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Procurement and supply management report for the WHO European Region, high MDR-TB priority countries, 2013

ABSTRACT

Drug-resistant TB poses a threat to population health in many countries throughout the WHO European Region. in order to decrease TB rates and to prevent the development and spread of resistant TB strains, capacities to diagnose and treat patients need to be increased, and the uninterrupted supply with adequate, high-quality, efficacious and safe TB medicines needs to be ensured. In order to provide comprehensive information on policies and procedures for procurement and supply management of anti-TB medicines in high-priority countries, the WHO Regional Office for Europe designed a questionnaire which was sent out to the 13 countries with the highest need for external support: the resulting country-level reports were the basis for this compiled regional report. Findings suggest that although progress has been made, several challenges still remain unsolved and need to be tackled further, including regulatory problems and funding issues.

Keywords

HEALTH POLICY
PUBLIC HEALTH
TUBERCULOSIS, EXTENSIVELY DRUG-RESISTANT
TUBERCULOSIS, MULTIDRUG-RESISTANT

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Abbreviations

ADR	adverse drug reaction
FDC	fixed dose combinations
GDF	Global Drug Facility
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	good manufacturing practice
INN	international non-proprietary names
M/XDR-TB	multidrug/extensively drug-resistant tuberculosis
NTP	national tuberculosis programme
PDR-TB	polydrug-resistant TB
SRA	stringent regulatory authority

Executive summary

The prevalence and incidence rates of TB are decreasing globally. Nevertheless, TB remains a major global health problem mainly due to the continuous spread of drug-resistant TB, particularly in the WHO European Region, which has the highest proportion of multi- and extensively drug-resistant TB (M/XDR-TB) in the world. In order to bring down the rates of TB further and prevent the development and spread of resistant TB strains, greater capacities to diagnose and treat patients are needed and uninterrupted supplies of adequate, high-quality, efficaceous and safe TB medicines ensured.

Since 2004, several initiatives have been started to facilitate the scaling-up of national TB programmes (NTP) by securing external funding and providing technical support. Despite the progress made since then, many countries are still struggling with stockouts of TB drugs and facing crucial challenges with respect to the rational use of medicines. The primary objective of this report has, therefore, been to collect comprehensive data on procurement and supply management in high MDR-TB priority countries in the Region as a basis for further and more targeted assistance.

The average TB incidence in the Region was 42 per 100 000 population in 2012, with a detection rate of approximately 78%. The prevalence of MDR-TB among new and previously treated patients was approximately 14% and 48%, respectively, with as many as 11% of these drug-resistant patients having XDR-TB.[1] Since 2005, a gradual decrease in treatment success has been observed, down to 67.2%, 49.2% and 48.5% among new, previously treated and MDR-TB cases, respectively. Within the former two categories this can be attributed to the increasing proportion of MDR-TB among them, while the lack of supply of quality-assured second-line drugs and their rational use are most likely the main factors with regard to the latter group. The vast majority of the TB burden in the Region occurs in 18 high-priority countries which are responsible for 87% of the TB incidence, 87% of the prevalence, 92% of the mortality caused by TB, 91% of TB/HIV co-infections and 99% of MDR-TB.

The WHO Regional Office for Europe, together with a wide range of partners, has been implementing the Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant Tuberculosis since September 2011 in order specifically to address the alarming problem of MDR-TB throughout the Region.[2] This Plan, which is aligned with the Global Plan to Stop TB 2011–2015, aims to contain the spread of drug-resistant TB by achieving universal access to prevention, diagnosis and treatment in all Member States. Specific targets to be met by 2015 include: to decrease the proportion of MDR-TB patients among retreatment cases by 20%, to diagnose at least 85% of all estimated MDR-TB patients and to successfully treat at least 75% of MDR-TB cases.

A key initiative of the Stop TB Partnership is the Global Drug Facility (GDF), which aims to increase access to high quality first- and second-line anti-TB drugs, diagnostics equipment (and related supplies) for implementation of the Stop TB Strategy by linking the demand for drugs to supply and monitoring, simplifying drug management, and strengthening TB programme performance.

[1] Global Tuberculosis Report 2013. Geneva: World Health Organization; 2013 (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf, accessed 28 November 2014).

[2] Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant Tuberculosis in the WHO European Region 2011–2015. Copenhagen: WHO Regional Office for Europe; 2011 (http://www.euro.who.int/__data/assets/pdf_file/0014/ 152015/e95786.pdf?ua=1 2014, accessed 2 December 2014).

Unlike individual organizations and country programmes, the GDF is able to leverage the extensive size of the Partnership network to implement a pooled procurement programme, through which countries with insufficient procurement capacity are able to obtain drugs and diagnostics equipment at low prices that result in considerable savings.

The GDF provides TB drugs to countries that could otherwise not afford them. It offers assistance to 15 of the 18 high-priority countries in the Region.

The Global Fund has helped to accelerate case detection and successful treatment in recent years, with 9.7 million new smear-positive TB cases detected and treated through its support globally between 2002 and the end of 2013. The Global Fund provides almost 90% of all international financing for TB, thus contributing substantially to procurement and supply management in WHO European Member States

In order to provide comprehensive information on policies and procedures for procurement and supply management of anti-TB medicines in high-priority countries, the Regional Office designed and sent out a questionnaire to the 13 countries with the highest need for external support – Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Romania, the Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan. The resulting country-level reports were the basis for this regional report.

Throughout the Region, main regulatory bodies governed by the respective ministries of health exist with legal powers comprising marketing authorization mechanisms (regulation). Although individual marketing authorizations procedures differ between countries, the registration of all pharmaceutical products on the market is required in all countries. Medicines are always registered by international proprietary name (INN) or brand name + INN, and registration procedures usually require a fee to be paid and, on average, take between three and seven months. Registration waivers and exceptions are, however, available in every country assessed in this study, albeit on different grounds. Drugs provided as humanitarian aid or procured in case of emergencies are the most common reasons for exceptions to be made.

All countries have a medicine law and/or medicine policies, including provisions for pharmacovigilance. These generally encompass safety monitoring of medicines and mandatory reporting of adverse drug effects (ADR). Standard forms and national ADR databases do not, however, exist everywhere, and the reporting of ADRs to the Global WHO ADR database in Uppsala is not always a routine procedure. National essential medicines lists or formularies in line with the WHO Essential Medicines List are available in most countries except Georgia and Romania, although certain fixed-dose combinations (FDC) and paediatric formulations are not included in the national essential medicines lists in Belarus, Kazakhstan, Romania, the Russian Federation and Ukraine.

All countries have a national procurement policy or a public procurement law, generally including a variety of operational principles of good pharmaceutical procurement, ranging from three out of 10 possible options in Kyrgyzstan to nine out of 10 in Azerbaijan, Kazakhstan and the Republic of Moldova. The most commonly applied principles are the application of competitive methods, procurement based on a national essential medicines list or formulary, and transparency management, all of them adopted in 12 countries. In contrast, only six countries make supplier prequalification a prerequisite for the public procurement of medicines.

Most countries use either external sources, such as Global Fund and GDF grants, or a combination of the public/central budget and other sources for the procurement of TB medicines. First-line drugs are quite frequently at least partly funded by the public budget, but second-line drugs are in most cases funded with external support. Among the countries surveyed, the Russian Federation is the only country that does not use any outside funding, while Armenia, Georgia, Kyrgyzstan, Tajikistan and Uzbekistan rely solely on external resources for first- and second-line drugs. Procurement systems vary widely between countries: half of the countries still lack standard operating procedures for medicines procurement, and Armenia and Georgia do not have a tool to forecast TB drug needs. In addition, buffer stocks for the procurement of second-line drugs in order to avoid drug shortages are mandatory by regulation only in Armenia, Belarus, Kazakhstan, Turkmenistan, Republic of Moldova, Russian Federation, Ukraine and Uzbekistan, and the amounts required vary widely. The majority of countries use open tender as the main procurement method, but a wide range of other methods is also usually available. In addition to registration in countries that procure the medicines, in most cases the drugs procured need to be registered in the country of origin, but compliance of producers with good manufacturing practice is not mandatory in Azerbaijan, Belarus and the Russian Federation.

Quality assurance systems differ considerably between countries. While marketing authorizations for medicines in all countries except Kyrgyzstan require adherence to good manufacturing practice, manufacturers are not always inspected. Post-marketing quality control provisions are reported to be in place everywhere except Georgia, but procedures vary and there are no requirements and standard procedures for collecting samples from TB medicines stocked in hospital pharmacies and warehouses in Georgia, the Republic of Moldova and Uzbekistan.

Good distribution practice and standard operating procedures for handling the import, transport, storage and distribution of TB medicines are in place in only half the countries. A system of product recall in case of quality issues has, however, been implemented in all countries except Georgia and the Republic of Moldova. The systems and frequencies of distribution differ between and within countries and are usually dependent on the level of the supply system and the drugs in question. While first-line drugs are delivered to regional levels mostly on a quarterly basis using a push system, the distribution of second-line drugs usually relies on pull systems with higher delivery frequencies. However, alternative schemes and systems do exist due to the varying degree of decentralization in different countries.

Selection of TB medicines is based on standard treatment guidelines, which are generally in line with international recommendations. Minor variations include the recommendation for FDCs, which are completely omitted from standard treatment guidelines in, for example, Azerbaijan, and the use of paediatric formulations, which are not routinely used in Azerbaijan, Belarus, Georgia, Romania or Ukraine. Deviations with respect to second-line drugs used for treatment are usually caused by the unavailability of certain drugs in some countries, either as a result of budgetary constraints or of obstacles to procurement such as missing marketing authorizations.

The management of side-effects of treatment with TB medication is handled quite differently. Side-effects are monitored but not always reported. Only in Armenia, Belarus, Kyrgyzstan, the Republic of Moldova and Ukraine is a central register for ADR in use. Ancillary drugs are not always available, although there are protocols for the treatment of side-effects in all countries except the Russian Federation, where they exist only in a few regions. In addition, patients usually have to pay for these drugs out of pocket, particularly those undergoing ambulatory treatment.

In contrast to international recommendations, anti-TB drugs, including some second-line drugs, are freely available from pharmacies in Armenia, Georgia, Kazakhstan, Kyrgyzstan, the Russian Federation and Ukraine, usually without a prescription and/or for inadequate indications.

All countries have registers for drug-sensitive TB as well as for DR-TB and a dedicated unit or person for TB drug management. TB drug management information systems exist throughout the Region. In most countries, these systems contain information about shelf life/expiry date and expired products, but the level of detail included depends on the level of the supply system – central, regional or local.

Several potential problems based on the findings of the survey should be highlighted. First, although systems for market authorization, drug procurement and supply and TB treatment are in place in all countries, usually based on international recommendations, the degree of successful implementation and the efficiency of some of these systems can be questioned. Second, national guidelines with respect to quality assurance, monitoring of suppliers and pharmacovigilance are quite frequently inadequate, and useful tools for medicine forecasting are sometimes lacking. Third, storage and laboratory capacities for testing the quality of medicines are in many countries still insufficient. Fourth, the use of available medicines is not always rational, patient compliance with treatment is generally too low and the management of side-effects needs improvement in most countries. Fifth, funding in some countries relies almost exclusively (or to a large degree) on external sources, and the lack of public/central funding will most likely have severe implications for national TB programmes in the future.

On the basis of the challenges and problems observed throughout the Region, some recommendations are made for future consideration.

Introduction

Although TB prevalence and incidence rates are decreasing globally and mortality rates continue to decline, TB remains a major global health problem, particularly in view of the high prevalence of drug-resistant TB. Multi- and extensively drug-resistant TB (M/XDR-TB) requires expanded treatment with more expensive and problematic second-line drugs. The continuous availability of quality-controlled drugs is, therefore, a prerequisite for the successful treatment of MDR-TB patients in order to prevent the further spread of TB and, in particular, of drug-resistant TB *(1)*. It is also essential that an increased capacity to diagnose M/XDR-TB be matched with supplies of quality drugs and scaled-up country capacity to deliver effective treatment and care, so as to ensure the effectiveness of national TB treatment programmes *(2)*.

