

Analysis of the Global TB Drug Market and Country-Specific Case Studies of TB Drug Distribution Channels

Russia Federation (RF) Case Study
Prepared June 2007



Executive Summary

- TB drugs are primarily purchased by the public sector. For 1st line drugs, this is increasingly decentralized to regions (oblasts) and for 2nd line drugs, it is mostly carried out by the federal government using funding from international donors (with the exception of Tomsk, which procures directly through the GLC using GFATM funding)
- The 1st line TB drug market is a public market valued between \$38M and \$47M USD (including contributions of both regional and federal programs and the World Bank)
- The 2nd line drug market is also a public market, covered by the federal program and external donors (World Bank, GFATM). In 2007 it will total approximately \$60M USD

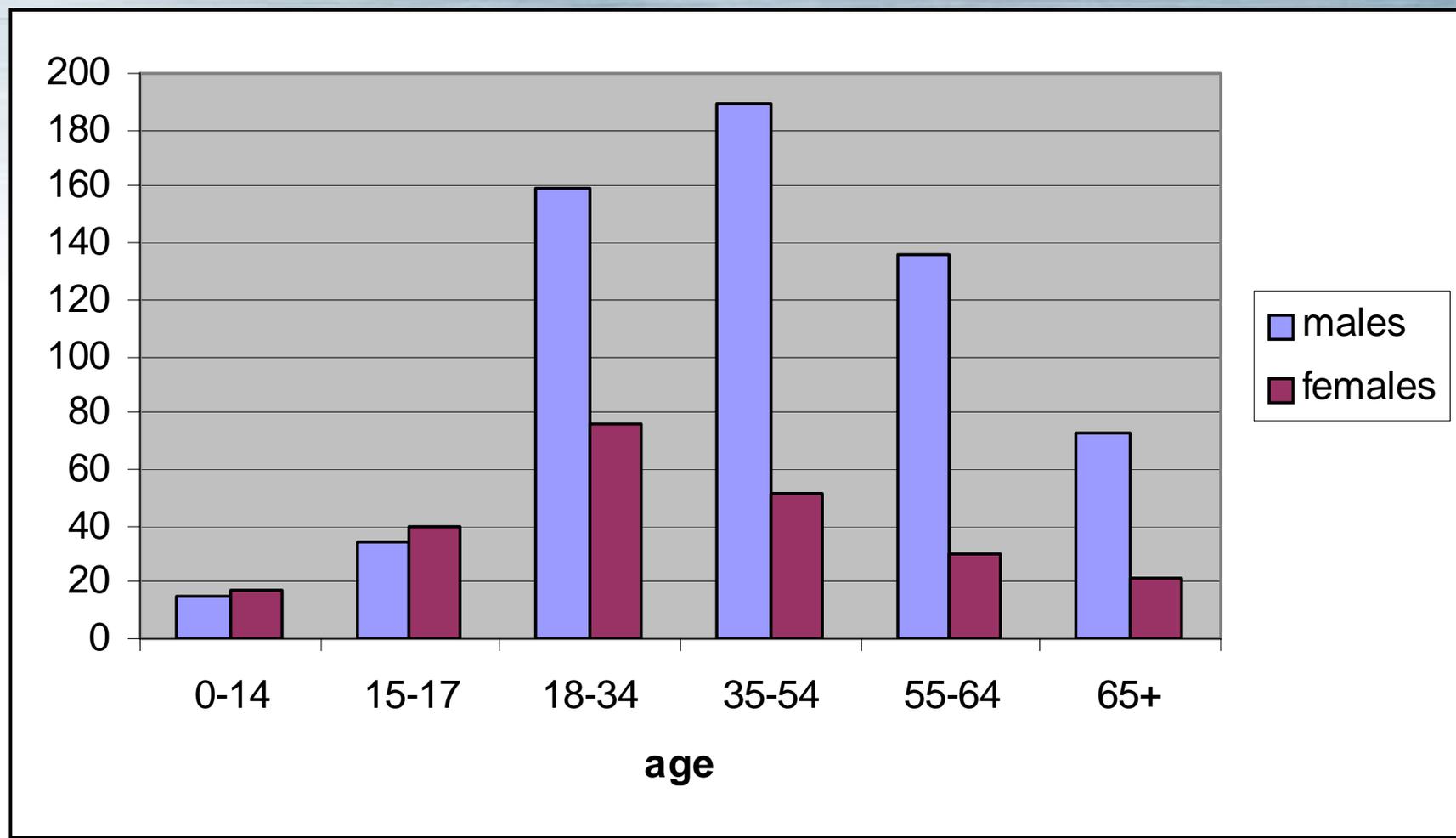
Executive Summary (continued)

- TB control in the RF is within the remit of the public sector and the government is responsible at both federal and regional levels. The National TB program is heavily centralized and falls under the MOH. Most policies are set at the national level
- TB control, including drug purchases, are budgeted through so-called federal and regional TB “target programmes”. These plans are adopted for 3 year periods and revised annually
- Treatment of TB at all levels of the health system is free for the patient
- TB Drugs purchase by the government increases each year, as the government places increased emphasis on TB control
- Purchase of 1st line drugs has shifted in recent years from the federal to regional governments
- The majority of 2nd line drugs are purchased by the federal government with funding from international donors (GFATM, WB). Only Tomsk is purchasing from the GLC using using GFATM funding)
- Procurement of 1st and 2nd line drugs are done on a tender basis. Tenders are conducted by federal and regional procurement department (federal tenders, through the MOH procurement departments)

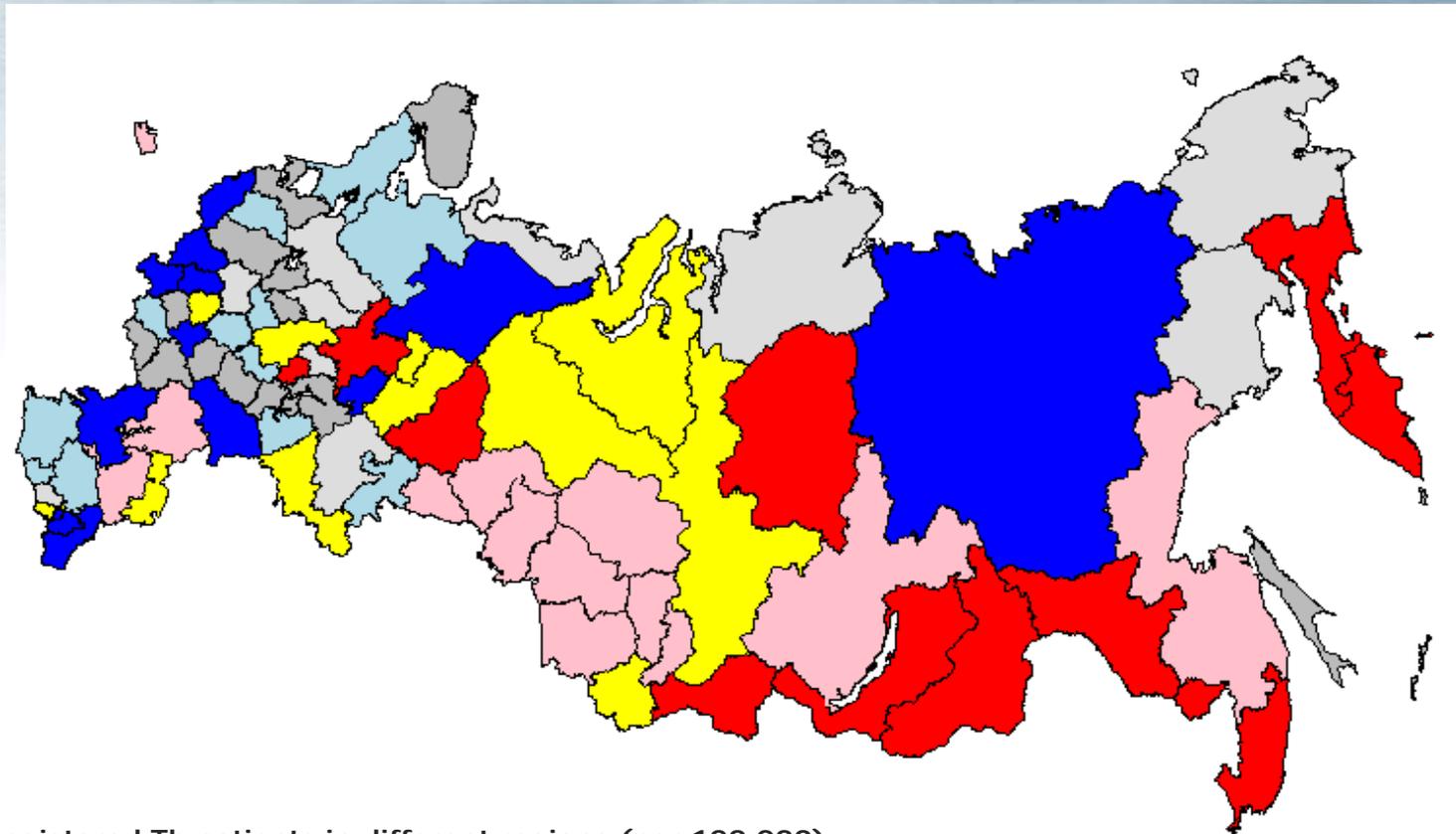
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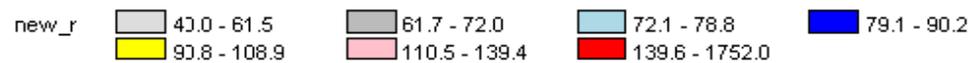
127,930 cases of TB were newly diagnosed in 2005. Tuberculosis in Russia is mostly a disease of young and middle-aged males



