ITPCru E.V.A. Simona+ CF «Candle»

To treat or not to treat?

Report based on the results of community research

ARV treatment procurement and provision in Russia

Saint- Petersburg
2012

Background

This report contains results of two studies that were carried out in 2011-2012 in Russia by the community of people living with HIV (PLHIV). Both studies focus upon different aspects of access to antiretroviral medicines in the Russian Federation.

The first study is a monitoring project Simona+ carried out by the community of patients. Its purpose has been to identify weaknesses in the field of access to medicines for PLHIV in different regions of the country. In 2011-2012, Simona+ focused upon identifying stock-outs of ARV medications in Russia, key barriers that patients face with respect to access to treatment, as well as the most frequently prescribed treatment regimens.

The second study is an analysis of the government procurement of ARVT in Russia on the federal level for the period of 2009-2012. This research has been conducted by the activists of the International Treatment Preparedness Coalition in Eastern Europe and Central Asia (ITPCru). The analysis focused primarily on the number of patients per year receiving treatment in Russia for the funds of the federal budget, the most frequently purchased drugs, distributors and manufacturers, as well as the cost of medicines in the federal procurement programme.

Both studies were conducted during the same period of time, which enabled the research teams to cooperate and exchange data; towards the end of the studies, it became evident that they complemented each other. In view of this, it was decided to issue a joint report combining the results of Simona+ and the ARVT government procurement monitoring project, which you are reading now.

This document is written for a broad range of readers who are interested in the issues of access to treatment for PLHIV in Russia, who face problems with access to treatment and seek solutions for the problems in this field: community activists, doctors, healthcare administrators and experts, as well as for our foreign colleagues. We tried not to overburden the reader with statistics and scientific data and, at the same time, we wanted to make this report as informative as possible. The first chapters of the document contain general data, followed by more specific and complicated issues.

Government procurement and prices for ARVT still remain a terra incognita for many people. We hope that this report will help the reader to find answers to the most important questions, namely what drugs are used for treating people living with HIV, how much treatment costs, what the problems and the solutions are etc.

This document is an invitation to dialogue. It is our attempt to tell all the stakeholders that it is time to take action in order to change the system regulating access to treatment. It is time to take measures to adjust the treatment provision system to the needs of the patients and the healthcare workers, to make it transparent and convenient for healthcare administrators, to make it economic for the budget and profitable for the manufacturers and distributors. We believe that the new HIV team that was formed within the Ministry of Health as this report was being prepared would successfully unite the efforts of experts and activists in order to take these very important actions.

Respectfully yours,
Research team:
Denis Godlevskiy, Alexandra Volgina, Sergey Golovin, Polina Girchenko, Andrey Skvortsov

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We especially thank the focal points of Simona+ project, Olga Timofeeva, Anastasia Solovyeva, Grigory Vergus, Vladimir Osin, Maria Godlevskaya, Ekaterina Zinger, Maria Yakovleva, Tatyana Fedorova and Egida Association, Ivan Begtin and Rosgoszatraty Project, doctors and patients who have taken part in the research and many other people who have made this research possible.

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Procurement Procedures

So the reader can better understand those parts of our report that deal with the procurement of ARV drugs in the Russian Federation, we decided to include a small introduction that highlights the technical aspects of this issue. We will include information about auction procedures, auction records, legislation and other normative legal acts regulating government purchases, and the financial basis for procuring ARV drugs.

Legal Basis

All state and municipal procurements must be conducted in accordance with Law No. 94-FZ "On Placing Orders for Goods, Works and Services to Meet State and Municipal Needs", as well as other applicable sections of current RF legislation, including the RF Budget Code, the RF Civil Code, etc. The chief goals of the law FZ-94 are to ensure effective budget spending, fair competition, openness and transparency as well as to prevent abuse and other violations during the course of the bidding process.

Procedures

In accordance with the current version of FZ-94, several procedures can be used for state procurements, such as: procurement from a single supplier (for purchases less than 100,000 rubles – approximately USD3000), quote requests (for purchases less than 500,000 rubles – approximately USD 16,500), public electronic auctions, and contests.

Thus, auctions and contests are used for procurements in excess of 500,000 rubles. The main difference between auctions and contests is that in auctions, the single, deciding factor is the **price** of the goods or services being purchased (the participant who offers the lowest price for goods or services wins). In contests, the winner is the entity who offers the best conditions for fulfilling the contract (including quality, delivery time, price, etc. Various parameters are assigned points in accordance with a specific system). It is important to note that since 2010, public auctions at the federal level are only held electronically via specific electronic trading platforms. All document interchange occurs in the form of electronic documents.

For the purposes of this report, we are interested only in **public electronic auctions**, inasmuch as this procedure is used for procuring medicines, including ARVT. The list of goods (work, services) which must be purchased by means of an electronic auction is provided in Decree No 236-r of the Government of the RF dated February 17, 2008.

A public electronic auction consists of a series of formal steps which must be completed by the customer (in our case, the Ministry of Health[1]). The main procedures include the formation of a commission, the publication of a notice on open bidding, the review of the first section of bids received, the timely conducting of the auction, the review of the second section of bids[2], followed by the distribution and publication of the final protocol as well as the signing of the contract by the winner.

[1] The Ministry of Health and Social Development (MoH) has been procuring ARVs at the federal level since 2010. In 2009, the Russian Federal Service for the Protection of Consumer Rights and Human Welfare acted as the procurer, but at that time the auctions were not held electronically.

[2] Summarized, the difference between the first and second sections of bids consists in the fact that the first section contains information about the goods or services being supplied, while the second section contains information about the bidder himself, including everything about licenses, permits, etc.

There are clearly stipulated time frames for the majority of these procedures. For example, publication and distribution of the notice regarding bidding takes place no less than 20 days before the bidding deadline if the starting price is ≥ 3,000,000 rubles (approximately 100,000 USD), and not less than 7 days from the bidding deadline if the starting price is ≤ 3,000,000 rubles. The deadline for signing the contract is not less than 10 days after the signing of the final protocol. In other words, for large orders of more than 3,000,000 rubles, it generally takes about one and half months from the publication of the auction announcement to the closing of the contract.

Over the course of state procurement, specific documents must be prepared and made publicly accessible, including the auction announcement, documentation about the electronic auction that contains detailed information regarding the conditions of the order and the contract draft, bids for participating in the auction, a protocol regarding the bidding review, and a summary protocol. Among other things, the contract draft should prescribe the delivery schedule, according to which the distributor must deliver the goods to the final recipient (delivery destination). In our case, this means the institutions that directly issue ARVT to patients (AIDS centres, infectious diseases hospitals, etc.).

Access to Data

Information about all public electronic auctions is uploaded for public access onto specialized internet platforms in accordance with the law and corresponding to the different stages in the auction process. This information is presented in the form of specific documents and includes details about awarding contracts and thus permits the online monitoring of all required information. Currently, there are five main sites for electronic trading. Information about all purchases is duplicated on the single portal www.zakupki.gov.ru. These documents are available for download by any internet user without registration of any kind.[3]

Financing and Determining Requirements

The procurement of antiretroviral drugs with financing from the federal budget is handled in accordance with a special decree of the Government of the Russian Federation. In 2012, auctions were conducted in accordance with the Decree of the Government of the Russian Federation dated December 31, 2010, No 1236 "On the Funding of Purchases for Diagnostic Tools and Antiviral Drugs for the Prevention, Screening, Monitoring and Treatment of People Infected with the Human Immunodeficiency Virus and Hepatitis B and C " as amended on 21 December 2011.

This decree spells out the rules for funding purchases, for granting subsidies from the federal budget to the regional budgets, determining purchasing agents, and likewise presents the list of diagnostic tools and antiviral drugs admitted for purchase. Currently, the list contains 26 items, of which 7 are drugs used in the treatment of hepatitis B and C. In addition, given the registration of combined drugs in accordance with this decree, 22 drugs must be purchased under their international non-proprietary names. Several drugs are available with different doses and thus, for one specific drug name, several auctions might be conducted.

In order to determine the demand in quantity for ARVT, as well as a list of essential drugs, the Ministry of Health has developed an application form for AIDS centres, who each year at the prescribed time submit the completed form in which they indicate the names and quantities of drugs required. These orders are then approved by the Ministry of Health, and on the basis of the approved orders, the auction documentation is developed.

[3] However, it should be mentioned that several electronic platforms do not work very well with all browsers and that problems sometimes occur when downloading documents.

The federal procurement of antiretroviral drugs is financed with funding from the National Priority Project Health (NPP Health). There are likewise regional and local programmes for counteracting HIV infection, within which procurement of drugs also takes place. An example of such a programme is the long-term target Project "Development of Health Care in the Amur District for 2012 – 2014" under the programme "HIV Infection".

Interesting select examples taken from practical experience of Russian state purchases within the sphere of HIV treatment can be found in Appendix 2.

What drugs are purchased in Russia?

Analyzing the drugs that are purchased in Russia for the funds of the federal budget in 2009-2012, we have come to a conclusion that, despite the emergence of many new drugs, and despite the fact that some of the newer drugs have recently been registered in Russia, the structure of the ARVT procurement programme remains roughly the same (see Table 1).

№	International Non-Proprietary Name	Remark
1.	Abacavir, tablets (300 mg) ABC	
2.	Abacavir, solution (240 ml) ABC	
3.	Abacavir+lamivudine, tablets (600+300 mg) ABC+3TC	
4.	Abacavir+zidovudine+lamivudine tablets (300+300+150) ABC+AZT+3TC	
5.	Atazanavir, capsules (150 mg) ATZ	
6.	Atazanavir, capsules (200 mg) ATZ	
7.	Darunavir tablets (300 mg) DRV	Purchased for the last time in 2009
8.	Darunavir tablets (400 mg) DRV	Purchased within the government procurement prorgamme since 2010
9.	Darunavir tablets (600 mg) DRV	
10.	Didanosine, chewable tablets (100 mg) DDI	Purchased for the last time in 2010
11.	Didanosine, capsules (125 mg) DDI	
12.	Didanosine, capsules (250 mg) DDI	
13.	Didanosine, capsules (400 mg) DDI	
14.	Didanosine, vials 2 g (2.0) DDI	
15.	Zidovudine, capsules (100 mg) AZT (ZDV is also used)	
16.	Zidovudine, tablets (300 mg) AZT	
17.	Zidovudine, solution (200 ml) AZT	
18.	Zidovudine, solution for infusion (20 ml) AZT	
19.	Indinavir capsules (400 mg) IDV	
20.	Lamivudine tablets (150 mg) 3TC	
21.	Lamivudine, solution (240 ml) 3TC	
22.	Lamivudine+zidovudine, tablets (300+150 mg) 3TC+AZT	
23.	Lopinavir/ritonavir (200+50 mg) tablets LPV/r	
24.	Lopinavir/ritonavir, oral solution (60 ml) LPV/r	
25.	Lopinavir/ritonavir (100+25 mg) LPV/r	Purchased within the government procurement prorgamme since 2012; paediatric formula
26.	Nevirapine (200 mg) NVP	
27.	Nevirapine, oral suspension (240 ml) NVP	Not purchased in 2011, paediatric formula

№	International Non-Proprietary Name	Remark
28.	Nelfinavir tablets (250 mg) NFV	Purchased for the last time in 2010
29.	Nelfinavir, powder (144 g (vial)) NFV	Purchased for the last time in 2010
30.	Raltegravir tablets (400 mg) RAL (RLV is also used)	
31.	Ritonavir, capsules (100 mg) RTV (or …/r when used as a booster for other drugs)	
32.	Saquinavir tablets (500 mg) SQV	
33.	Stavudine capsules (30 mg) d4T	
34.	Stavudine capsules (40 mg) d4T	
35.	Stavudine, powder for oral solution (1 mg/ml – 260 ml) d4T	
36.	Fosamprenavir, tablets (700 mg) fAPV	
37.	Fosamprenavir, oral suspension (225 ml) FSP	
38.	Phosphazide, tablets (200 mg) F-AZT	
39.	Lyophilised enfuvirtide (90 mg/ml) T20	
40.	Etravirine, tablets (100 mg) TMC125 (ETR is also used)	
41.	Efavirenz, tablets (200 mg) EFV	
42.	Efavirenz tablets (600 mg) EFV	

Table 1. List of antiretroviral drugs purchased within the federal procurement programme in 2009-2012.

So, with a reservation made for various dosages, **a total number of 22 antiretroviral drugs were available for adults living with HIV within the federal ARVT procurement programme by 2012.**

Over the same period (2009-2012), several new antiretroviral drugs were registered in Russia (new international non-proprietary names)[4]:

International Non-Proprietary Name	Trade Name ™	Manufacturer	Date of Registration
Tenofovir (TDF)	Tenofovir	Hetero Drugs/ Makiz Pharma	March 30, 2010
	Viread	Gilead	October 3, 2011
Tenofovir/emtricitabine (TDF/FTC)	Truvada	Gilead	September 29, 2011
Maraviroc (MVC)	Celzentri	ViiV (Pfiser)	July 14, 2011
Tipranavir (TPV)	Aptivus	Boehringer Ingelheim	November 3, 2011

Table 2. New antiretroviral drugs (international non-proprietary names) registered in Russia in 2009-2011

Here we have to make a few clarifying comments. The fact that the drug is registered in Russia does not mean that it will be purchased within the government procurement programme. It merely means that the drug can be imported into Russia, as well as sold here and prescribed by doctors.