The WHO European Region has the highest proportion of M/XDR-TB cases in the world and, consequently, the lowest treatment success rates globally. The majority of these cases in the Region are concentrated in 18 high-priority countries in eastern Europe and central Asia, where poor access to and misuse of essential medicines and medical supplies potentially jeopardize the effectiveness of TB control programmes *(2)*. Since 2001, initiatives such as the Global Drug Facility, the Global Fund to Fight Aids, Tuberculosis and Malaria and the Green Light Committee[1] have emerged and have led to dramatic increases in funding for TB control, improvements in the availability and accessibility of quality anti-TB medicines, and increased access to technical assistance to the countries in question and support for developing their capacities. Despite these gains, many countries still struggle with stockouts of first- and second-line TB medicines and thus the provision of uninterrupted treatment. In addition, the rational use of anti-TB medicines of assured quality, efficacy and safety is a challenge in some countries because of problems such as poor planning of the pharmaceutical management cycle, errors in quantification of TB medicine needs and forecasting, poor inventory management, and a lack of monitoring and evaluation systems.

Comprehensive information on policies and procedures for the procurement and supply of anti-TB drugs in high-priority countries is needed in order for countries to be provided with further and more efficient technical assistance for ensuring an uninterrupted supply of the necessary first- and second-line drugs to TB patients. As these data were not previously available, the primary objective of this report was to collect comprehensive data on procurement and supply management in the high MDR-TB priority countries in the Region.

Epidemiological situation of TB and M/XDR-TB in the WHO European Region

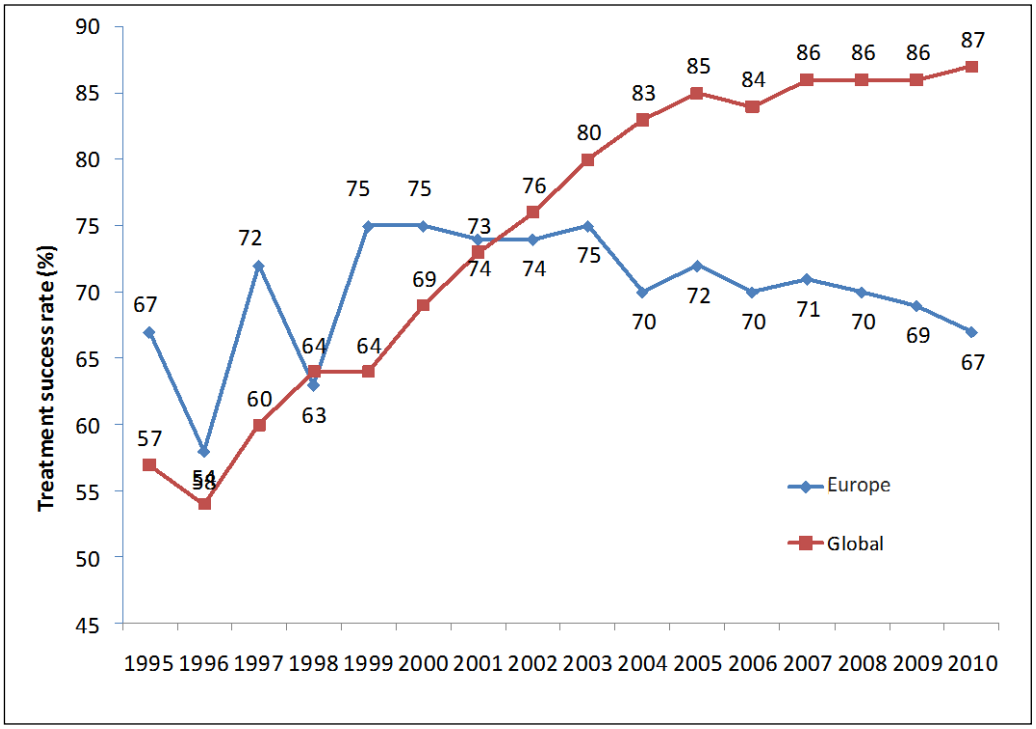
During the past decade, the absolute rate of TB in the Region has decreased in line with the targets in the Millennium Development Goals. In 2012, the average regional incidence rate was 42 per 100 000 population *(3)* compared with the global rate of 122 per 100 000 population *(2)*, albeit with substantial differences among and within countries. Of an estimated 380 000 new cases, 295 968 (approximately 78%) were detected in 2011, accounting for approximately 4.4% of the world's TB cases. Rapid detection methods for TB have recently been introduced in some countries within the Region so as to further improve the detection rates *(3)*.

[1] A technical body including WHO and partners that provides assistance, with support from the Global Fund, for developing national capacity to manage second-line drugs.

Nevertheless, despite the progress made, the Region has the highest proportion of M/XDR-TB cases in the world. In 2011, there were an estimated 78 000 cases of MDR-TB, of which 29 473 (38%) were detected. The prevalence of MDR among new and previously treated TB cases in the Region was 14% and 47.7%, respectively, and approximately 11% of MDR-TB cases tested for second-line drugs susceptibility in the Region had XDR-TB. Coverage of testing for resistance to second-line drugs is, however, still at a very low level (approximately 9% of MDR-TB cases) *(3)*.

Since 2005, a gradual decrease in treatment success has been observed (Fig. 1). Success rates are now down to 67.2%, 49.2% and 48.5% among new, previously treated and MDR-TB cases, respectively. The decrease in the first two of the three cohorts is mainly related to an increase in the proportion of MDR-TB among them. In the third cohort, the trend might be due to a rapid increase in reporting coverage to nearly double that of 2010 (from almost 7000 to over 12 000) and the lack of quality-assured administration of second-line drugs according to the most efficient regimens recommended by WHO *(3)*.

Fig. 1. Treatment success for new smear-positive cases in the WHO European Region and globally (%)



By far the largest proportion of the TB burden occurs in the 18 high-priority countries of the Region *(4)* (87% of the incidence, 87% of the prevalence, 92% of the mortality caused by TB, 91% of TB/HIV co-infections and 99% of the MDR-TB) (Table 1).

The WHO Regional Office for Europe, together with a wide range of partners, has been implementing the Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant Tuberculosis since September 2011 specifically in order to address the alarming problem of MDR-TB throughout the Region *(5)*. The Plan and its accompanying resolution EUR/RC61/R7 *(6)* were endorsed by all 53 Member States at the sixty-first session of the WHO Regional Committee for Europe in Baku, Azerbaijan.

Table 1. Estimated annual incidence of MDR-TB in the 18 high-priority countries in the WHO European Region compared to high MDR-TB countries in other WHO regions

Countries	Estimated annual incidence of MDR–TB	Estimated TB cases with MDR–TB out of the total notified (%)	
	Cases (95% confidence interval)	Newly treated (95% confidence interval)	Previously treated (95% confidence interval)
High MDR–TB burden countries in the WHO European Region			
Armenia	250 (220–280)	9 (7–12)	43 (38–49)
Azerbaijan	3 400 (3 200–3 700)	22 (19–26)	56 (52–60)
Belarus	2 000 (1 900–2 100)	32 (30–35)	75 (72–79)
Bulgaria	120 (90–150)	2 (1–3)	26 (19–33)
Estonia	100 (83–120)	23 (17–29)	58 (43–71)
Georgia	760 (700–820)	11 (10–12)	32 (28–35)
Kazakhstan	8 200 (8 000–8 400)	30 (29–32)	51 (50–53)
Kyrgyzstan	1 500 (1 400–1 700)	26 (23–31)	52 (45–58)
Latvia	120 (96–140)	13 (10–16)	29 (20–40)
Lithuania	360 (320–390)	13 (11–15)	50 (45–56)
Republic of Moldova	1 600 (1 500–1 700)	19 (17–22)	64 (60–67)
Romania	850 (650–1 000)	3 (2–4)	11 (8–15)
Russian Federation	44 000 (40 000–48 000)	20 (18–22)	46 (41–52)
Tajikistan	1 000 (910–1 200)	13 (10–16)	54 (48–59)
Turkey	560 (240–880)	1 (0–3)	38 (15–65)
Turkmenistan	0	4 (1–10)	18 (11–27)
Ukraine	9 500 (8 700–10 000)	16 (14–18)	44 (40–49)
Uzbekistan	3 000 (2 700–3 400)	23 (18–29)	62 (52–71)
High MDR–TB burden countries in other WHO regions (top 3)			
India	66 000 (58 000–73 000)	2 (1–3)	15 (13–17)
China	61 000 (54 000–68 000)	6 (5–7)	26 (22–30)
Philippines	11 000 (8 000–13 000)	4 (3–6)	21 (14–29)

Source: European Centre for Disease Prevention and Control *(3).*

With six cross-cutting strategic directions designed to safeguard the values of the Health 2020 strategy, the Plan aims to contain the spread of drug-resistant TB by achieving universal access to prevention, diagnosis and treatment of M/XDR-TB in all Member States. Its seven areas of intervention are aligned with the Global Plan to Stop TB 2011–2015, and include the following specific targets to be met by the end of 2015: (i) decrease by 20% the proportion of MDR-TB among retreatment patients; (ii) diagnose at least 85% of all estimated MDR-TB patients; and (iii) successfully treat at least 75% of all patients notified as having MDR-TB *(5).*

The continuous availability of quality-assured medicines is a prerequisite to address the last target of the Action Plan, namely to ensure the optimal clinical management and successful treatment of MDR-TB patients *(1).*

Procurement and supply management for first- and second-line TB medicines in regional high-priority countries

With regard to all medicines, the 2001 World Health Assembly resolution WHA 54.11on the WHO medicines strategy identified four main objectives: to frame and implement policy; to ensure access; to ensure quality, safety and efficacy; and to promote the rational use of medicines *(7).* The WHO Medicines Strategy 2008–2013 covers these objectives and aims to support all health-related Millennium Development Goals *(8,9).*

In the light of current trends in MDR-TB, it is essential to increase the capacity to diagnose MDR-TB in high-priority countries, to ensure the uninterrupted supply of adequate amounts of quality drugs, and to scale up countries' capacity to deliver effective treatment and care *(2)*. In January 2006, the Stop TB Partnership launched the Global Plan to Stop TB 2006–2015 which provides a roadmap for scaling up prevention and treatment. A principal mechanism developed to achieve the goals of this Plan is the Global Drug Facility (GDF). The GDF is designed to "provide TB drugs to countries that could otherwise not afford them, either in the form of grants or at the lowest possible price" *(10)*. The GDF operates according to a unique set of principles and offers a range of services, including technical assistance in TB drug management and the monitoring of TB drug use, as well as procurement of high-quality TB drugs at low cost *(10,11)*.

By 2011, 15 of the 18 high-priority countries in the Region as well as Bosnia & Herzegovina, Serbia and the former Yugoslav Republic of Macedonia (non-priority countries with lower burdens of disease) were receiving GDF assistance. Latvia, Lithuania and Turkey, although high-priority countries, did not receive assistance due to eligibility criteria (see below) *(12)*. In GDF-supported countries, drug procurement procedures are centralized through the GDF for medicines procured through grants or direct procurement mechanisms. Drug costs are lower and the availability of first- and second-line drugs is guaranteed according to the financial resources obtainable. Procurement of second-line drugs is carried out in consultation with the regional Green Light Committee mechanism *(1)*.

Technical note on data collection

In order to collect comprehensive information on policies and procedures for procurement and supply management of anti-TB drugs in high-priority countries, a questionnaire was developed by the Regional Office TB and M/XDR-TB Programme in collaboration with the Health Technologies and Pharmaceuticals Programme (Annex 1). This questionnaire was sent to WHO country offices, ministries of health and medicines regulatory authorities in high-priority countries in the Region where TB treatment is inadequate and which are most likely to need further support in optimizing the capacity of their national TB programmes, including for drug procurement and supply. Bulgaria and Estonia (although recipients of GDF assistance) as well as Latvia, Lithuania and Turkey were, therefore, excluded from this survey, as the drug management of TB cases in these countries is already considered adequate.

