MEETING MINUTES

Eastern European and Central Asian Community Advisory Board (EECA CAB)

and

ViiV Healthcare

February 7, 2013, Kyiv, Ukraine

Participants:

ViiV representatives:

Evgeniy Bukin, medical director of ViiV Healthcare representative office in Russia
Margarita Isliaeva, CIS business development manager
Boris Charchyan, General Manager of ViiV Healthcare in Russia
Scott Purdon, Director Access and Government Affairs
Marina Buchma, Area External Relations Manager Ukraine and BMC region

EECA CAB representatives:

Ehtiram Pashayev	Public organisation Against AIDS, Azerbaijan
Hovhannes Madoyan	Real World, Real People" NGO, Armenia
Zurab Danelia	Public organization "Tanadgoma Union", Georgia
Denis Maruha	League of PLWH in Republic of Moldova, CAB Moldova
Elena Bilokon	Kazakh Network of Women Living with HIV, Kazakhstan
Sergei Uchaev	Community of People Living with HIV in Uzbekistan
Aleksandrs Molokovskis -	Society "Association HIV.LV" Latvia
Sevara Kamilova	Community of PLHIV, Tajikistan
Svilen Konov	European CAB (ECAB), EATG
Grigoriy Vergus	ITPCru
Sergey Golovin	ITPCru
Andrey Skvortsov	"Patient Control", Russia
Albert Zaripov	Russian CAB (RuCAB), TatCAB, Russia, Tatarstan
Erika Matuizaite	Eurasian Harm Reduction Network, Lithuania
Elena Khodanovich	Belarusian CAB
Dmitriy Sherembey	Ukrainian CAB (UCAB)
Oksana Vaschenchuk	Ukrainian CAB (UCAB)
Vitaliy Tkachuk	All-Ukrainian Network of PLWH
Irina Borushek	All-Ukrainian Network of PLWH
Alexander Gatiyatullin	All-Ukrainian Network of PLWH
Olga Belyaeva	Community Council, Ukraine
Tatyana Khan	ECUO
Ekaterina Voinova	Estonian Network of PLWH

Moderator: Sergey Golovin

Introduction of participants. A minute of silence in memory of people who died waiting for access to treatment.

ViiV presentation

Scott Purdon:

Brief presentation of ViiV history
Company was established 3 years ago as a result of the merger of HIV departments of GlaxoSmithKline (GSK) and Pfizer. The reason for creating ViiV was to energize the process of new antiretroviral drugs development. Today, we will talk about the new drugs in development and discuss their efficacy and safety. We would also like to assure you that we are prepared to cooperate with the civil society. GSK has more than 20 years of experience collaborating with organizations such as GNP +, International Community of Women living with HIV, ICASO through the Positive Action programme. We are pleased to have this opportunity to conduct a dialogue with you today. We are also willing to talk about the partnership with NGOs and companies who produce generics medicines, and discuss issues related to access to treatment, because we know that you are very interested in these questions.

Evgeniy Bukin, new products

At the moment, the company's portfolio contains 17 molecules at different stages of development.
572 (international non-proprietary name (INN) – dolutegravir) is a next-generation integrase inhibitor. This drug completed some trails of phase 3. In December 2012, the dossier was submitted for registration with the FDA.
ViiV is a pioneer in the development of fixed-dose combination (FDC) of drugs. One of the future combinations is dolutegravir / abacavir / lamivudine. Another new integrase inhibitor is 744.

SPRING-2.
This research is conducted on treatment-naïve adults' population. It compares dolutegravir and raltegravir. The NRTI base is selected by the researchers.

SINGLE.
This is a comparison of the efficacy and safety of the combination of dolutegravir/ abacavir/ lamivudine and "Atripla" (emtricitabine / tenofovir / efavirenz).

SAILING.
Patients who have already received treatment, but not integrase inhibitors. This study compared dolutegravir and raltegravir.

VIKING.
Experienced patients who have received integrase inhibitors.

At the moment, there is a study of different doses of dolutegravir to be used for children.

In EECA region, the vast majority of studies with both naïve and experienced patients are carried out in Russia.

Question: Are these studies conducted in other countries of the EECA region?

Answer: So far, studies are carried out only in Russia mainly due to the technical capabilities of the centers. When selecting centers we evaluate their capability to carry out each single study, such as availability of laboratory facilities and professionals with appropriate training and experience.

Question: In which cities of Russia do you conduct the studies?
Answer: There are 12 centers, quite wide coverage, including central Russia.

Results of the studies with naïve patients, SPRING-2 and SINGLE.

Design of the SPRING-2: **multicentral double-blind placebo-controlled study. Inclusion criteria: ART naïve**, viral load (VL) was greater than 1000 copies per mL, patients were randomized into 2 arms: a group with dolutegravir - 50 mg OD + placebo raltegravir in combination with nucleoside backbone at the choice, and the group with raltegravir + placebo dolutegravir + nucleoside backbone at the choice. Duration - 96 weeks, followed by the open phase.

By week 48, 88% of patients from the dolutegravir arm achieved undetectable viral load (less than 50 copies per ml). The data in the raltegravir group - 85%. The immunological response is nearly the same. The average increase for 48 weeks is 230 cells.