[4] The term “new drugs” refers to international non-proprietary names that have not been registered in Russia before, according to the data of the state register of drug products http://grls.rosminzdrav.ru

In order to include the drug in ***the local procurement programmes funded by the city budget or the regional budget***, the following conditions must be met: a) there must be funds allocated for HIV response in the regional budget, and b) the local AIDS centre must send an order to regional healthcare officials with a request to purchase this drug.

In order to include the drug in the ***federal ARVT procurement programme funded by the federal budget***, the drug a) has to be included in the List of Essential Medicines, b) has to be included in the annual Decree of the Government of Russia on ARVT Procurement. However, the practice shows that the inclusion of the drug into the Decree of the Government could be enough.

Besides, the drug must be included into the form of the order for ARVT developed by the Ministry of Health and filled in regionally[5]. On the basis of the orders, MoH estimates the needs for antiretroviral drugs and develops the auction documentation on the basis of these estimates.

So, why has none of the drugs listed above been included into the ARVT procurement programme? When it comes to Viread, Truvada, Celzentri and Aptivus, it is more or less clear. Despite the fact that officially the drugs were registered at the end of 2011, by March 2012 the manufacturers had not received the marketing authorization from MoH, which is the main document proving that the drug has been registered. Without the marketing authorization, companies cannot import the drugs or apply for including the drugs in the List of Essential Medicines. This means that the manufacturers simply did not have time to take measures to ensure inclusion of the drugs in the procurement programmes.

The situation looks different with tenofovir by Hetero Drugs Ltd, represented in Russia by Makiz-Pharma[6]. This drug was registered already in the first quarter of 2010; the same year the company unsuccessfully applied for including tenofovir in the List of Essential Medicines. The second application in 2011 was also rejected.

Over the period of 2010-2011, community-based organization on several occasions sent letters to MoH, asking the officials to consider inclusion of tenofovir in the List of Essential Medicines and in the Decree on ARVT Procurement; however, those attempts also failed.

Tenofovir has been available for people living with HIV in the whole world since the mid-2000s (in the US, it was approved by FDA in 2001). In many countries, it costs less than USD100 per patient per year (see. Fig. 1)[7]. At the same time, it is one of the most efficient and one of the least toxic antiretroviral drugs. The World Health Organization (WHO) recommends tenofovir as the preferred first-line drug[8] for initiating treatment. The same recommendations have been adopted by expert societies in both developed and developing countries (for instance, EACS[9]).

Over the period of 2009-2012, 4 new drug products (international non-proprietary names) were registered in Russia. None of them was included in the List of Essential Medicines and in the federal procurement programme.

[5] Available at http://www.minzdravsoc.ru/docs/mzsr/projects/832/prilozhenie_45.rtf
[6] See the list of ARVT manufacturers in Russia
[7] According to MSF. http://utw.msfaccess.org/
[8] http://www.euro.who.int/__data/assets/pdf_file/0008/157166/e95794R.pdf
[9] European AIDS Clinical Society

In 2011, tenofovir was included as a first-line drug in the Russian recommendations developed by the Federal AIDS Centre; however, it is available in only few regions (Moscow, St. Petersburg, and Yekaterinburg). So far, it has not been purchased within the federal procurement programme.

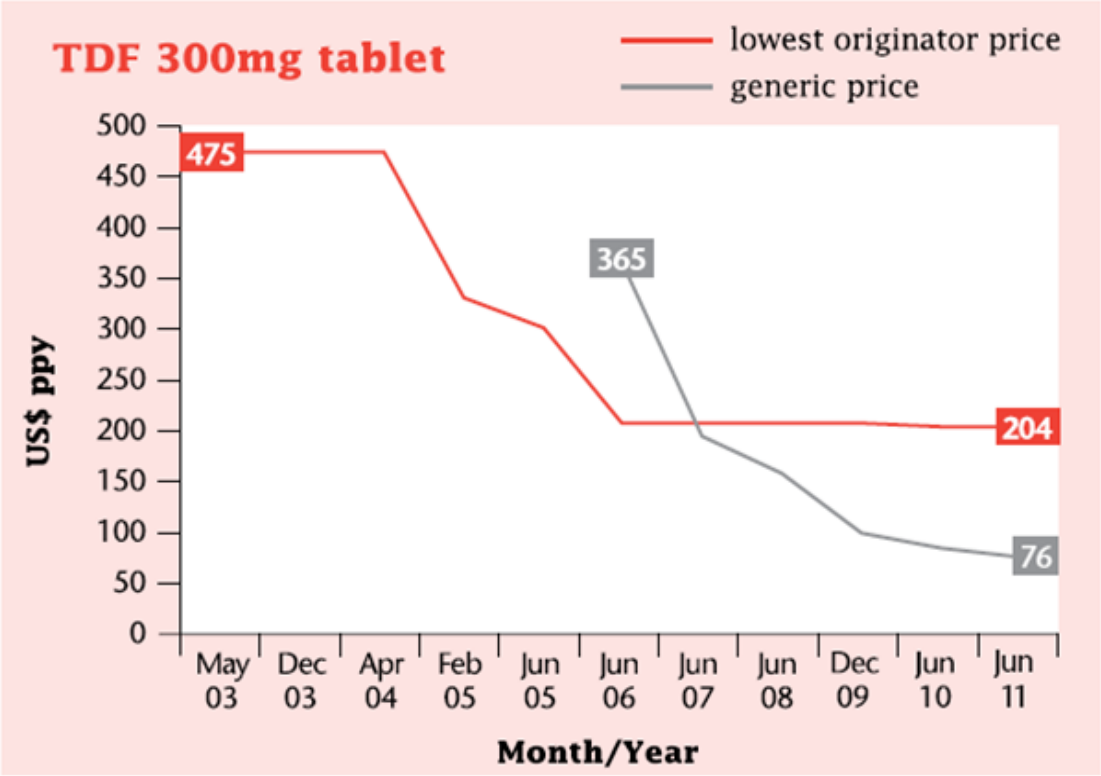


Figure 1. Cost of tenofovir in the world

So, what are the most popular drugs? If we look at the number of patients per year in the procurement programme (see Fig. 2), the obvious leaders for the last 4 years have been lamivudine+zidovudine (3TC+AZT, “Combivir”) and lopinavir+ritonavir (LPV/r, Kaletra). The graph below summarizes the most frequently purchased drugs in Russia for the period of 2009-2012. Appendix 3 contains more detailed information about the amount of drugs per patient per year purchased in Russia.

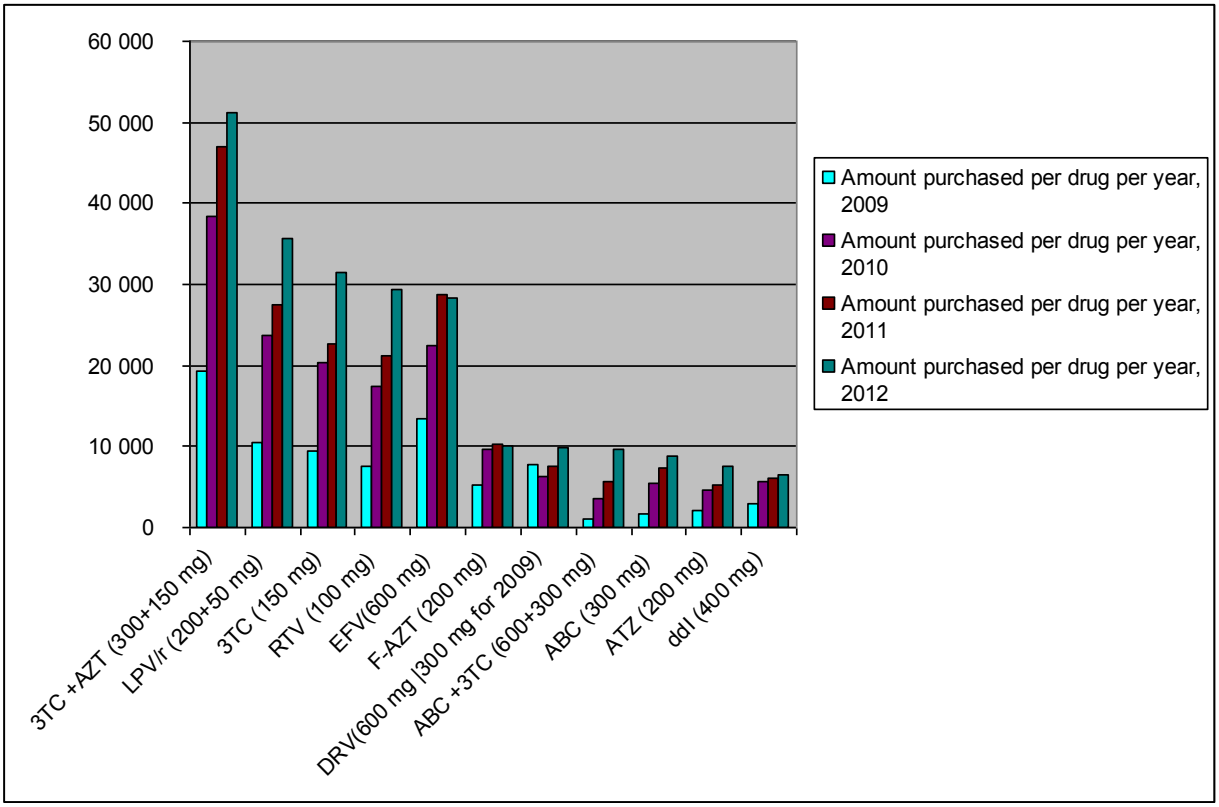


Figure 2. The most popular ARVs purchased within the federal procurement programme in Russia, 2009-2012

THE MOST POPULAR ARVT REGIMENS

Over the 8 months of Simona+ (September 2011 – April 2012), 1408 questionnaires from 23 Russian cities were analyzed, including 612 questionnaires for evaluating access to treatment (49.5% men and 50.5% women, average age 32.3) and 796 questionnaires for analyzing access to testing (47.9% men and 52.1% women, average age 31.7)[10].

Two important aspects must be noted:

1. The analysis did not take into account the source of medicines that were prescribed to the respondents. After the closure of GF programmes in Russia in 2010, patients started to receive drugs from different budgets (federal and local). Sometimes, patients can receive drugs purchased within different programmes. For instance, a patient has been prescribed zidovudine, lamivudine and atazanavir boosted by ritonavir (AZT, 3TC, ATZ/r). Lamivudine and atazanavir have been purchased for the funds of the federal budget, whereas zidovudine and ritonavir have been ordered locally. The figure below illustrates this situation:

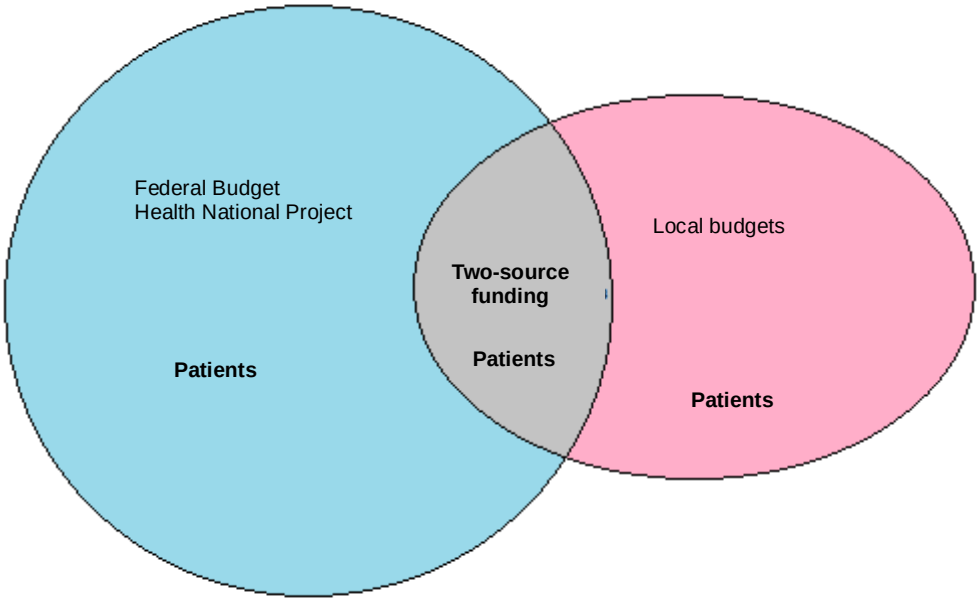


Figure 3. ARVT funding sources in Russia

This often leads to stock-outs of certain drugs at different levels and changes of regimens for some patients. Moreover, such “grey zones” make the procurement system less transparent and balanced. The level of transparency could be increased if complete regimens rather than separate drugs were purchased within one procurement system.

2. In both studies the drugs under analysis have been divided into three groups (see Table 3)[11] in accordance with WHO recommendations for first-line regimens: combination of two NRTIs as a backbone and NNRTI, PI or INSTI as a “third drug”.

[10] Appendix 1 contains a more detailed methodology.
[11] See note above.

