Impact of Donor Support on TB Pharmaceutical Systems: The Global Drug Facility Experience

Strengthening Pharmaceutical Systems

December 2011

Strengthening Pharmaceutical Systems
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This report is made possible by the generous support of the American people through the U.S. Agency for International Development (USAID), under the terms of cooperative agreement number GHN-A-00-07-00002-00. The contents are the responsibility of Management Sciences for Health and do not necessarily reflect the views of USAID or the United States Government.

About SPS

The Strengthening Pharmaceutical Systems (SPS) Program strives to build capacity within developing countries to effectively manage all aspects of pharmaceutical systems and services. SPS focuses on improving governance in the pharmaceutical sector, strengthening pharmaceutical management systems and financing mechanisms, containing antimicrobial resistance, and enhancing access to and appropriate use of medicines.

Recommended Citation

Strengthening Pharmaceutical Systems. 2011. *Impact of Donor Support on TB Pharmaceutical Systems: The Global Drug Facility Experience.* Submitted to the U.S. Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health.

Key Words

GDF, tuberculosis, technical assistance, drug management, donor support

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CONTENTS

ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
CDR	Case Detection Rate
CIDA	Canadian International Development Agency
DOTs	Directly Observed Treatment Short-Course
DP	Direct Procurement
FDC	Fixed Dose Combination
FEFO	First to Expire-First Out
GDF	Global Drug Facility
GLC	Green Light Committee
GNI	Gross National Income
HBCs	High Burden Countries
HIV	Human Immunodeficiency Virus
MDR-TB	Multi-Drug Resistant Tuberculosis
MoH	Ministry of Health
MSH	Management Sciences for Health
NEML	National Essential Medicines List
NTPs	National Tuberculosis Programs
PAHO	Pan American Health Organization
PPM	Public Private Mix
QA	Quality Assurance
QC	Quality Control
SPS	Strengthening Pharmaceutical Systems
TB	Tuberculosis
TGF	The Global Fund
TRC	Technical Review Committee
TS	Treatment Success
UNITAID	International Drug Purchasing Facility
USAID	U.S. Agency for International Development
WHO	World Health Organization

EXECUTIVE SUMMARY

Since 2001 the Global Drug Facility (GDF) has provided procurement services to National Tuberculosis Programs (NTPs) when it was established by international donors to fill the gap in procurement capacity of many countries. GDF is housed at the World Health Organization (WHO) within the Stop TB Department. GDF procurement services over the years have included free grants of medicines for adults and children, direct procurement services for those countries that obtained their own funding but still have weak procurement capacity, and technical assistance for in-country drug management.

Normally GDF conducts an annual monitoring mission in each country that is receiving support from GDF. This mission is conducted by GDF consultants. Although some pertinent data are extracted from the reports to present to donors there hasn't been a comprehensive analysis of the data contained in the reports. A study was conducted in August/September 2011 whereby mission reports were evaluated from 24 countries. The countries analyzed represent 26% of countries supported by GDF from 2001-2010 and 76% of the total number of patients treated with GDF medicines during this time period. Those selected for the study included: 13 of 22 high burden countries (HBCs)[1]; poorer countries (with GNI[2] less than US$ 3,000 per capita); and countries from the six WHO regions of the world.

Findings of the 24 countries analyzed show that during GDF support, 12 NTPs switched to use of fixed dose combination (FDC) medicines which contain all medicines in one tablet greatly facilitating pill taking and stock handling. The other 12 countries were already using some form of FDCs; this means all 24 countries are using the FDC products. Nine NTPs switched to patient kits which contain all TB medicines needed to treat one patient helping avoid medicine stock outs once patients begin treatment.

Of the two WHO core indicators 13 of 24 NTPs reached the target: case detection rate of 70%; and treatment success rate of 85%. Likewise, NTPs were able to expand their DOTs coverage to an average of 89% for the 24 countries analyzed. Several other programmatic management indicators improved including: establishing a 5-year DOTs expansion plan in 18 of 24 NTPs and standard treatment guidelines in 21/24 NTPs.

A number of drug management indicators improved in the 24 countries analyzed as well; decreased port clearance time in 14/24 NTPs; use of buffer stocks to avoid stock outs in 14/24 NTPs; practice FEFO[3] in 13/24 NTPs; use of stock cards in 18/24 NTPs; stock cards are kept up to date in 11/24 NTPs; medicines were out of stock over last 12 months in 19/24 NTPs with stock outs of 45-98 days on average.

Product quality assurance indicators revealed that drug registration is required in 19/24 (NTPs) but waivers are allowed for GDF medicines in 14/24 (NTPs); and product quality control testing is done in 16/24 NTPs on average.

[1] GDF has supplied TB medicines to 15 HBCs over the study period
[2] GNI = Gross National Income as reported on the World Bank website: http://search.worldbank.org/data?qterm=GNI%20per%20capita&language=EN
[3] FEFO = first to expire first out (should store first to expire medicines in front of others)

Recommendations are made to NTPs by the consultants and by GDF's Technical Review Committee based on previous mission reports. Of the countries reviewed, a total of 1047 recommendations were made; of the total, 854 (82%) recommendations were verified as completed by GDF consultants during subsequent missions.

GDF is a unique organization which has been able to make a significant impact on global TB control by: 1) greatly improving availability of quality medicines; 2) providing free medicine grants to needy countries; 3) procuring medicines for countries that still lack capacity to do their own procurements; and 4) supporting improvement in NTP programmatic and drug management performance. Hopefully donors will continue to fund the GDF well into the future.

INTRODUCTION

The Global Drug Facility (GDF) has provided procurement services to National Tuberculosis Programs (NTPs) since 2001 when it was established by international donors to fill the gap in procurement capacity of many countries. GDF is housed at the World Health Organization (WHO) within the Stop TB Department. In the beginning the medicines were provided as free grants funded by several donors. Eligibility for GDF support includes among others the basic requirement of Gross National Income (GNI) per capita of < 1000 US$, which was later extended to < 3000 US$ for adult patient grants and < 10,725 US$ for pediatric patient grants.

Concurrent with the founding for the Global Fund (GF) in 2002, the Stop TB Coordinating Board that governs GDF policy instituted the requirement that NTPs must transition from free grants within three years; this was later extended to six years during which time NTPs could satisfy preliminary GF requirements. Many of the countries have made the transition from GDF's free grants of first line drugs. The transitioning countries are now procuring from other sources or procuring from GDF as direct procurements with other funding (such as the GF, World Bank, other donors or government sources, etc.).

Based on its mandate[4] by the Stop TB Coordinating Board, during the period 2001-2010, the GDF also provided a level of technical assistance in tuberculosis (TB) pharmaceutical management through annual monitoring missions, field-training workshops and specific needs that GDF facilitated through experts it hired and through partners such as Management Sciences for Health (MSH), one of its major partners.

The USAID-funded program, Strengthening Pharmaceutical Services (SPS) managed by MSH, provides technical assistance to the GDF and the Green Light Committee (GLC)[5] in pharmaceutical management of tuberculosis (TB) at global, regional and country levels since 2001. This long standing partnership with GDF includes: the placement of MSH pharmaceutical management experts at GDF/GLC headquarters from 2001 to 2008 and 2009-2010; co-authoring WHO Stop TB publications including those on use of fixed dose combination drugs to combat TB[6]; conducting monitoring missions in countries to evaluate their pharmaceutical management capacity for managing 1st and 2nd line TB drugs[7]; and preparation of materials and facilitation of training workshops for GDF consultants, among others.

