company in India. It was established 80 years ago, and now it's the average company according to pharmaceutical standards. Its annual turnover is two billion dollars. 15 % of CIPLA's turnover is medications for HIV treatment, and it makes the company unique.

Now we have registered a lot of medicines for hepatitis, malaria and tuberculosis treatment. 16 years ago CIPLA's become one of the first companies that started production of generic antiretroviral drugs for HIV treatment. As you remember, at that time annual treatment cost amounted $11 thousands, and CIPLA set the price of $1 per day. It was a great revolution. And if we look at the prices of that time, we can say that the treatment was really expensive. At that time, and now, the treatment was accompanied by such drugs like Tenofovir. It costs $100 per year. And we hope that in a few years, such treatment regimen will cost just half of this price. Of course, it's the price CIPLA provides medicines to Global Fund, not private pharmaceutical sector.

Talking about ARV therapy, we are at second place after the MÁYLA Company. Like MÁYLA we are the only company that has access to the whole range of generic antiretrovirals.

I know that in this part of the world people are very concerned about quality of generics. All generics produced by CIPLA are approved by FDA (US Food and Drug Administration). FDA has the highest quality in the world. Today, 4 -5 million people take CIPLA drugs. And this number is just about the HIV treatment. If we are talking about other drugs, it is much more.

Question: In some cases you lose drugs prequalification because of untimely submission of documents needed for this procedure. Either you lose your registration in countries, again for the same reasons. Why not all the drugs you produce have prequalification?

Answer: It's a difficult question, but I will try to answer. When we apply for WHO prequalification, it takes about 2 years. And then, often, we need to register our products in countries as well. And it also requires a long time. I recently gave an example of case with Lopinavir and Ritonavir for children in South Africa. In 2010 we filed for registration of the syrup for oral use, and we were told that our registration will take place under the accelerated procedure. As a result, we have received the registration in November 2015 what means 5 years later. I don't want fast registration, I want slow registration - maybe it will be faster.

Question: You said that all your products have FDA registration. As well as FDA registration WHO prequalification is given to particular drug for specific manufacturing site. As far as I know CIPLA has a lot of manufacturing sites, and not all of them have FDA registration for drugs that are produced on these sites, and not all sites are prequalified by WHO. The question is how we can be confident that products arriving in our countries are produced on site which is FDA registered and WHO prequalified?

Answer: You should know that each product is manufactured only at one site, otherwise we would become bankrupt. The only exception is drugs such as Tenofovir which are a combination of drugs that are produced at three manufacturing sites. This exception is because of very large scales of production. And all these three sites have received prequalification.

Question: You have a generic Atazanavir and Atazanavir Ritonavir – both are not prequalified. In our region these drugs are needed and will be needed for sure. What are you going to do with this issue? Are you going to register? How soon?

Answer: If we are talking about Atazanavir and Ritonavir, we have applied for WHO prequalification in August 2014, and we were told that would get this prequalification till the end of 2016.

Question: Why so long?

Answer: It takes a long time. We applied both WHO and FDA. On average, the application examination takes 26 months in WHO and 11 months in FDA. There is one thing that WHO does faster. In case we change the manufacturing site, its review and approval takes 3 months in WHO, while in FDA it's 9 months.

Question: And what are the plans for registration of this drug in particular in the countries of region?

Answer: It's quite difficult to register this drug in the countries of region, and it takes a long time. For example, in Russia, it is connected to necessity of conducting clinical trials and there is no certainty the registration will be approved in the end.

Question: What about other countries of region? For example, in Ukraine the patent runs out and BMS is going to do nothing about this.