Backbones: NRTIs	Third drugs: NNRTIs, PIs, INSTIs	Other drugs (fusion inhibitors, 3 NRTIs)
Abacavir, abacavir +lamivudine, didanosine, zidovudine, lamivudine, lamivudine+zidovudine, stavudine, phosphazide	Nevirapine, efavirenz, etravirine, atazanavir, darunavir, indinavir, lopinavir, nelfinavir, saquinavir, fosamprenavir, raltegravir	Abacavir+lamivudine+zidovudine, enfuvirtide

Table 3. Breakdown of ARVs by classes

Clinical guidelines for antiretroviral therapy commonly agree that treatment regiment should consist of two nucleoside reverse transcriptase inhibitors (NRTI), often referred to as a “backbone”, and a third drug. The latter usually belongs to another class – either non-nucleoside reverse transcriptase inhibitor (NNRTI), protease inhibitor (PI) or integrase inhibitor (INSTI).

NRTI combination generally includes either lamivudine (3TC) or emtricitabine (FTC), for their nearly-perfect safety profile. Second NRTI may be a harder choice. Guidelines for developed countries (DHHS-2012, IAS-2010 guidelines) recommend tenofovir (TDF) as the first choice. The recently updated WHO protocols (WHO 2012) contain the same recommendation.

EACS guidelines provide grounds to use abacavir (ABC) as a first choice, but with certain limitations. In all above-mentioned guidelines zidovudine (AZT) is considered as a component of an alternative regimen, not the first choice.

In Russia the situation looks different, as emtricitabine is not registered and access to tenofovir is limited. Below follows an analysis of the study results, summarized in Table 4.

The most frequently used backbones in Russia are lamivudine combined with zidovudine and lamivudine combined with abacavir. Those could include both Combivir and Kivexa and separate drugs (trade names Epivir 3TC, Ziagen, and Zido-H). The main third drugs are lopinavir+ritonavir (Kaletra) and efavirenz (Stocrin).

Based on these data, patients in our sample mostly receive regimens, based on non-preferred backbone combinations. If we count ABC-3TC and TDF-3TC combinations as preferred backbone, then only 16.7% of patients receive them. Nevertheless older WHO guidelines (WHO-2007, WHO-2010) discuss use of regimens based on AZT or either more toxic drug – stavudine (d4T) because of their low price.

Drug Name	Total		First Year of Treatment	
Backbones	**N**	**%**	**n**	**%**
3TC+AZT	352	66	120	63.8
3TC+ABC	88	16.5	35	18.6
3TC+TDF	1	0.2	1	0.5
Other drugs	92	17.3	32	17.1
Total	*533*	*100*	*188*	*100*
Third Drug				
LPV/r	191	35.8	69	36.7
EFV	162	30.4	48	25.5
ATV/r	27	5.1	17	9
DRV/r	27	5.1	15	8
Other drugs	126	23.6	39	
Total	*533*	*100*	*188*	*100*
Most Frequent Regimens				
3TC, AZT, LPV/r	138	25.9	54	28.6
3TC, AZT, EFV	124	23.3	30	16
3TC, ABC, LPV/r	31	5.8	9	4.8
3TC, ABC, EFV	21	3.9	8	4.3
Other regimens	219	41.1	87	46.3
Total	*533*	*100*	*188*	*100*
Most Frequent Problems				
Not recommended by WHO[12]	82	15.4	27	14.4
Contains either didanosine or stavudine	60	11.3	26	13.8
Regimen not complete[13]	27	5.1	7	3.7
Drug not required[14]	14	2.6	4	2.1

Table 4. Results of Simona+. ARVs Prescribed.

Out of 533 respondents, only one had a regimen with tenofovir

So, the most frequently prescribed treatment regimens in Russia are:

- ***3TC+AZT+LPV/r (26% of the respondents on treatment and 28.6% of PLHIV interviewed within the project who have started treatment this year);***
- ***3TC+AZT+EFV (23.3% of all the PLHIV on treatment and 16% naïve patients).***

[12] Regimens not recommended by WHO, since they contain fewer than three components, unusual regimens (NNRTI + PI), regimens containing unboosted PIs.
[13] Regimens containing fewer than three antiretroviral drugs.
[14] Regimens with more than thee antiretroviral drugs.

Besides, many prescribed regimens have evident bottlenecks.

- ***15.4% of the regimens are not recommended by WHO;***
- ***more than 5% of the regimens consisted only of two drugs;***
- ***2.6% received an "extra" ARV drug;***
- ***11.3% included either didanosine or stavudine.***

The data of Simona+ fully correlate with the analysis of ITPCru in the section above. We see that doctors mostly prescribe the drugs that are purchased in larger volumes.

One may ask whether it can be vice versa: the drugs are prescribed by the doctors more often, and, therefore, are included in the government procurement programmes. However, it is hardly the case, as the choice of drugs doctors may prescribe is limited to the drugs included in the annual Decree of the Government and in the form of the order developed by the Ministry of Health.

No matter how often tipranavir is prescribed by the doctors, it will still have to be purchased within the local procurement programme, which is often miniscule. Besides, if the volume of the drugs in the regional orders is considered as inappropriate by the Ministry, the order will be "cut".

One may assume that patients in Russia do not receive preferred backbone combinations because of their higher price. But at the same time patients in our sample receive expensive third-drugs much more often than it needed if economic considerations are taken into account. For example, 46% of patients were given PIs, medications way more expensive than NNRTIs and not recommended in either WHO-2010 or WHO-2007 guidelines as a first choice. If we restrict our data only to patients who started treatment very recently (during the year preceding the study) the number of patients on PIs is even higher – 53%. However, talking about economy, we need to understand the real cost of ARVs in Russia.

When the obtained data were compared with the 2012 WHO clinical guidelines for Europe, it turned out that none of the patients received treatment in accordance with international recommendations due to unavailability of tenofovir. Only 16.7% received abacavir as a first-choice drug.

Cost of ARVT in the Federal Procurement Programmes in Russia

In order to understand the rationale behind the ARVT pricing policy in Russia, a few factors must be taken into consideration:

1. To include the drug into the List of Essential Medicines, the manufacturer must also register the so-called "maximum sale price". This measure has been adopted by the Government of Russia to regulate prices for drugs. The following algorithm has been developed by MoH for calculating this price:

"Maximum sale prices for **drug products manufactured in the Russian Federation** are calculated based on the average actual sale price of a specific drug product for the year preceding the date on which the maximum sale price is submitted for state registration...

…**FOR FOREIGN MANUFACTURERS**…based on the average actual import price of a specific drug product for the year including costs related to customs clearance (customs duties and fees) and transportation costs preceding the date on which the maximum sale price is submitted for state registration...

…**With respect to drug products which have not entered into circulation** on the territory of the Russian Federation during the year and with respect to original drug products, foreign manufacturers must indicate the minimal sale price of the manufacturer for the drug product in the country of the manufacturer and in other countries in accordance with Annex 5, including customs clearance costs (customs duties and fees) and transportation costs…"

List of reference countries for determining the maximum sale price for drug products in the List of Essential Medicines in Russia

N	Country
1.	Country of Manufacturing
2.	Bulgaria
3.	Germany
4.	Greece
5.	Spain
6.	Turkey
7.	Portugal
8.	Denmark
9.	Belgium
10.	Netherlands
11.	Ireland
12.	Italy
13.	Poland
14.	Belarus
15.	Kazakhstan
16.	Romania
17.	Slovakia
18.	Ukraine
19.	France
20.	Check Republic
21.	Switzerland
22.	Other Countries

Table 5.
List of reference countries

The reference countries for Russia are summarized in Table 5. By taking a closer look, we will see that half of the countries are EU countries with very high prices for medicines. Moreover, the Life Quality Index[15] shows that Russia occupies the 83rd place (between the Philippines and Namibia), whereas most reference countries lie in the top twenty.

This index is important because it takes into account the quality of healthcare, including access to medicines. This index, in our view, is far more indicative of the real situation in the countries than GDP, which has little relevance to the quality of life of ordinary people.

[15] http://nationranking.files.wordpress.com/2011/03/2011-qli2.png

Based on the Life Quality Index, Russia is on the 65th place in terms of healthcare in the list of countries covered by the research, whereas most of our reference countries are closer to the top of the list. In our opinion, it is more reasonable to compare Russia to BRICS countries. Besides, when registering prices for medicines it is not appropriate to rely merely on financial figures, without taking into account such factors as prevalence rates, disease burden etc. The use of the reference system has been criticized by experts in many countries, since this system contributes to keeping the price for drug products at a high level.

As an example, we can take Bulgaria, which is one of the reference countries for Russia, and is close to Russia both geographically and in terms of the level of healthcare. In Bulgaria, only a few hundred people are on ARVT, whereas in Russia this number will soon exceed 100,000. Evidently, prices in these countries should differ, given the difference in the epidemic and in the number of patients on treatment. In most reference countries, tenofovir has been available for patients for a long time, whereas stavudine is not recommended for use. In Russia, however, the situation is precisely the opposite.

The pricing issue is important because, according to the estimates of experts, the number of patients in need of treatment will have increased from 98,000 in 2011 to more than 350,000 in 2015, whereas the cost of medications will have gone up to 63 billion rubles (USD2.1 bln)[16].

The Russian government already spends 12 billion roubles on ARVT (USD400 mln), covering only half of PLHIV[17] with the CD4 count below 350. The cost of antiretrovirals included in the federal procurement programme in 2009 -2011[18] is given in Table 6 below:

International Non-Proprietary Name	PPY, RUB, 2009	PPY, RUB, 2010	PPY, RUB, 2011	PPY, USD, 2009	PPY, USD, 2010	PPY, USD, 2011
Abacavir+lamivudine, tablets, (600+300 mg)	223,778	198,140	77,811	7 474	6 587	2 474
Abacavir+zidovudine+lamivudine, tablets (300+300+150 mg)	278,239	264,399	165,177	9 293	8 790	5 252
Abacavir tablets 300 mg	57,174	57,334	56,210	1 910	1 906	1 787
Atazanavir capsules 150 mg	81,599	80,417	79,234	2 725	2 607	2 519
Atazanavir capsules 200 mg	108,631	107,149	105,040	3 628	3 562	3 340
Darunavir tablets 400 mg	NA	195,538	192,640	NA	6 338	6 242
Darunavir tablets 600 mg (2/300 mg tablets for 2009)	78,895	146,657	144,500	2 635	4 754	4 682
Didanosine capsules 125 mg	NA	NA	41,325	NA	NA	1 314
Didanosine capsules 250 mg	27,218	24,495	24,061	909	794	765
Didanosine capsules 400 mg	34,854	31,368	30,047	1 164	1 017	955
Zidovudine tablets 300 mg	22,163	21,681	5 541	740	721	176
Indinavir capsules 400 mg	24,813	22,163	25,601	829	718	812
Lamivudine tablets 150 mg	20,798	22,041	21,520	695	733	683
Lamivudine+zidovudine tablets (300+150 mg)	43,282	43,523	42,639	1 446	1 411	1 356
Lopinavir+ritonavir tablets (200+50 mg)	98,608	82,709	81,088	3 294	2 750	2 578
Nevirapine tablets 200 mg	19,579	14,856	14,856	654	494	472
Nelfinavir tablets 250 mg	179,835	154,176	NA	6 007	4 998	NA
Raltegravir tablets 400 mg	413,946	372,599	372,599	13,826	12,078	11,847
Ritonavir capsules 100 mg	21,480	21,079	21,079	717	701	669
Saquinavir tablets 500 mg	73,905	72,489	71,051	2 468	2 350	2 266

[16] http://www.hivrussia.ru/pub/2011/01.shtml, estimates of the Federal AIDS Centre, accessed June 22, 2012

[17] Presentation of Aza Rakhmanova, Chief Infectious Disease Specialist of St. Petersburg, International Conference "Screening and Treatment of TB among Drug Users, including HIV-Positive Drug Users. May 21, 2012, St. Petersburg.

[18] We have not included the prices of 2012 in our comparison, as not all the contracts were concluded at the time of publishing this report. Changes in the exchange rate may significantly influence the dollar values.