Data collection occurred between September and December 2013 with assistance from national procurement agencies, pharmacovigilance units, national TB programmes and Global Fund principal recipients. Using this data collection tool, country-level reports were developed by collating additional information from GDF monitoring mission reports, Green Light Committee monitoring mission reports, WHO pharmaceutical sector country profile reports and other recent WHO country reports, so as to present a detailed overview of existing TB procurement and supply management systems.

The results presented in this analysis are based on the procurement and supply management data collection tool and individual procurement and supply management country level-reports. The countries surveyed for this report were: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Romania, Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan.

Review of procurement and supply management in 13 high MDR-TB priority countries in the Region

Regulation of the pharmaceutical sector

Main regulatory bodies

The main regulatory authorities and governing bodies are shown in Table 2. Most of the 13 countries surveyed have a drug regulatory authority which is part of the ministry of health. In Armenia, Azerbaijan, Kyrgyzstan and the Republic of Moldova, the medicines regulatory authorities are semi-autonomous agencies under the Ministries of Health. In Belarus, the Ministry of Health itself functions as the official main regulatory authority.

Table 2. Main regulatory authorities and governing bodies

Country	Regulatory authority	Governing body
Armenia	Scientific Centre of Drug and Medical Technology Expertise	Ministry of Health
Azerbaijan	Analytical Expertise Centre of Medicines	Ministry of Health
Belarus	Ministry of Health	
Georgia	State Regulation Agency for Medical Activities	Ministry of Labour, Health and Social affairs
Kazakhstan	National Expertise Centre for Medicines	Ministry of Health
Kyrgyzstan	Department of Drug Supply and Medical Equipment	Ministry of Health
Republic of Moldova	Medicines and Medical Devices Agency	Ministry of Health
Romania	National Medicines and Medical Devices Agency	Ministry of Health
Russian Federation	Department of State Regulation of Medicines Supply	Ministry of Health
Tajikistan	State Supervision Service for Pharmaceutical Activity	Ministry of Health and Social Protection of Population
Turkmenistan	State Centre on Drugs Registration	Ministry of Health and Medical Industry
Ukraine	State Enterprise National Expert Centre	Ministry of Health
Uzbekistan	Head Department of Drug and Medical Products Quality Control	Ministry of Health

All 13 countries have legal provisions establishing the powers and responsibilities of the main regulatory bodies; these comprise marketing authorizations mechanisms (registration) and medicine laws and policies, including pharmacovigilance regulations.

Marketing authorization (registration)

In *Armenia*, legal provisions require marketing authorizations for all pharmaceutical products on the market, but registration waivers are available for drugs procured through the GDF. Medicines are registered by international non-proprietary (INN) name + brand name, and a fee is payable for market authorization based on the application procedure. For medicines procured through the GDF, however, no registration fee for the applicant is required although state tax is payable. Registration procedures may take up to six months, with possible acceleration for drugs prequalified by WHO and drugs with pre-existing stringent regulatory authority (SRA) registrations.

In *Azerbaijan*, legal provisions require marketing authorizations for all pharmaceutical products on the market, with the exception of drugs needed for humanitarian purposes, rare medicines and medicines used to cure diseases that require specific treatment, as well as for WHO prequalified

drugs. Medicines are registered by INN + brand name and a fee is payable for market authorization. Registration procedures can take up to seven months.

In *Belarus*, marketing authorizations are required for all pharmaceutical products, although exemptions are available for humanitarian aid. Registration is waived for drugs procured through the GDF. The Centre for Examination and Tests in the Health Service under the Ministry of Health is responsible for the assessment of all applications. There are no provisions for the acceptance of WHO prequalified medicines or SRA-registered products.

In *Georgia*, registration is required for all pharmaceutical products on the market, with exceptions in special conditions such as epidemics or for the treatment of rare diseases. Registration is also waived for drugs procured through the GDF. Medicines are registered by INN + brand name and a fee is payable. The registration procedure can take up to three months. There are no provisions for acceptance of WHO prequalified medicines, but registrations done by EU countries are recognized. A fast-track mechanism for registration of prequalified products is being developed.

In *Kazakhstan*, all medicines on the market have to be state registered and subsequently certified. Exceptions and waivers exist for orphan drugs as well as for medicines arriving as humanitarian aid, including drugs procured by the GDF. A fee is payable for state registration. The assessment of applications may take up to seven months.

In *Kyrgyzstan*, registration is required for all pharmaceutical products on the market. Special permissions for the import of non-registered drugs are possible on humanitarian grounds, such as for medicines procured through the GDF. However, all imported drugs need to be certified based on quality control procedures. Medicines are registered by INN + brand name. The registration process, for which a fee is payable, may take up to six months, although simplified fast-track registration is available for WHO prequalified medicines.

In the *Republic of Moldova*, legal provisions require marketing authorizations for all pharmaceutical products on the market, issued by the Ministry of Health on the basis of a recommendation from the Medicines Commission of the Medical and Medical Devices Agency. Exemptions and waivers exist, for example in cases of catastrophe and epidemics, for drugs registered in their countries of origin, although there are no general mechanisms for recognition of WHO prequalifications or registrations done in other countries. Medicines are always registered by INN + brand name, and a fee is payable for the application procedure which may take up to three months.

In *Romania*, all pharmaceutical products require marketing authorizations, although registration waivers are available to accommodate special needs, as well as in the case of emergencies, such as epidemics. Exemptions are also made for drugs procured through the GDF. In line with EU regulations, registrations made with the European Medicines Agency via a centralized procedure are recognized.

In the *Russian Federation*, legal provisions require all pharmaceutical products to be registered. The import of non-registered medicines in emergencies is possible but subject to authorization by the Ministry of Civil Defence, Emergencies and Disaster Relief. Medicines are registered by INN + brand name, and a fee is payable for the application. Procedures may take up to seven months. There are no mutual recognition procedures for medicines, with the exception of Belarus and Kazakhstan.

In *Tajikistan*, marketing authorizations are required for all products on the market, although registration waivers are available in cases of natural disasters and for drugs imported as humanitarian aid. Medicines are registered by INN + brand name, and a fee is payable. The application procedure may take up to six months. There is, however, a fast-track registration mechanism in place for products received from international organizations and for medications used to treat certain diseases such as TB and AIDS. This procedure may only take up to three months and is free.

In *Turkmenistan*, registration is required for all pharmaceutical products on the market, with exceptions granted for medicines imported as humanitarian aid on a case-by-case basis, including drugs procured through the GDF. Registration waivers are also available in emergency situations such as epidemics and natural disasters. Medicines are registered by INN + brand name, and an application fee is payable. The procedure usually takes up to three months but accelerated processing of registration is possible.

In *Ukraine*, only medicines registered in the country can be placed on the market, with exceptions in, for example, cases of natural disasters, catastrophes and epidemics. However, due to quarantine rules for non-registered products, drugs procured through the GDF have not been used previously although a registration waiver has been issued. Medicines are registered by INN + brand name, and a fee is payable. The rather complicated application procedure may take up to seven months. In order to improve availability of high-quality drugs for TB and other priority diseases, an amended assessment procedure is being implemented for WHO prequalified medicines with accelerated processing time and reduced fees.

In *Uzbekistan*, registration of all medicines on the market is required but one-time waivers can be issued for purposes of humanitarian aid, including drugs procured through the GDF. Exemptions are also available in case of emergencies such as epidemics and natural disasters. Nevertheless, all non-registered imports need to be certified based on quality testing and then approved by the government. Medicines are registered by INN + brand name. The application procedure, for which a fee is payable, usually takes between three and six months but may be accelerated in special circumstances.

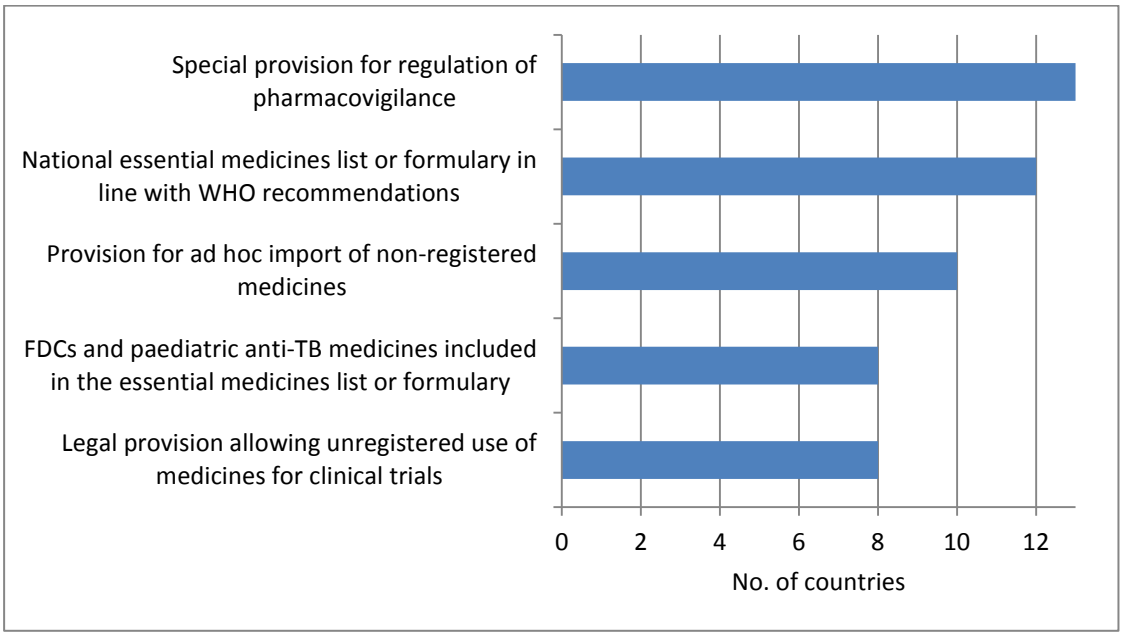
Laws and policies regarding medicines

All 13 high-priority countries have a medicines law regulating the manufacture, marketing authorization, import, distribution and post-marketing surveillance of drugs. Policies vary, however, especially with regard to the use of unregistered drugs and the use of national essential medicines lists (Fig. 2).

Turkmenistan and Uzbekistan do not have a provision for the ad hoc import of non-registered medicines for the period until they are registered. Azerbaijan does not have a provision allowing unregistered use of medicines for clinical trials, which are usually a prerequisite for medicines to be registered in the respective country.

All countries generally have provisions for the regulation of pharmacovigilance, encompassing the safety monitoring of medicines and mandatory reporting of adverse drug reactions (ADRs). Most countries have standard forms for reporting ADRs as well as ADR databases, although their efficiency differs and the number and quality of reports are inadequate. Tajikistan and Turkmenistan are not members of the Global Drug safety monitoring programme, and Azerbaijan and Georgia are only associate members.

Fig. 2. Summary of policies for regulation of the pharmaceutical sector



All countries except Georgia and Romania have national essential medicines lists or drug formularies in line with the WHO Essential Medicines List, including first- and second-line drugs. However, fixed-dose combination (FDC) (two, three and four FDCs) and paediatric anti-TB drugs are not included in the national essential medicines lists of Belarus, Romania, the Russian Federation and Ukraine.

Regulation of medicines procurement

Currently all 13 countries have a national procurement policy or a public procurement law, and all countries' regulations on procurement of essential medicines include operational principles of good pharmaceutical procurement. However, the range of the principles applied varies between countries (Fig. 3).

The principles of good pharmaceutical procurement implemented in each of the 13 countries are shown in Table 3. The number of principles currently implemented ranges from three out of 10 in Kyrgyzstan to nine out of 10 in Azerbaijan, Kazakhstan and the Republic of Moldova. Although the use of competitive methods for public procurement of medicines is almost universal, most countries also have provisions for other methods, usually for direct procurement in special cases. In the Russian Federation, Turkmenistan and Uzbekistan non-competitive procurement methods are not, however, explicitly regulated.