Answer: The situation with Atazanavir in Ukraine is different. Because the patent is still valid, theoretically, I shouldn't register a generic product before the patent ends; otherwise it may lead to legal proceedings - to claim by the patent holder. It's hard to explain, but the situation for companies like CIPLA has changed over the last 10 years. In 2005 India adopted the Law on Drug Patents. We could easily produce generics until this law was passed. But now to provide access to the drug for India's population we have to negotiate with the patent holder and to obtain a license, not just make a copy. Now we're discussing with BMS different products and license agreements issues. I can't go against the BMS patent in Ukraine without their opposing. I could have done it 10 years ago, but not today.

Question: Nikita Trofimenko, All-Ukrainian Network of People Living with HIV. Please, could you clarify a little about what kind of document from BMS is needed for Atazanavir? Maybe it's some kind of a letter approving that they will not enforce a patent in Ukraine. In fact, the validity of patent expires in 1.5 year, and the company has closed its Ukrainian office in 2007. Since that time it has minimal presence on our market, and it's clear that there is no Atazanavir in this country at all.

Answer: We do it all, but don't get any written confirmation. It's all quite informally. For example, CIPLA has registered Sofosbuvir in the country not included in the Patent and License Agreement. During the phone call Gilead Sciences have said that they are not against such action, but they will never be able to declare this officially. You know, we really act on the edge, and very often personal relationships play an important role. The company has never officially give you access to the patent, but unofficially during the phone call they can say that it's ok. If you want I can try to deal in same way with Atazanavir in Ukraine.

Question: I am from Kyrgyzstan. Just two weeks ago we've got a method of simplified registration. We have already applied to the Ministry of Health for drugs inclusion in the list of medicines allowed for trade in the country, and we hope that they will be included at the

beginning of next year. It means that companies that want to come to Kyrgyzstan just have to confirm a product quality certificate. So, I would like to ask whether you are willing to enter our market.

Answer: Well, I have good news for you. Two weeks ago we had a meeting in Georgia, and we've prepared and sent a package for our products registration in Kyrgyzstan, as well as in other countries of the region. To be more precise, we filed a registration dossier on the Hepatitis C treatment drugs in Kyrgyzstan.

Question: Is it understood that they are already in our drug supply department?

Answer: Yes.

Question: I am from Kazakhstan. I have two questions. I would like to ask whether it planned to purchase products for 2017 in frames of UNICEF international procurement. Does CIPLA participate in this process in Kazakhstan?

Answer: Yes

Question: What ARV products?

Answer: All of them.

Question: In which EECA regions CIPLA presents children's pediatric form?

Answer: We have all the available pediatric formulations. It's our specifics. The only exception is the syrup Lopinavir and Ritonavir. Now it is substituted with microtablet pellets, due to the fact that the syrup contains alcohol. We use these drugs, pellets, in those countries where the number of HIV infections among children is the largest – in countries such as Kenya, Botswana and South Africa, but not in EECA countries yet.

Question: I want to ask about pellets price. Why so expensive?

Answer: It's a very complex form. It took us more than two years to stabilize this formulation and these pellets. They are in capsules, and special equipment is needed in order to fill the capsules. This is a very complex technology.

Question: Of course, it's all technology and so on. But we say that there is a certain amount that country can provide a patient for a particular treatment. And suddenly there is a better treatment improved due to the fact that the treatment used before is not acceptable. Hence, now this new treatment should be at the same price, but not three times as expensive.

Answer: I had a similar discussion in South Africa. The fact is that children simply spit out the syrup, so it's not the cost of treatment, it's just wasted money. Therefore, it may be less expensive, but this treatment doesn't work. And so, now we're producing three thousand packs of pellets per month, and we're going to produce 20 thousand. Today, the package price is $26. Our turnover from this drug production is $ 0.5 million. We have invested in equipment and production of this drug $1.2 million. It is always a very unpleasant conversation about the price, and everyone wants to get a lower one. And in the beginning, when we received FDA approval, but haven't begun to manufacture products yet, there were complaints about too high price.

Question: Do you plan to localize CIPLA manufacturing in Russia? If so, with whom? If there's somebody, then when? What drugs and approximate prices?