International Non-Proprietary Name	PPY, RUB, 2009	PPY, RUB, 2010	PPY, RUB, 2011	PPY, USD, 2009	PPY, USD, 2010	PPY, USD, 2011
Stavudine capsules 30 mg	30,996	6 023	6 022	1 035	195	191
Stavudine capsules 40 mg	32,522	27,944	27,944	1 086	906	887
Fosamprenavir tablets 700 mg	155,059	139,620	139,642	5 179	4 642	4 440
Phosphazide tablets 200 mg	45,048	39,387	39,387	1 505	1 309	1 252
Enfuvirtide 90 mg/ml	812,541	798,803	783,137	27,139	26,556	24,854
Etravirine tablets 100 mg	332,281	294,540	222,752	11,098	9 548	7 218
Efavirenz tablets 200 mg	15,045	14,290	14,290	503	463	454
Efavirenz tablets 600 mg	10,439	10,198	9 676	349	331	308
Didanosine chewable tablets, 100 mg	40,099	39,683	NA	1 384	1 286	NA

Table 6. Price per patient per year for antiretroviral drugs in Russia, (RUB, USD)

Below is the cost of the most common regimens as per the results of Simona+ (2012 prices):

MAX. Combivir+Kaletra = USD3934

MIN. 3TC 150 mg + AZT 300 mg + Kaletra = USD3437

MAX. Combivir + Stocrin (200 mg) = USD1810

MIN. 3TC 150 mg + AZT 300 mg + Stocrin (600 mg) = USD1167

The price reduction rate since 2009 is miniscule for the five most expensive drugs:

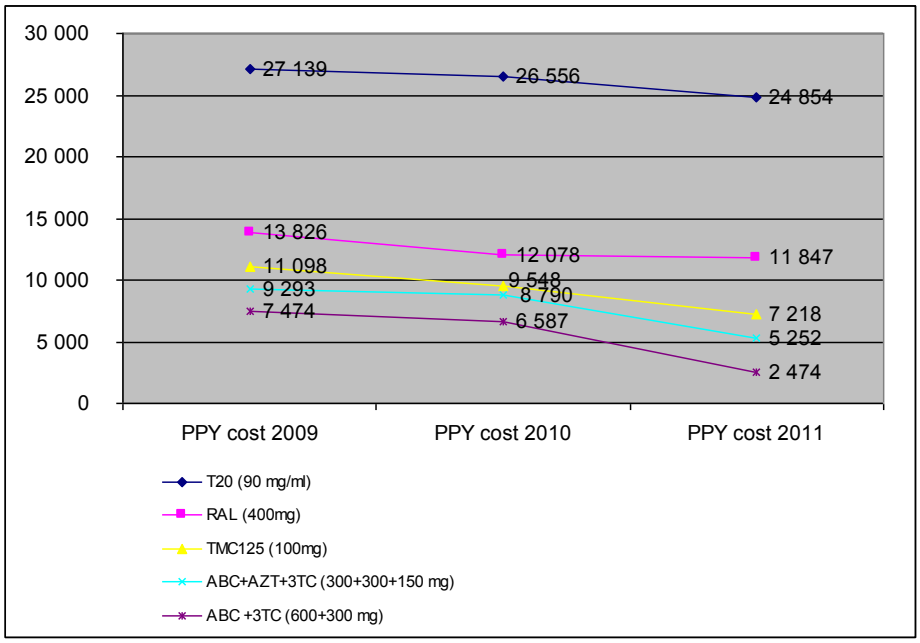


Figure 4. Price dynamics of the 5 most expensive antiretroviral drugs in 2009, 2009-2011

The most interesting example is the case of abacavir+lamivudine (600+300 mg). The price for this combination was reduced as a result of the action of the Ministry of Health with the active support of community representatives. Unfortunately, this is one of the few positive examples of such practice. Despite the company's saying that they would be supplying the drugs almost at a loss, a comparison of ViiV's prices in Russia with the prices in the UK

shows, that before this reduction the drug was supplied at a price higher than that in Britain[19] (see Fig. 5).

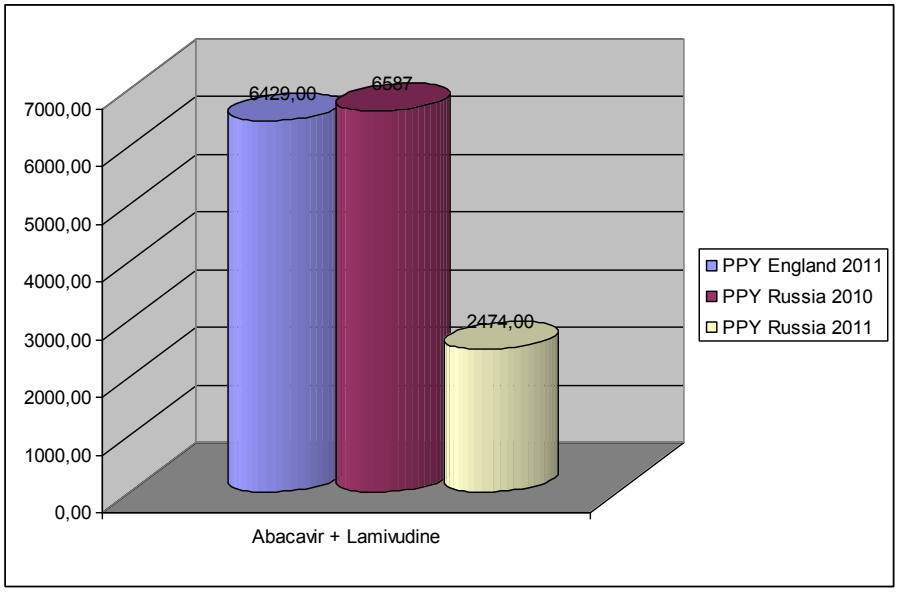


Figure 5. Price for Kivexa in Russia and in England

On average, the prices for ARVT in Russia are higher than the prices in the world. In 2010-12, MSF) conducted a study focusing on prices for ARVT in different countries, both developed and developing. We compared the results[20] with the prices for the same drugs in Russia in the most popular regimens listed above.

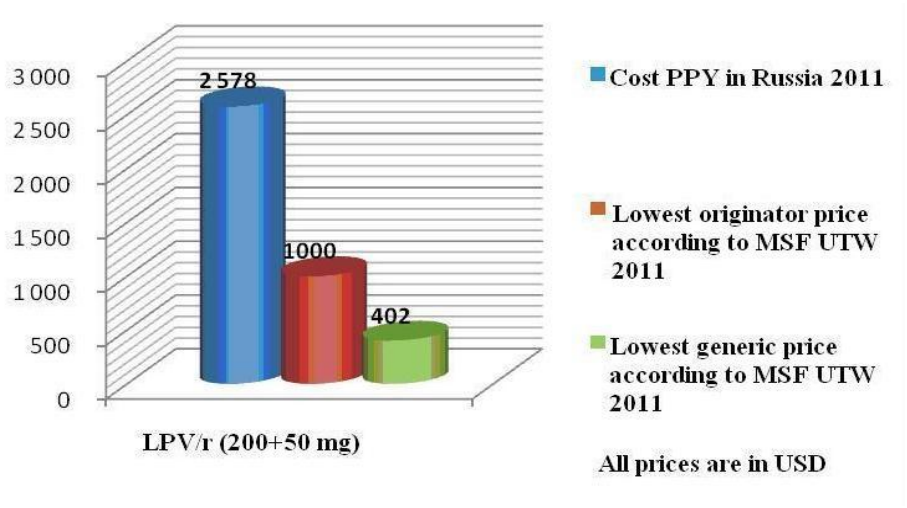


Figure 6. Comparison between the price for LPV/r in Russia and the data of MSF

The graphs show that by introducing generic drugs on the market, the prices for ARVT by hundreds of times. Obviously, at the same time generic drugs must undergo strict quality control; this applies both to imported and domestic generics.

[19] British National Formulary, 2011
[20] http://utw.msfaccess.org

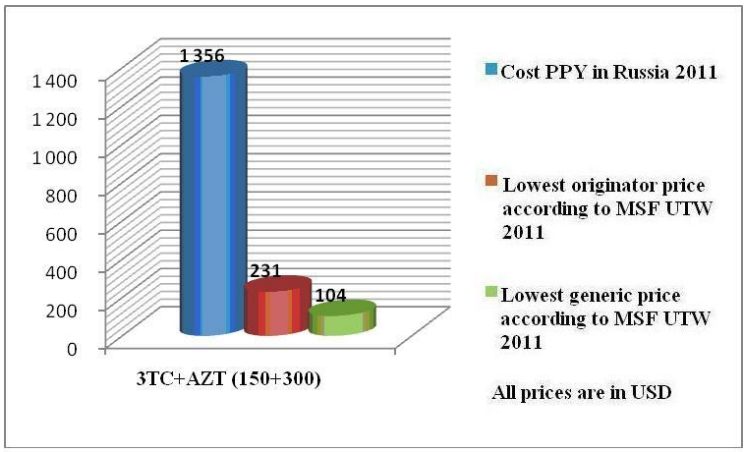


Figure 7. Comparison between the price for 3TC+AZT in Russia and the data of MSF

It is a very positive fact that several generic products have already been registered in Russia, and some generics are undergoing clinical trials for registration. If this trend is to continue, generic ARVs will become more available within the framework of the Strategy for Development of Pharmaceutical Industry in Russia till 2020.

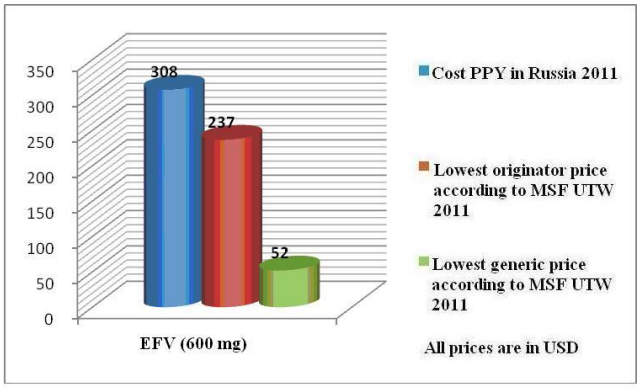


Figure 8. Comparison between the price for efavirenz in Russia and the data of MSF

Foreign brand and generic manufacturers are already making efforts to localize their manufacturing process. Over the last few months, Abbott Laboratories, ViiV Healthcare, Aurobindo have announced plans for manufacturing localization in Russia and started to build strategic alliances with Russian companies.

It is definitely a positive trend both in terms of pricing policy and budget saving and the development of the industry in Russia and the strategic goal to become independent of foreign manufacturers.

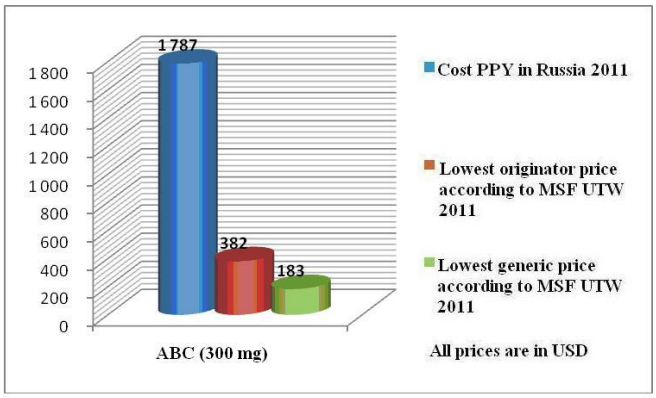


Figure 9. Comparison between the price for ABC in Russia and the data of MSF

However, a number of serious measures must be taken by the community and by the specialized government bodies in order to ensure quality of the products to be included in the government procurement programmes.

Another complicating factor is that there is a widespread belief in the community of PLHIV in Russia that generic drug products are always of lower quality, although they buy generic drugs in drug stores every day and never feel the difference, apart from the saved income. In view of that, besides the quality control, there is a need in educational activities for PLHIV and a system of feedback from patients to manufacturers concerning adverse effects.

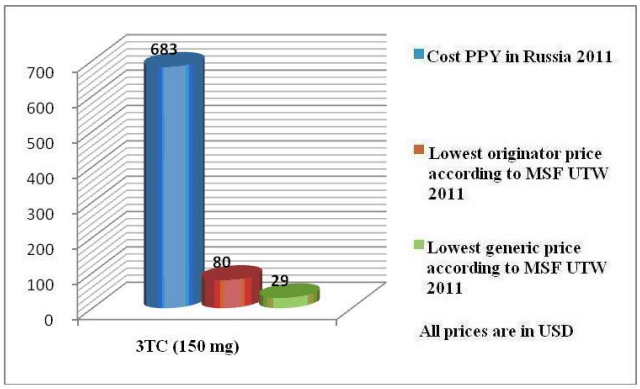


Figure 10. Comparison between the price for lamivudine in Russia and the data of MSF

Trying to answer possible criticism regarding the fact that comparison with Europe is more appropriate in the case of Russia, we would like to provide another example of a possible saving. GF programmes in Russia were closed in 2010 and declared ineffective. Here we shall focus only on the treatment component, without discussing the prevention side. Table 7 presents prices for two drug products in GF programmes and within the Health National Project.

Price per Pill	GF, 2010	MoH, 2011
Lopniavir+ritonavir	$1.73	$1.83
Efavirenz	$0.74	$0.90

Table 7. Difference between the national procurement programme price and Global Fund price

The price per pill at first glance seems miniscule, only about 10-16 cents. However, as it has been noted above, the number of patients per year on Kaletra in 2011 was 27,442 (40,064,640 pills per year), whereas the number of patients on efavirenz was 28,739 (10,489,830 pills per year). By multiplying the difference, we get an overpaid amount of USD12 mln on only two drugs.

At the same time, in 2010 MoH decentralized the procurement of test kits for immune status and viral load, one of the reasons being lack of funding. Looking at the data above one can come to a conclusion that the problem lies mostly in the ineffective financial management, rather than in the lack of resources. To avoid budget deficit, possible measures could include discontinuation of the practice to levy customs duties on ARV drugs, negotiations with brand companies on price reduction, negotiations with generic companies on in-country manufacturing etc.

To sum up, the price reduction activities can be much more effective that the current efforts. Today, the economy achieved by means of auctions is represented by the following figures:

Year	Savings	
	Absolute figures	Percentage of the Initial Budget
2009	+2,555,154	+0.42%
2010	-148,640,089	-1.45%
2011	-179,949,547	-1.52%

Table 8. Economy achieved by means of auctions and changes in contract conditions, 2009-2011

As seen in the table above, in 2009 the government spent more than was planned initially, and in the following years the government saved 1.5% (including the 60% price reduction for Kivexa).

Below follows a table containing names of manufacturers and distributors in the Russian Federation.