Purpose of this paper

A study was conducted in August/September 2011 to understand the evolution of countries' pharmaceutical systems related to international donor support and systems strengthening as

[4] *Global TB Drug Facility prospectus – founding principles*, http://www.stoptb.org/gdf/whatis/principles.asp
[5] Green Light Committee http://www.who.int/tb/challenges/mdr/greenlightcommittee/en/
[6] *Operational Guide for National Tuberculosis Control Programmes on the Introduction and Use of Fixed-Dose Combination Drugs* [WHO/CDS/TB/2002.308 - WHO/EDM/PAR/2002.6] http://www.stoptb.org/gdf/whatis/documents.asp
[7] 1st line = for susceptible TB; 2nd line = previously treated TB

promoted by the GDF through its various activities. The specific objectives of the study are the following:

- Identify major funding sources for NTP-donor relationships in key countries
- Report on pharmaceutical management issues and changes in performance over years of donor assistance (2001-2010)
- Identify shifts in NTP reliance on donor funding and associated factors
- Analyze and report on trends in the shift from GDF free grant support to other funding sources (eg. major funding from Global Fund)
- Identify trends in NTP performance likely related to GDF support

This paper describes the findings and conclusions reached during the study including a section on suggestions for GDF to enhance its services. USAID provided funding for the study through the FY2010 MSH/SPS activity work plan.

Methodology

The GDF through SPS and other Stop TB partners has been conducting annual monitoring missions to the grant recipient countries since 2002. The reports of these missions contain a TB situation analysis based on standard TB indicators and description of pharmaceutical management practices including: government commitment; promoting access to medicines through policies, regulation, financing; drug registration; quality assurance of non-GDF medicines; procurement practices; storage and distribution; and rational use of medicines. An important part of the mission reports is a section on recommendations from both the GDF mission consultants and the Technical Review Committee (TRC) members and progress made on implementing the previous recommendations. The recommendations are directed to the Ministry of Health/National TB program, donors/partners, and the GDF secretariat for improving the countries' TB control programs. Therefore, the monitoring reports contain a wealth of important data that have not been comprehensively analyzed for trends, such as: possible reasons for success or failure of TB programs, stock-outs or wastage of medicines and supplies; and total impact of GDF activities on Pharmaceutical Management for TB in the countries it has served.

GDF provided support to a total of 94 countries over the study period; 15 are high burden countries. SPS conducted the study using the GDF mission reports related to data for first line adult and pediatric medicines, with a focus on high burden countries, countries with weak TB programs and countries that enjoyed GDF support for multiple years. NTPs were identified as "weak" by GDF's TB program consultants. A total of 24 countries were selected that meet the aforementioned criteria. These 24 countries are also representative of the six WHO regions. See Annex 1

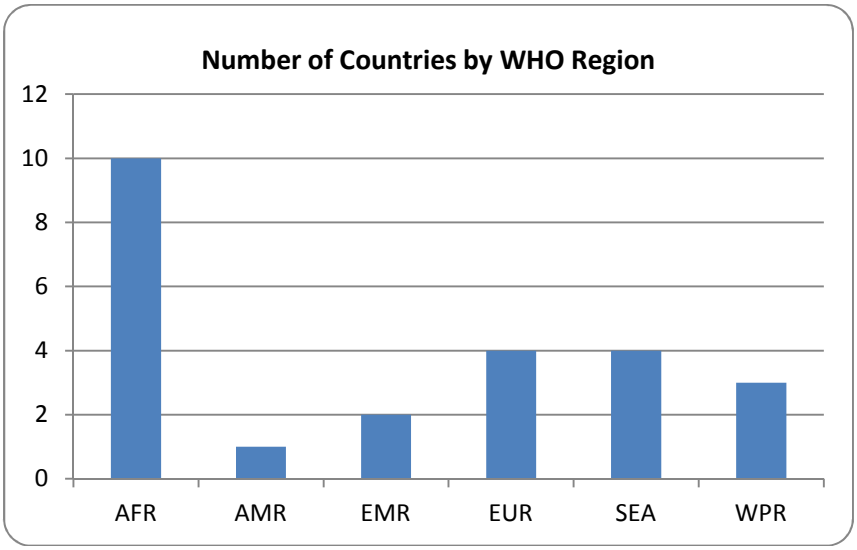
It is notable that data were missing (not reported by GDF consultants) at the rate of 1-22 times on average taking all mission reports that were reviewed into account and depending on the data element. Thus some of the data above could be skewed as a result of under reporting.

FINDINGS AND DISCUSSION

Selection of countries

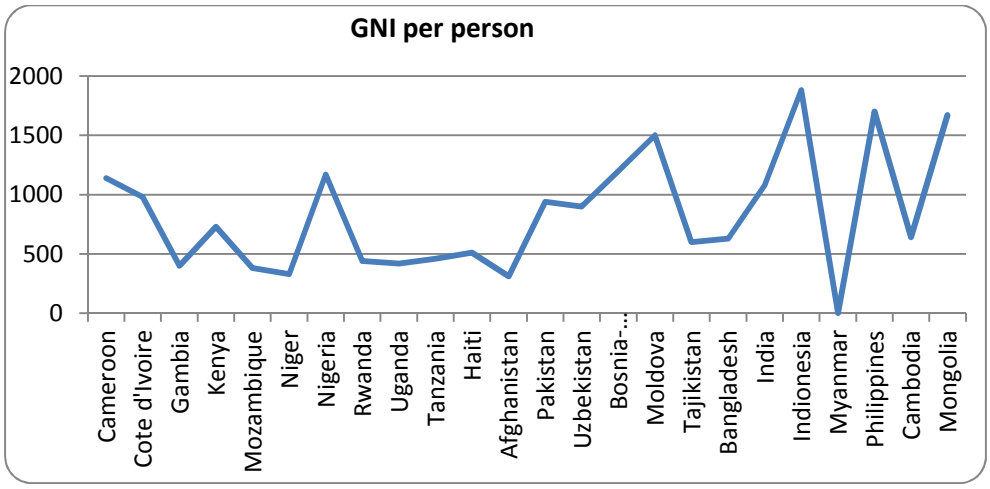
Of the 25 countries selected for this study, one did not have sufficient data to report. Thus the remaining 24 countries represent 26% (24/94) of the countries supported by GDF from 2001-2010. Further, a compilation of the total number of patients treated shows that the 24 countries represent 76% (13.8 million) of the 18.1 million patients treated through support from GDF. Some of the countries excluded from the study have very small TB programs (eg. 50 TB patients) such as the smaller island nations in the Western Pacific Ocean. Other countries not selected received only one or two years of GDF support and consequently there is not enough information in those reports necessary for this study.

Part of the criteria for country selection was to represent all six WHO regions to obtain a global picture. Notice in the graph below there was only one country from the Americas region which is appropriate since only three countries received support from GDF in that region over the study period. On the other hand is the inclusion of ten countries from the Africa region which is appropriate because of the large number of countries served by GDF in that region.



The GNI requirement of countries was met as evidenced below for all 24 countries studied. These figures represent the GNI during the first GDF mission to that country[8].

[8] http://search.worldbank.org/data?qterm=GNI%20per%20capita&language=EN



Monitoring Missions

Most NTPs receive annual monitoring missions conducted by several TB partners to evaluate program performance and to provide technical assistance helping NTPs reach TB programmatic goals established by the World Health Organization and international partners. Two of these goals are to find 70% of the TB cases in the population and to reach a target of at least 85% treatment success. As defined by WHO, treatment success includes numbers of patients who completed treatment plus those that are cured.