Answer: I think you can answers almost all these questions by yourself. About a month ago, we've signed an agreement on manufacturing products with NIC which is a part of Rostec. And everything would be fine, but then we haven't heard anything from the NIC. NIC Director contacted us and intended to start the discussion again. It's happened only a month ago. I don't know, on what stage we are. We are opened to dialogue with other organizations as well. And you know that the new law was passed. It takes effect next year. It says that active ingredients for drugs manufacturing must be carried out here in Russia. And it makes difficulties for our company. The less we lead the process, the less control we will have over the situation, hence, over prices.

Question: The question about Belarus. The same as Russia, but about Belarus. That's because HETERO have some business in drugs manufacturing in Belarus. So, as I understand, there are some conditions in Belarus more attractive than in Russia?

Answer: Indeed, it is more favorable to establish business relationships in Belarus, but we don't know whether the drug produced in Belarus is considered for market in Russia. We are negotiating with the Belarusian Academpharm, and we will supply API and technology transfer.

Question: Which drugs will be produced in Belarus?

Answer: It depends on our cooperating companies in Belarus. We are ready to give them API, i.e. the active ingredient and technology, but most likely they will want to manufacture products that are already in use. I wish it was one-pill-a-day drugs, but most likely it will be formulations used before.

Question: There is the foreground domestic manufacturer in Belarus. It means that everything we produce here will be purchased in frames of governmental procurements after the transition to national funding. Today we are dealing with a drug packed at the Farmateh factory. Global Fund pays part for it. And now there is a niche for you. As patients, we would like to see CIPLA in Belarus as a domestic manufacturer. There are forty-two thousand boxes of Dolutegravir and Kaletra were purchased during the last year, and Atazanavir for the last three years, i.e. there is a wide range.

Answer: We don't have problems with domestic manufacturer. What we offer them are API, the active ingredient, technology and quality control. And after that it depends on domestic manufacturer how they going to sell products to government.

Question: My question is about Daclatasvir in Ukraine. There is a great need in it. Why don't you produce it?

Answer: We are going to collect the dossier for Daclatasvir registration till the end of the year.

Question: Concerning Dolutegravir. Ukraine, Moldova and Armenia were included to the license. So, will CIPLA deliver this drug? And if so, when?

Answer: We are going to deliver Dolutegravir in Ukraine. In Armenia the situation is different. I think there are no more than ten people who need this drug, so in this case it will better to use Global Fund's delivers than register our product.

Question: Is it such a purchase system without registration because of few patients? But what are your plans after the Global Fund financing is over?

Comment: We understand the Global Fund mechanism effectiveness. But there are two things: the first, according to our CAB policy, we strongly recommend to register; and the second, the true number of people who need a particular range of ARV combination is artificially reduced (due to lack of information, patients tracking, low access to regular monitoring etc.). Therefore, it should be revised. Maybe in Armenia it is relevant, but overall, I would never act using just patients' evaluation data. We are extremely interested in the pediatric form of pellets. As a father of three children, I can say that the pellet are fine, but there is a certain time period when we have to use syrup until children can take pellets. You are the only reclassified competitor of brand syrup and what we want is you to continue manufacturing syrup for the same price, because children under three years old wouldn't even take this beautiful sweet pill. Thank you.

Comment: If we are talking about Moldova in particular we have to understand that for many years about ten hundreds people are on Kaletra. Your drug is such a replacement scheme which can remove side effects, especially dystrophy (which is the reason for youth to leave treatment, so we had youth deaths). We are waiting for your registration and good suggestions.

Answer: Of course, we have to register these products in Moldova as soon as possible.

Question: Do you monitor the situation in Eurasian Customs Union (ECU)? If everything's ok, are you going to enter the market of this union and make a joint purchase for all 5 countries if requested?

Answer: We understand the idea of ECU, but we can't understand registration process yet. For example, it's not clear if any product registered in Kazakhstan would automatically be sold in Russia.