SINGLE. This is a double-blind and placebo-controlled study. Duration - 96 weeks, then the open phase follows. Virologic response in dolutegravir group - 88%, in the "Atripla" group - 81%, the difference is statistically significant. In the dolutegravir arm, VL dropped to undetectable levels in 28 days on average. In the "Atripla" arm, VL dropped to undetectable levels in 84 days on average.
The growth of cells was significantly higher in the dolutegravir group – the average increase was 267 cells from the baseline. In the "Atripla" arm, the average increase was 208 cells. "Atripla" group has a higher patient dropout rate due to adverse effects (AEs).
Conducted genotypic and phenotypic resistance tests indicate a high barrier of resistance of dolutegravir.

SAILING. This study includes therapy-experienced patients who have not received commercially available IIs (raltegravir, elvitegravir). The inclusion criteria – defined HV (400 copies) + confirmed resistance to two other classes of ARVs. There are two groups: first group received dolutegravir + optimized background therapy (chosen according the profile of resistance) and second group received raltegravir + optimized background therapy. Study takes 48 weeks, then open phase. Interim data analysis (24 weeks) are included in the registration dossier, soon they will be introduced at international conferences, including next conference in Atlanta (CROI-2013).

VIKING-3. Patients with resistance to the first generation IIs. Two phases, first phase – patients received functional monotherapy - then the "unsuccessful" regimen was

supplemented by a double dose of dolutegravir (50 mg 2 times a day). One of the first end points - the study of the antiviral activity at day 8. After the first 8 days the base therapy regimen was optimized. The period after the monotherapy phase was 24 weeks.
After 8 days of monotherapy, the viral load decline by about 1.5 log in almost all the patients. By week 24, 63% of patients achieved full viral suppression.

Safety data:

SPRING-2. The overall incidence of adverse effects that led to withdrawal was less than 2% (7-10 patients in absolute numbers). The incidence of serious adverse events is extremely low. There was one death in each group; these two cases are not related to the drug intake (criminal case and suicide).

SINGLE. Similar data on safety – 10 people (2%) dropped out due to adverse effects in the arm receiving dolutegravir. In the "Atripla" arm every 10th patient opted to drop out. No fatal case of adverse effects was recorded in the dolutegravir group.
Dolutegravir is a new single-dose II drug that does not require boosters, it has favourable drug-drug interaction profile. It is as effective as raltegravir.

Question: SPRING-2 and SINGLE studies had problems with creatinine. Are these problems resolved?
Answer: Indeed, there is evidence that dolutegravir has effect on serum creatinine level to elevate it by binding to one of the transport proteins that breaks indirect recapture of creatinine, but this does not indicate renal toxicity.

Creatinine level increases for 4-8 weeks and then in the future it maintains at the same permanent level without any dangerous clinical implications for the kidneys.

There is a plan to study the efficacy and safety of the drug in special groups of population; especially among HIV-infected women who are more difficult to treat. Also, we plan to study the switch from PIs to dolutegravir, to study in populations with HCV and TB. We plan to investigate novel strategies on dolutegravir-containing regimen.

In Russia, there is a study FLAMINGO, it compares dolutegravir with darunavir.

Question: Which countries will be included in studies in patients with coinfection?
Answer: It is too early to talk about the countries; we are still developing the protocol. Tentatively, the studies are scheduled to be carried out in Russia. It will be finalized during 2013.

Question: Wouldn't the increases of creatinine be dangerous in the long term? Was it only creatinine level or urea level as well?
Answer: No, only the creatinine level. There is no evidence that the increase in the creatinine level is of any clinical relevance. There were laboratory data changes that were not associated with any clinical implications.

Question: Will you conduct the study on drug-drug interaction of dolutegravir with substitution therapy drugs?

Answer: Some pharmacokinetic data are already available. Clinically significant interactions in such drugs as methadone and buprenorphine have not been identified.

Question: Is it possible to give a little more information on the research of pediatric forms?
Answer: Pharmacokinetic studies are conducted to define the doses for children; then, we will study the effectiveness and safety. In 2014, we will receive the data on usage in children population.

Suggestion: ViiV can share the draft versions of the research protocols with the regional community.

Question: What is the purpose of the studies in patients coinfected with HIV / HCV and HIV / TB? To study the interaction with the drugs or to see the influence on the course of the co-infections?
Answer: We study effectiveness and the safety of the drug in specific populations – patients with coinfections, possibility of relevant therapy prescription.

Question: Is it possible to know the list of cities / centers where the studies with HCV will be conducted? It is a question of early access, sometimes these clinical trials are the only chance for the patients.
Answer: We can discuss this question taking into consideration information confidentiality requirements.

Question: Are there any interactions of dolutegravir with boceprevir and telaprevir? Have you conducted any studies?
Answer: We included the study of the interaction of dolutegravir with PIs for HCV treatment in the research strategy.

Question: What characteristics will you explore in the trials involving HIV-positive women as a specific population?
Answer: Women tend to respond worse to treatment as compared to men. Thus, we are looking at the effectiveness of the drug and its safety. Long-term adverse effects associated with ARV can represent a problem.

Question: Will female drug users be included / excluded from the study?
Answer: The protocol is currently under development. At the moment, it is impossible to say whether they will be excluded from the study. Typically, one of the exclusion criteria is poor adherence to therapy as researchers state; drug users may fall into this category.

Question: Studies have shown superiority of dolutegravir over raltegravir, can you explain why dolutegravir is better than raltegravir in simple terms?
Answer: SPRING study did not show the superiority of dolutegravir. The difference was 3% which is not statistically significant. Superiority of dolutegravir was observed over the drug "Atripla" (7%) in SINGLE study. 414 patients received dolutegravir combined with the base therapy (abacavir + lamivudine), 419 patients received the drug "Atripla".

Question: Increased ALT / AST was recorded as a side effect. Is there a risk for patients with HCV? Will the HCV genotype sampling be conducted for the inclusion into the study?