The GDF requires an annual monitoring mission before a country can receive medicines for the subsequent year. To enable this, the GDF established a consultant monitoring template to collect information related to GDF requirements, and some basic national programmatic information. The template allows the consultant to remind NTP managers about WHO TB treatment goals, but also to provide a level of technical assistance on what constitutes good pharmaceutical management for TB. The template was expanded over the years to include more salient information that could be used to provide additional support including technical assistance.

GDF Requirements for Support

The WHO DOTS strategy was adopted by ministries of health in developing countries as the most efficient and cost-effective approach to the prevention and control of TB. The success of the DOTS strategy depends on the adequate implementation of several key components, including the following which are directly related to appropriate handling of medicines:

- Standardized short-course chemotherapy available for all TB cases, under proper case-management conditions including direct observation of treatment
- Uninterrupted supply of quality-assured medicines with reliable pharmaceutical programming, procurement, and distribution systems

- Recording and reporting system enabling outcome assessment of each and every patient and assessment of overall program performance

GDF based its support requirements on the WHO DOTs strategy and its mandate as established by the Stop TB Coordinating Board. GDF's basic requirements[9] are the following:

- Countries must fall within a GNI per capita of no more than 3000 US$ for adult patient grants and a GNI per capita of no more than $10,725 for pediatric support
- Drugs supplied by the GDF are only used to treat TB patients, free of charge, in treatment regimens following WHO guidelines
- National programmes are following guidelines for DOTS implementation, in accordance with a multi-year plan for DOTS expansion, to reach the global targets of TB control
- The NTP assumes responsibility for GDF drugs beyond the agreed point of delivery, including the payment (or waiver) of import duty or tax, storage fees or insurance levied on GDF drugs
- The NTP facilitates the process for registration of GDF drugs, if relevant; GDF directs its medicine suppliers to provide required registration information
- A medium to long term plan to ensure quality of medicines is established
- GDF support has not inadvertently displaced committed funds for DOTS
- Financing and technical assistance for other aspects of DOTS (not medicines) is available
- The government TB budget has increased from the last year
- Public sector/donor funding for TB control activities has not been reduced during the period that GDF grants are received
- A Ministry of Health/NTP budget exists for the required TB drugs, treatment of adverse effects, prophylaxis, and pharmaceutical management including: logistics; procurement; and quality control
- DOTS expansion increased or maintained 100% coverage since the last year
- The country achieved an acceptable level of cure rates in DOTS coverage areas
- Other TB medicines used in the country from sources other than the GDF are of good quality and of similar specifications to those provided by GDF
- The NTP is moving towards standardized formulations and dosage presentations of TB drugs

[9] http://www.stoptb.org/assets/documents/gdf/whatis/GDF-Prospectus.pdf

Types of GDF Support

In the beginning GDF provided free grants of first line drugs for adult patients to eligible countries. These grants were designed to cover any gaps in TB treatment created by lack of sufficient government funding. In some poorer countries especially those with smaller numbers of TB patients the GDF support was 100% of TB medicine needs. As mentioned before, the GF came on board to provide support to national programs in controlling TB, HIV/AIDS and Malaria based on countries meeting specific criteria. In the beginning few GDF countries requested funding for TB medicines from the GF; but as the three year (and later six year) maximum period of GDF support were approaching, more and more countries began applying for support from the GF for TB medicine funding as well.

With GF grants there is currently no requirement for countries to procure their TB medicines from the GDF (exception: MDR-TB[10] medicines). Therefore, after applicant countries began receiving TGF medicine support they went to other sources. Some countries however, lack procurement capacity to do this and requested the GDF to continue to provide their TB medicine needs. GDF established its direct procurement (DP) mechanism to fulfill this need.

In 2007 GDF received funding from UNITAID to supply pediatric formulations to NTPs as grants. NTPs need to meet the same GDF support requirements as mentioned above. Since the maximum grant periods (three to six years) have not been met by the current recipient countries, all GDF supply of pediatric medicines currently continues as free grants.

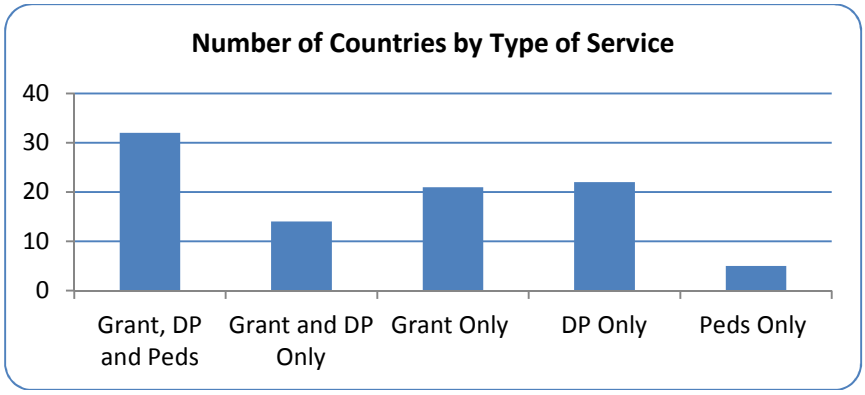
In the meantime, based on needs discovered during monitoring missions and through discussion with other TB partners, GDF developed two kits that would help NTPs quantify, procure and assure quality of the medicines and supplies they need for TB control. One of these kits, called the "Stop TB Kit", contains all medicines needed for full treatment of one patient. That way, to calculate medicine needs is simplified (1 patient = 1 kit), whereby only one item is handled by storeroom managers instead of the five or six TB drugs normally stocked; with kits patients are assured that all their medicines are available when they need them. The other kit developed by GDF is the TB diagnostic kit. There are variations of this kit depending on the needs of the NTP, such as one containing slides, testing reagents and sputum cups for microscopy, one containing a microscope and one containing only microscopy slides.

As GDF was being launched, WHO and partners were developing a four fixed dose combination tablet (4-FDC) to treat TB. This tablet contains all four TB drugs recommended by WHO for first-line treatment and in dosage strengths that allow appropriate numbers of tablets for different patients' weights[11]. GDF adopted the 4-FDC and later a 3-FDC[12] which helped standardize the handling of medicines from time of quantification of drug needs by the NTP until administered to the patient. GDF consultants demonstrated the usefulness of these dosage forms during monitoring missions, and NTPs proceeded to change their standard treatment guidelines, to train their health workers how to handle these very useful products and then began to procure them.