Question: Concerning Dolutegravir. In Kazakhstan branded Dolutegravir goes with annual price of about $ 3000. If you enter the market, what approximate price you'll set?

Answer: About $100-500.

Question: How much?

Answer: $ 150

Question: Per year?

Answer: Per year. Dolutegravir itself costs $150 per year. Actually, the price of 50 mg of Dolutegravir is the same as for 600 mg of Efavirenz. Maybe, the price for combination will be lower than $100, but we don't know what combination it should be. We have to wait 2-3 years.

Question: I have a question concerning components of complex formulations – Tenofovir, Lamivudine, and Emtricitabine. Do you have registration in countries? If so, where? Is there an experience of entering drug procurement bidding with these formulations in countries? If not, why? And important question: why this formulation is more expensive than the same pharmaceutical drugs formulation? It is clear that it's complex production, etc.; we've heard all these fairytales. I would like to hear the real answer, because we know the technology, so, we understand that it can't be as more expensive as the other drug.

Answer: Well, triple drugs can't be sold in the EU. We've already got a patent for Lamivudine, so it's ok to deliver it. Emtricitabine and Tenofovir individually are not eligible yet - they are protected by a patent.

Question: I'll try to specify this question. There are many situations in Russia when multicomponent products are purchased because they have lower price. We can talk a lot about benefits for patients, better treatment adherence, etc., but they understand only one thing – cheaper price. And the question is how much cheaper you are ready to deliver in region comparing to multicomponent price? In which countries? And in which countries you are ready to register?

Answer: We provide the Global Fund with a combination of Tenofovir, Lamivudine, and Emtricitabine for $85 million annually. Due to large sales volume it is reasonably to keep a low price. We don't sell these drugs individually. The exception is only Tenofovir for the Hepatitis B treatment.

Question: The Global Fund will leave in some time. Was there the drug procurement bidding entering for three-component drugs in region? And what is connected to, excepting payments? UNDP can purchase as an alternative to the Global Fund.

Answer: Yes, we've participated tenders in Ukraine and in other countries of the region, it was UNICEF and the UNDP. UNDP is Global Fund, but in order to participate in tenders in the country itself. It's necessary the drug has been registered in the country, but these drugs are available not in all countries of the region and we're working on it now.

Question: How Ukraine can purchase if it doesn't have registration?

Answer: Triple drugs? There is registration for Tenofovir, Emtricitabine, and Efavirenz. Thus, the Atripla is patented in many countries of the region. We propose to replace the Lamivudine component with Efavirenz. But if we do that, we'll need to register again.

Question: Where? When? Where and when we will have Lamivudine Atripla?

Answer: I don't have a complete list of countries where this drug is registered, I didn't expect you will be so much into the details, I'm sorry that I am not fully prepared, but in most, many countries still have a patent for Tenofovir.

Question: Is it possible to clarify if I understood correctly? For example, you say that you have three triple formulations. You enter some country for registration and if any of the three components of triple formulation still has valid patent in this country, then you won't be able to register anything? Or you can register a new triple formulation?

Answer: Yes, if one of components of this triple drug is still under patent, we can't register it. But it's better to explain: pharmaceutical company registers and enters the market of country when it's easier to register and when more people who need these drugs. The African country with three million patients will be more attractive for us than, for example, Armenia. The same applies to countries with complicated registration process, including availability of valid patents for some of components.

Question: I have two questions concerning Tenofovir. I have heard that CIPLA is developing a new 100 mg Tenofovir formulation that will be as effective as the 300 mg formulation, and will have fewer side effects at the same time. I would like to clarify when you plan to launch it on the market, and so on.

Answer: I want to explain a little of Pharmacology: when you take Tenofovir, in fact, you are not taking Tenofovir as such a substance. You take just a medicine, substances, one of which is TDF, and the other is TAF, and then in the cells these two substances transform into Tenofovir. So, more TDF you take, than less Tenofovir is in cells.