There is a significant discrepancy in TB rates in different regions



Rate of registered Tb patients in different regions (per 100 000)

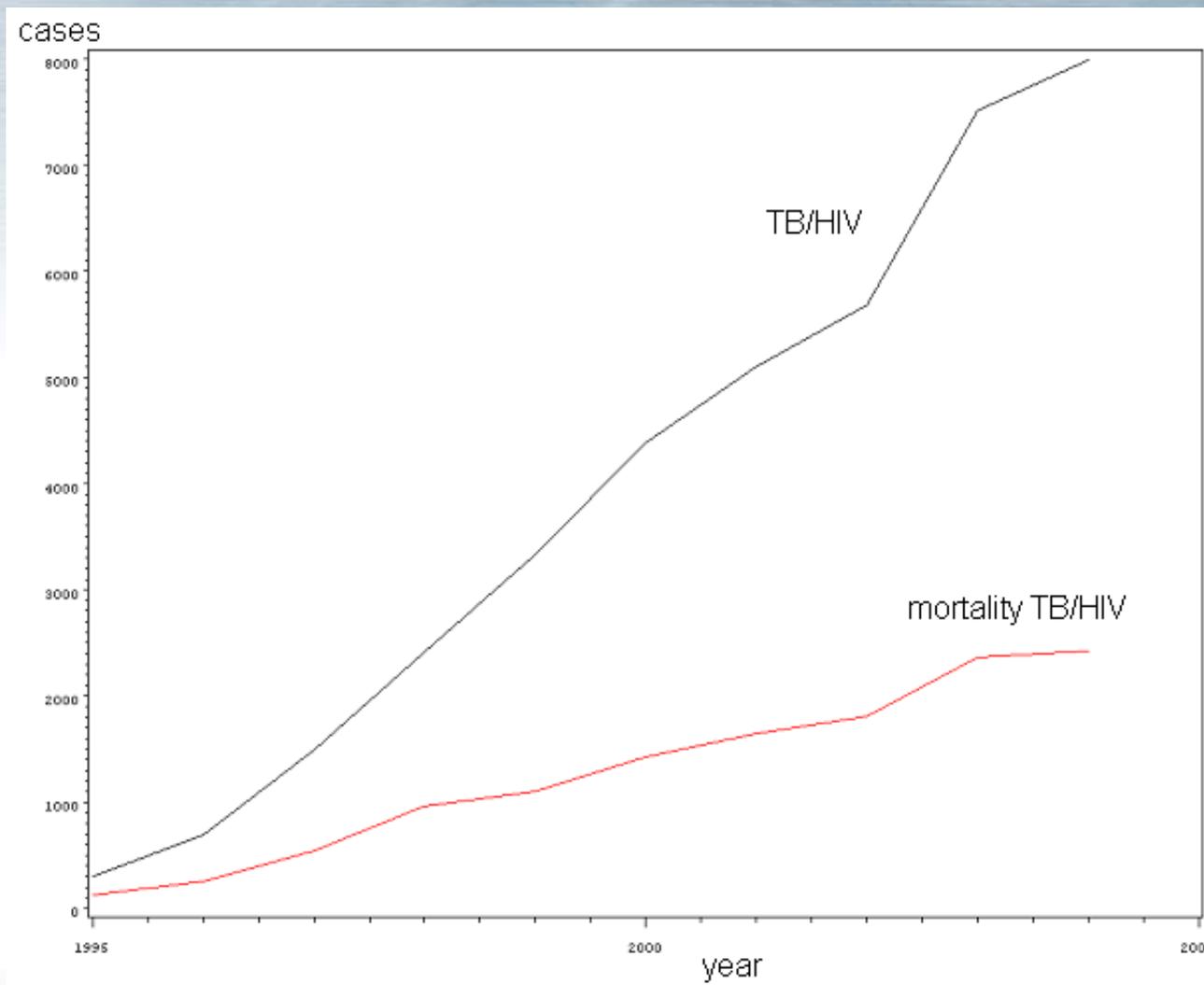


Estimates on prevalence and incidence of MDR-TB Russia range dramatically, but all are significant

- WHO estimates and studies done in Samara and Tomsk show approximately 20% of all TB cases are MDR
- US CDC data on Eastern Europe/Central Asia (includes surveillance in Russian labs) shows up to 35% of all TB cases are MDR and 14% are XDR
- Russian experts estimate that incidence of MDR TB is about 5-7% of newly diagnosed TB cases, but this figure is considered an underestimate because of lack of appropriate diagnostics capacity