Answer: There will be no genotype stratification. On of the exclusion criteria is the need for the treatment of HCV.

Question: Will you stratify by type of TB (MDR-TB, XDR) in the scheduled study in HIV/TB population?
Answer: At the moment, there is no information whether this is planned in the design.

The drug 744 is an integrase inhibitor. Clinical data of the early stage study has showed the same effectiveness results as of dolutegravir. Now, we are studying two forms: oral form in tablets and solutions and a long-acting parenteral form. There are pharmacokinetic data of healthy volunteers, as well as initial data of studies in patients with HIV.
Long-acting pharmacokinetics of 744 in healthy volunteers. Parenteral dose – 5 and 30 mg. Monotherapy for 10 days, transfer patients from the placebo group in the triple therapy group (does not include the studied drug). Regardless of the dose, a significant decrease in the viral load was observed at day 10. Genotypic and phenotypic studies have not shown the development of resistance. No serious adverse effect were observed.
Parenteral injection - from 100 to 800 ml, subcutaneously or intramuscularly. Almost in all the doses, the suppressed viral load concentrations remained for a long time (24-28 weeks).
Study of a 2-components therapy regimen containing 744 and rilpivirine is planned.
We received a question about the future of 761 and lersivirine. The studies of 761 are suspended, modification is possible, and so far, we do not have any serious plans.
Lersivirine (NNRTI): at the end of December, we made a decision to stop the study, because this drug would not have any advantage over the already available drugs.

Question: 744 - injection (in association with enfuvirtide), were there any side effects associated with the injection procedure?
Answer: Yes, they included redness, nodules, but no other clinically significant effects.
For developing a long-term form, we use a so-called technology of Nanoemulsions, this technology is not new.

Question: When will 744 be available on the market?
Answer: On average, it takes from 7 to 10 years; it is difficult to specify the exact date.
We are looking forward to new opportunities in the treatment and in the preventive care. One injection monthly, perhaps quarterly.

Question: Will the study be carried out in the region?
Answer: Large-scale studies are available only in the third phase, now it is phase 2. It's highly probable that study centres in Russia will be included, perhaps – in Ukraine, taking into account the readiness of the centres, as well as any legislative aspects (experience in conducting research, etc.).

Question: Is there any information on a fixed dose combination?
Answer: We are planning phase 3b studies.

Presentation №2. Margarita Islyaeva.

Epidemiology, demographic and economic parameters of the region.

According to the data, only three countries (excluding Russia) in the EECA region can be defined as high-and middle-income countries, namely Kazakhstan, Belarus, and Azerbaijan. All other countries are considered as low-income (including Ukraine).
The incidence data is provided by UNAIDS in 2010. The updated data is available for Azerbaijan and Belarus (2012, press releases and reports, Republican AIDS Centre).

Comment: Data for Georgia and Ukraine is inaccurate (in Ukraine 32,000 people receive treatment).

Answer: The data may be inaccurate, we would be grateful for more accurate information.
Government programs: Russia, Ukraine (GF and government), Kazakhstan (only MOH). Belarus (Government / GF - 30% and 70%), Moldova – the funding comes from the GF, there are reports that in the second half of 2014 there will be some financial support from the state.

Question: You didn't mention Tajikistan, do you have any data?
Answer: In Tajikistan there is only GF.

Comment: By the end of 2012, in Azerbaijan the public funding share of the ARV therapy is 60%.

Comment: There is no government program in Armenia. It was not drawn up. The estimated number is 3500 according to the latest data. UNAIDS is very slow in collecting and publishing information. It is possible to use more dynamic sources, such as reports of ECUO.

Comment: to gather the information is not the responsibility of ViiV; rather, it is the responsibility of the government and UNAIDS. However, even the information we have shows that very few people are covered by the therapy, and it is a very big problem.

Question: How do you comment on that third column? Poor commitment, the reluctance of the people to be treated? This table does not make sense without these comments.
Answer: The reason is the lack of funding for the therapy programs by the government or donors, as well the problem of poor adherence, patients' reluctance to take medicines, and poor infrastructure. We believe that the main reason is underfunding.
The basic sense of the table is to show where people require treatment the most. It is possible to question the statistics provided by UNAIDS, but for us it is important to work with you to hear your opinions and experiences on the topic who receives and who does not receive treatment. It is important to understand how many people should be treated according to WHO recommendations. Other results are important as well: how many people were tested, how many people received results, how many people require treatment, how many people drop out of the treatment, etc.

Question: The table does not include Lithuania, Latvia, Estonia. Are you not interested in the opinion of these countries?

Answer: The challenge for us is that the company is divided into several regions, including Europe, Asia and Latin America. We took part in the ECAB meeting last week. To discuss the Baltic countries, we need to think about bringing to the meeting an expert who is responsible for the European region.

Comment: Originally, EECA-CAB was formed as a discussion platform for 15 countries of the former USSR, representatives of these countries (except Lithuania) were on the first meeting with ViiV.
Answer: We can discuss it and invite the representatives who are responsible for the region to the next meeting. Also, we can forward questions about Baltic countries to our colleagues.

Drugs registrations

The drugs supplied by GF do not require registration in the country. The company has plans for product registration in each country, in some of them we have already applied for registration.