Comment: I know this process very well. I will explain quickly. I've been talking about side effects of Tenofovir for three years. It has strong toxic effects, primarily on the kidneys and bones. When using TAF it doesn't occur and, thus, side effects are reduced.

Question: You have already applied for registration? When it will be?

Answer: Well, we've conducted all the clinical trials and now we're at the stage of registration. This drug will be registered till the end of 2017. Also we're going to use TDF for Hepatitis B treatment. This would require a 100 mg of the drug as well.

Question: I have a question. Efavirenz has 600 mg formulation, and the WHO already recommends 400 mg. Could you tell us more about it?

Answer: According to clinical trials, 400 mg of Efavirenz works as well as 600 mg, but gives less strain for the body and side effects. Therefore, we filed for WHO registration of Efavirenz 400, as well as the combination of Lamivudine, Emtricitabine, and Efavirenz.

HEPATITISES

Question: When you are going to fill any drug dossier for Kyrgyzstan?

Answer: We've applied for Sofosbuvir registration in Kyrgyzstan.

Question: What about other countries? Which drugs?

Answer: Just Kyrgyzstan for now.

Question: At what price you are planning to sell? I'll inform you with lower prices. NATCO and HETERO factory prices are around $ 100-130 for Sofosbuvir and $ 30 for Daclatasvir. Maybe we'll agree at $ 20? Will your price be comparable? We have Grateziano. It's really expensive, but it was just the first batch. What are your plans about prices?

Answer: We sell Sofosbuvir for three months for $ 400 in India at the moment. In Kyrgyzstan we can't sell cheaper.

Question: Why only Kyrgyzstan? Why don't you consider other countries? We are ready to provide you with any kind of assistance; including situation when you called me and we went to pass registration documents together. And I can control the whole process. Kazakhstan, Belarus and other countries are waiting for you.

Answer: It's hard for us to register in other countries.

Question: Please tell us about situation between Gilead and Pharco in Ukraine?

Answer: Currently Gilead doesn't have patents. Patents position that has been filed on their applications appeared potentially blocking, but Gilead sued Generic on data exclusivity. Gilead lost the First Court Instance. The Court sided with Generic, because it believes that it is forbidden to use the materials of the registration dossier for the purpose of filing the

application, and just so happened that the Generic filed for registration earlier than Gilead. Perhaps, Gilead will appeal.

Comment: I just want to say once again that this example tells us that you need to come, register, and then we will deal with situation.

Comment: I know in details how to pass the registration process for the first and the second drug. The question is what we've got at the end, at the last procurement bidding. The price difference between Gilead and Egyptian drug amounted $ 10. That is 2.5% percent difference between Gilead drugs and generic (Natco). Therefore, it's a separate issue. And such schemes where generic drugs are 2.5% cheaper than a brand should not be tolerated.

Question: In fact, if we evaluate the potential market of Russia, there is a sufficient number of people living with hepatitis - five million. Also there is a sufficient number of people who are ready to pay reasonable prices for treatment themselves.

Answer: You can buy the necessary drug in Kyrgyzstan and in India, but we can't sell it in Russia. It is simply forbidden.

Question: As I understand there is a mechanism when prescription is sent to manufacturer, i.e. you, and you can send the drug. Do I correctly understand such mechanisms on prescription for personal use?

Answer: But not in Russia. In Kyrgyzstan. The British, for example, can buy Sofosbuvir in India and bring it home, because it is for personal use, but we can't deliver the drug to the UK.

Question: You have a very good price on Abacavir. What about registration, sales and plans for countries of our region?

Answer: I don't know what's the situation with Abacavir and a patent for it, but we have an adult version as well as a pediatric one.

Comment: We really like your price. We invite you and look forward to see on our market! Register. Dennis, thank you very much for coming and giving a lot of new ideas. I hope that we also managed to convey what we wanted. Thank you so much!

End of the meeting.