TB/HIV co-infection is rising

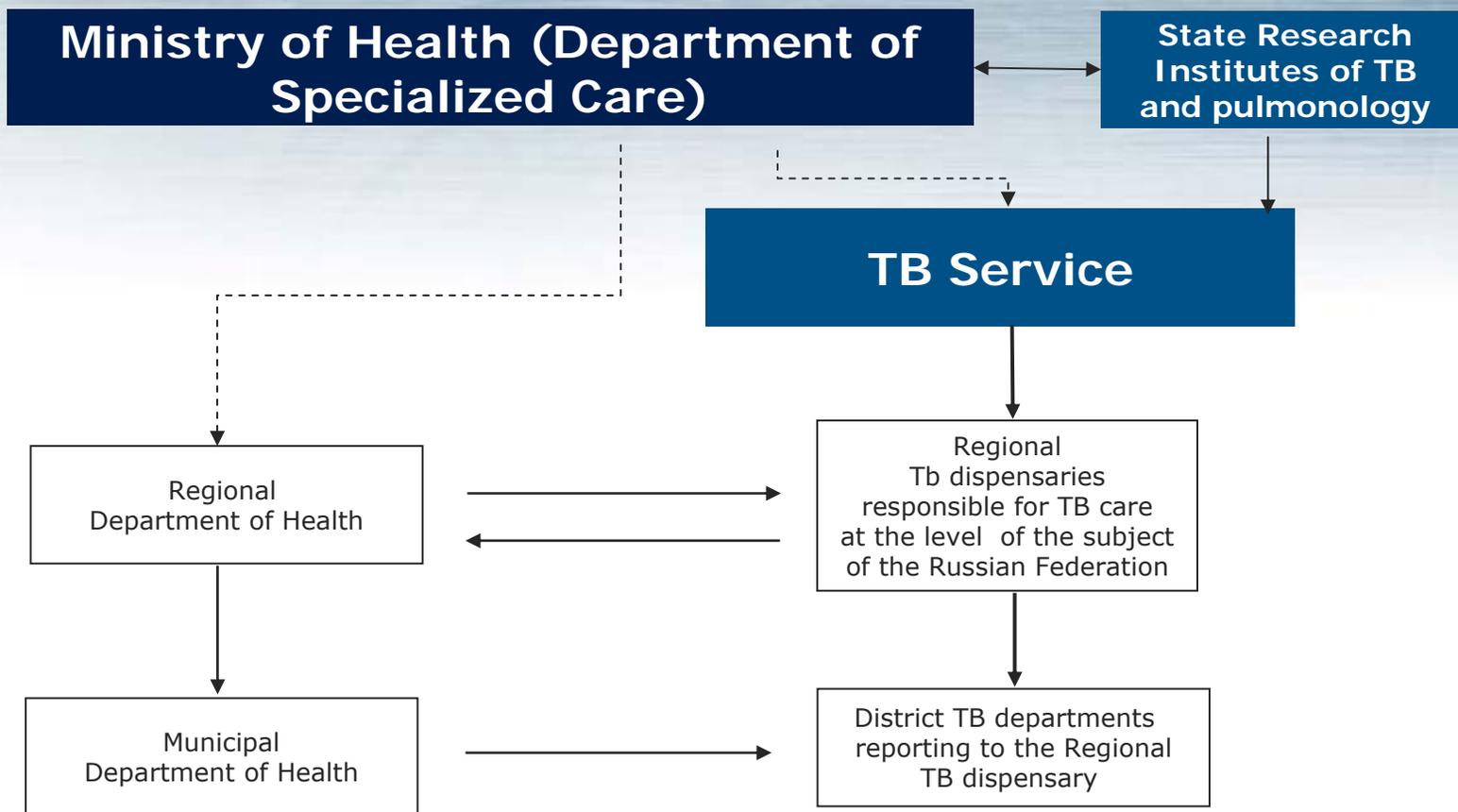


The Russian penitentiary system has a severe burden of TB

- 48,370 TB patients were in Russian prisons in 2005
- More than 10% of all incidence cases in RF are registered in prison sector.
- There is obligatory testing for men and women entering the prison system
- The majority of new cases are identified upon admission, indicating that the number of civilian cases is underestimated
- Prevalence of MDR and XDR TB in prison sector is 8-10% of new cases and significantly higher than the in the civilian sector



The MOH of the federal government is responsible for setting policy and implementing TB control measures



Federal Target Programme on TB Control in Russia

- The Russian Federal Target Programme “Prevention and Control of Social Diseases (2002–2006)”, with the sub-program “Urgent Measures of TB Control in Russia” was approved in 2001. The Programme covers strengthening the capacities of health facilities, research institutes and centers that carry out prevention, detection, diagnosis and treatment. It is also responsible for purchase of drugs.
- Several federal laws and regulations have been developed to support the TB control programme.
- Within the federal TB control programme, five research institutes are responsible for organizing and supervising research, training and implementation of TB control in a wide network of more than 500 TB control facilities in 88 regions of the Russian Federation.
 - Research Institute of Phthisiopulmonology of Sechenov Moscow Medical Academy (RIPP MMA)
 - Central TB Research Institute of the Russian Academy of Medical Sciences (CTRI RAMS)
 - St Petersburg Institute of Phthisiopulmonology
 - Ural Research Institute of Phthisiopulmonology
 - Novosibirsk TB Research Institute.

Examples of support laws includes the federal law "On prevention of tuberculosis spread in Russian Federation" (N 77, 18.06.2001 with changes from 22.08.2004)

- Guarantees TB diagnostics and treatment by the state
- Divides responsibilities for TB control between federal and regional governments, with regional and federal governments both responsible for provision of drugs.
- Stipulated that 1st line treatment is a responsibility of regional governments (since 01.01.2005 the article demanding involvement of local governments in TB treatment has been abolished). As a result, 1st line drugs are becoming more of a regional responsibility while provision of 2d line drugs remains the responsibility of federal government.



Tb Control System in Russia

- In 2004 in Russian Federation there were:
 - 470 regional and local TB dispensaries
 - 120 TB hospitals
 - 9 children TB hospitals
 - 479 TB dispensaries (502 dispensaries in 1998),
 - TB departments and out-patient clinics in the territories with population less than 80 thousand people
 - 61 adult TB sanatoriums and 144 children TB sanatoriums (versus correspondingly 75 and 166 in 1998).
- Number of TB beds – 73,266; bed occupancy - 326.2 days/year.
- Number of TB specialists- 9,027 (0.63 per 10 000 population)
- Under the Ministry of Justice, 37 hospitals and 57 treatment facilities provide treatment for TB patients within the penitentiary system.



According to the MOH, DOTS expansion and strengthening the TB program has been a major focus in recent years

DOTS progress to date:

- **Started to be introduced in 1997**
- **According to the WHO, coverage reached 26% in 2004 and was expected to increase substantially in 2005**
- **DOTS Plus started in some regions**

2005 achievements:

- **Increased government funding for TB control**
- **Intensified case management**
- **Set up of diagnostic tools in the majority of Regional TB dispensaries and hospitals**

TB treatment: TB suspects are most often referred to a TB dispensary where they have access to free diagnosis and treatment

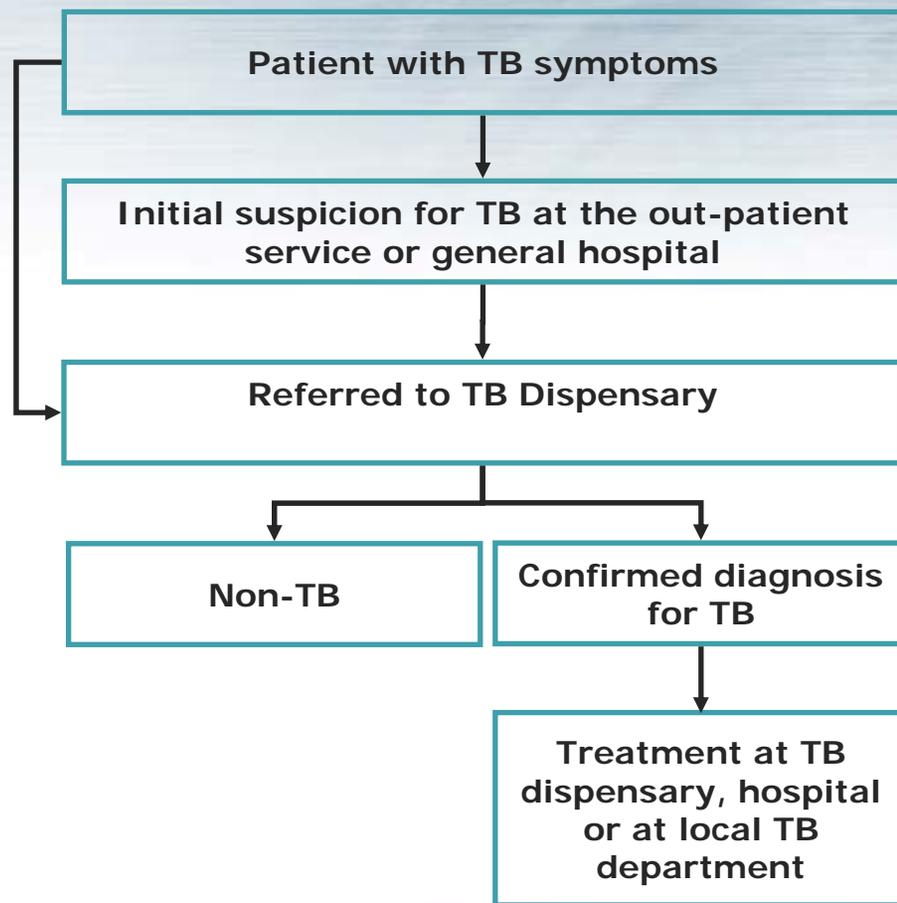
Diagnosis

- X-ray for patients suspected of having TB
- Smear test for patients with abnormal X-ray photo
- Smear tests for patients during free treatment (a lot of tests done with poor quality)
- Low number of patients primarily diagnosed through smear tests