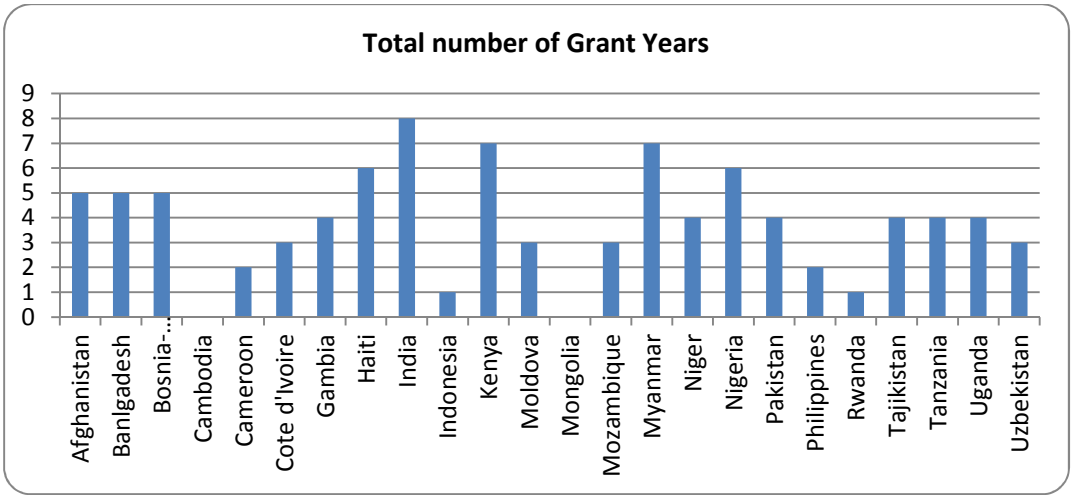
[10] MDR-TB = multidrug resistant TB: patients resistant to the drugs isoniazid and rifampicin
[11] 4-FDC = rifampicin 150 mg/ isoniazid 75mg / pyrazinamide 400 mg/ ethambutol 275 mg
[12] 3-FDC = rifampicin 150 mg/ isoniazid 75mg / ethambutol 275 mg

Another fundamental area of medicine packaging for the NTP is whether to use bottles containing loose tablets or to use tablets packaged individually in blisters. Taking NTP needs into consideration, GDF supported the use of TB medicines in blisters because this maintains the quality of each tablet until it is pushed from the blister sheet and given to the patient to ingest. With loose tablets, there is the danger of giving the wrong medicine (the four drugs are often supplied as all round white tablets); also there is the hygiene factor where health workers dispense loose tablets from bottles using their ungloved hands. With the FDC and blister presentations in hand, GDF was able to simplify even more the Stop TB kit under development, which today requires little adjustment, based solely on a patient's weight.

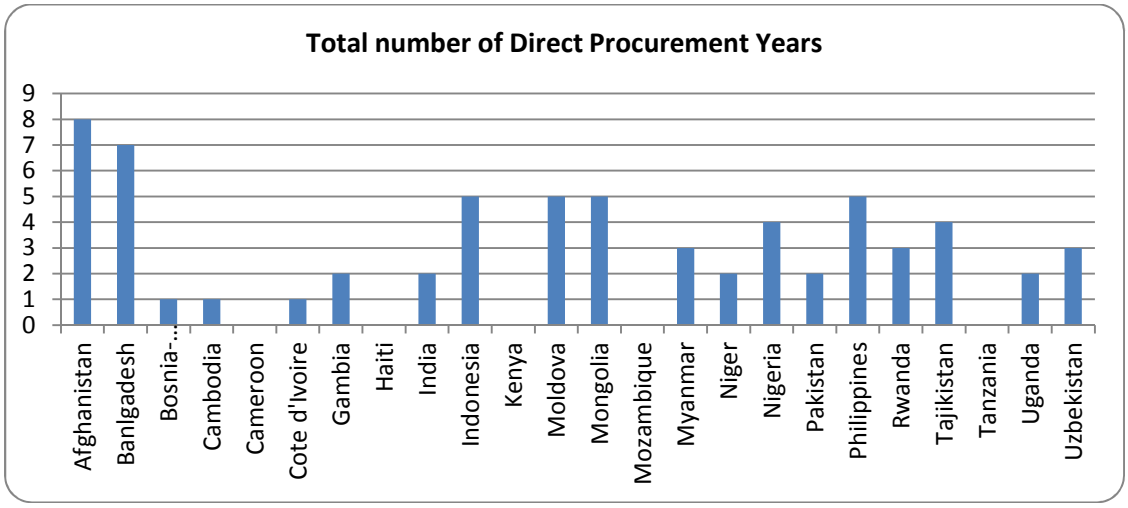
The following graph shows findings during the data analysis related to type of service from the GDF: adult grants (grant), direct procurement (DP) or pediatric grants (Peds).



Concerning grants and DP services provided by GDF, the following two graphs show the number of years each of the 24 countries procured medicines through the GDF, one for grants (adult and pediatric), and the other for direct procurements. These data helped select the countries to be studied.

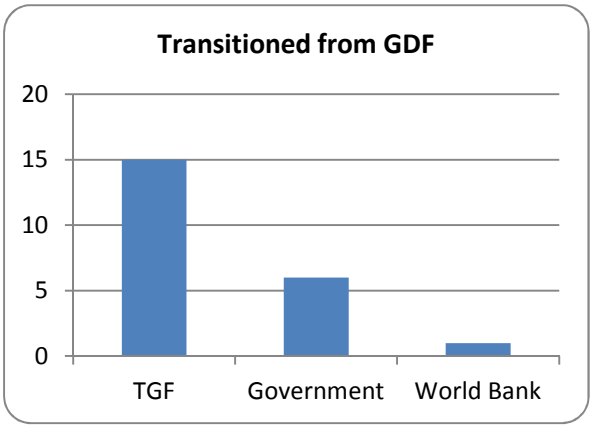


Notice that for three countries above the number of grant years exceeded the maximum of six years. This was due to special circumstances and GDF's Technical Review Committee and the Stop TB Coordinating Board had to approve these exceptions.



The graph above shows that some countries did not use the GDF beyond the free grant years, once they boosted their efforts by either funding the TB medicines themselves or through funding by the GF and other international partners.

As mentioned earlier, GDF policy requires that countries must transition from GDF support after six years of TB medicine grants. For the 24 countries studied, this visual shows that 14 countries transitioned to the Global Fund (TGF) and six countries transitioned to government funds. Data provided showed transition of one country to World Bank funding.



The table below shows for transitioned countries what percentage of the budget was covered by the new source of funding. The figures show the range of medicine funding when combining data for the different countries.

Transitioned to:	Medicine Budget Covered
TGF	25-100%
Government	10-50%
World Bank	Not reported

Linked to the transition requirement is the expectation that governments should increase their TB program or medicine budgets during each year of GDF support. That way when GDF support is no longer available there would be less of a funding gap to fill. The following data from the 24 countries analyzed show that eight countries did in fact increase their budgets for the national TB program activities and seven countries increased their budgets for TB medicines over the years of GDF support. The percentage (%) increase in funding while under GDF support was not always reported by consultants; however, where reporting did take place the figures are listed.

	Government increased funding to NTP program (Number of Countries)	% increase in funding to NTP while under GDF support	Government increased funding for TB medicines (Number of Countries)	% increase in funding for TB medicines while under GDF support
Yes	8	3, 6, 7, 39	7	4,7,13,15, 21,40, 80
No	8		10	
Not reported	8		7	

Program Guidelines, Treatment Regimens and Dosage Presentations

For the 24 NTPs analyzed, 12 switched to fixed dose combination (FDC) products. However for the other 12 countries, they had requested FDCs from GDF since the beginning meaning that all are using 2, 3 and 4-FDC products to treat TB in their countries. Of the 12 NTPs that switched to FDC products, nine are from high burden countries (HBCs).

A further nine NTPs switched to the Stop TB patient kit all of which contain FDCs as well; and six of the nine NTPs switching to Stop TB patient kits were also HBCs.

The FDCs and Stop TB Patient Kit dosage presentations as mentioned previously allow much easier handling of TB medicines for all concerned: easier to calculate medicine needs by NTP; easier to handle one item rather than the four or five TB medicines if procured singly; and storage and accountability are much easier, likewise because of fewer products to handle.

Concerning use of loose tablets versus tablets packaged in blisters, the following table shows the number of countries switching to blisters, those that were already using blisters and those that continued to procure loose tablets. Tablets packaged in blisters allow quality control all the way up to ingestion by the patient plus avoiding manipulation of loose tablets in a non-hygienic way.