Market Share, Manufacturers (money)				
Company	**Market Share 2009**	**Market Share 2010**	**Market Share 2011**	**Abs. figures, 2011 USD, approx.**
ViiV Healthcare	30.5%	35.6%	33.6%	130,328,582
Abbott Laboratories	20.4%	20.1%	19.7%	76,335,312
Janssen Cilag	14.0%	13.8%	15.0%	58,182,403
Bristol-Myers Squibb	10.0%	10.3%	10.0%	38,594,327
Merck Sharp & Dohme	5.4%	5.2%	7.2%	27,927,553
Hoffmann La-Roche	8.4%	5.4%	6.0%	23,272,961
Makiz/Hetero Drugs	4.9%	5.5%	5.0%	19,432,922
AZT-Pharma	4.6%	3.9%	3.5%	13,459,529
Aktavis	0.9%	n/a	n/a	n/a
ZAO Obolenskoe	n/a	n/a	0.1%	310,306
Boehringer Ingelheim	0.9%	0.1%	n/a	n/a

Table 9. Market share of ARV manufacturers in Russia, 2009-2011

Market Share, Distributors (money)				
Name	**Market Share 2009**	**Market Share 2010**	**Market Share 2011**	**Turnover, 2011 USD, approx.**
OOO "Optimalnoe Zdorovie"	44.6%	29.6%	0.1%	387,882
ZAO "Apteka Holding"/ "Alliance Healthcare)	22.9%	18.4%	18.4%	71,176,472
ZAO "R-PHARM"	18.1%	19.2%	42.4%	164 501 046
ZAO Firma "ZV Proteq" / OOO "Proteq 50"	13.3%	16.5%	16.2%	62,992,147
OAO "Pharmaceutical Import Export"	n/a	10.3%	7.8%	30,099,696
OAO "Pharmstandard"	n/a	3.6%	15.2%	58,803,014
OOO "Irvin 2"	n/a	2.4%	n/a	n/a
ZAO "ORFE"	0.9%	n/a	n/a	n/a
OOO "Orto-Pharma N"	0.2%	n/a	n/a	n/a

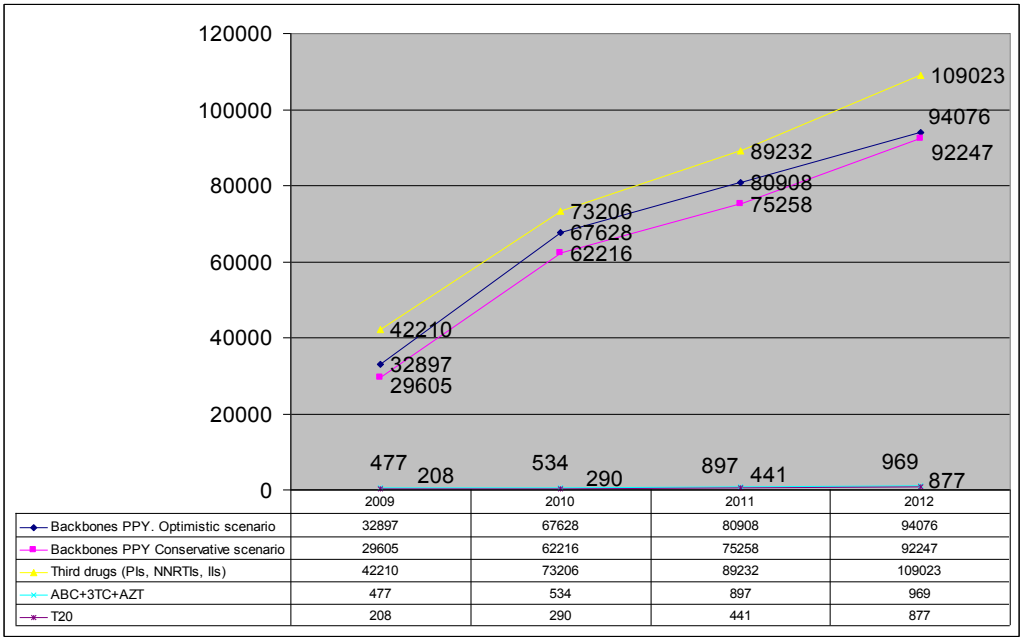
Table 10. Market share of ARV distributors in Russia, 2009-2011

Number of Patients on ARVT and Availability of Treatment

On the one hand, the efforts undertaken by the government and other relevant agencies over the course of the last four years in the area of increasing the coverage of antiretroviral therapy for PLHIV are quite impressive. A few statistics are given below.

The number of patients receiving the drug combination abacavir+lamivudine (TM Kivexa) increased by 476% in 2011 as compared to 2009. For the same time period, coverage of the most frequently used drugs Combivir (lamivudine + zidovudine) and Kaletra (lopinavir/ritonavir) increased by 144% and 162% respectively.

In absolute numbers, the achievements appear quite solid.[21]



	2009	2010	2011	2012
Backbones PPY. Optimistic scenario	32897	67628	80908	94076
Backbones PPY Conservative scenario	29605	62216	75258	92247
Third drugs (PIs, NNRTIs, IIs)	42210	73206	89232	109023
ABC+3TC+AZT	477	534	897	969
T20	208	290	441	877

Figure 11. Annual quantity of treatment regimens which can be made from drugs purchased through the federal budget between 2009 and 2012.

It should be noted that this data diverges from information published on the Ministry of Health's website[22] regarding the supply of ARVT to those patients requiring it. For comparison, we used data both about the possible number of backbones (NRTIs in the optimistic scenario) and data which we obtained that focused only on the third drug. The maximum theoretical number of PLHIV who could be treated with drugs purchased through the federal budget was calculated. The analysis focused only on the third drug, assuming that drugs forming the backbone could be used in any combination without need of recommendation. The following formula was used in the analysis:

V (drug quantity per person per year) = (NNRTI+PI+INSTI)+FI+3 NRTI

[21] The calculation methodology is contained in Appendix 1.
[22] http://www.minzdravsoc.ru/health/prevention/36

MoH Estimates	ITPCru Analysis	
	NRTI (optimistic scenario)	NNRTI+PI+INSTI+FI+3NRTI
2006 – 15,000 patients	n/a	
2007 – 30,000 patients	n/a	
2008 – 45,000 patients	n/a	
2009 – 52,000 patients	32,897 ppy	42210+208+477 = 42 895 ppy
2010 – 70,000 patients	67,628 ppy	73206+290+534 = 74 030 ppy.
2011 – 100,000 patients	80,908 ppy	89232 +441+897 = 90 570 ppy.
2012 – 105,000	94,076 ppy	109023 +877+969= 110 869 ppy

Table 11. Number of patients on treatment, Ministry of Health estimates vs. ITPCru analysis

We deliberately did two things when conducting the comparison. First, in terms of the data, we are not discussing the quantity of people here, because we assume that at the cost of one annual treatment regimen it is possible to treat more than one person. This point of view is expressed in the methodical recommendations of the Federal AIDS Centre and is based on the fact that the requirements for annual treatment regimens vary for different groups of patients, specifically:

- Patient, continuing treatment – 1 annual treatment regimen
- Patient beginning treatment – .50 of an annual treatment regimen (with uniform inclusion of patients in treatment)
- Chemoprophylaxis of vertical transmission of HIV – .25 of an annual treatment regimen
- Post exposure chemoprophylaxis – .08 of an annual treatment regimen

Second, by adding the third drugs "in one pile" we deliberately violated all possible rules, and thus attempted to calculate the maximum (even if absolutely absurd) number of people who could supposedly be supplied with such "treatment".

Because of these two facts, we did not conduct any direct parallels between the data from the Ministry of Health concerning the quantity of people and the data that we received from counting tablets. However, one cannot help but notice that between the number of PLHIV provided with treatment and the number of purchased regimens there are absolutely no parallels to be found. **So it becomes clear that the number of NRTIs purchased via federal programmes, even in the most optimistic of scenarios, is not enough to supply the needs of all PLHIV**. At the same time, the "skew" was confirmed towards the purchases of more expensive drugs that were not supported by purchases of NRTI combinations for forming the backbone of treatment. The project Simona+ had already made note of this tendency at the prescription level done by doctors[23].

There is still one serious problem which is a cause for extreme concern: the plans of the Ministry of Health to accept only 5,000 people for treatment in 2012. This stands against an annual increase starting in 2009 of more than 20,000 people and a "waiting list" of 100,000[24]. In such a situation, it is completely clear that for the most part, PLHIV who need ARVT are not going to be receiving it in 2012. Under these circumstances, one can hardly expect that IDU or migrants will have access to treatment.

[23] See the section containing the most frequently prescribed treatment regimens.
[24] Presentation of Aza Rakhmanova, Chief Infectious Disease Specialist of St. Petersburg, International Conference "Screening and Treatment of TB among Drug Users, including HIV-Positive Drug Users. May 21, 2012, St.Petersburg.

To summarise, let us direct the reader's attention once again to a number of problem areas.

1. Only 5000 naïve patients will start treatment in 2012 according to MoH plans.

2. There is no connection between the statistics about patients on ARVT as presented in public reports by the Ministry of Health and the quantity of drugs that have been purchased.

3. There is an obvious skew in favour of purchasing "third" drugs, as a rule, expensive protease inhibitors that are not reinforced with NRTI combinations.

4. As was mentioned earlier, the prescribed regimens frequently do not comply with international recommendations.

5. The amount of drugs on hand is not adequate to cover all PLHIV estimated to need ARVT (approximately 200,000 people in 2012 based on data from Russian Federal Service for the Protection of Consumer Rights and Human Welfare).

6. There is still another problem which we have not yet mentioned, but which clearly deserves attention. Over the course of the analysis, we became aware of serious shortages in lamivudine and ritonavir during all years of procurement. In 2009, from the drugs that were purchased using funds from the federal budget, it would have been possible to supply a maximum of 32,897 annual "backbone" treatment regimens (2 NRTIs). At the same time, there arose a certain amount of remnant NRTIs. In order to create from these remnants a complete "backbone" and to simultaneously observe the WHO guidelines on permissible drug combinations, it would be necessary to purchase an additional 6,585 regimens of lamivudine.

In 2010, 67,628 backbone drug regimens were purchased, but a shortage of lamivudine still continued and reached 10,825 annual regimens (now and hereafter, with regard to the shortage of ritonavir and lamivudine, see the table below). In 2011, 80,908 annual regimens of backbone drugs were purchased. Meanwhile, the lamivudine shortage reached 11,271 regimens. And only in this year has the situation started to change. 94,076 backbone drug regimens were purchased, and the lamivudine shortage was sharply reduced to 3,659.

The ritonavir shortage was identified after we compared the purchased amount of ritonavir with the amount that is needed for boosting protease inhibitors, for which it is required.

Ritonavir shortages:	Lamivudine shortages
2009: 6 833 ppy	2009: 6 585 ppy
2010: 2 921 ppy	2010: 10,825 ppy
2011: 4 604 ppy	2011: 11,271 ppy
2012: 6 741 ppy	2012: 3 659 ppy

Table 12. Deficit of RTV and 3TC

Of course this could all be explained if the needed drugs are being purchased at the regional level. However, in this case, the publications posted on the Ministry of Health's website lead the reader astray, assuring him that everything is provided using funds from the federal budget. Furthermore, such a system is extremely opaque and vulnerable in terms of the sustainability of treatment programs, as we already mentioned at the beginning of this report. When we speak about system vulnerability and about the risks associated with providing ARVT to PLHIV, we are speaking first of all about shortages. And this brings us logically to the next section of our discussion.

Shortages in Providing Treatment

Shortages (stock-outs) in the supply of ARVT drugs are a traditional and very serious problem for Russia. This problem was raised by communities of patients as early as in 2008, but only in 2010, when it reached a catastrophic scale and after the General Prosecutor's Office intervened (also at the initiative of community organizations), did it finally receive an "official" status. The main tools for informing the community about shortages has traditionally been the Internet (contact and meet-up forums for PLHIV, the website www.pereboi.ru, emails from NGOs and community organizations) as well as the project Simona+.

Currently, both experts and representatives from community organizations agree that the shortages can be traced to several main causes, from which the following can be delineated:

1. Problems with on-site planning. One can imagine the situation in which a significant number of newly diagnosed patients appears at an AIDS Centre. These patients have a low immune status and must immediately begin ARVT, but their arrival was not anticipated at the time of determining ARVT purchases, or the actual number of patients may have exceeded the doctors' expectations. In such cases, doctors and administrators are faced with a dilemma. Either they delay the beginning of treatment, risking the life of their patients, or they start everyone on ARVT, but thereby risk not being able to "stretch out" supplies until the next delivery, which entails running into shortages and having to start replacement regimens.

2. Problems at the stage of approvals of orders. Again, given the Russian reality, it is easy to imagine a situation in which the budget provisions for procurements simply are not enough to cover all of the stated needs of the various regions. In such cases, the orders are "slashed".

3. An absence of tools that would help increase the effectiveness of planning and transparency in the usage of various drugs, such as a unified patient register that takes into account data from clinical and laboratory observation and also clinical records, that regulate all prescriptions and that are binding for the doctors involved.

4. Logistic problems associated with the physical transportation of drugs, including procedures for clearing customs, delivery to warehouses or pharmacies, and so forth.

In 2011-2012, within the framework of research conducted by Simona+, 22.6% of respondents replied that they had changed their treatment regimen within the last six months, 5.6% of the doctors surveyed reported that the drugs which they needed were out of stock. The table below shows the changes in regimen according to month.