Treatment

- 5 Categories of patients (1, 2a, 2b, 3a, 3b, 4) in accordance with the MOH Order N109 from 2004 based on WHO recommendations
- All patients go through public health sector
- Self-treatment does occur but in a small scale and it should not be taken into consideration (as state is taking care of control of socially determined diseases as priority)

Most patients suspected of having TB are referred to a TB dispensary for further diagnosis and treatment



Typically present at urban and rural primary health care facilities.

Usually hospitals that have capacity to conduct x-rays and sputum microscopy in their facilities provide initial diagnosis on site. There is a trend to strengthen capacity of general health care facilities in diagnosing TB in the World Bank project.

Most patients are referred to TB dispensary for treatment and monitoring. Some of them - for diagnosis as well.

The majority of patients are treated on an inpatient basis for the first few months/weeks and then continue through the out-patient setting

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Overview of drug purchase and distribution

- All drugs are provided for free to patients at TB institutes/dispensaries
- TB drug procurement is done through the public sector but specific channels depend on the route of funding.
- TB Drugs are procured in accordance to the national rules common for all drugs purchased by the government health system
- Procurement is carried out through annual bids and tenders, independent of the funding source.
- A very small amount of drugs are available from general pharmacies for urgent purposes (mainly isoniazid, rifampin), mainly for children when drug shortages occur. Such situations are not common.

Regional procurement procedures

- Procedures are common for all drugs in the public sector
- Annual bids and tenders are conducted by regional Procurement Departments (reporting to the regional administrations)
- Procured drugs must meet necessary requirement common for all purchased drugs in RF
- Usually 4-5 big national distributors win tenders depending mostly on prices but as well as on the other conditions: storage, transportation time, etc.
- Drugs are delivered quarterly to the store of the Regional TB dispensaries from the warehouses of the distributors situated nearby Moscow
- TB dispensaries then distribute them to municipal TB clinics
- The Department of Health of Ministry of Justice submits their annual demands to MoH, thus drug procurement and distribution for the prison sector is totally centralized



Role of federal government in supply of 1st line drugs

- Regional TB dispensaries submit applications for annual supply of drugs to the regional department of health and MoH (Department of Specialized Care) and allocations are made according to epi data, so-called “regional quotas” in the federal funding framework, and total funding for the Russian TB program
- Half-year buffer stock of drugs is taken into consideration when the demand is submitted in compliance with the national order of MoH
- These demands are revised and adjusted. Usually they are considered jointly and the overall approach is that MoH donates to the poorest regions
- The proportion of regional funding for the 1st line depends on the economic level of the region

Procurement process at the national level is similar for the 1st and 2d line drugs independent of the source of funding (ie. Federal Target Programme or WB project)

**“Organizing company”
that arranges the tender
is selected...**

- Tenders for procurement of drugs within civil and prison sector are organized by GONGO “Russian Health Care Foundation” closely linked to MoH

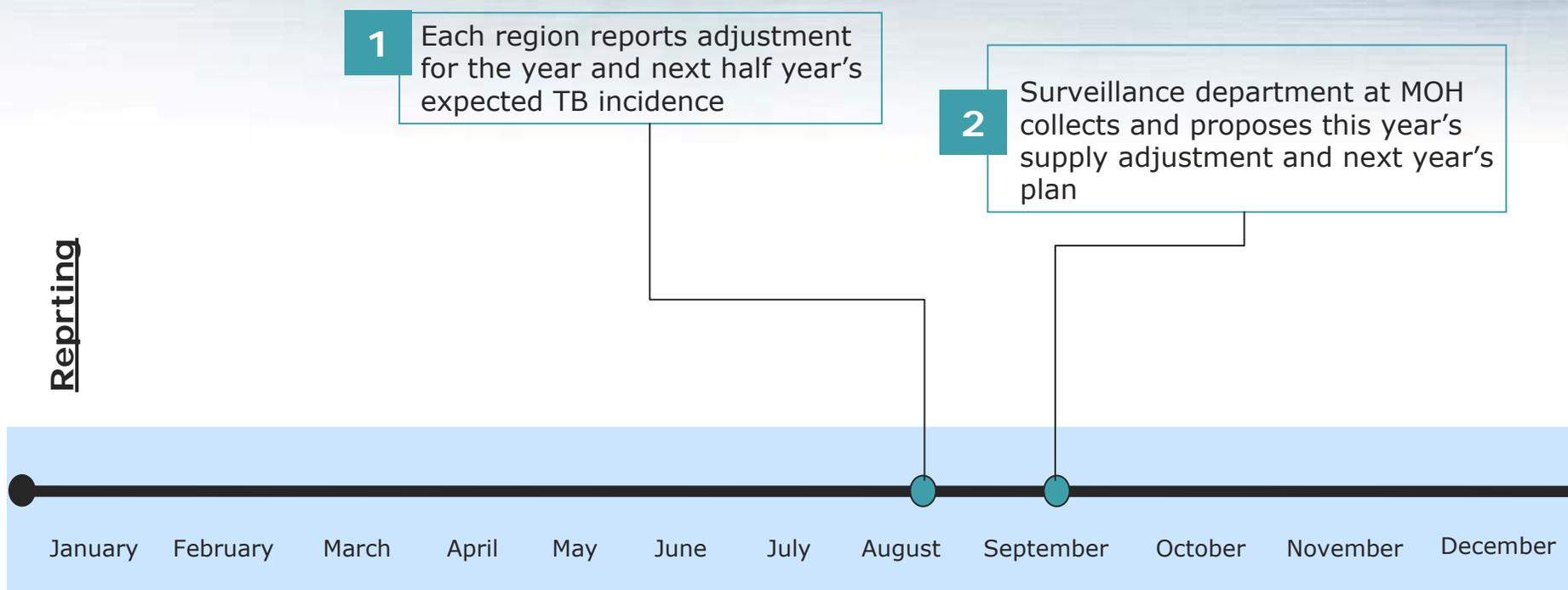
**...International
competitive bid
floated to public...**

- Domestic and international manufacturers are eligible to submit bids
- Manufacturer must be MOH approved (Pharmaceutical Commission)

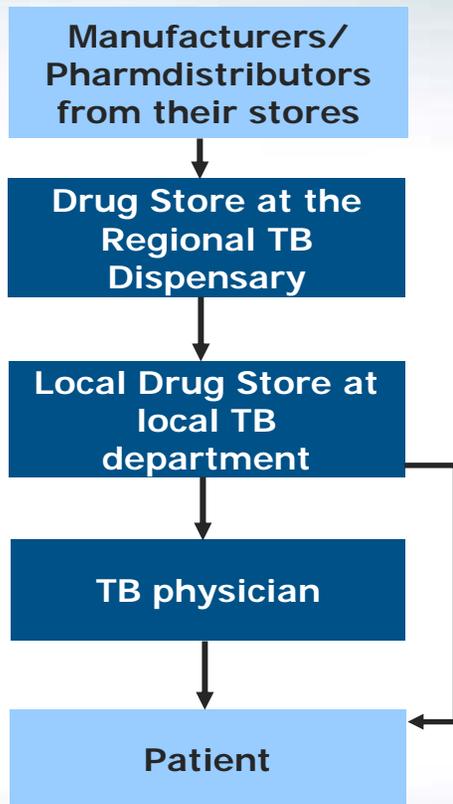
**...Limited number of
suppliers win the bid
for the next year**

- Generally 4-5 companies
- Winning bid is highly based on price
- Tender issued for 1 year

The procured drugs are delivered directly to each region in accordance with the official demand quarterly. When there is a deficit of drugs they are re-distributed between regions.