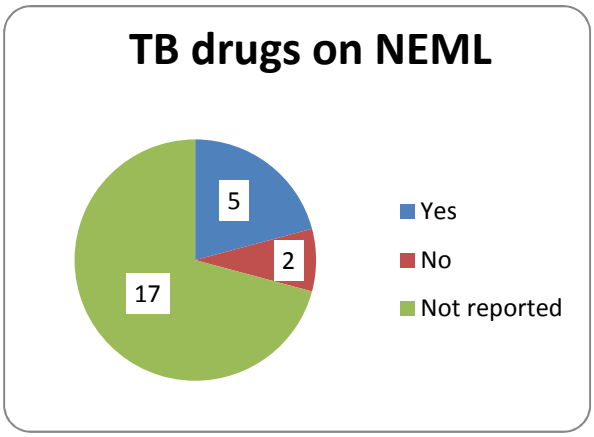
	Number of Countries
Switched from loose to blister	16
Began as blister	6
Remained as loose	2

One GDF requirement is to have a multiyear plan in place that includes DOTs expansion, standardized treatment regimens and program guidelines that are available to health care providers and managers. GDF would recommend during missions that training must take place on the program guidelines for health providers so that TB patients are treated in a standardized way. This table describes the outcome of the 24 countries analyzed including other program aspects such as DOTs coverage.

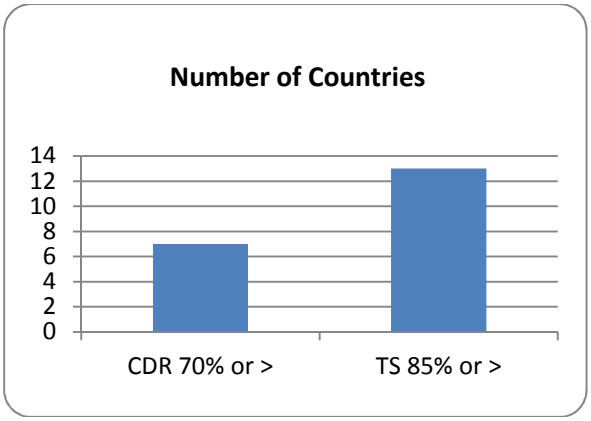
	Have NTP 5 yr plan	Have TB Program Guidelines	DOTS coverage	Have STGs	Improved STGs while under GDF support	Have Child TB Manual
Number of Countries	18	21		21	12	16
Later prepared guidelines	2			2		
Average %			88.9			
Range %			56-100			

In the area of drug management often guidelines are not available and GDF consultants during the annual missions to these countries encourage NTPs to work with essential medicine programs to develop one. Nine of the countries analyzed reported they now have drug management guidelines while six of these countries developed them as a direct result of GDF requirements. For one country drug management guidelines were never developed and 14 countries did not report on this issue. Guidelines are important for training and for standardization of work activities so that medicines are handled in a similar quality way.

Every Ministry of Health should have an approved list of medicines called a National Essential Medicines List (NEML) so that providers will treat patients only with appropriate medicines following standard treatment guidelines. During monitoring missions GDF consultants would collect information on this indicator and encourage NTPs to become involved when TB medicines were not on the approved list. This graph shows that of 24 countries surveyed, five indicated that all TB medicines in use were included on the NEML; two countries indicated they had not yet done this; one country was able to update the NEML with TB medicines during GDF support and for 17 countries, this indicator was not reported. Working with essential medicine departments, NTP managers should encourage the MoH to make this a reality.



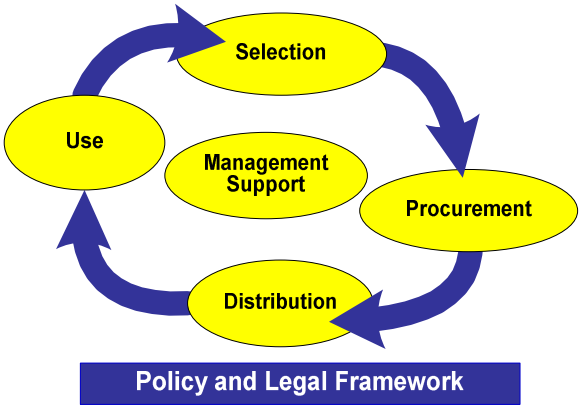
Two core indicators that WHO and partners strongly recommend NTPs to monitor are *case finding rate* for smear positive (sm +) patients and *treatment success rate*. The case finding rate (CDR) is important because it shows how well the program is expanding to meet the needs of the TB population in the country. The treatment success rate (TS) is made up of two figures, the number of sm+ patients who completed treatment plus those that were cured. WHO and partners have established targets of 70% for CDR and 85% for TS. The graph below shows the results of the analysis.



It is evident that countries have had difficulty reaching the CDR (only 7 countries so far), but greater success was reached in treating patients since 13 of 24 countries (54%) reached the TS core target. It takes time to implement good TB control, consequentsly NTPs still have much work to do in that regard.

Drug Management Elements of TB Programs

The Drug Management Cycle pictured below shows the various elements of a drug management system[13]. Within each element are several activities that must be managed in order to have medicines available when patients need them. For the medicine *Selection* component, WHO and partners have recommended appropriate treatment regimens for new, relapse, previously treated and multidrug resistant TB[14]. All medicines supplied by GDF meet these recommendations. For the other components, results of the survey will be discussed one by one except for medicine *Use*, since this was not a mandate of the GDF. *Quality assurance of medicines* is an important activity that exists within every element of the Drug Management Cycle. This will be discussed below as well.



One activity within the *Procurement* element of the Drug Management Cycle is quantification or estimation of medicine needs. For TB grants, GDF consultants help NTPs calculate quantities of each drug needed for next year's consignment. For direct procurement quantities, GDF provides this assistance as requested by the NTP.

The *Distribution* element of drug management includes receipt, port clearance, distribution within the country, stock management and ordering. GDF consultants discuss details of these activities with NTPs and medicine managers as a way of providing technical assistance while simultaneously monitoring the capacity of the program to handle TB medicines.

The **port clearance** activity is carefully monitored since delays are detrimental to quality control and for reducing shelf life of the products. For this study, 10 days for port clearance was used as a measuring point since GDF secretariat encouraged countries to facilitate clearance within five - 10 days of shipment arrivals. Nine of 24 countries exceeded 10 days on average. However, it was interesting to see that 14 of 25 countries had improved port clearance time in recent deliveries when compared with previous deliveries. Causes of the delays were several, for example: not

[13] *Managing Drug Supply: The Selection, Procurement, Distribution, and Use of Pharmaceuticals, 2nd edition,* http://www.msh.org/resource-center/managing-drug-supply.cfm
[14] *Treatment of Tuberculosis Guidelines, 4th addition* http://www.stoptb.org/assets/documents/gdf/drugsupply/who_TB%20treatment%20guidelines%202009t.pdf

preparing to pay the port clearance fees in advance; consignee was away from the country and could not accept the delivery; and too many authorities needed to approve payment of handling costs.

Distribution of medicines within a country, consist of several activities such as: distribution responsibility, delivery schedule, method of ordering and use of buffer stocks. The table below shows the results of data gathered during the survey. For the ordering activity, *push* means the NTP decides how many medicines to distribute to districts and treatment centers and *pull* means the districts and treatment centers decide how many medicines they need and request these based on numbers of patients treated and other medicine consumption data. The responsibility for distribution may be *central* if the national level actually delivers medicines to the periphery and *district* if medicines are delivered from port directly to districts which then deliver to treatment centers. *Mixed* means that central level receives medicines from Port and *district* picks up medicines from central level for storekeeping and later delivery to treatment centers. The amount of buffer stock to keep at district level is measured to see if the supply system can handle unknown demands on quantities of medicines needed by the treatment centers such as an unexpected increase in number of patients diagnosed with TB.