Регистрационный статус

	Тризивир	Комбивир	Кивекса	Зиаген	Эпивир	Ретровир	Телзир	Целзентри
Армения								
Азербайджан								
Белоруссия								
Грузия								
Казахстан								
Киргизстан								
Молдавия								
Россия								
Таджикистан								
Туркменистан								
Узбекистан								
Украина								

Green – registered, purchased/included in the EML

Yellow – Not registered, purchased within the GF programme (or by other donors or by the state)*

Blue – documents submitted for registration (year when registration is expected)*

Question: Is there any information on specific dates, for example in Moldova and Armenia?
Answer: We have made our decisions about the majority of the countries; the timing will depend on the procedures in each country. The yellow colour means that we have decided to register. The internal procedures of the company also need to be taken into account. By the end of the year, we will have concrete plans, if they are interesting for you, we are ready to give further information.

Question: "Combivir" is in the list of registered agents in Azerbaijan.
Answer: Maybe it is a generic drug (lamivudine + zidovudine). This may also be due to the import of drugs by the GF program, which does not require registration.

Question: There is a concern that GF will curtail its programs in the region, and some countries will remain completely without drugs. Are there medications which you will promote and register quicker? For example, "Kivexa" and "Combivir" (which is unfortunately still widely used in the region).
Answer: Many countries have a generic version of "Combivir", for example, Azerbaijan and Kazakhstan. In some countries, the original "Combivir" has never been distributed. There is no patent, no registration, but patients have access to generics. The focus of our registration efforts will be on "Kivexa", "Telzir", "Celsentri" (new drugs). We do not see the point in competing with generic products on low-income markets. 2013 will be devoted to the preparation of the dossier; in 2014, we will start the registration. By 2015, when GF leaves, we hope these drugs will have been registered. If generics do not register their products and there are problems, we will solve them directly with the governments. However, we do not think that generics will refuse to register.

Question: Which of the EECA region is the most difficult in terms of its registration procedure from the political point of view?
Answer: There is no universal registration procedure for countries; it might be relevant when the customs union is organized. Probably, the most difficult procedure is in Russia. For many countries (e.g. Ukraine), Russia is not a reference country. We have to prepare the dossier for each country and this complicates the process. Georgia and Armenia have simplified procedures for the drugs registered in the EU.

Comment: Registration procedures in Georgia have become complicated.

Question: Are there any problems with registration specifically in Moldova?
Answer: Preparation of dossiers; it takes about six months. In different countries the review period may take from 6 to 18 months.

Question: In many countries, it is GSK who register ViiV drugs, and they are not willing to do it and consider it a burden. This often hinders the process of registration. Sometimes, the community tells us that the company does not consider our market as attractive. You mentioned that in December you will define the plans for registration; if we get them we would be very happy. Is it possible to get the document with specific dates and countries?
Answer: We will register, but at the moment it is difficult to give specific information on the dates and products.
This is a common misconception when people say that we as a company are not interested in certain markets. We always try to achieve a balance between the needs of the governments and community of patients. In many countries of the EECA region, donor funding accounts for 50 to 70%; such donors as the Global Fund can import drugs without registration using special procedures. With regard to dolutegravir, we are now applying for a patent in advance; the same will apply to the registration procedure. As for the criticism associated with a lack of attention to the small markets, in South Africa, for instance, we have issued voluntary licenses for all our products to generic drugs, and we do not earn money there, even though the market volume is about $ 2 billion. It is a question of social responsibility.

Question: In Tajikistan, as I understand it, we plan to register the drugs. The drugs available in our country are generics and we do not have brands. At the moment, we have funding up to 2015. What plans does ViiV have in Tajikistan after 2015?

Answer: The generic drugs have been supplied to your market for several years, and it is their responsibility to be registered. At that, ViiV takes the responsibility to register and supply its products in case of necessity.

Question: What will be the financial policy of the company on prices after 2015, when GF leaves? Will you keep the commitment to the price, or will it be pure business? In Georgia, ViiV drugs are bought within the GF programs. Now, the price is, say, $ 3. Will the price remain at the same level when GF leaves or will the drugs cost $ 5 because it is the government who will buy it?
Answer: When it comes to ViiV drugs, the price will remain the same, even if the level of income in the country increases.

Question: Can you provide information on patents?
Answer: We have patents in Russia and Ukraine, and 3 drugs have patents in Kazakhstan; in the rest of the countries, we do not have patent protection, it is part of our access policy. This information will be updated.

Question: Do all drugs in Ukraine have patent protection?
Answer: Abacavir-containing medications and "Telzir" are protected in Ukraine; the old drugs do not have patent protection.

Question: What are the plans on Turkmenistan? As we understand it, you have some information on this country?
Answer: We hope that by the time GF finishes its program, our innovative products will be registered there.

Question from ViiV: Why is the community in Turkmenistan not engaged?
Answer: We do not have contacts with the patient community there, and the government there denies the fact of epidemic. In 2005, at an international conference, a representative of Turkmenistan said that they had only two HIV-positive patients in the country. Even at the Central Asian level, representatives of this country do not make contact.

GSK has offices in each country of EECA region, so it is possible to receive all updated information from them. We can take responsibility to share updated information on registration status.

Question: What is ViiV's policy in respect of prosecution those who violates patents? At the ECAB meeting, the company said that it had quite loyal policy, is this true (possibly, it was translation problems)?

Answer: We have a policy of issuing voluntary licenses (VL) for many countries (all the least developed countries, all low-income countries and Sub-Saharan Africa – 75% of people living with HIV). For other countries we apply differentiated pricing depending on the epidemic, income level and commitment of the government. We also supply drugs to GF, "Doctors Without Borders», «PEPFAR», UNICEF, UNITAID. Patents are tools for the protection of innovations that enables investment in new development. We also recognize the right of governments to use TRIPS flexibilities.