Once supply reaches the Regional TB Dispensary drugs are distributed between the dispensary and other TB local departments in accordance with epidemiological indicators and local demand.



- Drug management functions are undertaken at 3 levels of the supply system: central, regional and local (in distant rural areas)
- Usually the process is similar in each territory

Procurement of drugs in prison sector

- Prison sector from all the regions receive 1st line drug supplies through federal tenders
- They are conducted according to the same scheme as in civil sector under supervision of MoH and are based on the applications that Ministry of Justice provide to MoH on the annual basis
- Department of TB control of the health services of Ministry of Justice collect the applications from the regional Departments of Justice based on the regional epi data on TB in prison sector

Procurement of 2nd line drugs

- Second line drugs are purchased under the Federal TB Program
- GFATM Round 4
 - Drugs to be delivered to 2 regions in 2007
 - In total 3000 in 12 regions patients will be covered
 - Drugs are purchased by GONGO “Health care foundation” through the Netherlands based IDA and distributed directly to the regions
 - Number of patients is different in various regions
 - Average price per patient per year differs by treatment regimen but not More than USD 3.500
- GFATM Round 3 (Tomsk Project)
 - Purchase and procurement from GLC

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1st line and 2nd line TB drugs markets

Overall TB Market

1st line market

- Sources of funding:
regional budgets in the framework of regional TB programmes, federal budget in the framework of NTP and National Priority Project, WB loan funds (beginning with 2006-2007)

2nd line market

- Sources of funding:
Federal budget in the framework of NTP
International Projects - GFATM 3, 4
- GFATM Round 3 is implementing locally in Tomsk Region
- Round 4 TB project has just started (with 2007) and supply is not well regulated yet.

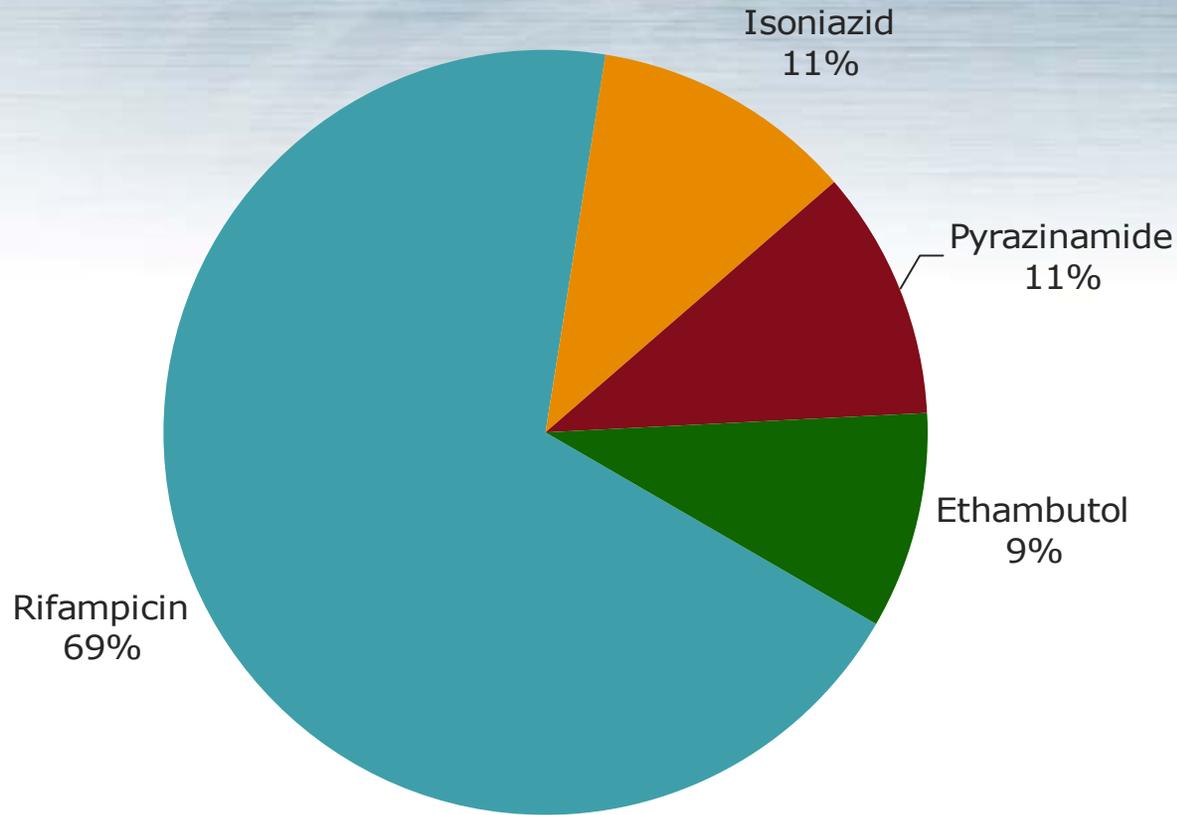
Value estimates for 1st line drugs range from \$38M to \$47M

Source	Total (Million USD)
Regional Budgets*	34-38
Federal TB Program	4-5
WB Projects**	4

*Share of funding for 1st line drugs differs by region, but it ranges from 45-70%, with the remainder covered by the federal program.