	Has your treatment regimen been changed over the last 6 months?	Has your doctor told you that your drugs were not available over the last 6 months?
	YES	YES
September	29.0%	12.9%
October	35.4%	6.1%
November	23.1%	4.5%
December	19.0%	1.6%
January	23.0%	8.0%
February	12.0%	4.8%
March	19.3%	2.3%
April	21,1%	5,1
Total	**22,6%**	**5,6%**

Table 13. Changes of treatment regimens by months

We also asked our respondents about the explanations their doctors gave with respect to regimen changes. The answers are summarized in Figure 12.

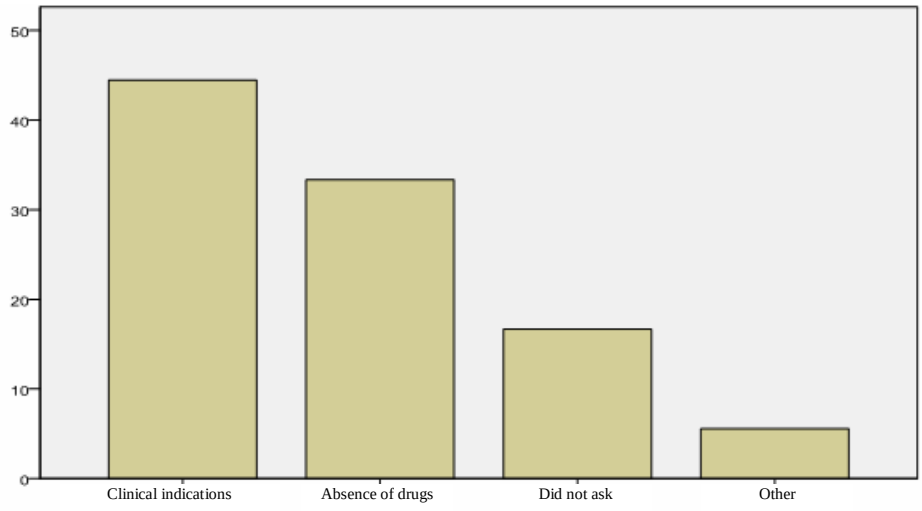


Figure 12. Reasons for changing the treatment regimens according to doctors (%)

Likewise, we compiled a list of cities, in which changes in ARVT regimens were observed most frequently (Fig. 13), as well as cities where, according to patients, the problem of stock-outs was mentioned most often (Fig. 14).

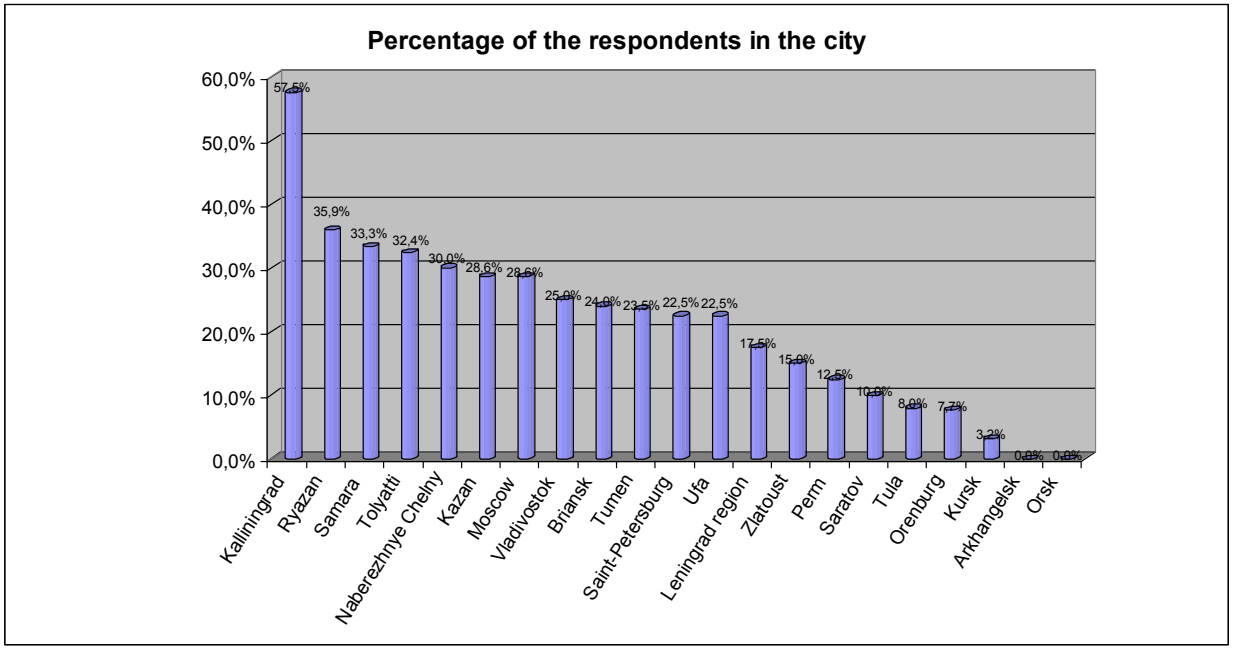


Figure 13. Changes in ARVT regimens registered in different cities

Below follows a list of cities where, according to patients, doctors most frequently referred to the problem of stock-outs.

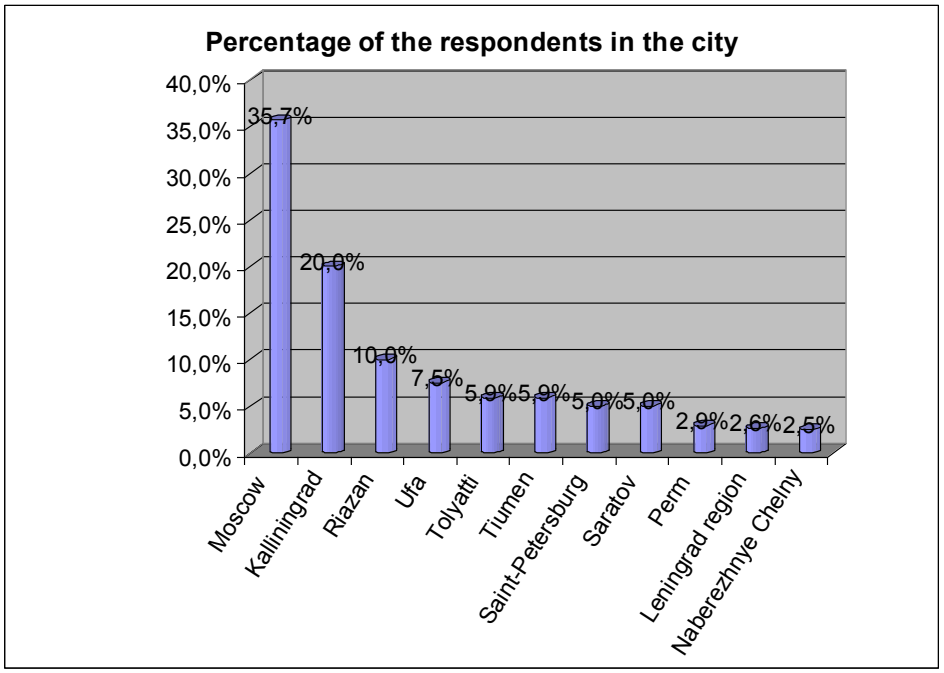


Figure 14. Stock-outs of antiretroviral drugs registered in different cities

Furthermore, within the framework of the current research, we investigated reports that were posted on the website www.pereboi.ru. All the messages about stock-outs at the website were taken as 100%.

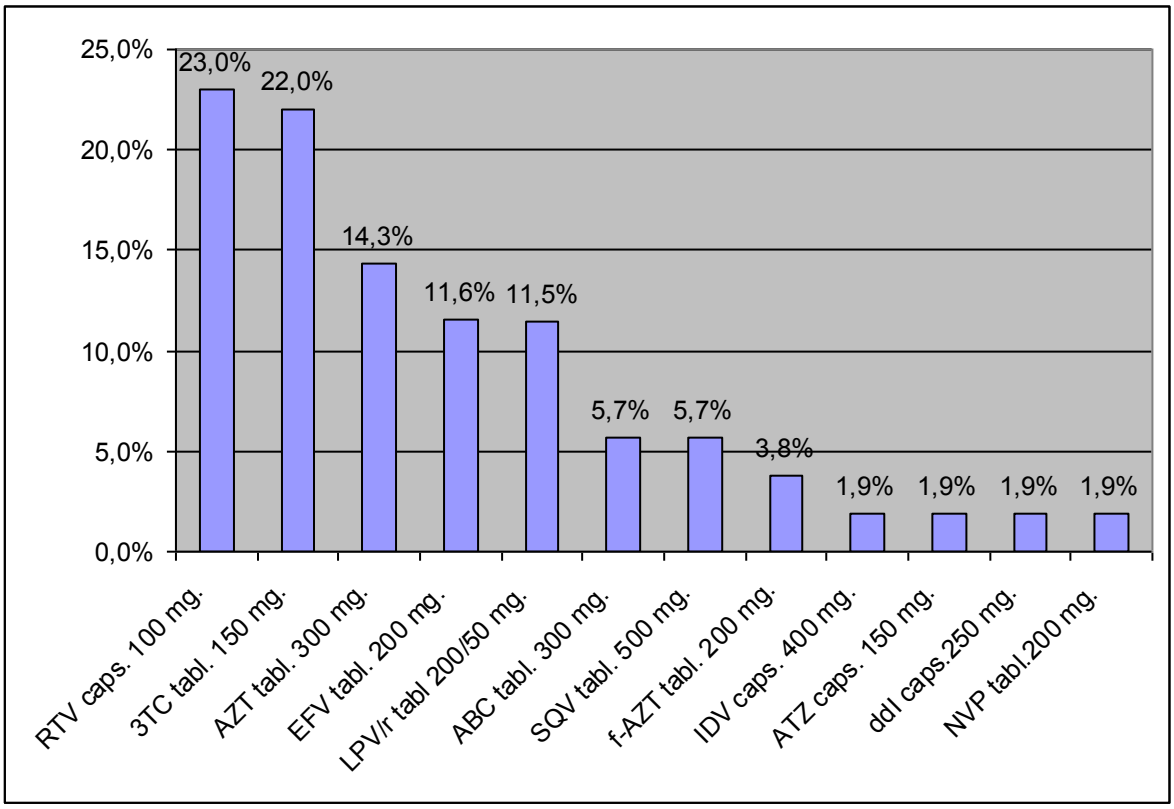


Figure 15. Frequency of messages about stock-outs of ARVs at www.pereboi.ru

These messages prove that the deficit of lamivudine and ritonavir in the federal procurement programme revealed by the ITPCru analysis is a very likely cause of stock-outs, treatment deficit, and regimen changes. As we see, in 2011 most messages about stock-outs concerned ritonavir and lamivudine; their deficit was 4 604 and 11 271 ppy respectively.

Besides, starting from 2011 Simona+ has also monitored availability of immune status and viral load testing. It was due to the fact that following the decentralization of test kits procurement, the number of messages about stock-outs of test kits at www.pereboi.ru became so high that we even had to make a separate section. The situation with test kits shows that the idea to decentralize ARV procurement in Russia may be premature.

The following two indicators were taken into account for evaluating the situation with the availability of test kits:

a) Number of analyses prescribed (both viral load and immune status)

b) Number of tests actually made

In an ideal system the difference between these two parameters will be close to zero, with certain minimal fluctuations caused by forgetfulness of patients etc. Moreover, this difference will be more or less the same in all the cities. However, at the figure below we see precisely the opposite: in some cities (Arkhangelsk, Kazan, Naberzhnye Chelny, Tula) the situation with testing was positive (N=0). On the contrary, in Zlatoust, Leningrad region, and Vladivostok it was far from optimal.

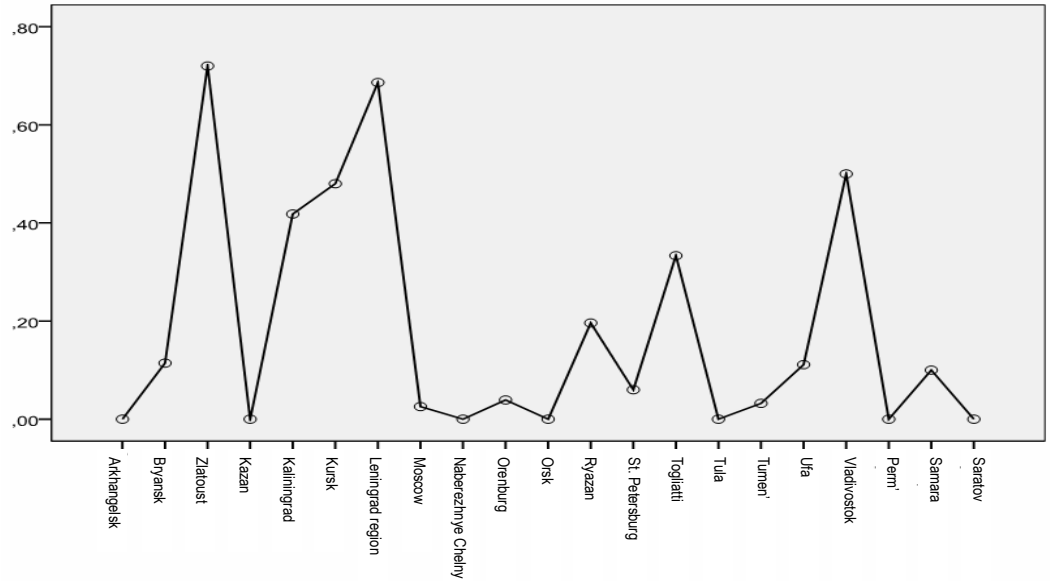


Figure 16. Difference between the prescribed and actually made viral load tests

The same was observed with respect to CD4 tests, with Kursk being least fortunate city (N> 60).