Question: Can we see the list of countries? Can we get information about the criteria for the list? How can Ukraine get into the first list?
Answer: We are happy to provide you with the list of countries. We mainly issue VLs for pediatric forms. VLs cover 118 countries with 98% of children living with HIV in the world. Ukraine is not a least developed country and it is not a country with low income. Ukraine can provide treatment to people. It is important to understand what the government's position is, and what the barriers are: how many people are tested, how many are diagnosed, etc.

Question: Will you continue to sue the Ministry of Health and the All-Ukrainian Network of PLHIV regarding abacavir?
Answer: The trial is not with the All-Ukrainian Network of PLHIV, but with companies violating our patent rights.

Question: ViiV's policy as to establishing the list of countries is different to the policies of other brand companies. The criteria are based on official data. Is it possible for the company to take a unique position and to take into consideration the point of view of the civil society? EECA CAB may be an accumulating body and can provide data from unofficial sources. Often, the data provided by the government does not reflect the real situation.
Answer: The short answer is yes. We have a list of countries formed by the Bank of Reconstruction and Development. However, the prices in Ukraine are not set on the basis of this paper. We are negotiating with the government.

Question: For abacavir, there is an "evergreen" patent; first, you register the substance, then you register the salt, etc. In Ukraine, out of the 300,000 people living with HIV, only 9% are provided with treatment. 2000 of them receive abacavir. Do you plan to continue the trial?
Answer: Now, there is a dispute over the abacavir patent, which ends in 2018. We discussed this information at one of the UCAB meetings. Certain decisions were taken. Last year, to avoid interruption of treatment, we donated approximately 50 million of hryvnia[1]. We fully understand our social responsibility. On the one hand, we defend our patent rights; on the other hand, we do our best to make our products available, and to avoid interruption of therapy. The price of abacavir in Ukraine is at the level of the generic price.

Comment: it was the day before yesterday the company did not show up at the court hearing. The hearing was postponed till May.

Answer: We do not have the opportunity to comment on that now.

Question: What are the criteria for the decision on registration of maraviroc? For example, why will it be registered in Armenia, Azerbaijan, but not in Moldova? Complex registration procedure, unattractive markets, something else?
Answer: It is hard to prepare all the dossiers at once. The Belarus dossier, in particular, is very similar to the Russian one. It is more simple to prepare it in comparison to other countries of the region. Maraviroc is a new dossier, a new drug.

Question: If in these countries there is one person who needs maraviroc, will he/she get it?

[1] ~6,25 mln. USD

Answer: The company has a program of global access to medicines; patients can get the drug directly in the case of emergency, even if it is not registered. Russia is an exception due to legal aspects.

Question: Is it possible to provide GSK contact details in Azerbaijan and Georgia?
Answer: Yes, this is possible (contacts attached).

Question: Are hypersensitivity and tropism test systems registered? Why are they not included into this table?
Answer: We have been in contact with the producers about the plans in the region, but it should be a two-way process. Governments must come up with a proposal to companies.

Question: Are you as a company interested in it?
Answer: We do not have an opportunity to influence these manufacturers. There is a test system developed by "InterLabService"; it is registered in Russia and Ukraine. The test system is available commercially and can be used. If you have a question about a specific country, we can contact the producers and raise the issue.

Question: On the 1st of March, Ukraine introduces a license for imported pharmaceuticals; it can lead to restrictions on import. What are your comments?
Answer: This is a very important issue for all. We began bringing up this issue a year ago. Now, the secondary legislation that defines the rules is not adopted. It is less than one month before the project is coming into legal force. To obtain a license, a huge list of documents is needed and it is only 30 days. There are negotiations with the government and with the Minister of Health. According to the current situation, no company will be able to get a license. Now, a way out would be either to cancel this rule, or to put in on the shelf and modify it.

Question: Can ViiV make emergency supplies?
Answer: We have considered this and foresee this possibility, but we are talking only on behalf of ViiV.

Question from ViiV: As for hypersensitivity tests, we supply our original products only in Russia and Ukraine. Which countries have problems with hypersensitivity tests?

Comment: Ukraine does not have access to hypersensitivity tests.

Answer: The test is registered in Ukraine. We have been discussing this issue with patient organizations and with the Ministry of Health for 2 years; there are problems on the part of the government. We cannot take over the functions of MoH. If initially the original drug had been supplied to Ukraine, the issue would have been resolved. This is one of the side effects associated with the supply of generics.

Comment: Sometimes it happens that generic companies supply the drugs. There are situations when generic companies supply products at a price slightly lower than ViiV's drugs. There is a risk that in the absence of your registered products generic prices could be super-high.
Answer: We agree. There are situations when we make a bid at a price of $ 3 and generics win at a price of $ 2.99; the bids are submitted in sealed envelopes.

Comment: We do not absolutely agree with you that the availability of hypersensitivity tests completely depends on the issue of generic drugs. Russia has original abacavir, but there are many people who were not offered the test and who have never heard of its existence.

Answer: ViiV has been making charitable deliveries since 2007. Last year, we have supplied tests free of charge to 23 centres, covering more than 6000 patients. This year, the program will continue in Russia.

Question: What about other countries?
Answer: ViiV drugs exist only in Ukraine and Russia, in other countries, there are only generics. Apropos the question of prices, today with Georgia we discussed that when GF curtail their program our prices will remain on the same level, in this aspect we expect patients community demand from generic companies to do the same.