Procurement of TB medicines

Most countries use either an external source, such as Global Fund grants, or a combination of public/central budget and other sources to procure TB medicines (Fig. 4). The Russian Federation uses only public budgetary funds (including federal sources and regional budgets) for the procurement of first- and second-line drugs. Azerbaijan and Belarus use only central budgetary funds for procurement of first-line drugs.

Fig. 3. Principles of good pharmaceutical procurement

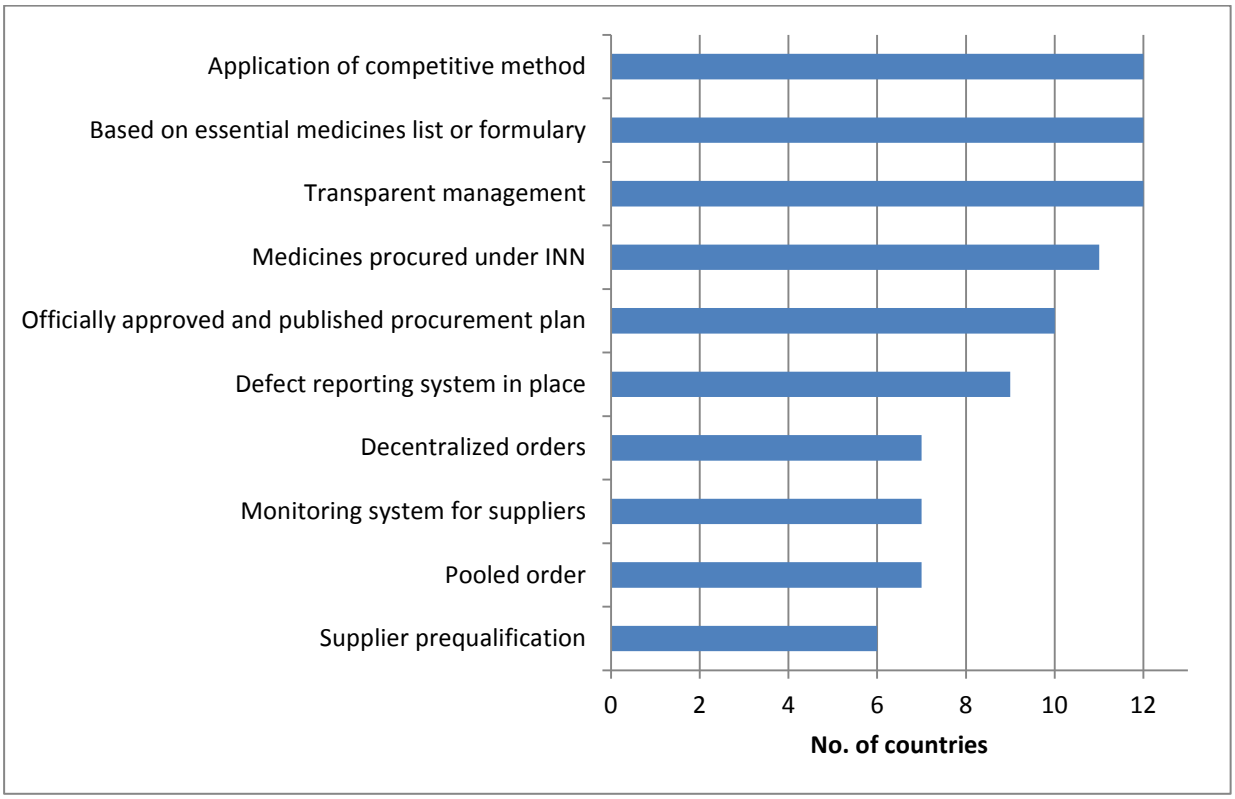
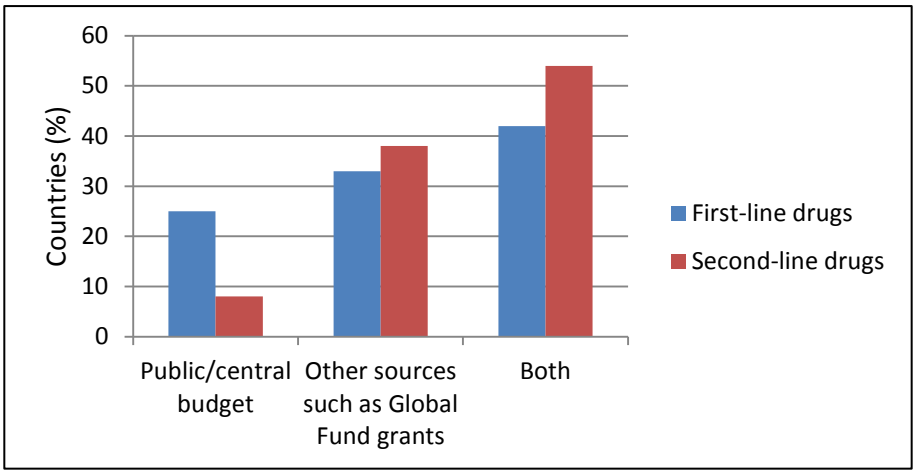


Fig. 4. Sources of supply and procurement of TB medicines



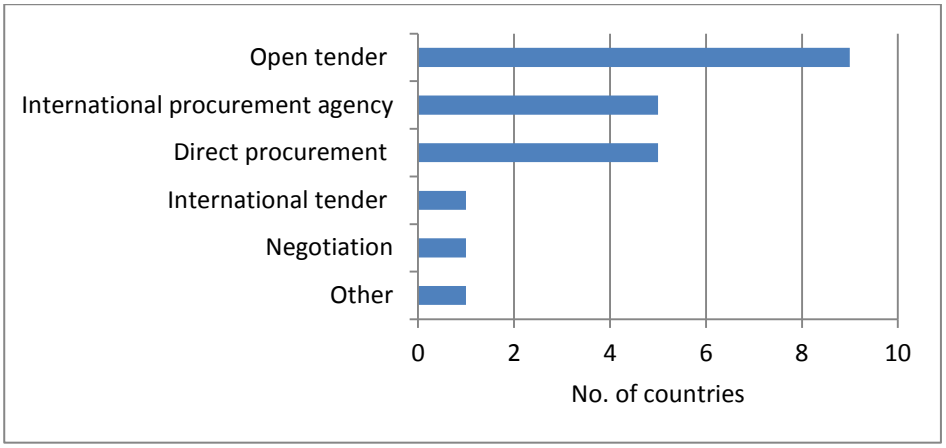
Procurement systems for TB drugs vary widely between countries. Half of the countries – Azerbaijan, Republic of Moldova, the Russian Federation, Tajikistan, Ukraine and Uzbekistan – have no standard operating procedures, and guidelines on medicines forecasting are missing in Azerbaijan, Belarus, Georgia and Tajikistan. Nevertheless, most countries except Armenia and Georgia have a tool in place to forecast the needs for TB medicines, either manually or electronically, and six countries require a mandatory buffer stock for procurement of second-line drugs: Armenia (50%), Belarus (50%), Kazakhstan (25%), Turkmenistan (25%), Ukraine (100%) and Uzbekistan (50%).

Table 3. Principles of good pharmaceutical procurement as currently implemented in individual countries

Principles of Good Pharmaceutical Procurement	Armenia	Azerbaijan	Belarus	Georgia	Kazakhstan	Kyrgyzstan	Republic of Moldova	Romania	Russian Federation	Tajikistan	Turkmenistan	Ukraine	Uzbekistan
Transparency management (written procedures, working groups decision, advertisement)	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓
Based on EML or national formulary list	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
Pooled order (cumulative order at the national level)		✓	✓		✓		✓				✓	✓	✓
Prequalification of suppliers	✓	✓		✓			✓			✓	✓		
System of monitoring of suppliers and post qualification of suppliers		✓		✓	✓				✓	✓		✓	
Official approved and published procurement plan	✓	✓	✓	✓	✓		✓	✓		✓	✓	✓	
Competitive method applied	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Decentralized orders	✓		✓	✓	✓			✓	✓	✓			
Medicines procured under INN	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	
Defecting system in place	✓	✓	✓	✓	✓		✓		✓			✓	✓

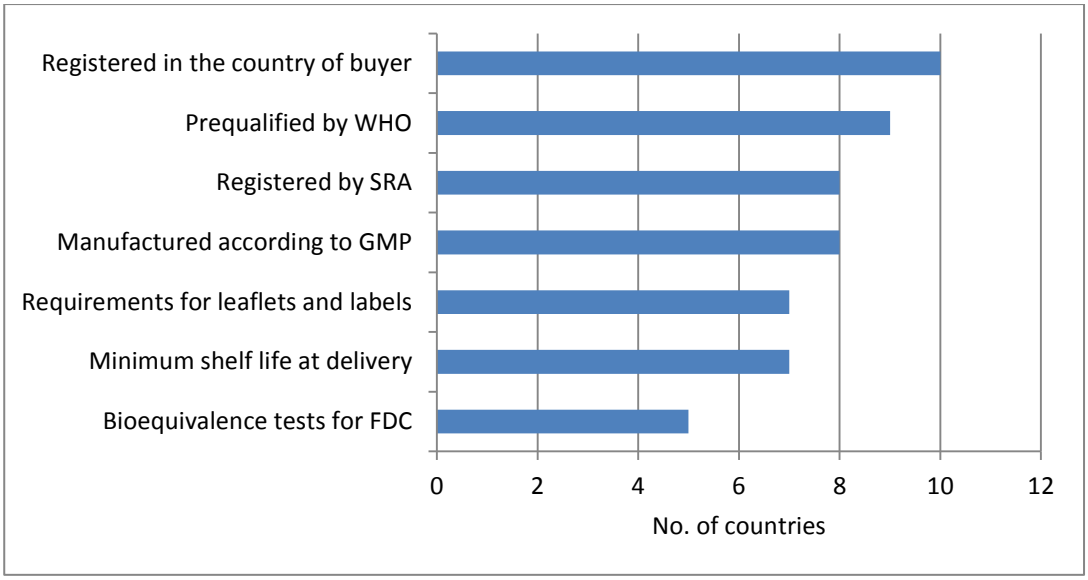
The methods used for procuring TB medicines vary across the countries, with the majority using open tender (Fig. 5). The GDF direct procurement mechanism is used by all the countries when Global Fund or other external sources of funds are available for procurement of anti-TB medicines. When funding for anti-TB medicines stems from the public budget, current regulations do not allow the procurement of drugs from international agencies.

Fig. 5. Methods used for procurement of TB medicines (not mutually exclusive)



Countries vary with respect both to the combination of special provisions they apply in the regulation of procurement of TB medicines and as regards the overall extent of procurement specifications which range from one out of seven in Kazakhstan to all seven possible options in Belarus. Every country has its own combination of regulation provisions, the most common being the requirement for a procured drug to be registered in the country of the buyer (Fig. 6). When procurement is local, TB medicines always need to be registered in the country. Compliance with good manufacturing practice (GMP) is not, however, mandatory in Azerbaijan, Belarus and the Russian Federation.

Fig. 6. Special provisions in the regulation of TB drug procurement



Mechanisms for monitoring suppliers are implemented in most countries (except Kyrgyzstan, Republic of Moldova, Tajikistan and Uzbekistan), and always include the criteria for delivering

medicines according to the terms of the contracts, respecting the schedule of delivery, assuring storage conditions during transport and respecting minimum shelf life. The criteria applied in Romania are unclear.