	Use buffer stock (Number of Countries)	Amount of buffer stock at district level (months)	Stock orders: Push or Pull (Number of Countries)	Distribution responsibility (Number of Countries)
Yes	14	1-12; Average 3	Push 6 Pull 12	Central 16; District 2; Mixed 3;
No	1			
Not Reported	9		3	3

Stock management consists of various activities that are monitored by GDF mission consultants. The results of the 24 countries survey are listed in the following tables.

	Number of Countries		
	Practice FEFO	Use drug cards	Drug cards up to date
Yes	13	18	11
No	2	2	7
Not reported	9	4	6

FEFO in the table above means "First to expire – First Out" as a means of using medicines that will expire first to avoid stock outs by storing them in front of other medicines. It is important to monitor dates of expiry in order to avoid loss of medicines and scarce financial resources. Use of individual medicine cards or registers is important for inventory control as well as actually recording stock movement on a daily basis. Ideally where a "pull" system is used for ordering medicines, the facility will need good data to accurately order quantities needed for the next order period. Notice that many countries in the table above are following these principles, but some lapses were found during the GDF mission. In the recommendations section of this paper data will show how many countries actually improved their drug management practices while under GDF support.

The following table shows various activities that constitute **good storage practices** of medicines:

	Number of Countries						
	Storage away from sunlight	Storeroom has climate control	Moisture in store room found	Drugs stored on floor	Evidence of pests	Separate expired stock from good	Has storeroom security
Yes	11	8	1	2	2	3	13
No	1	4	10	11	8	2	0
Not Reported	12	12	13	11	14	19	11

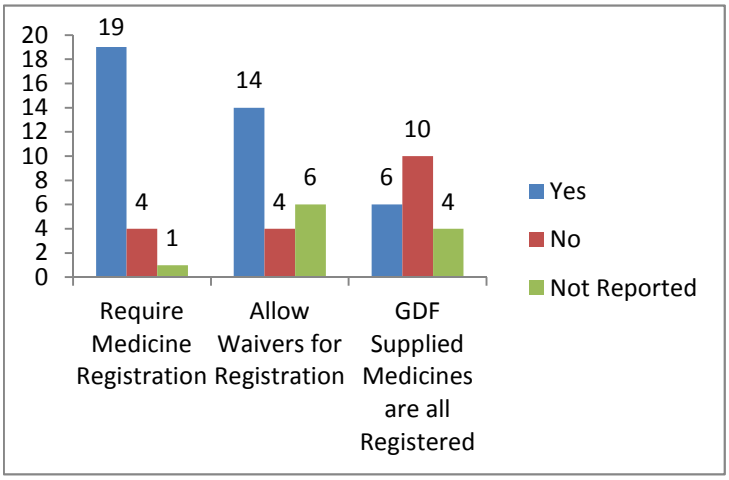
Storing medicines in direct sunlight will eventually cause them to become unusable for patients (eg. would discolor or disintegrate). Moisture is detrimental to medicines causing some of them to swell and disintegrate while in storage, especially if the packaging is of poor quality. Having a method to control temperature, ideally an air conditioner, but at least air circulation throughout the storeroom is important to help control temperature and moisture. Drugs stored directly on the floor are sure to pick up moisture and pests; thus storing medicines on pallets and having a good pest control system are a necessity anywhere in the world. For those products that have actually expired, good storeroom management requires that these are removed to a quarantine area so they will not be given mistakenly to patients. Medicines are expensive and are open to theft or other diversion if security for the storeroom is not in place. All of these factors must be considered to maintain good storeroom practices and to protect medicines. Otherwise TB products will be lost and not available when patients need them and scarce financial resources will be wasted. It is interesting to note that GDF consultants reported in subsequent missions that three more countries began using individual drug cards for record keeping, one updated the NEML, two began to practice FEFO, two established storeroom security and one began storeroom treatment to eliminate pests.

The above activities will also avoid *medicine expiry* and medicine *stock-outs*, other activities that are monitored during the GDF consultant missions and reported to GDF. Data from the missions

are reported together for central and district warehouses and clinic storerooms that were included in the visit. Findings regarding medicine expiry and stock-outs from data analysis revealed the following:

	Number of Countries			
	Expired drugs seen on shelves	Reported that drugs had expired	Any drug was out of stock for any period of time	Average days out of stock all drugs (days)
Yes	5	9	19	47-98 days
No	12	12	4	0
Not Reported	7	3	1	4

The Quality assurance of medicines element of drug management is a very important activity which is dispersed throughout all elements of the Drug Management Cycle. Quality determines if the medicine is usable by the patient, if there is loss of medicine due to expiry or deterioration during storage. It is known that some unscrupulous drug suppliers actually prepare medicines with no active ingredient (counterfeit), the medicine that is needed to actually fight the TB germ. In all cases the patient would be affected since poor quality or counterfeit products if given to patients will not treat their TB and can cause adverse effects for the patient causing them to become even sicker. For those reasons, before receipt and distribution of a medicine within the country, the procuring agency, whether GDF or another source must be sure that manufacturers are producing medicines that meet international quality standards. GDF does this by procuring only from manufacturers who have met the WHO prequalification standards, been approved by a stringent regulatory authority or those on track for approval by the WHO prequalification scheme[15] through the Expert Review Panel mechanism[16]. During monitoring missions, GDF consultants collect data about several quality-of-medicine activities.



Another important quality assurance activity is **drug registration**, whereby a national drug regulatory agency assesses each product of each manufacturer procured for distribution within the country. Some countries have no such agency or because of insufficient human resources to carry out registration activities agree to provide a waiver for the GDF products. However, where required, GDF works with its

[15] http://apps.who.int/prequal/
[16] http://www.stoptb.org/gdf/drugsupply/quality_sourcing_process.asp

manufacturers to provide all required documentation for product registration. Data collected during this analysis show that 19 of the 24 countries studied require medicine registration; and 14 of 24 countries allow waivers of registration for GDF and other international sources which they deem "for humanitarian purposes". Concerning GDF medicines, only six of 20 countries had actually registered the GDF medicines they import[17].

Data for other quality assurance activities of the 24 countries are listed in the following table. Receiving a batch certificate with each shipment should be mandatory indicating to the recipient that samples were taken and passed quality control testing. Some countries accept medicines based on the batch certificate and a visual inspection of the products received due to lack of resources for more stringent quality control activities. When adequate resources are available however, some countries go an additional step and test in their own laboratories or have an independent laboratory test for in-coming products. Notice in the data below that some of these activities were poorly reported by GDF consultants, such as the data element, "Reports that Quality Control (QC) Problems Occurred for Distributed Drugs" where no data were reported for 22 of the 24 countries. This should be improved for future missions since determining quality of medicines is a critical activity if patients are to be cured and the NTP is to succeed in TB control.