Question: Will all the six drugs that ViiV intended to register in Moldova be for sale simultaneously?
Answer: As far as possible, but we are not talking about the six drugs, it is primarily "Kivexa", "Telzir" and "Celsentri." Moldova requires an EU dossier so it has to be translated.

Comment: You were talking about charity actions with regards to the supply of test systems; we do not quite understand why this is charity, when we are talking about the life of patients?
Answer: We agree that as a company we have to mitigate the risk; maybe, “charity” was a wrong word. Free provision of test systems is a small part of risk minimization. We conduct seminars for doctors who prescribe ARVs, etc. Unfortunately, even the test does not eliminate the risk. Careful clinical monitoring is very important.

Question: When will the CCR5 tropism test be available in Russia?
Answer: We have done everything to make maraviroc and tropism tests available for everyone. There are some Russian products; there is a central system of testing funded by the company. The situation with "Celsentri" is very complex; we have applied for inclusion of maraviroc into the Russian Essential Drug List; however, it has been included neither in the ENL nor in the standards of care. We are taking measures to include maraviroc into these documents.
We have sponsored research to develop a local tropism test at the Federal AIDS Centre. The equipment (sequencers) is available only in 7 centres; we have had negotiations with others, but so far without success. The Staff is not trained. We have conducted training seminars, established a system of transportation of samples to the laboratory in Moscow at ViiV’s cost. This year, we do not expect access to maraviroc to be improved. The Russian tropism test is cheaper than the Western tests. The owner (Central Research Institute of Epidemiology) can register it in other countries if necessary.
The cost of one test system for 50 tests about 110 thousand rubles. The problem is that in some centres there are fewer than 50 patients. Therefore, ViiV have organized logistics and continue educational trainings for the centres where the equipment is available.

Question: Do you plan any actions to reduce the price for this test?
Answer: We cannot do this, as this test does not belong to us. We are discussing this issue. However, the price of the Russian equivalent is lower than the Western product.

Comment: In the UK, the price for one test is about 120 pounds (genotypic test).

Question: Did maraviroc receive MA for naïve patients, or for both naïve and experienced?
Answer: Only for experienced patients (initially, it was Pfizer, who submitted the registration dossier); now, we are planning to register a new indication in the MA for naïve patients.

Review of voluntary licensing and patents.

The development of one drug can take from seven to ten years, and the cost can be 1-1.4 billion dollars. The whole point of the patent restrictions imposed by TRIPS is to motivate companies to develop new drugs. The company will have exclusive rights to recoup their investments in the drug development. As well, we invest in such activities as testing and community projects (Positive Action). In addition, we invest in the development of test systems, for example, in abacavir hypersensitivity tests.
With regard to the question why Ukraine is not included in the list of countries where we issue voluntary licenses – the company's policy is to issue voluntary licenses for the least developed countries and low-income countries
There is such a TRIPS mechanism as compulsory licensing. In this regards, ViiV is ready to discuss each individual case to find solutions with respect to all of the existing mechanisms.

Question: So, for each country, the price of each product will be discussed individually?
Answer: Yes.

Question: The question regards CA countries, possibly, except Kazakhstan. Tajikistan, Uzbekistan, Kyrgyzstan, and, perhaps, Turkmenistan have long been buying Indian drugs. How will you convince our governments to buy your products, if your price is higher?
Answer: We are not planning to convince governments of these countries to buy our products, which are more expensive than generic products, and we do not intend to compete with generics. We assume that generic manufacturers will continue to sell and promote their products in those countries. They can set a low price, and the government will be able to afford their products.

Question: Has there ever been a case of a compulsory license issued with regard to your drugs?
Answer: There are several examples where governments negotiate compulsory licenses, such as for protease inhibitors in Brazil. Very often, the mechanism of compulsory licensing is used for political purposes, as, for example, last year in Indonesia, where a compulsory license was issued. There are 360,000 people in need of treatment, and only 26,000 people on ART. 2 months prior to the introduction of compulsory licensing, we had a meeting with Indonesian representatives with regard to issuing licenses to local generic companies. 2 months later, the new Minister of Health held an appointment and, without any debates, he issued a compulsory license for seven ViiV drugs.

Question: Could you please repeat a summary of the patents.
Answer: Last year, in Russia patents on lamivudine and "Combivir" expired; we still have patents on abacavir and "Trizivir", "Kivexa", "Telzir", "Celsentri" (maraviroc). We have the same patents in Ukraine. In Kazakhstan, we have patents on three drugs: "Kivexa", "Trizivir" and "Telzir". We do not have patents in any other countries of the region.

Question: Do you get the patents directly in other countries, and not through the Eurasian Patent Office?
Answer: Yes.

Question: Does the company consider itself as a participant of Medicines Patent Pool (MPP)?
Answer: We have been negotiating with the MPP for about two years; we were one of the first who took part in the negotiations. As you know, MPP aims to obtain licenses from originator companies to transfer these licenses to the generics companies. We provided a wide range of technical assistance to MPP, which included monitoring of possible negative side effects, quality monitoring etc. The aim of MPP is to improve the licensing conditions. Our company has over a decade of experience in providing VL that we started in 2001. As of today, we have issued 13 different VL to the leading generics companies.

Question: Is ViiV planning to patent dolutegravir in the same three countries [Ukraine, Russia, Kazakhstan]? Are you planning to expand the list of the countries?
Answer: We will try to obtain the patent for dolutegravir wherever possible, as this is an innovative product. Once we receive the approval of FDA, we will immediately start negotiations on granting voluntary licenses to generics companies whose products cover 75% of people living with HIV in the least developed countries, in the countries situated South of the Sahara, and in low-income countries.