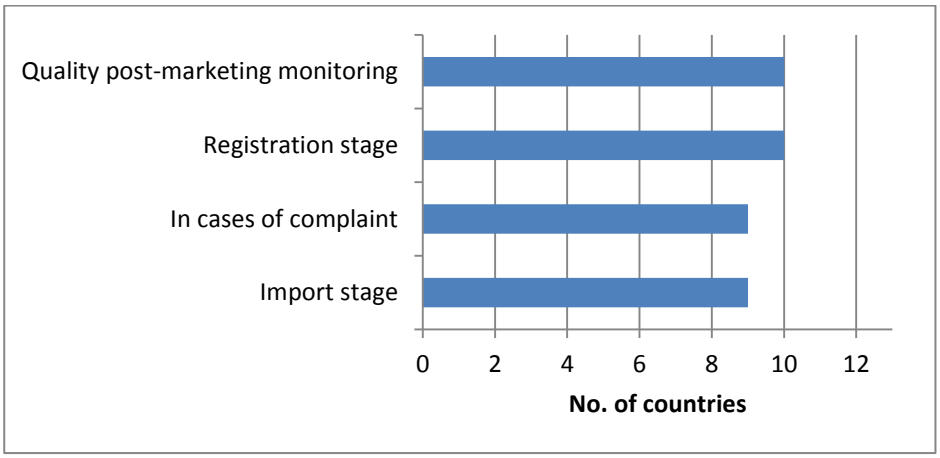
Quality assurance

Although good manufacturing practice is a legal requirement for the registration of medicines in all countries except Kyrgyzstan, manufacturers are not always inspected for GMP compliance: in most cases foreign manufacturers are inspected but local producers are only inspected in Armenia, Belarus, the Republic of Moldova, Romania, Ukraine and Uzbekistan. No quality control policies with regard to medicine production currently exist in Turkmenistan. Mandatory compliance with GMP guidelines will be introduced in the Russian Federation by 2014 and in Kazakhstan by 2015. In Armenia, Azerbaijan, Georgia and Tajikistan, no TB medicines are currently manufactured locally.

Good distribution practice is a legal requirement in Azerbaijan, Belarus, Romania, Ukraine and Uzbekistan. Armenia and the Republic of Moldova are in the process of developing provisions for good distribution practice.

Provisions for post-marketing quality control also vary between countries. Regulations for monitoring the quality of medicines, including TB medicines, are in place in almost all countries but the procedures for implementing them differ, especially as regards timing and sampling procedures for drugs to be tested. In the Republic of Moldova, medicines with funds from the Global Fund are tested at the import stage. Since the national quality laboratory is not WHO prequalified and does not have International Organization for Standardization, TB medicines are also tested at the contracted laboratory that corresponds to the Global Fund quality requirements. In Georgia, the overall lack of quality assurance provisions means that drugs are only tested in cases of complaint. In Kyrgyzstan, Romania and Tajikistan, medicines from Turkmenistan and Uzbekistan are only tested at the import and registration stages, respectively (Fig. 7). Nevertheless, in all countries receiving the Global Fund grant, quality control testing is done for samples of drugs procured through this grant according to the Global Fund quality policy.

Fig. 7. Procedures for testing medicines



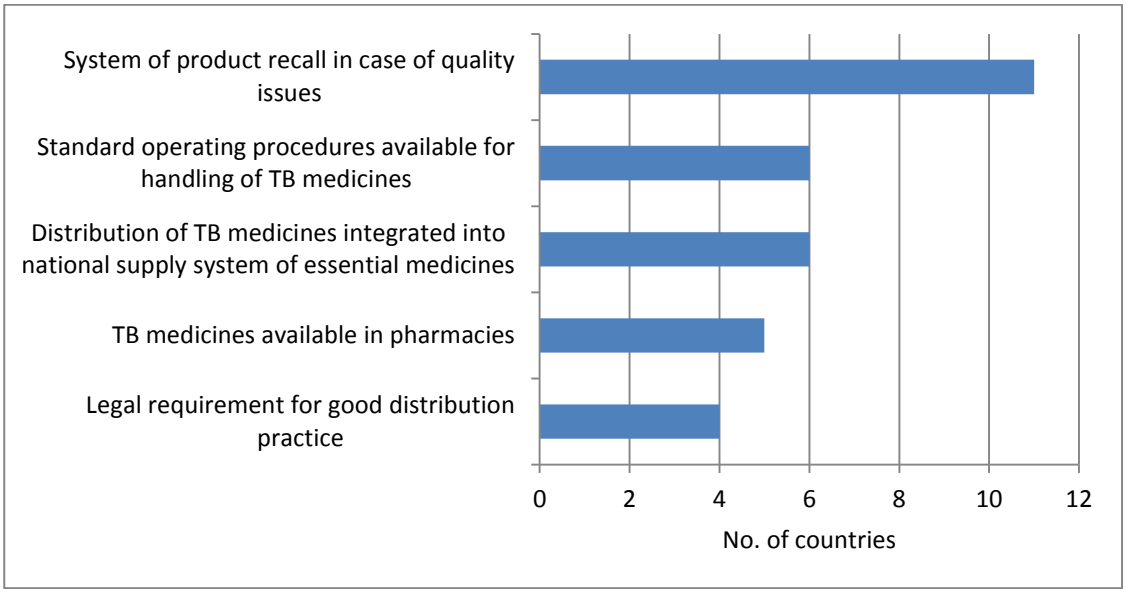
All the countries (other than Georgia and Uzbekistan) have requirements and standard procedures for collecting samples from TB medicines stocked in pharmacies or warehouses during inspections for post-marketing quality control. With the exception of Kazakhstan and the

Russian Federation, appointed inspectors are authorized to perform unexpected inspections and sampling. Testing usually takes place in appointed quality control laboratories, although not all national medicine quality testing laboratories in the countries surveyed have been accredited by international standards or prequalified by WHO.[2]

Distribution of TB medicines

The distribution of TB medicines is in general part of the overall programme management structure of national TB programmes but is not always integrated with the national supply system for essential medicines. Standard operating procedures for handling the import, transport, storage and distribution of TB medicines are only in place in half the countries: Azerbaijan, Georgia, Kazakhstan, the Russian Federation, Ukraine and Uzbekistan have yet to introduce them. All countries except Georgia and the Republic of Moldova have implemented a system of product recall in case of quality issues (Fig. 8).

Fig. 8. Summary of provisions for distribution of TB medicines

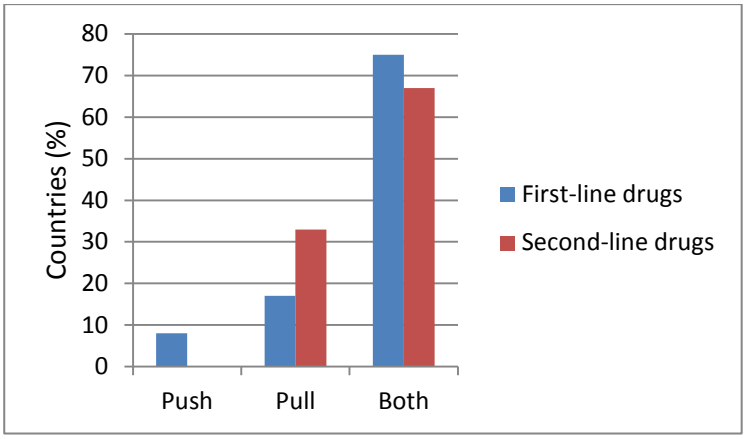


The distribution of TB medicines differs between countries, and the distribution systems as well as the distribution frequency usually depend on the level of the supply system and the drugs in question. First-line drugs are usually delivered to regional levels on a quarterly basis using a push system, and onward to local levels through a wide range of systems. The distribution of second-line drugs usually relies on pull systems with a higher delivery frequency (Fig. 9). Alternative schemes and systems do, however, exist: in Kazakhstan, annual supplies of second-line drugs and paediatric formulations are delivered to regional levels due to a lack of storage capacities for these medicines at the central level. In Ukraine, the annual distribution of TB drugs

[2] In close cooperation with national regulatory agencies and partner organizations, the Prequalification Programme aims to make quality priority medicines available for the benefit of those in need. This is achieved through its evaluation and inspection activities.

to the regional level is usually sent straight on to local levels due to a shortage of regional storage facilities. Romania does not have a centralized system, so delivery schedules are designed for each hospital individually on the basis of estimated demand for TB medicines and the available funding.

Fig. 9. Distribution systems for TB medicines



In addition to being dispensed by health personnel in TB hospitals and dispensaries or administered in primary health care facilities and through specially trained TB supervisors, TB drugs are also available free from pharmacies in Armenia, Kazakhstan, Kyrgyzstan, the Russian Federation, Ukraine and Uzbekistan, although usually without a prescription and for inadequate indications, often contrary to existing legislation.

Selection and use of TB medicines

Selection of TB medicines is usually based on national standard treatment guidelines (in all the countries) and the national essential medicines list or formulary. In most countries, national standard treatment guidelines are designed according to WHO recommendations, although some minor variations exist with regard to primarily recommended second-line drugs and the use of FDC. In addition, the registration status of medicines in the respective country is taken into consideration; thus, non-registered drugs are sometimes excluded from the national essential medicines list, potentially limiting the availability of theoretically possible treatment options.

Although FDC are recommended in all standard treatment guidelines (apart from Azerbaijan), their use is sometimes restricted usually through unavailability. This is particularly the case for paediatric FDC, which are not routinely used in Azerbaijan, Georgia, Romania and Ukraine. Azerbaijan does not procure paediatric FDCs due to funding problems. In Georgia, previously procured paediatric FDCs have not been used due to a lack of information about their use. In Romania and Ukraine, only a few FDCs are registered so that most FDCs cannot be procured or made available for use. Nevertheless, Tajikistan and Uzbekistan have comprehensively introduced patient kits providing FDC for all TB patients treated with first-line drugs (four FDC during the intensive phase and two FDC in continuation phases).

The second-line drugs recommended in existing standard treatment guidelines are generally in line with current WHO treatment guidelines. The deviations observed are usually based on budgetary limitations and/or procurement obstacles such as missing marketing authorizations. Non-recommended drugs, for example ciprofloxacin, are thus sometimes still in use, and in at least one country (Romania) separate guidelines exist for patients provided with externally funded medicines versus patients treated with drugs obtained through the central budget. Selection of second-line drugs for treatment of M/XDR-TB is based on drug susceptibility testing, whenever possible, but resources required to test for resistance to second-line drugs are scarce in many countries, resulting in the use of standardized treatments rather than individual

schemes. In addition, not all recommended second-line drugs (especially those categorized as group 5 medicines) are always available (Table 4).