	Receive batch certificate each shipment	QC done by independent lab	In country QC lab testing	In-country QC visual inspection	Require QC tests only for non-GDF drugs	Reports that QC problems occurred for distributed drugs
Yes	13	3	15	17	4	1
No	1	10	8	0	14	1
Not Reported	10	11	1	7	6	22

Data on results of QC tests though reported to GDF too infrequently by the consultants does give an idea of medicine problems encountered for the 24 countries analyzed. There were four countries reporting that some TB medicines failed QC testing. These data show that the failed products represent 0.5, 1.2, and 2.5 percent of all products procured. Although the data collected were incomplete, it was clear that the poor quality products were sourced primarily from local manufacturers. For the one country that reported QC problems, these problems were identified as follows: tablets that were crushed, discolored and disintegrated[18].

[17] GDF medicine registration data were only collected beginning in 2008; thus 4 of the 24 countries had no such data
[18] Tablet breaks down into smaller parts changing its composition and usefulness: http://www.merriam-webster.com/dictionary/disintegrate

For GDF, its own quality control activities consist of batch certificates of the quality control results from the prequalified manufacturer and laboratory testing by an independent laboratory for each batch procured through GDF and sent on to country programs. Through these QA activities, GDF has emphasized to NTP managers the importance of quality medicines in TB control.

Recommendations to National TB Program Manager

Each GDF consultant mission report contains recommendations made to the NTP manager. The recommendations come from both the consultants and also GDF's Technical Review Committee. There were a total of 1047 recommendations made to NTPs in the 24 countries analyzed for the study period (2001-2010). Of these, 854 (82%) were verified as completed by GDF consultants during subsequent missions. This section discussions examples of the recommendations made, first for pharmaceutical management and then for program management.

TB pharmaceutical management

It is not uncommon for TB drugs to be available for sale in private pharmacies. This is not a good practice since development of TB drug resistance can increase due to poor prescribing, dispensing and drug taking. Some countries have national regulations prohibiting this practice, but too often the national drug regulatory authority is not able to monitor all or any of the pharmacies and the practice continues. In the table below GDF consultants made recommendations about this practice to five NTPs. Other recommendations had to do with strengthening various pharmaceutical management activities so that quantities of TB medicines procured would be correct; or the whole supply chain needs improvement at all levels; or the drug information system for recording and reporting drug consumption is more accurate for better quantification of medicine needs.

Recommendations Related to Pharmaceutical Management (Reported as Number of Countries)	
TB drugs available in the private sector	5
Supply chain needs improvement/strengthening	4
Quantification needs strengthening	3
Need mechanism to transfer drugs from one location to another (avoid drug expiry)	2
Drug Information system needs strengthening to capture quantities consumed	5

TB program management

For TB program performance, WHO's Stop TB Department and partners expanded the concept of TB control to eventually include all populations of a country including private sector, prisons and persons living with HIV/AIDS. Persons living with HIV/AIDS are more likely to present with TB than the normal population since their body systems are already compromised. A national Public Private Mix (PPM) program involves private clinics, private pharmacies and private industry in the national TB control schemes, so that patients will be treated in a standardized, appropriate way.

The following table shows the frequency of recommendations to NTPs for the 24 countries analyzed related to the expanded NTP populations. Also included are two recommendations that are basic components for good TB control: monitoring and supervision, and a well-functioning laboratory network.

Recommendations Related to TB Program Management (Reported as Number of Countries)	
Laboratory Network needs strengthening	5
Monitoring and Supervision activities are weak or non-existent	4
Prison population included in NTP activities	3
TB/HIV activities weak or non-existent	2
Need to implement (PPM)	5

It is clear from the data above that many countries need technical assistance and additional resources to expand their TB control programs. It is likely NTPs are receiving technical assistance in the weak areas of their programs due to the large number of partners working in the field and the interface GDF has developed with Stop TB partners and funders such as the GF, USAID[19], CIDA[20] and World Bank. The next section discusses this topic further.

Technical Assistance

Data were collected about the need for technical assistance (TA) by NTPs for improved TB control relative to pharmaceutical management (DM TA) and program management (PM TA). Only 20 or the 24 countries had recent data about TA since this information was not part of the GDF template in earlier years. The following data show the frequency of such requests, if funding from the Global Fund (GF) were approved for TA, and if multiple partners are already providing TA to the countries.

[19] USAID = United States Agency for International Development
[20] CIDA = Canadian International Development Agency

	DM TA requested	DM TA included in GF grants	Multiple partners provide DM TA today	PM TA requested	PM TA included in TGF grants	Multiple partners provide PM TA today	Requested TA from TB Team
Yes	19	17	11	19	18	19	8
No	1	3	9	1	2	1	11
Not Reported							1

The above data show that TA is very much needed by NTPs to improve TB control in their countries (19 of 20 countries)[21]. Technical assistance can be expensive and requests were made by NTPs to the GF to include TA in 17 (DM TA) and 18 (PM TA) countries respectively. The trend is increasing to request outside funding for TA since NTPs made requests in multiple Global Fund grant rounds in four countries for DM TA and six countries for PM TA.

The WHO "TBTEAM" initiative was established in 2009 to consolidate requests for TA by NTPs. Of the 24 countries studied only eight have bought into the concept and made formal requests to TBTEAM so far.

In most countries, several partner organizations are involved in TA in the countries studied. These are illustrated in the table below showing the number of countries requesting TA from each partner. It was interesting to find that in four countries, GDF was the only partner providing DM TA, that being through the annual consultant monitoring mission.

[21] Technical assistance data were only collected beginning in 2008; thus 4 of the 24 countries had no such data

TA in Drug Management		TA in Program management	
Partner	Number of Countries	Partner	Number of Countries
WHO *	8	WHO	1
GDF	11	GDF	4
Project Hope	2	Project Hope	2
MSH	9	MSH	4
UNDP	2	UNDP	2
GLC	2	GLC	2
Greenstar	1	Greenstar	1
JSI	2	JSI	2
Italian cooperation	1	Italian cooperation	2
Damien	1	Damien	3
RIT	1	RIT/ JICA	3
UNION	1	UNION	1
TBCap	3	TBCap	6
		PATH	2
		CDC	5
		KNCV	2
		MSF	4

*Technical assistance could be from headquarters, regional or country offices of WHO

Data were collected on the type of TA requested by NTPs. These varied considerably from one TA element to another as reported in the table below. In drug management the most frequently requested TA was for: procurement; quantification; stock management; rational drug use; DMIS[22] and managing SLDs[23]. The DM TA request for "strengthen NDRA[24]" is an interesting one since WHO recommends that countries enact legislation to prevent the sale of TB medicines in private pharmacies unless an agreement has been reached to follow NTP guidelines. The NTP manager can only request this of the NDRA who then must work with the legislature to pass a regulation to that effect. For TB program management the most frequently requested TA was for: MDR-TB; childhood TB; laboratory/microscopy; MIS[25]; infection control; monitoring and evaluation; and ACSM[26].

[22] DMIS = drug management information system
[23] SLDs = second line drugs for MDR-TB
[24] NDRA = National Drug Regulatory Authority
[25] MIS = management information system for monitoring, case management and reporting
[26] ACSM = advocacy,communication,social mobilization
http://www.who.int/tb/people_and_communities/advocacy_communication/en/

TA in Drug Management		TA in Program management	
Type of TA Requested	Number of Countries	Type of TA Requested	Number of Countries
Procurement	8	Case management	2
Quantification	13	All aspects of TA	1
Distribution	8	MDR-TB	8
Stock management	14	Childhood TB	5
Rational drug use	10	Laboratory/microscopy	5
DMIS	15	MIS	6
Pharmacovigilance/ adverse reactions	3	Update operational guidelines	3
Post marketing surveillance	1	Infection control	7
Manage SLDs	4	Drug sensitivity testing	1
Manage pediatric drugs	2	Adverse drug reactions	1
How to use patient kits	1	Operations research	3
Strengthen NDRA	1	Monitoring/Evaluation	4
Monitoring/Evaluation	1	TB/HIV	3
		ACSM	4
		DOTS expansion	1
		Public Private Mix	2
		Prevalence survey	1
		Human Resource development	2
		Update training materials	2
		PAL[27]	1

Some of these processes take time and will require persistence from Stop TB partners to continue working with NTPs as needed, so that global TB control will become a reality.