Question: Will the company defend their patents in Russia and Ukraine?
Answer: We have patents in these countries and we ask the generics companies to respect our rights. Besides Ukraine and Russia, we have patents in Kazakhstan. In other countries, we have no patents so generics can compete there. As for the situation in Ukraine, it was a matter of principle on our side. Not only that, given that the situation was quite complicated, we supply abacavir to Ukraine under special conditions at the price of generic companies.

Question: Ukraine adopted TRIPS + with regards to patent protection and drug registration. How would you comment on the fact that countries adopt TRIPS + and do not use flexible conditions?
Answer: TRIPS is an effective mechanism to ensure investments in the development of new products.

Question: We would like to know the situation with abacavir, not in Ukraine this time, but in different countries. Now in Russia we are observing two situations at the same time. The first situation is a decentralization of procurement; previously, it was the Ministry of Health who purchased the drugs; now, each region will purchase the drugs independently. The second situation is a development of the generic drugs industry. You probably know that in Russia we have at least two companies who are starting development of ARVs. Abacavir is among the drugs they are developing. Hypothetically, some regions will buy the generics and, thus, they will violate your patent. The question is what would you do?
Answer: We will go to court.

Question: If the situation happens in a small region where due to the small budget is not possible to regulate this situation so there will be a risk of interruptions in the drug supply, what are your actions?

Answer: First, the situation is hypothetical, and secondly, our lawyer will deal with the litigation, thirdly, the ligation starts post factum. One of the mechanisms of the company is to inform the generics companies and the Ministry of Health in advance to prevent the drugs getting to the tender.

Question: So you do this kind of activity?
Answer: Generics companies have the right to register the drug, but they do not have the right to introduce it to the market. Each of these companies has received a letter from our legal team that we have rights with respect to this drug, and we ask them to respect our rights etc. In return, we have received a letter from them saying that they are aware of this and now they are simply registering the drug. We do not expect these companies to violate our rights. Supply interruptions may occur not because of patents, but due to the regionalization of business, because of the chaos and incompetence, and due to the distributors not knowing what to do. Of course, we will supply drugs at no cost, if supply interruptions occur.

Comment by ViiV: A more worrying situation is with the pediatric forms. For example, some distant region would announce a tender for five packages of the drug, and none of the distributors would want to supply it. So now we are working on this issue with the distributors and AIDS centres and here we may need support from your side.

Issues on access to specific drugs

Maraviroc

Comment from EECA CAB: This product is registered in Russia, it was in procurement for a first time; in St. Petersburg, the price was 17 dollars per tablet which is about 15 thousand dollars a year + test for hypersensitivity.

Comment from ViiV: I find it difficult to judge why the distributors' price was 60% higher, because our price is about 7,7-8 thousand dollars a year, the smaller dosage is about 5 thousand a year.

Question: Could you please clarify the situation with maraviroc? Despite the high price, and access to the tests, the drug is important for patients. What is really going on?
Answer: We do not expect that a large number of patients will have access to it. About 15 major centres in Russia are already planning to buy the drug this year. We still do not know the amount and for how many people; and this is despite the fact that the drug is not included in the list of essential drugs. Now, we are working to include it in the standards of care. The competitors of the drug are darunavir and raltegravir. All our competitors are 2 or 2.5 times more expensive. Despite the fact that the drug is not cheap, it gives the opportunity to save the budget.

Comment from ViiV: Maraviroc will take its place for those patients who have a limited choice of drugs for the treatment (failure of the previous regime, etc.).

"Combivir"

Comment from EECA CAB: Latvia signed the order of the Cabinet on all products that are listed in the compensation system; if the patent term expires in three years, the applicant (not necessarily the manufacturer) has to reduce the baseline compensation price by 30%. Since we now have "evergreen" patents, we are trying to introduce a proposal that if a drug has been on the market for 10 years, the applicant must reduce its price by 30%.
At the meeting in Tbilisi, we found that one of the barriers which we can influence is registration. Since February, the cost of registration in Latvia has been reduced; before the cost of registration of a new drug was 10,000 lats, now, it is 4 000 lats.

Question: Why is the price for older drugs, such as "Combivir", not reduced in Latvia? Why is it kept at $ 400 per package? We cannot provide 400 people with treatment! This is an old drug that has many side effects, and it has paid itself long time ago. The policies of pharmaceutical companies saying that they will reduce the price if the government spends more for the procurement of ARVs is very clear. But the patients are in the middle.
Answer: We do not try to promote drugs with toxic side effects, and I am not ashamed of the drug; we try to make the next generation of drugs less toxic, for example, dolutegravir. The price in Latvia is set in accordance with the prices in EU, it is a pricing benchmark.
Of course, I apologize. I would like to have a meeting with you and representatives of GSK in Latvia and try to resolve the question as to why there are 400 people on the waiting list for the drug. Do these patients need Combivir or other drugs?

Comment: They are waiting for the start of treatment. In Latvia, the crisis time rules clearly indicate that treatment begins with "Combivir" and "Stocrin"; if something does not work, they are replaced by “Kivexa”. But the first choice is "Combivir". Patients are waiting for treatment in general.

Comment from EECA CAB: We have a lot of dialogue within the community about “Combivir”. The drug is out of date; the side effects are very strong. On the other hand, it is cheap and easy. Given the fact there are many IDUs in our region and supply failures and problems with the procurement we have, this drug is advantageous. On the other hand, if we demand price reduction, the governments will start with a drug which is not very good and not very new. The same situation is in Russia, we are afraid that the centres will buy Combivir, which would be based on the financial costs. What is preventing you from reducing the price for Combivir, when its days are almost over? ViiV’s position on "Combivir" is irritating. We do not really want this drug, but we cannot do without it anyway. What concessions could ViiV make?