**Planned for 2006 but not expended until 2007

Volume of 1st line TB drugs sector: regional + federal

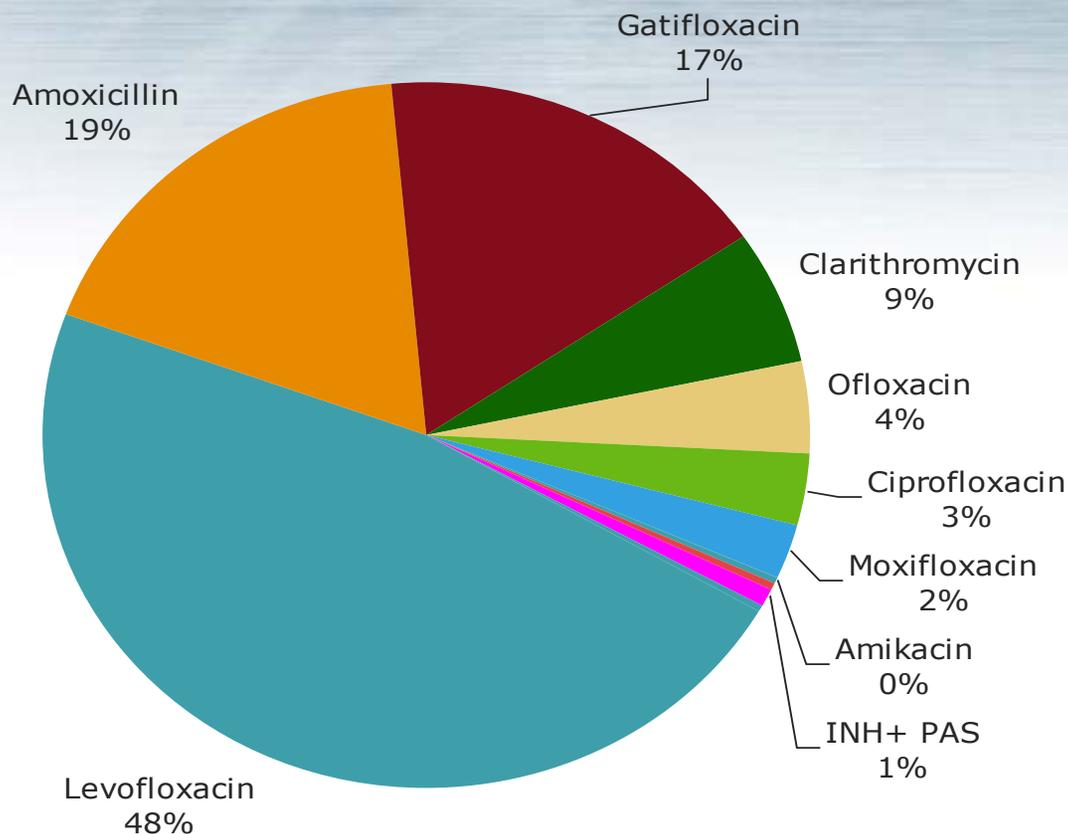


Value estimate for 2st line drugs in 2007 totals approximately USD56.7M

Source	Total (Million USD)
Federal TB Programme	50
GFATM Round 3	1.2
GFATM Round 4*	5.5

Scheduled to begin in 2007

The volume of 2nd line TB drug market in the framework of National Target TB programme.



Funding trends for purchase of TB drugs

- Drugs procurement (1st and 2d line) is funded by government (federal and regional budgets) and donors (Global Fund and WB projects)
- Procurement is done through national and regional bids
- In 2002-2004 the majority of 1st line TB drugs were procured by the federal government through national bids. Now about 70% (volume) of 1st line drugs are procured through regional bids
- Federal bids still account for procurement of 2d line drugs and about 30% of 1st line drugs. These are then distributed mostly to economically poor regions as donations

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Overall funding for TB control in the Russian Federation

- The total budget planned for TB control per year for 2004 and 2005 was approximately US\$ 316 million (almost US\$ 3000 per new TB patient). For these years, approximately US\$ 250–260 million was made available from the government (including funds from the World Bank loan), a substantial increase compared with 2003.
- The largest budget line is for staff working in TB control (US\$ 113); initiatives to increase case detection and cure rates (US\$ 84 million); investment in buildings and equipment (US\$ 60 million); and, second-line drugs (about US\$ 45 million).
- While these figures are substantial in comparison to other HBCs (reflect the country's extensive network of dedicated TB control facilities and the large number of patients with MDR-TB) a funding gap of about US\$ 40–50 million per year was estimated. The gap included needs around second-line drug purchase (US\$ 18 million) and investment in buildings and equipment (US\$ 24 million).

External funding sources

WB	<ul style="list-style-type: none"> • Equipment, training and 1st line drugs for 88 regions of the Russian Federation (additional to 1st line drugs purchased by government)
GFATM Round 3	<ul style="list-style-type: none"> • Specialists' training, monitoring, drug and equipment procurement, social support to TB patients in prison and civil sectors in Tomsk Region
GFATM Round 4	<ul style="list-style-type: none"> • TB control among civilian and prison population, the project will gradually cover about 20 regions of the RF with the population of about 30% of the total of the country population. 2d line drugs, trainings.
PIH	<ul style="list-style-type: none"> • Tomsk Region - training, monitoring, drug and equipment procurement, social support to TB patients in prison and civil sectors
DFID	<ul style="list-style-type: none"> • Samara Region "Improvement of TB Control in Samara Region (DOTS)" (finished)

Donor assistance for TB drugs

- World Bank project (USD 50M)- lab equipment, trainings, epi monitoring, 1st line drugs (drugs purchasing to start in 2007)
- GFATM Round 3 (regional project in Tomsk) USD 10.5M – 2d line drugs (purchased through regional bids), trainings
- GFATM Round 4 (USD 90M) –lab equipment, trainings, 2d line drugs (purchased by GONGO “Russian Health Care Foundation” through IDA (International Dispensary association) and GLC
- WB and GFATM Round 4 are only at the start of purchasing drugs.

Donor funding of TB drugs – World Bank

- WB project (started in 2003) intended to provide 1st line drugs for 86 regions of RF. At that time, this was urgent because 1st line drugs were not procured at the regional level (in the majority of regions), overall funds were limited and assistance was needed to ensure appropriate supply.
- There was a significant delay initiating of drug procurement (collecting applications from the regions, tenders, etc) and a simultaneous increase of regional funding for 1st line drugs
- As of the beginning of 2007 the WB was ready to start procurement of 1st line drugs but process for distribution between regions was still under discussion given that now regional budgets provide for almost 100% of 1st line drugs