Table 4. Medicines included in national standard treatment guidelines

Country	TB	MDR-TB	XDR-TB
Armenia	H, R, Z, E, S; including FDC	Z, E, Km, Cm, Lfx, Mfx, PAS, Pto, Cs, Cfz, AmxClv	E, Cm, Mfx, PAS, Pto, Cs, Cfz, AmxClv
Azerbaijan	H, R, Z, E, S; including FDC for adults but not for children	Z, Am, Lfx, PAS, Pto, Cs	Z, Cm, Mfx, PAS, Pto, Cs
Belarus	H, R, Z, E; including FDC	Z, Cm, Km, Am, Lfx, Ofx, Eto, Pto, PAS, Cs	Z, Cm, Km, Am, Mfx, Eto, Pto, PAS, Cs, Cfz, Lzd, Amx/Clv, Thz, Imp/Cln, Clr
Georgia	H, R, Z, E; including FDC; no widespread use of paediatric formulations	Z, Cm, Km, Lfx, Mfx, PAS, Pto, Cs	Z, Cm, Mfx, PAS, Pto, Cs, Cfz, Lzd, Amx/Clv, Ipm/Cln, Clr
Kazakhstan	H, R, Z, E, S; including FDC	Z, Cm, Km, Am, Lfx, PAS, Eto, Pto,Cs	Z, E, Cm, Km, Am, Mfx, Eto, Pto, PAS, Cs, Amx/Clv, Clr
Kyrgyzstan	H, R, Z, E, S; including FDC for adults and children	Z, E, Cm, Km, Lfx, PAS, Pto, Cs	Z, Cm, Am, Mfx, PAS, Pto, Cs, Amx/Clv, Clr
Republic of Moldova	H, R, Z, E, S; including FDC	Z, Cm, Ofx, Lfx, Eto, Cs	Z, Cm, Mfx, PAS, Eto, Cs, Amx/Clv, Clr
Romania	H, R, Z, E; restricted availability of FDC, no paediatric formulations	Km, Am, Cm, Ciprofloxacin, Lfx, Ofx, PAS, Pto, Cs	Km, Am, Cm, Mfx, PAS, Pto, Cs, Clr
Russian Federation	H, R, Z, E, S; including FDC (including uncommon combinations)	Cm, Am, Km, Lfx, Mfx, Ofx, PAS, Eto, Pto, Cs, Rifabutin	
Tajikistan	H, R, Z, E, S; including FDC	Z, E, Cm, Am, Ofx, PAS, Pto, Cs,	Z, E, Cm, Am, Lfx, Mfx, PAS, Pto, Cs
Turkmenistan	H, R, Z, E, S; including FDC for adults and children	Z, Cm, Km, Lfx, Pto, Cs	Z, Cm, Km, Ofx, Ciprofloxacin, PAS, Pto, Cs
Ukraine	H, R, Z, E, S; FDC included but rarely used;no paediatric formulations	Z, E, Km, Am, Cm, Lfx, Ofx, PAS, Eto, Pto, Cs, Thz	Z, E, Km, Am, Cm, Lfx, Mfx, PAS, Pto, Cs, Thz, Cfz, Lzd, Amx/Clv, Clr
Uzbekistan	H, R, Z, E, S; including FDC (HRZE, HR)	Z, E, Cm, Km, Lfx, PAS, Pto,Eto,Cs	
WHO recommendations (first- and second-line drugs, and reserve antibiotics)	H, R, Z, E, S	Am, Km, Cm; Lfx, Mfx, Ofx; PAS, Eto, Pto, Cs, Trd	Cfz, Lzd, Amx/Clv, Thz, Ipm/Cln, high-dose H, Clr

Key.

Am	Amikacin	Cm	Capreomycin	Km	Kanamycin	Pto	Protionamide
Amx	Amoxicillin	Cs	Cycloserin	Lfx	Levofloxacin	R	Rifampicin
Cfz	Clofazimine	E	Ethambutol	Lzd	Linezolid	S	Streptomycin
Cln	Cilastatin	Eto	Ethionamide	Mfx	Moxifloxacin	Thz	Thioacetazone
Clr	Clarithromycin	H	Isoniazid	Ofx	Ofloxacin	Trd	Terizidone
Clv	Clavulanate	Ipm	Imipenem	PAS	p-Aminosalicylic acid	Z	Pyrazinamide

TB treatment as set out in national standard treatment guidelines is aligned with international recommendations in all countries. Nevertheless, differences exist, and adherence to treatment according to standard treatment guidelines also differs between and within countries, especially with respect to duration of treatment and use of second-line drugs.

In line with WHO guidelines, directly observed treatment is implemented in the countries surveyed, mainly in ambulatory settings. In Kazakhstan, Kyrgyzstan, Romania, Turkmenistan,

Ukraine and Uzbekistan, however, the intensive phase at least is usually conducted within a hospital setting, with the patient referred to a primary health care facility only for the continuation phase. Support programmes to ensure patients' adherence to treatment protocols have not been fully implemented in all countries.

Side-effects of treatment with TB medicines are generally monitored but not always centrally collected or analysed. In Azerbaijan, Georgia and the Russian Federation, ADR are registered in the patient's file but not reported further. In Kazakhstan, only severe side-effects are reported. Armenia, Belarus, Kyrgyzstan and the Republic of Moldova register and analyse ADR using a centralized system. The reporting system in Ukraine is underused, while in Romania, side-effects are neither registered nor reported.

In line with international recommendations, TB drugs are available free to patients in all countries. Auxiliary drugs for the management of side-effects during M/XDR TB treatment are, however, not always available for everybody without additional cost. In Kazakhstan, Kyrgyzstan, the Russian Federation and Ukraine, these drugs are provided free for inpatients but not for outpatients. In Belarus and the Republic of Moldova all patients have to pay for them. Protocols for the treatment of side-effects are in place in all countries except the Russian Federation, but in Kyrgyzstan and Ukraine the availability of auxiliary drugs is not always guaranteed.

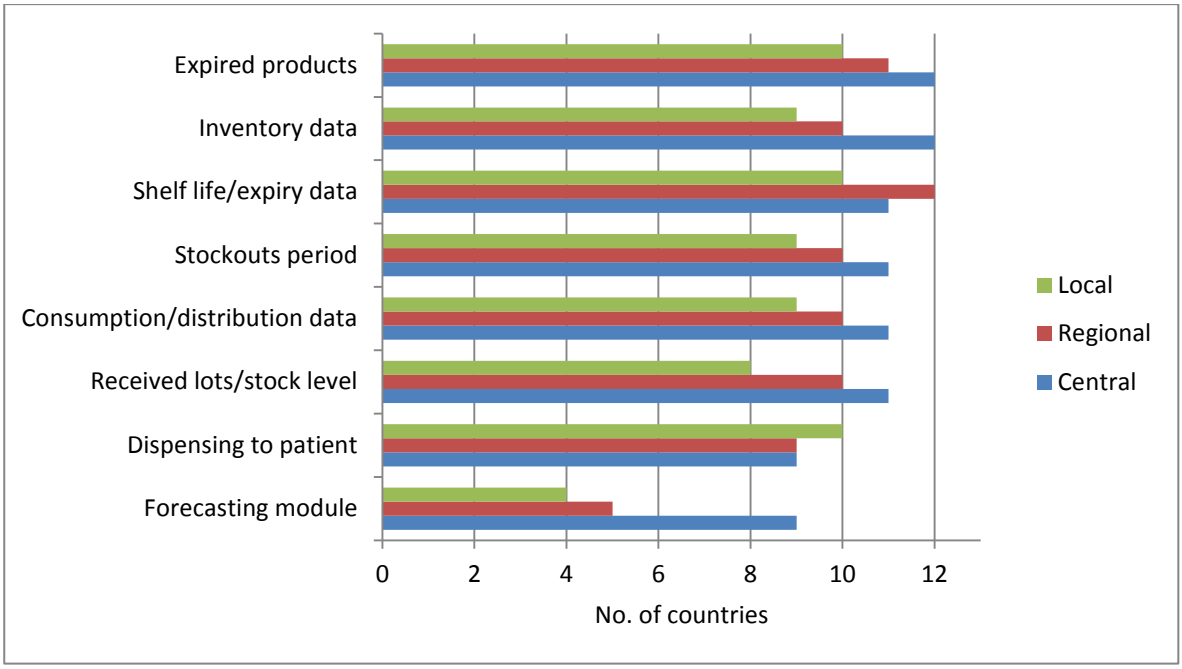
Programmatic and drug management data provisions for TB and DR-TB

National TB control programmes (NTP) are established in all countries with the exception of Georgia, which has no official NTP but does have a TB centre at the central level.

In general, NTPs are under the responsibility of the respective ministry of health. However, the organization of these programmes varies between countries, as do the responsibilities of different departments or administrative levels. While in most countries a single central organization is responsible for overall programme management and policy issues, regional TB centres in Kazakhstan, the Russian Federation and Ukraine have considerable individual responsibility. In Georgia, the recent restructuring of the health system has led to shared responsibility for the NTP by two different agencies.

A dedicated unit or person for TB drug management is appointed in all countries, either at central or regional level depending on the structure and organization of the NTP. TB drugs management information systems are also available everywhere, although these systems are paper-based in Azerbaijan and Georgia. Information about pharmaceuticals management is generally recorded at different levels of the supply system (central, regional and local), but the degree of detail differs with the most detailed information usually found in central records. Shelf life/expiry data, inventory data and expired products are the kinds of information most often recorded (Fig. 10). In addition, all countries have registers for drug-sensitive TB and DR-TB, although the data are not always disaggregated, thus limiting adequate drug management. These data are usually recorded at central, regional and local levels, with two exceptions: the Russian Federation, where no central TB register exists, and Kyrgyzstan, where data are registered centrally and regionally but not locally. In most cases, the procedures for data registration are either automated, using computerized files and/or databases, or both automated and manual. TB registration at local level is done manually in Georgia, the Russian Federation, Tajikistan and Uzbekistan, while DR-TB registration is done manually in Georgia, the Russian Federation and Tajikistan. In Turkmenistan, all registers are completed manually as automated registration procedures have not been implemented.

Fig. 10. Information recorded on pharmaceutical management, by supply system level



Discussion

Several positive aspects are highlighted in the country reports, based on the survey, which should be mentioned and discussed briefly.

Despite the differences between the countries, and sometimes the unfavourable circumstances resulting from the economic crisis and political unrest in many areas, all the countries have adopted basic laws and provisions necessary to govern the pharmaceutical sector in general and TB programmes in particular. Medicines regulatory authorities, in cooperation with national ministries of health, are present in all countries, and rules and regulations exist with respect to marketing authorizations and pharmacovigilance. Procurement and supply of medicines are based on rules adopted from international recommendations. NTPs have been both financially and technically assisted to provide centralized focal points for policy development, programme management and surveillance of operational aspects. In addition, treatment guidelines, national essential medicines lists and selection of medicines in the countries surveyed basically follow international recommendations and guidelines. Many countries have only recently adopted these guidelines, and several developments and improvements are in progress.

Most importantly, considering the high prevalence of TB and MDR-TB in the Region, all countries actively support the combined efforts of international organizations and individual governments to achieve the targets set by the Consolidated Action Plan.

Although the survey underlines the progress made so far by exemplary highlighting of existing policies and available resources for the adequate treatment of TB and MDR-TB, it also pinpoints some challenges the individual countries and, hence, the Region as a whole, still face. Some of these challenges need to be discussed further in order to understand the underlying reasons and potential problems and the implications they might have.

The main issue throughout the countries surveyed is the discrepancy between policy and practice on several levels and with respect to a variety of factors. All countries have adopted regulations for the pharmaceutical sector and procurement and supply management systems in line with international recommendations. Nevertheless, unavailability and stockouts of medicines still occur quite frequently, and medicines and supplies placed on the market as well as drugs procured through national procurement systems do not always comply with international quality requirements. Many reasons can be seen as responsible for this discrepancy, although naturally not all of them are applicable in every country. Only those crucial aspects applicable in the majority of countries will be discussed further, with mention of countries where these issues are most prominent.

The most important reasons for the inefficiency of regulatory systems are probably structural in nature. In many countries, the current legislation was implemented quite soon after the change from a collectivist-based to a market economy-based model. Some countries privatized their health care systems quickly, using existing frameworks and systems and adding some new regulations and structures. This may have led to the observable existence of parallel structures, vertically as well as horizontally. In addition, the presence of various international aid agencies and their sometimes suboptimal coordination – each with separate procurement and supply management structures and regulations – potentially exacerbates already complicated situations.

In some countries, there are separate routes for marketing authorizations for essential and non-essential medicines (for example, Tajikistan and Ukraine), and exceptions are sometimes made for locally produced medicines in order to foster national pharmaceutical industries (for example, Belarus, Kazakhstan, the Russian Federation, Turkmenistan and Ukraine). Parallel structures for the procurement of drugs based on the country of origin, source of funding or registration status are prevalent in almost all countries. An example is the existence of parallel and, in some cases, completely unrelated procurement structures for first-line drugs on the one hand and second-line drugs on the other, which might be due to the use of funding from a variety of external sources and the involvement of several external partners. In many countries, first-line drugs are procured using governmental funds, while second-line drugs are procured using Global Fund grants or other bilateral external sources, effectively resulting in two separate routes for selection, procurement, supply, storage and distribution based on divergent requirements. This puts a further strain on already strained resources.