Answer: The patent on "Combivir" expired in 2012. The cost per patient per month is about $100; its generic analogue is cheaper by 13-14%. This year, the price of the drug will match the price of the generic. The danger is that patients will receive neither the original nor generic "Combivir" and will receive a combination of individual drugs. We get many signals that centres consider procurement of individual drugs instead of combined drugs because the total price is lower.
We are ready to negotiate and reduce the price, but there was no invitation for negotiations from the governments.

Comment from EECA CAB: I understand that the question of "Combivir’s” prime cost will remain unanswered. We see the price of $ 100 for an annual course in Africa. You can lower

the price so the combination of monotherapies will be more expensive than the combined therapy. The price can be reduced tenfold, this is our position.

Answer: The position is interesting, but the price hardly can be reduced by ten times. Last year, our company did not participate in the tender on lamivudine, but the price reduction did not happen.
Comment from EECA CAB: Your comment about the fact that generics are not much cheaper than the original drugs applies only to our region, where the corruption component is high. In other countries, they are much cheaper. Generic companies produce and profit by selling "Combivir" at a price ten times lower than the cost of the original drug. The opportunity for price reduction does exist.

Question: As I understand, we have the Federal AIDS Centre, which forms the suggested retail price on drugs. For example, if the Baltic States have a high price, that will affect pricing as well. Is it right?
Answer: Latvia is not a reference country for Russia.

Question: Would you say that the prime cost of a tablet is different in different countries?
Answer: The prices in different countries are different. Russia has one of the lowest prices for Combivir in the world. We do not plan to compete with generic companies in terms of prices. However, if generics reduce their prices, it will allow the Ministry of Health to provide more people with treatment. This year, our price will be identical to the price on generics. If their price is lower, they can win the auction.

Question: Are you prepared to sell the same "Combivir" at a lower price in Russia? We have more and more people on the waiting list.
Answer: We are ready to consider the question, of course, within reason. But, again, in the current situation with tenders in the country it is very difficult to predict the winner and the amount, etc. MoH has never contacted us with regard to the increase of the supply amount.
Last year, the quantity of "Combivir" amounted to 622 thousand packages; 30 thousands packages were generics. Both production and storage are expensive. If we deliver 600,000 packages to the country and someone else wins the tender, the batch is likely to be destroyed. In addition, it is important that it is the FDC and not a combination of monotherapies wins the tender.

Pricing policy.

The price includes the prime cost, income level, the prevalence of the disease and the commitment of governments. Russia is a middle-high income country; Ukraine is a middle-low income country. In the EU and U.S., the prices are higher. The most expensive drugs are in Japan.

Question: Is there any information on a possible price for dolutegravir?
Answer: We are not yet ready to talk about it, because the drug is not registered.

Question: With regard to pharmacovigilance: what is the patient feedback mechanism; how to contact you, is it possible according to the law? In the EU, the "Yellow Card" was introduced only a few years ago.

Answer: The law does not prohibit it; we are constantly monitoring the Internet resources; all the information is accumulated in the head office. You can reach any member of ViiV. The answerphone is on all day and records the information. This information in an anonymised form should be passed on to the central committee on clinical safety within 24 hours.

Question: Is there contact information in Uzbekistan?
Answer: You can contact the local office of GSK, if they do not react, you can contact the Russian office. We have a contract with GSK whereby they serve the markets where we are not represented. The same applies to Tajikistan.

Question: Is there a list of contacts in the region? Can we get it?
Answer: There is only the list of GSK contacts; ViiV is represented only in Russia. We can provide contacts (list attached).

Position of EECA CAB announced to ViiV.

- EECA CAB finds that ViiV should review its pricing policy in the region in the direction of a significant price reduction in order to improve access to treatment, especially with respect to the widely used drugs in the EECA region (including "Combivir", "Kivexa" and “Ziagen”). At the moment, the prices are oriented towards the formal classification of countries by income and they do not reflect the specifics of the epidemic and the situation with public health service in the region.
- EECA CAB believes that ViiV’s policy on drug registration in several countries in the EECA region could jeopardize access to treatment; and ViiV should take steps towards registration of their products in the countries where they are not registered yet and can be delivered only through donor programs, thereby eliminating the risk of treatment interruption after the donors withdraw the programs.
- EECA CAB believes that after the curtailing of GF programs in EECA region, ViiV’s drugs should be available to governments for a price not higher than the price within the GF program.
- EECA CAB believes that ViiV should include countries of EECA region into the list of countries covered by voluntary licenses in bilateral agreements with generic companies and in the agreements made with Medicines Patent Pool.
- EECA CAB considers that in all the EECA countries hypersensitivity tests for abacavir-containing drugs and CCR5 tropism tests for maraviroc should be available at ViiV’s cost for patients receiving treatment with the respective ViiV’s products.

Additional questions:

Question: Are there any plans for the development of drugs for other diseases?
Answer: No, ViiV deals only with HIV. If you need to get information on the drugs for the treatment of HIV and TB which are developed by GSK and Pfizer, you should apply directly to these companies.

Comment: We would like to receive information on the Baltic States at the meetings of EECA CAB.

Answer: Indeed, there are two options: either you join meetings of ECAB, or we can bring the people who are responsible for the European region to EECA CAB.

End of the meeting