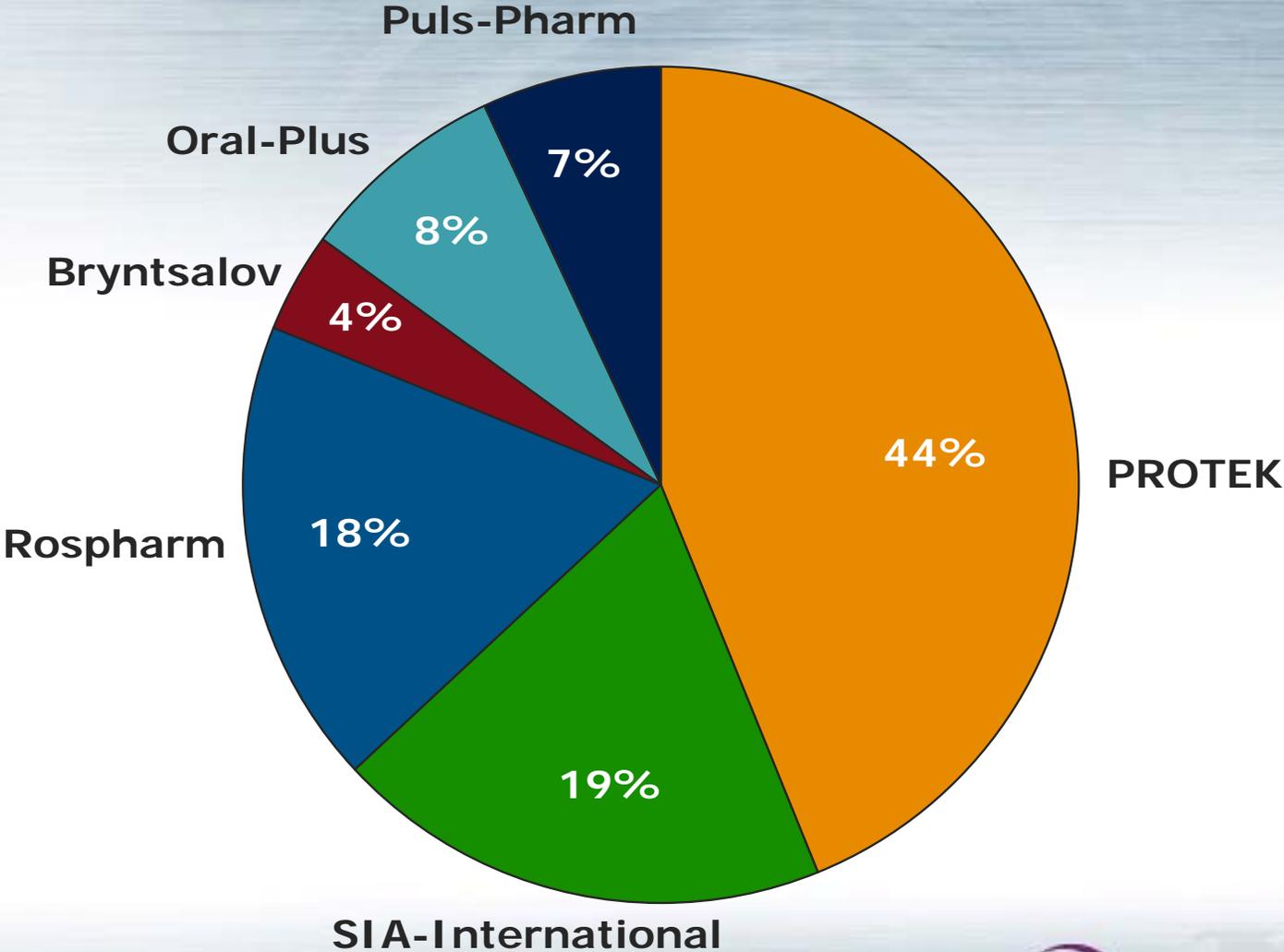
Donor funding for TB drugs - GFATM

- GFATM Round 3, started in 2004, covers 2d line drugs in Tomsk region through regional bids (the only one region in RF procuring 2d line drugs through regional bids)
- GFATM Round 4 (started in 2006) covers 2d line drugs through national bids with distribution planned for 12 regions.
 - Selection of regions is based on a number of factors (epi situation, participation in projects, etc.) but all of them should go through GLC approval

Russian TB drug production

- According to WHO, 13 Russian plants producing TB drugs have applied for prequalification
- Three producers are now recognized GMP compliant
 - ZAO Zio-Zdorovie (ЗАО «Зио-Здоровье»)
 - ZAO Makiz Pharma (ЗАО «Макиз Фарма»)
 - ZAO Veropharm (ЗАО «Верофарм»).
- Other producers include:
 - Akrikhin
 - Pharmsyntez
 - Ferrein
 - Mospharmchimpreparati
 - Aspharm
 - PROTEK
 - SIA-International
 - Rospharm
 - Bryntsalov
 - Oral-Plus
 - Puls-Pharm

Main TB drug producers and their respective market shares



Treatment regimens

- Treatment is done in compliance with the Order of MoH from 2003
- Patients are divided into 5 categories: I, IIa, IIb, III, IV
- I-firstly detected smear+ TB, IIa-repeated course after interruption with low risk of drug-resistance, IIb- the same with high risk of drug resistance, III-firstly detected smear- TB, IV- Drug-resistant TB
- Treatment is divided into 2 phases: intensive and continuation
- Abbreviations in the schemes : H-isoniazid, R-rifampicin, Z-pyrazinamide, E-ethambutol, S-streptomycin, Rb-rifabuthin, K-kanamycin/amikacin, Pt-prothyonamid, Cap-capreomycin, Fq-ftorhynolons, Cs-cycloserin, PAS-PASK

Treatment regimens (continued)

- I - PHASE I: 2 HRZ E/S; PHASE II:4 HR
- IIa- PHASE I: 2 HRZES+1HRZE; PHASE II: 5HRE
- IIb -PHASE I: 3 HRZE [Pt] [Cap]/[K][Fq]; PHASE II: the same as I, IIa or IV depending on resistance
- III- PHASE I: 2 HRZE; PHASE II: 4HR
- IV – PHASE I:min 5 drugs without resistance to them for 6 months, 3 drugs for 12 months

- Figures show duration of treatment in months

Samara case study

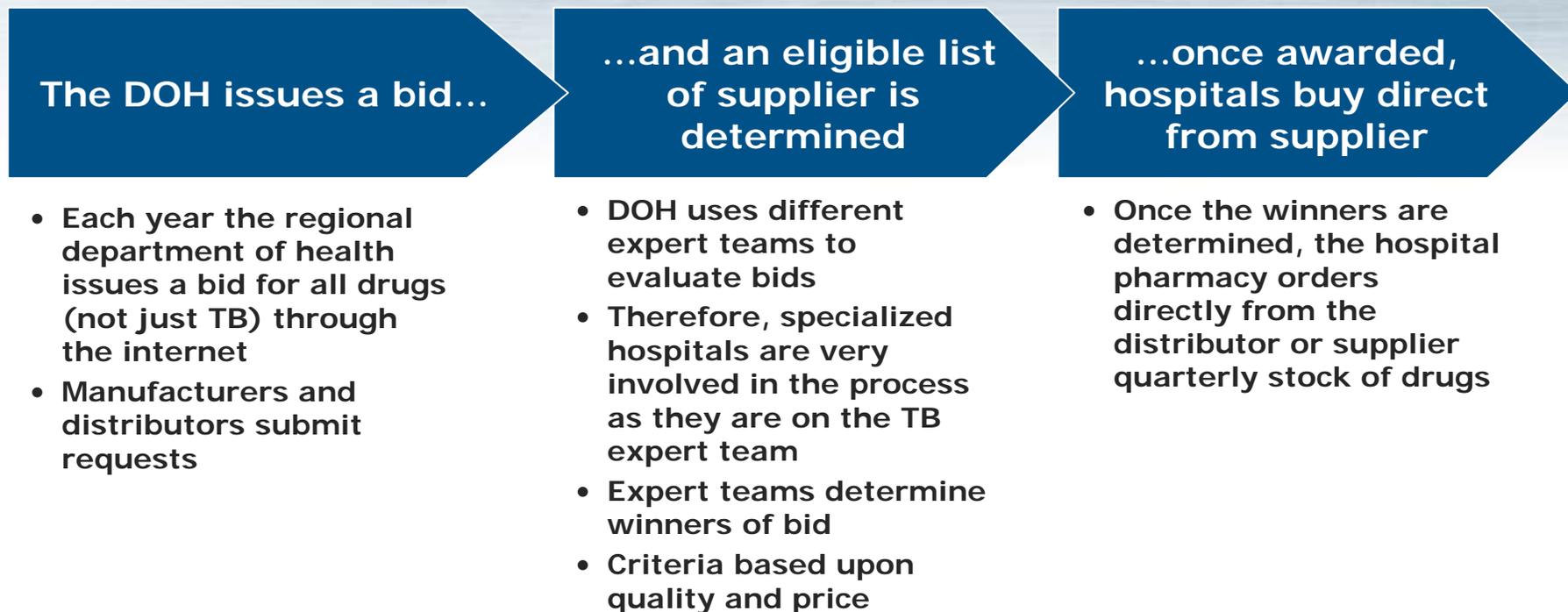
- DFID-funded project was implemented in Samara region in 1994-2005
- It aimed at the introduction of DOTS strategy at the regional level
- As a result the laboratory services were partly reformed (number of new labs were opened, number of various lab tests improved, staff trainings were conducted)
- At present time drugs are purchased through regional bids (1st line drugs), received from the federal level in the framework of federal target programme (2nd line drugs), GFATM Round 4 (planned for the coming months)
- Region received approval of GLC for 2nd line drugs in 2006