Additional bureaucratic requirements in some cases prevent prompt customs clearance (for example, Kyrgyzstan, Kazakhstan, Ukraine and Uzbekistan), and the forwarding of procured medicines from the central level to subordinate levels or between regions faces further obstacles from excessive paperwork, strict hierarchies and ambiguous responsibilities which may hamper the alleviation of drug shortages in one region by forwarding overstocks from another region. Moreover, complicated and sometimes even contradictory regulations and policies inhibit the accessibility and availability of certain drugs. While a product procured with external grants may, for instance, be exempt from registration in a country, this might not be the case when procurement is with public funds. In addition, even though a registration waiver may exist, thus enabling the import of unregistered medicines into the country, the use of this medicine for the treatment of patients may still be impossible on legal grounds, or the financial coverage of this medication by national health insurances might not be guaranteed (as in, for example, Kazakhstan, Romania and Ukraine).

Most countries seem to lack monitoring and evaluation of processes and outcomes and thus the adjustment of insufficient or inadequate procedures and methods. The introduction of structural

and organizational surveillance systems would increase the efficiency of regulatory and procurement and supply management systems, but in view of the heavy workload of most medicines regulatory authorities and NTPs, this should probably be done only when additional resources can be made available, at least temporarily. Were procedures to be simplified and bureaucracy slimmed (as recommended in many country reports), resources might be set free which could be used to maintain adequate, functional monitoring and evaluation systems.

Another problem regarding the procurement and supply management systems in several countries is the absence of regulations covering areas such as legal requirements and standard operating procedures. No standard operating procedures for either procurement or distribution of anti-TB medicines exist in, for example, the Russian Federation, Ukraine or Uzbekistan. There is no legal requirement to adhere to principles such as GMP, good pharmaceutical practice or good distribution practice in, for example, Armenia, Kazakhstan or the Russian Federation. Although laws and policies with respect to manufacturing, procurement and distribution exist in every country (at least to some extent), the implementation of legal norms and regulations remains inadequate in all the countries surveyed. Simple, practical and easy to read and follow procedures and guidelines usually increase adherence to rules and regulations and would, therefore, improve the working of the systems already in place. Fortunately, in many countries such guidelines are being developed or are in the process of being implemented. Nevertheless,to be effective, standard operating procedures and other guidelines should be mandatory, ideally include monitoring of adherence and regularly adjusted and adapted to changing circumstances.

Improved procurement and supply management depend on both legally binding guidelines and the availability of correct estimates of expected demand. Although most of the countries surveyed have tools for forecasting the demand for medicines, these are quite often not functional or inadequate (for example, in Azerbaijan and Ukraine), resulting in the procurement of inappropriate quantities of drugs. Only about half the countries have requirements with regard to buffer stocks of second-line drugs. This may hamper the continuous supply of medication to patients, leading to interruptions in care or complete treatment default with a resulting negative influence on drug resistance patterns. This might pose a serious problem, especially when plans are made to scale up drug susceptibility testing in order to increase MDR-TB case detection. Some countries already face shortages of second-line drugs due to inaccurate estimates and insufficient drug procurement (for example, Romania, the Russian Federation, Tajikistan and Ukraine), resulting in long queues for MDT-TB treatment (Azerbaijan, Kyrgyzstan, Tajikistan). Inadequate procurement is, however, not only a result of inaccurate estimates of demand: lack of funding and personnel shortages are additional challenges, as well as generally substandard organizational practices (in, for example, Tajikistan and Ukraine).

As regards TB treatment, some crucial aspects have to be highlighted. Although national essential medicines lists and standard treatment guidelines are in place in most countries and usually designed according to international recommendations, non-adherence to treatment guidelines as well as irrational use of medicines is seemingly a greater problem than had been anticipated. Treatment schemes sometimes deviate from recommended schemes through the use of uncommon combinations or inappropriate medicines, formulations or dosages, or changes in treatment durations or schedules (for example, in the Republic of Moldova, Romania, the Russian Federation and Ukraine). In particular, the treatment of children is frequently not based on paediatric standard treatment guidelines, or includes adult formulations instead of child-friendly paediatric ones (for example, Azerbaijan, Georgia and Kazakhstan). The compliance of some patients with their treatment is clearly poor, considering the high default rates in some countries (such as Armenia and Georgia). The management of side-effects is poorly structured in

many countries, including, for instance, a lack of guidelines for the treatment of side-effects of anti-TB drugs and a lack of ADR surveillance (for example, Azerbaijan, Georgia, Tajikistan and Turkmenistan). Moreover, TB drugs are sometimes freely available (in, for instance, Armenia, Kazakhstan, Kyrgyzstan, the Russian Federation and Ukraine) and thus used to treat inappropriate conditions. These are all important factors to be taken into account in the fight against TB and, in particular, MDR-TB, since they could well contribute to the spread of drug resistance.

Several reasons for the irrational use of medicines are theoretically conceivable, but unfortunately the actual causes are unclear. Most likely a multitude of factors are responsible, including the non-availability of drugs, inadequate information for patients and health care personnel, side-effects, and the long duration and affordability of treatment. Although TB medicines are in general free for all patients in every country, this is not always the case for ancillary drugs and other aspects of treatment (for example, in Belarus, Ukraine and Uzbekistan).

Adding to the structural and organizational shortcomings described above, aspects of storage and laboratory capacities also call for heightened attention. Storage capacities, for example, are far too low in many countries, especially at central level. This has crucial implications: storage might not comply with international standards because of insufficient space, resulting in crowded conditions, confusion and reduced quality of medicines, or leading to untimely delivery of inappropriate amounts of drugs to peripheral levels, eventually overburdening regional or even local storage facilities (for instance, in Armenia, Kyrgyzstan and Ukraine). Storage facilities at lower levels in particular, as well as being far too small, are usually not equipped to retain large amounts of medicines for longer periods: they might not have air-conditioning, refrigerated space is in general limited, and the personnel might not be qualified to deal with large stocks appropriately (for example, in Azerbaijan, the Russian Federation, Tajikistan and Ukraine).

Similar concerns can be raised with respect to laboratories. Although most countries have fully equipped and, in most cases, adequately qualified laboratories for monitoring the quality of medicines, it is doubtful whether they could handle an ever-increasing workload in view of the constraints on their capacity (for example, Georgia, Kyrgyzstan, the Republic of Moldova, the Russian Federation, Tajikistan and Ukraine). Apart from the fact that most testing laboratories are centrally situated and that as a result some regions (particularly rural areas) are potentially underserved (for example, Azerbaijan and Uzbekistan), unfavourable working conditions in many regions might lead to a shortage in qualified personnel. It is also not clear to what extent the laboratories currently depend on external assistance, especially in terms of technical support, and whether problems might arise when this support ceases. In addition, budgetary limitations might impair efficiency and usefulness, which will potentially worsen when external funding stops. Although the necessary equipment will be available until then, uncertainty hangs over further supplies of sometimes expensive laboratory materials and the maintenance of existing functions.

A final, important, aspect for consideration is the availability, origin and sustainability of funds in general. In several of the countries surveyed, certain components of NTPs are already underfunded, which has implications particularly for storage and distribution as well as ancillary drugs. Public budgets are rarely sufficient to cover all necessary expenses apart from the procurement of second-line drugs and other externally funded activities, and these challenges will be amplified when GDF support and funding from the Global Fund eventually stop. Programmes will most likely need more funding in the future instead of less, bearing in mind the

targets set to increase diagnosis, treatment and drug susceptibility testing. It is uncertain how long the Global Fund will be able to financially support the high MDR-TB priority countries.

Knowledge gaps

In order to reduce overall TB incidence rates and, in particular, halt the spread of MDR-TB, NTPs need to be adequately staffed and function efficiently. The survey this report is based on highlighted some of the prevailing issues regarding procurement and supply of TB medicines as well as TB treatment within the countries reviewed, but several questions still need to be answered. It is also unknown whether a potential lack of monitoring and evaluation can be ascribed to insufficient planning, a shortage of resources or organizational issues. In addition, the reasons for the problems with regard to pharmaceutical management, such as inadequate record-keeping or drug supplies, need to be addressed further; this includes the overall regulatory framework as well as individual aspects of existing procurement and supply management systems.

Although not directly connected to pharmaceutical management issues, another crucial aspect of NTPs which is posing additional questions is treatment compliance. There seems to be a problem with patients defaulting on treatment; the reasons for this are uncertain and need to be investigated further in order to increase treatment success and reduce the risk of drug resistance.

External factors may also have to be given greater consideration. The influence of political instability on the performance and sustainability of TB programmes as well as the ramifications of economic disturbances are difficult to predict and may pose serious problems in several countries.

Recommendations

Although the countries reviewed are diverse and, therefore, recommendations on an individual basis are necessary, some recommendations can be made that are applicable to the majority of the countries. More specific recommendations are in the individual country reports.

First, sustainable funding for all aspects of NTPs needs to be secured, not only for drug procurement and supply, but also for programme and drug management, information systems, storage capacities and the distribution of medicines. Most programmes rely heavily on external funding, and underfunding of at least some parts of the programmes is already apparent in all countries. This is likely to worsen when external funding ceases. The supply of second-line drugs in particular is usually funded by external grants, mostly from the Global Fund, and facilitated by the GDF procurement mechanism.

Second, structural and organizational redundancies within procurement and supply management systems should be reduced, not only with respect to the level of the supply system (central, regional, local) but also with respect to the source of the funding. Existing systems for TB registration and drug management should be integrated and unified at all levels so as to enable the uncomplicated exchange of data and prompt analysis. Programmes need to be structured more efficiently to improve the overall performance of NTPs, with clear responsibilities and effective data management systems.

Third, the availability of FDC, paediatric formulations, a wider range of second-line drugs and ancillary medicines needs to be improved in most countries. Unavailability arises for different reasons in different countries, but in general, a simplified registration process for medicines and increased public funding are necessary to deal with this problem. In-country registration of TB medicines should be facilitated on the basis of the outcomes of the WHO prequalification of medicines programme as well as mutual recognition procedures.

Fourth, medicine procurement needs to be based on good pharmaceutical practice and good distribution practice guidelines and backed up with updated standard operating procedures, regardless of the origin of the procured drugs and the source of the funding. Only GMP-certified producers should be acceptable for supplying TB medicines. The import of unregistered medicines needs to be facilitated in some countries but needs to be based on binding rules with respect to qualification of the manufacturers, quality of the medicines, distribution procedures and interim storage practice.

Fifth, laboratory capacities and performances should be scaled up in line with the European Laboratory Initiative. Additional capacities are necessary, particularly for quality testing of medicines which should be done in a qualified laboratory according to international standards. Drug susceptibility testing should be made more widely available: this is particularly important for testing of second-line drugs resistance.

Sixth, the capacity of storage facilities needs to be increased and their working practices improved. In many countries, central warehouses lack storage capacity, which results in overcrowded spaces, inadequate storage practice, lack of inventory transparency and waste. Inadequate storage capacity may lead to the delivery of unnecessary and unused amounts of medicines to lower levels. At the regional and local levels, storage capacities are also usually insufficient, and storage units may lack the necessary equipment (such as air conditioning and refrigeration) to store medicines for extended periods of time. This should be supported with the improvement of information management systems in order to avoid stockouts and reduce the amount of waste.

Seventh, to minimize the risk of exacerbating drug resistance, the rational use of medicines needs to be emphasized. The unrestricted sale of TB drugs in pharmacies without prescription and/or for inappropriate indications must be abandoned, adherence to treatment guidelines by health personnel enhanced and treatment defaults by patients reduced.

Finally, adequate and ethically acceptable pharmacovigilance systems should be implemented or strengthened in all the countries, to enhance patient care and safety and to support NTPs with reliable, balanced and up-to-date information.