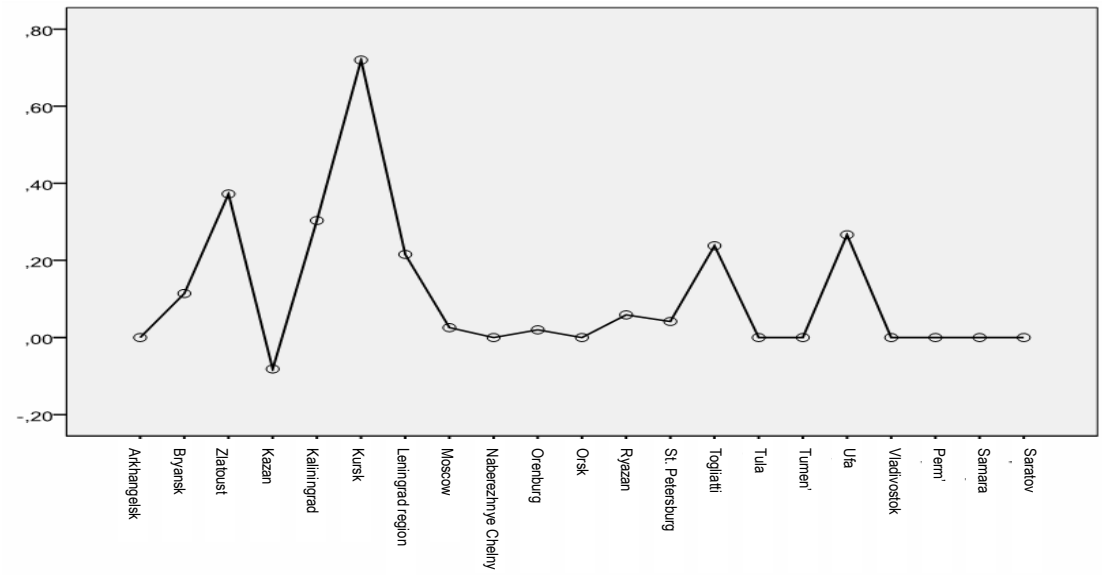


Figure 17. Difference between the immune status tests prescribed and actually made

Besides, the analysis showed that people who were already on treatment were prioritized before patients who had not been prescribed ART: patients on treatment visit the doctor and make tests more often that patients not taking ART (see Table 14)[25].

[25] All the differences are statistically significant.

	Are you taking ART?	N	Average	STD
Over the last year, how often did you visit your doctor for HIV monitoring?	Yes	556	5.16	3.653
	No	238	3.10	2.405
How often were you referred for a viral load tests over the last year?	Yes	549	2.71	1.290
	No	236	1.97	1.402
How often did you make a viral load test over the last year?	Yes	551	2.52	1.318
	No	234	1.79	1.443
How many months ago did you make a viral load test?	Yes	545	2.46	2.456
	No	225	3.10	3.340
How many times per year were you referred for an immune status test?	Yes	554	3.04	1.589
	No	236	2.26	1.393
How many immune status tests a year did you make?	Yes	554	2.93	1.632
	No	236	2.12	1.437

Table 14. Data on testing based on the results of Simona+, absolute figures

Thus, notwithstanding important achievements that have been reached in the area of access to treatment for PLHIV in Russia, the current situation remains pressured and requires further steps in order to strengthen not only general organization and the planning process but also the treatment process itself, with the goal of reducing barriers of access to treatment. More information about this is found in the next section.

Access to and Preparedness for Treatment

All cities participating in the Simona+ research were classified in accordance with the level of prevalence of the HIV epidemic. The results of the data analysis demonstrated that the higher the prevalence of HIV in a city, the greater the quantity of specialists that a patient is required to visit before he or she is able to start ARVT: thus, in cities with an HIV prevalence lower than 300 per population of 100,000, the median number of specialists whom a patient was required to see before starting ARVT was one. But in cities where the prevalence of HIV was higher than 1,000, the median number of visits to specialists required before starting ARVT was five (see table).

HIV Prevalence	Median number of specialists and consulations which were needed before ARVT was prescribed.
Lower than 300 (per 100,000)	1
300-500	2
500 -1000	4
1000+	5

Table 15. Number of consultations prior to ART initiation and level of HIV prevalence

Moreover, there were practically no phthisiatricians among these specialists (only 53.2% of patients went through some kind of screening for tuberculosis), but there were plenty of meetings with psychiatrists, proctologists and dentists.

Inasmuch as every visit to specialist requires time and in some cases also money, each additional consultation increases the threshold to ARVT access. Thus, the higher the prevalence of HIV in a city, the higher the threshold to receiving ARVT.

Patients reported that before starting ARVT, 96.7% to 99.2% were tested respectively for viral load and immune status. Meanwhile, only 74.8% and 61.1% had, respectively, biochemical and clinical blood tests performed.

Among 88 patients who were placed on a treatment regimen that included abacavir, only 22 people, 25.6%, were tested for hypersensitivity to abacavir.

If you take into account that the average time period from the moment of starting ARVT reached 26.4 months, then those respondents who began ARVT were basically already within the time frame when the problem of combined pathology of HIV and tuberculosis was becoming extremely urgent. The fact that only half of the respondents were tested for tuberculosis is therefore extremely alarming.

448 (85.7%) patients in our study receive their medications only in the AIDS Centre – the specialized state-run clinics. Only a minority of the respondents said that they can receive ARVs in other medical facilities, without visiting centralized clinics.

The majority of patients (222; 42.3%) refill their treatment supply monthly, 127 (24.2%) do so every other month, 170 (32.4%) once a quarter or even less frequently, taking larger refills at a time. **In the study sample, 149 individuals (31.6%) reported having to face such impediments as long waiting lines, inconvenient working hours at clinics or similar issues.**

Another important problem is the lack of understanding about what ARVs are all about. Antiretroviral therapy requires a long-term commitment from the person receiving it. Thus, it is crucial that the goal of treatment and the basic rules are clear to the patient.

467 (87.9%) respondents said that after talking to a physician they fully understood how to take medicines, 59 (11.1%) admitted that they left without a firm understanding of how to take ARVs, and 5 (0.9%) of the patients said the doctor did not explain basic rules or requirements to them at all.

RECOMMENDATIONS

The first group of recommendations is aimed at improving the forecasting mechanisms and planning procedures relating to the procurement of ARVs in the Russian Federation.

1. **Bring the current clinical protocols for HIV treatment into compliance with the most recent WHO recommendations (2012 guidelines for the European region) and make them mandatory by issuing an appropriate order.** Order No 109 of the Ministry of Health on improving tuberculosis control activities in the Russian Federation can be taken as an example.

2. **Introduce a unified confidential computerized register (an electronic database) of patients living with HIV throughout the Russian Federation ensuring non-disclosure of the personal data.**

    a. Ensure training for specialists working with the register;

    b. Establish a special division within the structure of Federal AIDS Center or another specialized institution responsible for maintaining the register.

3. **Discontinue the practice of providing one and the same patient with ARV drugs purchased within different procurement programmes (federal and local)**. The required volume of the ARV drugs within one and the same procurement programme shall be calculated on the basis of full treatment courses (treatment regimens containing all necessary drugs for one person) rather than individual drugs that make up these regimens.

4. **Shift to the planning of purchased medication based on the number of required treatment regimens rather than individual components.**

    a. The use of the following system may be considered: all the patients on ARV treatment at the end of the current calendar year (when the orders for the next year are being filled), as well as the patients who are very likely to need treatment in the next calendar year based on the data in the register (with the immune status close to 350 CD4 cells and other indications in accordance with the guidelines), are covered by ARV treatment purchased within the federal procurement programme.

    b. At the same time, all the ARV drugs given to patients detected at a late stage (with indications for immediate initiation of treatment), pregnant women etc. can be then recovered by means of additional purchases financed by the local budget (or, alternatively, by means of additional auctions at the federal level). Treatment regimens should be prescribed in strict compliance with the updated guidelines (e.g. WHO EURO 2012).

5. **Synchronize the planning of ARV procurement and the budget planning for the planning period.**

6. **When planning the local budget for ARV drugs, one shall allocate funds in an amount enough to cover the maximum number of patients who may need treatment in a given fiscal year.**

7. **Optimize budget expenditures by revising the list of purchased drugs. For example, stavudine, didanosine, indinavir, nelfinavir and other drugs not recommended for wide use in patients with HIV by the leading international agencies including WHO** should be excluded from the procurement programmes, or their share should be minimized.

The second group of recommendations includes possible measures to improve access to treatment by reducing prices of antiretroviral drugs and providing more alternatives for treatment. As a result of these measures, a real competition between manufacturers should appear. The auction mechanism is not ideal for reducing prices in a situation with a monopolized market characterized by a limited number of manufacturers. This problem could be tackled by creating favourable conditions for generic companies to enter the market, which could, in turn, improve the competitive environment.

1. Government agencies should conduct systematic work aimed at reducing prices of originator drugs. This should include meetings involving manufacturers, government agencies, non-governmental organizations, regulatory agencies and oversight bodies (such as the Federal Antimonopoly Service), independent observers (members of the Public Chamber of Russia, the President's Council, etc.)

2. Government authorities should create conditions for introducing generic drugs in Russia in line with the Strategy for the Pharmaceutical Industry Development until 2020. This work can be carried out in several ways:

    a. Make the Russian market more attractive for Indian and other companies producing generic drugs;

    b. Establish local production of generic drugs;

    c. Negotiate with manufacturers on localization of manufacturing and subsequent price reduction.

3. In order to improve the quality of generic drugs it is necessary to develop specific requirements for the quality of products purchased within the "Health" national project.

    a. For example, only generic drugs prequalified by WHO, or approved by FDA for use in the U.S., or approved by EMEA for use in the EU shall be approved for inclusion into the federal procurement program. The drugs must also be produced at the same plant with the use of the same substances. In other words, the registration dossier of the drugs must be completely identical to the registration dossier of the drugs approved by other stringent regulatory agencies.

    b. For national manufacturers, such requirement must include compliance with GMP standards etc.

    c. At the same time, the pharmacovigilance system and the system of monitoring adverse events must be improved. Simplified mechanisms for providing feedback from patients to manufacturers and oversight bodies must be developed. In addition, information about how and where to report adverse events should become an integral part of patient education programs implemented on the territory of the Russian Federation both by manufacturers of drug products and NGOs.

4. Provide a simplified registration mechanism of antiretroviral drugs (clinical trials must not be necessary for the registration process). Simplify the mechanism for including the newly registered ARVs in the relevant decrees of the Government regulating ARV procurement in the Russian Federation. As an example, all the newly registered ARVs could be

automatically included into the relevant Decree, becoming available for patients within a year.

The last group of recommendations relates to legal aspects of ARVT procurement process and other aspects affecting the stability of the ARVT supply system.

The current system stipulated by federal law FZ-94 is not optimal for the procurement of medicines. Disruptions in the supply of antiretroviral drugs and drugs for treating tuberculosis, diabetes, multiple sclerosis

1. The new revision of the law on state and municipal orders must take into account the customer's responsibility for the execution of public contracts.

2. Non-governmental organizations and associations operating in the interests of the target groups (PLHIV) shall have access to full information relating to the particular auctions, including planning requirements, auction planning and execution, full text of contracts, as well as information on the contract execution.

3. With regard to medicines used for treating socially significant diseases, the law shall stipulate the possibility of additional requirements for bidders, such as experience of successful deliveries in the respective fields.

4. Provide a thorough legal basis for broad implementation of patient education programs on a regular basis (so-called "schools of the patient") as part of public procurement programmes. These programmes shall be developed with participation of NGOs and community organizations and take into account the needs of various risk groups.

APPENDIX 1

METHODOLOGY

Main Information Sources

Name	Link
Official public procurement website of the Russian Federation	www.zakupki.gov.ru
Official public procurement website of the Russian Federation (archive, contains information relating to public procurement before 2010)	www.zakupkiold.gov.ru
ZAO "SberBank - AST" electronic trading platform	www.sberbank-ast.ru
Register of Public Contracts	www.reestrgk.roskazna.ru
Project “RosGosZatraty”. Monitoring of public contracts	www.rosspending.ru
Unified State Register of Medicinal Products	www.grls.rosminzrav.ru

Algorithm for collecting and processing information:

1. The above-listed websites were used for collecting the necessary documents, ranging from announcements about the auctions to public contracts.

2. The price of each drug per patient per year was calculated by multiplying the price per pill by the number of pills that must be taken daily, and then by 365.

3. For calculating prices in USD, we used the average exchange rate between the ruble and the US dollar (as per the data of the Central Bank of The Russian Federation) for the quarter of the reporting year (2009-2011), in which the customer paid the distributor for the drugs delivered.