Tomsk Case Study

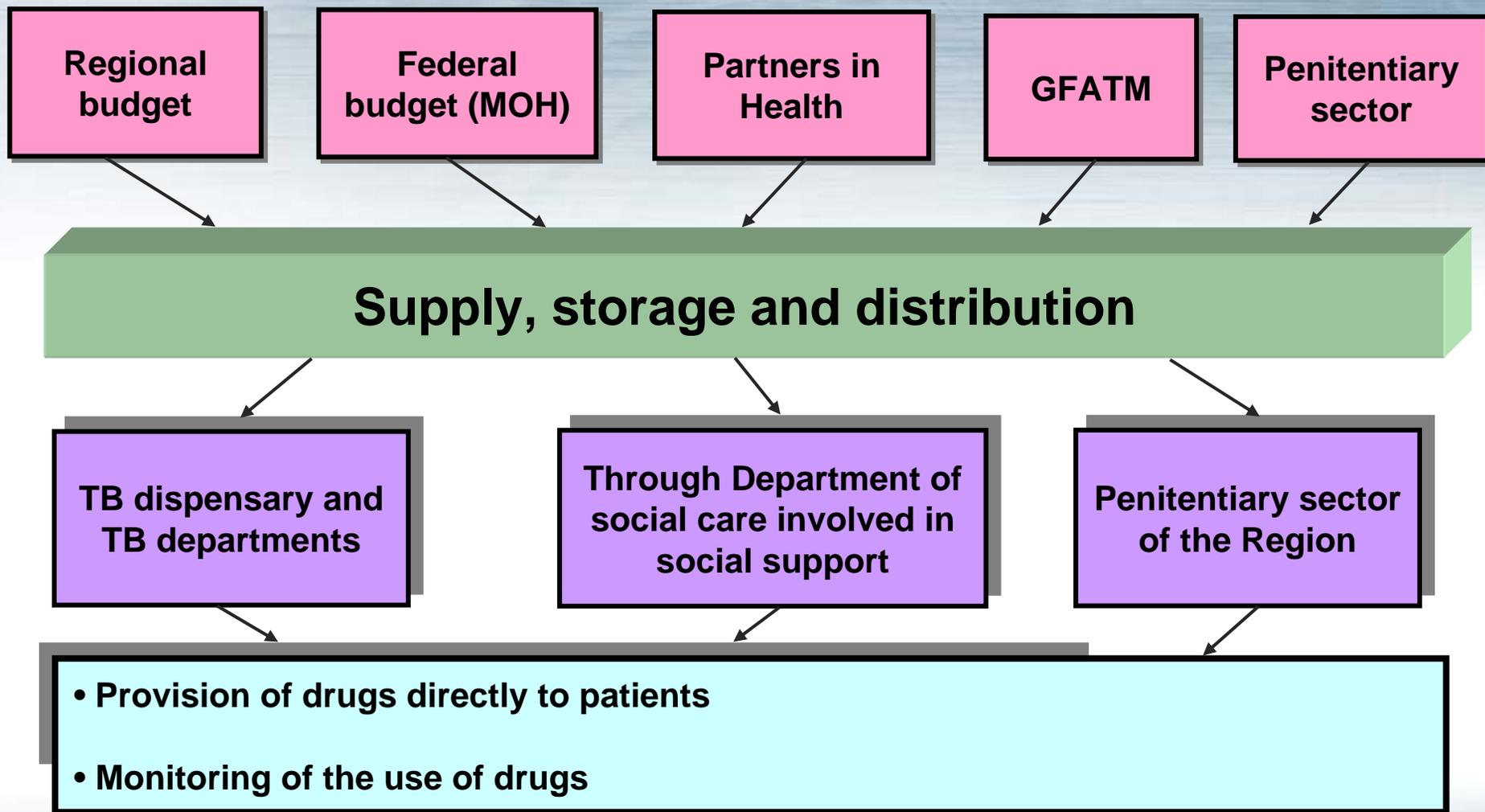
The GFATM Round 3 project “Comprehensive approach to TB control” is a pilot program in Tomsk region of total 10.7M USD 5-year budget started in 2004. 33% of funds pay for 2nd line drugs.



Tomsk Case Study: region administers an annual bid to determine eligible suppliers of products used by public hospitals



Tomsk Case Study: The Central Drug Store of TB medicines was established in 1998



Tomsk Case Study: Cost of DOTS Plus per patient with MDR-TB

- Before the project start and approval of the Project by Green Light Committee USD\$7500 - \$15000
- After approval of the Project by Green Light Committee reduced to approximately USD\$3500

Tver case study: total budget and patient numbers (2006)

- Budget

- 1st line drugs – USD 180.400 - regional budget
- 2d line drugs - USD 182.900 (est.) – federal budget

- Number of treated

- With 1st line drugs – 1825 patients
- With 2d line drugs – 106 patients

Tver case study: price per regimen (most frequently used) for locally bought drugs (2006)

Regimen			Intensified			Continuation			Total Cost RUR	Total Cost USD
			Per unit RUR		# of months	Per unit RUR		# of months		
Cat I	HRZE	HR	400		2	250		4	20,600	\$70
Cat IIa	HRZE	HRE	400		2	500		5	31,700	\$120
Cat III	HRZ	HR	350		2	250		4	24,800	\$95

Tver case study: examples of products, yearly purchases and manufacturers (Tver Regional TB Dispensary, 2005)

	Doses	Cost per year RUR		Manufacturer
Rifampicin, Tablets	150 MG	45 000		"Bryntsakov", Russia
Rifampicin, Tablets	150 MG	23 500		"Belmedpreparati", Republic of Belarus
Ethambutol, Tablets	400 MG	12 300		"Makiz-Pharma", Russian Federation
Pyrazinamide, tablets	500 MG	11 800		Lupin LTD, India
Ethambutol, Capsules	400 MG	9 500		Lupin LTD, India
Cycloserin, Tablets	250 MG	7 300		"Shelkovski vitaminnii zavod", Russian Federation
Isoniazid, Tablets	300 MG	12 100		"ROSPHARM", Russian Federation
Rifacomb (capsules) (Rifamycin, Isoniazid, Pyridoxin)		10 000		Ipca Laboratories, India
Streptomycin, Injections		6 700		"Biokcimik", Russian Federation

Interviewed Stakeholders

Individual	Organization	Position
Dr Gyldara Guleeva	Ministry of Health	Deputy Chief of Department of Specialized Care
Dr. Vladimir Grechukha	World Bank loan project on TB Control (RHCF)	Director
Dr Olga Frolova	Federal HIV/AIDS Centre	Director
Dr. Svetlana Sidorova	Ministry of Justice, Federal Service of Penitentiaries	Head of TB Department
Dr Svetlana Safonova	Ministry of Justice, Federal Service of Penitentiaries	Deputy Head of TB Department
Dr. Vieslav Yekybovyak	WHO, Moscow Office	Director of Tb Control Programme
Dr. Mikhail Bionyshev	Programme of the TB control of GFATM Round 4 (RHCF)	Deputy Director
Dr. Ivan Berezkin	Federal Health Service	Chief expert on infectious diseases
Dr. Natalia Frolova	Federal Health Service	Chief specialist
Dr. Sergei Mishustin	Tomsk Regional TB Dispensary	Chief TB Specialist of Tomsk region
Dr. Victor Lebedev	Tver Regional TB Dispensary	Chief Physician
Dr. Natalia Shirkova	Moscow TB Hospital No7	Director of Drug Store
Dr. Tatyana Izotova	Tver TB Dispensary	Deputy head

Interviewed Stakeholders

Individual	Organization	Position
Ms. Veronika Agapova	Russian Red Cross	Deputy Chief
Dr. Aleksandr Gorbunov	Moscow Scientific Centre on TB control	Consultant
Oksana Ponomarenko	Partners in Health	Director of Russian office
Dr. Viktor Punga	Central Institute of Phtiziopulmonology	Head of monitoring department
Dr. Aleksei Korobitsin	WHO, Moscow Office	TB Programme officer
Dr. Vieslav Jekybovyak	WHO, Moscow Office	Director of Tb Control Programme
Dr. Dmitri Pashkevich	WHO, Moscow Office	Medical Officer, TB control programme