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Annex 1

QUESTIONNAIRE ON PROCUREMENT AND SUPPLY MANAGEMENT OF FIRST- AND SECOND-LINE TB MEDICINES

Part A. Data on key stakeholder responsible for providing data

Country:		
Names of partners involved in completing the questionnaire (for example, public, private, donors, civil society) and their responsibility in the procurement and supply of TB medicines:	Partners:	Responsibilities in procurement and supply management:
Representative of organization interviewed:		
Position:		
Address:		
Email:		
Tel:		

Part B. General background on procurement and supply management

1.	**Regulation of pharmaceutical sector**		
1.	Is there a medicines law? If yes, please provide the last updated version or the link	Yes☐	No☐
2.	Please provide the last updated version or the link to the provision on registration of medicines.		
3.	Is there a provision for the ad hoc import of non-registered medicines (for the period until they are registered)?	Yes☐	No☐
4.	Is there a legal provision allowing unregistered use of medicines for clinical trials?	Yes☐	No☐
5.	Is there a special provision for regulation of pharmacovigilance? If yes, please provide the lastupdated version or the link.	Yes☐	No☐
6.	How many reports on adverse events were reported in 2012?		
7.	Is the national essential medicine list or formulary in line with the WHO Essential Medicines or Formulary? If yes, please provide the last updated version or the link.	Yes☐	No☐
1.7.1.	Are fixed-dose regimens 2, 3 and 4 and paediatric medicines of anti-TB drugs included in the essential medicines list or formulary?	Yes☐	No☐

2.	**Regulation of medicines procurement**		
2.1.	Is there a national procurement policy or public procurement law? If yes, please indicate the year of the last update of both documents and provide the most recently updated version of the list or the link.	Yes☐	No☐
2.2.	Does the regulation on procurement of essential medicines include operational principles of good pharmaceutical procurement? If yes, please tick the applied criteria below.		
	Transparency management (written procedures, working groups decision, advertisement)	☐	
	Based on essential medicines list or national formulary list	☐	
	Pooled order (cumulative order at the national level)	☐	
	Prequalification of suppliers	☐	
	System of monitoring of suppliers and post-qualification of suppliers	☐	
	Officially approved and published procurement plan	☐	
	Competitive method applied	☐	
	Are there regulations for other methods?	Yes ☐	No ☐
	Decentralized orders	☐	
	Medicines procured under INN	☐	
	Defect reporting system in place	☐	
2.3.	Is there a fast track registration procedure? If yes, please provide a brief description:	Yes ☐	No ☐
3.	**Regulation of anti-TB drugs**		
3.1.	Are there national standard treatment guidelines for TB, MDR-TB, PDR-TB, XDR-TB? If yes, please attach the most recently updated version.	Yes ☐	No ☐
3.2.	Are fixed-dose combinations of TB medicines recommended in the treatment standards?	Yes ☐	No ☐
3.3.	Please describe the list of medicines included in the treatment guidelines separately for sensitive TB, MDR-TB, XDR-TB?	TB-sensitive: MDR-TB: XDR-TB:	

4.	**Procurement**			
4.1.	What are the sources of supply and procurement of TB medicines in the country?			
	First-line TB medicines	Public/central budget ☐	Other sources. Please specify (Global Fund grant, etc.) ☐	Both ☐
	Second-line TB medicines	Public/central budget ☐	Other sources. Please specify (Global Fund grant, etc.) ☐	Both ☐
4.2.	What type of procurement system of TB medicines is applied in the country from the public budget?			
	Centralized ☐	Regional ☐	Decentralized ☐	
4.3.	What are the methods for procurement of TB medicines? Please select from the list below			
	Open tender ☐	Request for quotation ☐		
	Direct procurement ☐	International tender ☐		
	Negotiation ☐	Through international procurement agency ☐		
	Other (please describe) ☐			
4.4.	What are the special provisions in the regulation of procurement of anti-TB medicines? Please select from the list below.			
	Minimum shelf life at the delivery date ☐			
	Registered in the country of buyer ☐			
	Prequalified by WHO ☐			
	Manufactured according to GMP? ☐			
	If yes, please describe how GMP status is verified:			
	Registered by the stringent regulatory authorities ☐			
	Bioequivalence tests for FDC ☐			
	Requirements for leaflets and labels ☐			
	Others: please specify ☐			
4.5.	Are there any standard operating procedures for procurement of TB medicines?	Yes ☐	No ☐	

4.6.	Please provide the information regarding the organization(s) and respective source of funding that conducts anti-TB drugs procurement and their most recently updated version of standard operating procedures(s).		
4.7.	Is there a tool for forecasting TB medicines (electronic or manual)? Yes ☐ No ☐ If yes, please specify for first- and second-line anti TB drugs.		
4.8.	Is there a guideline on forecasting? Yes ☐ No ☐		
4.9.	Is a buffer stock a mandatory requirement for procurement of second-line drugs? Yes ☐ No ☐ If yes, what is the percentage of buffer stock allowed? 100% ☐ 50% ☐ 25% ☐		
4.10.	If procurement is done locally, what are the technical specifications for TB medicines?		
	Complied with GMP ☐	Non-registered, but prequalified by WHO ☐	
	Non-GMP ☐	Prequalified by WHO ☐	
	Registered in the country ☐	Testing of medicines at the prequalified laboratory ☐	
	Other (please describe) ☐		
4.11.	Is there a mechanism of monitoring suppliers? Yes ☐ No ☐ If yes, please tick the criteria applied for monitoring supplier's performance		
	Medicines delivered are according to of contract's ☐	Operative to solve issues related to products delivered ☐	
	Schedule of deliveries are respected ☐	Storage conditions during transportation are assured ☐	
	Minimum shelf life is respected ☐		
	Other (please describe) ☐		
4.12.	Is there any mechanism for exception/waiver of registration for anti-TB drugs procured or granted from WHO GDF? If yes, please provide brief description:	Yes ☐	No ☐
5.	**Quality assurance**		
5.1.	Is good manufacturing practice (GMP) a legal requirement for registration of medicines?	Yes ☐	No ☐
5.2.	Are local manufacturers inspected for GMP compliance?	Yes ☐	No ☐

5.3.	Are foreign manufacturers inspected for GMP compliance?				Yes ☐	No ☐
5.4.	Is there a legal requirement for good distribution practice?				Yes ☐	No ☐
5.5.	Is there any provision and procedure for acceptance of WHO prequalified medicines or of products registered by the stringent regulatory authorities?				Yes ☐	No ☐
5.6.	Are there any national laboratories accredited with ISO 17025 or prequalified by WHO?				Yes ☐	No ☐
5.7.	When are medicines tested? Please tick below the procedures applied.					
	At the registration stage ☐		Only for public procurement ☐			
	For monitoring of post-marketing quality ☐		In case of complaints ☐			
	At the import stage ☐		At the prequalified laboratory ☐			
	Other (please describe) ☐					
5.8.	Is there a regulation on post-marketing monitoring of quality of medicines, including TB medicines? If yes, please provide the last updated document or give a brief description.				Yes ☐	No ☐
5.9.	Are there procedures (requirements) for collecting samples of the TB medicines stocked in the pharmacy or warehouse by the inspectors for post-marketing quality control?				Yes ☐	No ☐
5.10.	Do inspectors have the authority to perform unexpected inspections and/or sampling post-marketing?				Yes ☐	No ☐
6.	**Distribution of TB medicines**					
6.1.	Are TB medicines available from pharmacies?				Yes ☐	No ☐
6.2.	Is the distribution system of TB medicines integrated into the national supply system for essential medicines?				Yes ☐	No ☐
6.3.	If no, please describe the distribution system for first-line and second-line drugs in your country.					
6.4.	Are there standard operating procedures for handling the import, transport, storage and distribution of TB medicines? If yes, please provide the last updated standard operating procedures or a link to them.				Yes ☐	No ☐
6.5.	Is there a system of product recall in case of quality issues? If yes, please provide the last revised document or the link.				Yes ☐	No ☐
6.6.	What kind of distribution system is in place?					
	First-line drugs	Push ☐	Pull ☐	Both, depending on the level of distribution (central, regional) ☐	Please provide brief description	

	Second-line drugs	Push ☐	Pull ☐	Both, depending on the level of distribution (central, regional) ☐	Please provide brief description

7.	**Use of TB medicines**				
7.1.	What procedures/measures are in place to ensure compliance of TB and MDR-TB treatment with WHO recommendations? Please provide brief description.				
7.2.	Are there any protocols for treatment of side-effects to second-line drugs?			Yes ☐	No ☐
7.3.	What mechanisms are in place for reporting/recording side-effects of first- and second-line anti-TB drugs? Is this reporting mechanism linked to a data information system for TB patients? Please provide a brief description.				
7.4.	Are drugs for management of side-effects provided free during outpatient treatment with second-line drugs?			Yes ☐	No ☐
8.	**Data management information system for programmatic management of TB and DR-TB**				
8.1.	Is there a register for TB-sensitive patients? Please tick below the procedure in practice			Yes ☐	No ☐
	Central level	Automated ☐	Manual ☐	Both ☐	
	Regional level	Automated ☐	Manual ☐	Both ☐	
	Local level	Automated ☐	Manual ☐	Both ☐	
8.2.	Is there a register for DR-TB patients (MDR-TB, PDR-TB, XDR-TB)?			Yes ☐	No ☐
	Central level	Automated ☐	Manual ☐	Both ☐	
	Regional level	Automated ☐	Manual ☐	Both ☐	
	Local level	Automated ☐	Manual ☐	Both ☐	
8.3.	Is there a TB drugs management information system?			Yes ☐	No ☐
8.4.	What type of information on pharmaceutical management is recorded? Please describe by level of supply system of TB medicines.				
	Received lots/stock level	Central ☐	Regional ☐	Local ☐	
	Consumption/distribution data	Central ☐	Regional ☐	Local ☐	

	Stockouts period	Central	☐	Regional	☐	Local	☐
	Inventory data	Central	☐	Regional	☐	Local	☐
	Shelf life/expiry date	Central	☐	Regional	☐	Local	☐
	Expired products	Central	☐	Regional	☐	Local	☐
	Dispensing to patient	Central	☐	Regional	☐	Local	☐
	Forecasting module	Central	☐	Regional	☐	Local	☐
8.5.	What are the procedures for quality assurance of data on drug management? Please present brief description (e.g. data flow from different levels).						
9. Management							
9.1.	Is there a dedicated unit or person for TB drug management?					Yes ☐	No ☐
9.2.	Please provide brief description of the responsibilities of this unit or person.						
9.3.	Who is responsible for selection of TB medicines for procurement?						
9.4.	Who is responsible for development of technical specifications for bids for TB second-line medicines?						
9.5.	Are there any training programmes for TB medicines supply for the NTP? If yes, please describe briefly.						

Part C. Key stakeholders/partners involved in procurement and supply management of first- and second-line TB medicines in the country

No.	Names of stakeholders/	Second-line TB medicines	First-line TB medicines

		Area of procurement and supply management	List of responsibilities or type of assistance	Period of implementation /budget	Area of procurement and supply management	List of responsibilities or type of assistance	Period of implementation /budget
1		Selection			Selection		
2		Procurement			Procurement		
3		Distribution			Distribution		
4		Drug management information system			Drug management information system		
5		Prescription/use of TB medicines			Prescription/use of TB medicines		
6		Pharmacovigilance programme			Pharmacovigilance programme		
7		Quality assurance			Quality assurance		
8		Management: training/continued education programmes			Management: training/continued education programmes		

PART D. MDR-TB estimates, treatment enrolment, drug procurement and funding

Data variables	2012	2013	2014	2015	2016	Reference document
Estimated number of MDR cases (WHO)						(WHO report or other document)
Total number of MDR-TB cases, including poly-drug resistance, enrolled and planned for treatment with second-line drugs, of which: – are procured/to be procured internationally – are procured /to be procured domestically						(National MDR-TB response plan or other document)
Total number of XDR-TB cases enrolled and planned for treatment with second/third line drugs, of which: – are procured/to be procured internationally – are procured /to be procured domestically						(National MDR-TB response plan or other document)
Available and planned funding for second- and third-line drugs from government (US $)						(National programme, Ministry of Health strategic plan or other document)
Available and planned funding for second- and third-line drugs from Global Fund grants (US $)						Global Fund grant number
Available and planned funding for second- and third-line drugs from other donors (US $)						Programme title and donor name