4. For calculating the total number of patients per year for each drug separately, the total number of pills purchased was divided by the number of pills that must be taken daily and then by 365.

5. For calculating the number of patients who can be treated, all the antiretroviral drugs were divided into the following three groups:

Backbone	Third drug	Other
ABC, ABC+3TC, ddI, AZT, 3TC, 3TC+AZT, d4T, f-AZT	NVP, EFV, TMC125, ATZ, DRV, IDV, LPV, NFV, SQV, FPV, RAL	ABC+3TC+AZT, T20

6. After obtaining information about the number of patients per year who can be treated by each drug separately, we had to take into account different combinations of antiretroviral drugs. The number of drugs for making backbones was calculated using two methods referred to as “conservative optimistic” and “optimistic”.

   a. “Conservative optimistic” scenario – calculating combinations of NRTIs according to EACS and DHHS.

b. “Optimistic” scenario – adding half of the sum of all the NRTIs (ppy) to the sum of all the combination drugs (two NRTIs).

c. The third drugs (PIs, NNRTIs, INSTI) were summed (taking into consideration the necessity to boost them with ritonavir) based on the daily doses according to recommendations.

d. Enfuvirtide and abacavir+lamivudine+zidovudine were considered separately.

The table with international non-proprietary names and brand names is based on the Unified State Register of Medicinal Products available at grls.rosminzrav.ru.

Legal aspects of the procurement process have been analyzed with the support of EGIDA Legal Association.

SIMONA+ Methodology 2011-2012

Every month in every city seven new respondents got involved into the study - two not taking ARVs, and five PLWH on ARV treatment.

This method of data collection allowed us to reach a large sample size: during 8 months of data collection (September 2011 - April 2012) **1408** questionnaires were collected in 23 cities of the Russian Federation, of which **612** questionnaires (49.5% men and 50.5% women, med. age 32.3 years) were designed to explore access to treatment and **796** questionnaires (47.9% men and 52.1% women, med. age 31.68 years) were aimed to assess access to HIV testing.

Geography of the project "Simona+" in 2011-2012 covers 23 regions: Biysk (Altai), Perm, Zlatoust (Chelyabinsk region), Tyumen, Kazan, Kaliningrad, Samara, Saratov, Kursk, Moscow region, Naberezhnye Chelny, Volgograd, Orsk, St. Petersburg, Leningrad Oblast, Togliatti (Samara region), Ufa, Vladivostok, Orenburg, Bryansk, Arkhangelsk, Tula, Ryazan.

Demographic Data of Simona+, Russia, 2011-2012

	Total
Age	32,36 (SD=6,352)
Sex	Male 49,0% (N=265) Female 50,3% (N=268)
N of respondents in the region	North-West 24,2% (N=121) Central 26,1% (N=130) Volga Region 39,3% (N=196) East Siberia and Far East 10,4% (N=52)
Division of respondents from regions according to HIV prevalence	Less then 300 to 100 000 - 25,2% (N=137) 300-500 to 100 000 - 28,3% (151) 500-1000 to 100 000 - 17,4% (93) More then 1000 to 100 000 - 28,5% (152)

APPENDIX 2

Russian governmental procurement in the area of HIV treatment: selected examples

Increased prices due to auctions

In 2009, an interesting case was noted involving increased prices due to an auction. And so, in general, as a result of the way auctions were conducted (at that point they still were not conducted electronically) 0.46% more was spent than was originally planned (if you add all the initial auction prices).

This occurred because a whole number of companies retracted bids that they had originally filed. In particular, this was the case with the drugs darunavir, abacavir + zidovudin + lamivudin, abacavir + lamivudin as well as a number of other drugs. Subsequently, the contracts were concluded at a higher price in comparison with the one which was originally announced at the auctions.

Audits by the General Prosecutor's Office of the Russian Federation

On 1 December 2010, the General Prosecutor of the Russian Federation issued a statement in which a number of violations were described that had been allowed by the Ministry of Health and Social Welfare during the procurement of ART. The audit by the General Prosecutor of the Russian Federation was in large part initiated by appeals from community organisations. Several related citations are reproduced below.

"So, **for a long time the Ministry did not purchase diagnostic tools or antiviral drugs**. As a result of the late posting of notices about electronic public auctions, public contracts for the drug deliveries were finalised only between 26 June and 14 July of the current year... In this regard, the Ministry started purchasing antiviral drugs in the fourth quarter of 2010...

In the Primorsky Krai and the Moscow, Omsk, Tyla, Ulyanovsk and Chelyabinsk regions there is **evidence of shortages for antiretroviral drugs for the treatment of HIV-infected people** based on public contracts concluded in 2010. Thus, this year in the Ulyanovsk region the supply of the drug stavudine was 35% of the required amount whereas phosphazide was 21%. In the Chelyabinsk region, the supply of didanosine was 6.8%, in the Omsk district it was 2.4% and in the Primorsky Krai 44.8%. In the Irkutsk district, the supply of the drug entecavir was only 7.1%, in the Omsk district, the supply of zidovudine was 1.7% and in the Moscow district 35.9%.

Likewise, over the course of the audit, evidence came to light of concerted actions that violated laws of competition in bidding organised and implemented by the Russian Ministry of Health, concerning the right to public contracts for supplying diagnostic tools and antiviral drugs for the treatment of people infected with the viruses hepatitis B and C…"

Auctions for the Children's Form Nevirapine that Did Not Take Place

In 2011, the auction for paediatric form of the drug nevirapine did not take place for the reason that not a single bid was placed. The phrase "the auction did not take place" is generally used in cases where one bid is placed. In this situation, the customer has the right to conclude a contract with this one bidder at a price that does not exceed the initial price. However, in the case of nevirapine, there were no bids at all. According to information received, the price of 606 rubles per vial did not entice suppliers, who were not eager to enter the auction at such a low price. It is worth noting that in this case, the Ministry of Health set the starting price at 606 rubles because this was the closing price at the auction held the year before. However, in 2011 not one supplier was ready to participate in the auction at the price listed by the Ministry of Health. According to experts, in this case the given price could be considered monopolistically low, inasmuch as it limits the possibility

of other company suppliers participating in the auction. In addition, certain issues (to put it diplomatically) affected the quantity of delivered goods. The total number of vials – 13,853 – greatly differed from the quantity of vials sent to the recipients. In other words, if you add the number of vials of nevirapine, which according to electronic auction documentation was ordered by medical institutions in each district, you get a number that is much higher than 13,853. Judging by the numbers in the documentation, the Moscow Health Department's Infectious Clinical Hospital No. 2 was alone supposed to receive over (!) 200,000 vials, while the documentation specified more than 60 recipients.

In 2011, the auction did not take place, despite the fact that activists and medical experts made a number of protests. In 2012, an auction was again announced at the same price. One bid was received and the contract was closed at a price of 606 rubles per vial. The winner was the company R-Pharm, which in 2011 and 2012 became the largest provider of ARVT in the Russian Federation.

ANNEX 3

Amount of medications per patient per year, purchased in Russia in 2009-2011 within the federal procurement programme (solid forms + enfuvirtide), in decreasing order

MNN	2009	2010	2011	2012
3TC +AZT (150+300 mg.), tabl.	19,228	38,433	46,902	51,165
LPV/r (200+50 mg.), tabl.	10,470	23,658	27,442	35,599
3TC 150 mg., tabl.	9 401	20,311	22,734	31,367
RTV 100 mg., caps.	7 529	17,313	21,185	29,431
EFV 600 mg., tabl.	13,366	22,445	28,739	28,308
f-AZT 200 mg., tabl.	5 161	9 721	10,266	10,002
DRV 600 mg./ 300 mg. in 2009. tabl.	7 752	6 293	7 597	9 756
ABC+3TC (600+300 mg.), tabl.	976	3 472	5 622	9 715
ABC 300 mg. tabl.	1 735	5 428	7 250	8 784
ATZ 200 mg. caps.	2 181	4 610	5 328	7 541
ddI 400 mg. caps.	2 955	5 576	6 125	6 450
SQV 500 mg. tabl.	2 045	3 432	4 304	6 317
ATZ 150 mg. caps.	1 622	3 573	3 974	5 498
d4T 30 mg. caps.	1 427	3 927	3 641	4 092
NVP 200 mg. tabl.	2 151	3 964	4 183	3 587
TMC125 100 mg. tabl.	490	1 197	1 871	2 907
FPV 700 mg. tabl.	449	1 441	2 157	2 841
RAL 400 mg. tabl.	324	766	1 492	2 644
ddI 250 mg. caps.	787	1 997	2 799	2 635
DRV 400 mg. tabl.	0	622	1 296	2 602
AZT 300 mg. tabl.	2 412	3 101	2 348	2 159
EFV 200 mg. tabl.	662	763	805	1 395
ABC+AZT+3TC (300+300+150 mg.) tabl.	477	534	897	969
T20 90 mg/ml.	208	290	441	877
d4T 40 mg. caps.	1 509	1 386	1 392	816
ddI 125 mg. caps.	0	0	214	88
IDV 400 mg. caps.	95	49	44	28
NFV 250 mg. tabl.	603	393	0	0
ddI 100 mg. Chewable tabl.	146	284	0	0

International Treatment Preparedness Coalition in Eastern Europe and Central Asia

"Black Box"

Russian HIV Policy and Its Economic Effectiveness

Summary
July 2012

Russian HIV policy resembles a "black box." The input is a substantial amount of HIV funds provided by the federal government, which have grown 6-fold from 2006 to 2011 and amounted to 63 billion rubles (about USD$2 billion) overall. The output is the number of new HIV infections in Russia, which jumped 10% compared with the last year, and increased mortality among Russians with HIV.

The International Treatment Preparedness Coalition in Eastern Europe and Central Asia developed a review of the economic effectiveness of Russian HIV policy. The report aimed to assess whether Russia is obtaining maximum benefits from its HIV funds, especially in lieu of the fact that HIV spending will stagnate at the level of 2012 for the next two years. We analyzed data from HIV budgets and programs, interviewed experts, and assessed the prioritization of HIV allocations vis-à-vis the specifics of the Russian epidemic and outcomes of cost-effectiveness research.

The assessment demonstrated that Russian HIV spending is ...

… not linked to a national strategic plan or transparent system for monitoring and evaluation. Russian HIV budget is not tied to the National HIV/AIDS Strategy, which has not been developed after 25 years of the Russia epidemic.

... not aligned with the specific nature of the HIV epidemics. The HIV epidemic in Russia continues to spread through high-risk groups. The majority of new infections are still registered in people who inject drugs (58% of all new cases) and their sexual partners. Russian studies found that the increase of registered drug users by 10% leads to an increase in the new HIV cases by almost 30%. Nevertheless, the half of Russian HIV prevention resources is targeted for communication on social and behavioral change and no single dollar goes into needle and syringe programs for people who inject drugs. Such an investment policy is mismatched with evidence on the cost-effectiveness of needle and syringe programs, documented for Russia, as well as many other countries, including Ukraine and China. Besides prevention programs, HIV screening and treatment programs provide insufficient coverage of high-risk groups and overlook their specific needs.

Tuberculosis remains a major cause of death among Russians with HIV, however TB-HIV funding and programming are insufficient and inadequate. The number of people co-infected with HIV and TB in the past five years increased by almost 3-fold, despite the fact that during the same period, government spending for HIV increased 6-fold, and for tuberculosis – 4-fold. 75% of those co-infected with TB/HIV are people who use drugs, 40% of whom fall out of long-term inpatient TB treatment programs. Nevertheless, public expenditures are still not shifted toward outpatient TB treatment, including highly efficient DOTS programs.

... not informed by the best patients' interests at the stage of planning ... Even when the Russian government makes significant investments in the treatment of people with HIV, it does not take accompanying steps to rapidly scale-up access to treatment. The procurement of ARV drugs is guided by the essential medicines list, which does not include new and effective drugs such as tenofovir, but contain obsolete and highly toxic medications, such as stavudine. The government is rarely negotiating with pharmaceutical companies to reduce the costs of patented drugs and procuring a very limited number of generic ARVs.

... and inefficiently organized at the stage of disbursement. Government tenders for supply of ARVs and HIV prevention services are being conducted with limited transparency and competitiveness that repeatedly attracted the attention of the Prosecutor General of Russia and Federal Anti-Monopoly Service. The opaque tendering processes attributed to the procurement of high priced ARVs. Moreover, in 2009-2011, the composition of procured ARV drugs was inadequate for making up the required number of treatment regimens. In addition, the 2011 tender for procurement of HIV prevention services for key populations - announced by government for the first time over the previous two years – set such unrealistic outcomes and deadlines, that was "the impractical and inefficient spending of public money," according to an independent evaluation.

On the whole, the report demonstrated that despite clear increase in HIV funding over the last six years, this money has not been used to achieve maximum impact on HIV prevention and treatment in Russia. On the one hand, the process of setting priorities for allocation of HIV resources is flawed at the stage of planning. On the other hand, HIV funds are spent in a non-transparent manner, without targeting quality indicators, and with the lack of accountability for outcomes. As a result, in today's Russia, not 150, as in 2008-2009, but already 160 people become infected with HIV daily, and there are still cases of regiments change due to stock-outs of ARV drugs.

All these mistakes will lead to further government spending and the escalation of new infections and deaths among people with HIV.

COMING SOON!