[27] PAL = practical approach to lung health http://www.who.int/tb/health_systems/pal/en/index.html

DATA CONSIDERATIONS

The data in this report were obtained from GDF electronic monitoring mission reports. The denominator used for most calculations was 24 countries for relevant information presented herein. However, the study set was reduced to 20 countries for two additional topics later added to the original data collected: (1) technical assistance; and (2) number of GDF products actually registered in countries. Reduction to 20 countries was necessary because four of the original 24 countries did not have this information since monitoring mission templates had been modified over the years to include more and more information such as the need for technical assistance. It is duly pointed out to the reader in the relevant sections whether 20 or 24 countries are used as the denominator.

The 24 countries studied represent 26% (24/94) of the countries supported by GDF from 2001-2010 for first line drugs. As mentioned in the "methodology" section the 24 countries were chosen based on several criteria, one of which was multiple uses of GDF services. Therefore most of the countries not included in the study (70/94) were either single users of GDF services or the countries have extremely small populations, such as Pacific Island nations and Ministry of Health drug management systems are non-existent. Although this could skew the results presented in this report, this is not expected by those familiar with GDF operations.

It is notable that data were missing (not reported by GDF consultants) at the rate of 1-22 times on average taking all mission reports that were reviewed into account and depending on the data element. Thus some of the data presented in the report could be skewed as a result of under reporting by consultants.

CONCLUSION

The expansion of GDF services over the years 2001-2010 show how GDF has been able to make significant impact on global TB control[28]. Several main areas of impact were: 1) greatly improving availability of quality medicines; 2) providing free medicine grants to needy countries; 3) procuring medicines for countries that still lack capacity to do their own procurements; and 4) providing technical assistance in drug management.

In the area of availability of TB medicines, GDF has helped standardize treatment regimens by promoting 3- and 4-FDC medicine use and patient kits. Of 24 countries analyzed, 12 NTPs switched to FDC products, with nine of them from HBCs. Nine NTPs adjusted their treatment regimens to the Stop TB patient kit, six of which were also from HBCs. These products helped promote world-wide the WHO recommendations on appropriate TB treatment.

From monitoring missions GDF learned that some NTPs were struggling to procure good quality diagnostic products which directly affected the NTPs' capacity to expand DOTs services. GDF stepped in and developed a diagnostic kit that contains: sputum cups, microscopy slides and reagents and even a microscope depending on the needs of a specific country.

GDF promoted the Stop TB partners requirement of having a five-year plan for DOTS expansion, and having treatment guidelines for TB. Of the countries surveyed 18 and 21 NTPs respectively, developed a five-year plan and standardized treatment guidelines which they used to train NTP staffs; pediatric treatment guidelines and drug management guidelines were developed by 16 and six NTPs respectively.

GDF criteria helped drive medicine support and technical assistance to those programs most needing GDF services by way of the GNI maximum and mandate that national programs agree to use GDF medicines only for TB patients and providing them free of charge. GDF was established to fill the gap in TB medicine needs of countries, but for very poor countries this often meant 100% support until the NTPs could secure other funding for medicines and TB control. During support by GDF, DOTS coverage of countries averaged 88.9%, with a range 56-100%. Likewise, GDF tries to respond quickly to emergencies and urgent needs for medicines, although this has not been the mandate of GDF.[29]

GDF support has had a major impact on the two core indicators for national TB control established by WHO and Stop TB partners through the TA provided by GDF consultants during monitoring missions. As a result, NTPs have been able to approach these targets incrementally as evidenced by the 13 of 24 NTPs that reached the treatment success rate of 85% or greater and the seven of 24 NTPs that reached the case detection rate of 70% or greater.

GDF worked hard over the years to support improvement of drug management activities in countries. According to its mandate, GDF is not responsible for medicines beyond the port of entry; but hearing from Stop TB partners that in-country drug management is very weak, GDF

[28] See the following website for various reports of GDF contributions and success to global TB control: http://www.stoptb.org/gdf/whatis/documents.asp

[29] *Supplied 10 Million Treatments in 6 Years*, GDF Achievement Report, 2007 http://www.stoptb.org/gdf/

has used its monitoring missions as a way to provide technical assistance in this area. The monitoring mission template used by consultants lists many significant policies and activities required of a good drug management system. During the mission itself consultants take this opportunity to discuss with NTP management and storeroom managers how they can improve their drug management practices. Some of the policy and operational standards promoted include: having TB medicines added to the national essential medicines list; development of guidelines and training for staffs; checklists for monitoring how medicines should be stored; necessity of having buffer stocks; use of blister products instead of loose tablets; how to quantify TB medicine needs; monitoring of port clearance time; and monitoring of medicine quality during receipt and storage of TB medicines. All of the foregoing promotes standardization and safety of medicine use, access to TB medicines by patients and monitoring of medicine quality until it is administered to the patient.

During monitoring missions the MoH and NTPs were encouraged to search for other financial support since GDF assistance is time limited. GDF often provided help to countries in preparing their procurement and supply management applications to funders such as the Global Fund. Of the countries analyzed for this study 14 of 24 countries transitioned to the Global Fund. More importantly six countries transitioned to government funds, showing their commitment to support national TB control.

GDF has helped establish a global awareness of quality assurance (QA) of medicines through its QA policy of procuring only medicines approved according to international standards.[30] GDFs QA policy includes the issuance of a manufacturers batch certificate and an additional batch certificate from an independent laboratory. This has helped NTPs understand the importance of product quality in good TB control – that with poor quality medicines, patients are not cured and can develop drug resistance to TB.

Suggestions were made to GDF to improve consultant training and preparation, mission template updating and working closely with the TBTEAM mechanism to facilitate TA needs in countries, all of which should help GDF make an even greater impact.

GDF is a unique organization that has made a huge contribution to TB control around the world[31]. Even if the landscape for TB medicine procurement changes significantly in the years ahead, there is a place for GDF to continue to provide the same high level of support it has shown during 2001-2010. Obviously, without the major donors contributing to GDF the picture would have been different. Hopefully, the donors can see how their support must be continued so that the GDF can continue its contributions to TB control and carrying them far into the future.

[30] For complete GDF QA policy see website: http://www.stoptb.org/gdf/drugsupply/quality_sourcing_process.asp
[31] *GDF: Innovative Global Procurement*, Journal Tuberculosis and Lung Diseases, 8(1) 130-138, 2004 IUATLD

ANNEX 1: COUNTRIES INCLUDED IN STUDY

Country name	High Burden Country (Yes = √)	WHO Region [a]
Afghanistan	√	EMR
Bangladesh	√	SEA
Bosnia-Herzegovina		EUR
Cambodia	√	WPR
Cameroon		AFR
Cote d'Ivoire		AFR
Gambia		AFR
Haiti		AMR
India	√	SEA
Indonesia	√	SEA
Kenya	√	AFR
Mongolia		WPR
Mozambique	√	AFR
Myanmar	√	SEA
Niger		AFR
Nigeria	√	AFR
Pakistan	√	EMR
Philippines	√	WPR
Moldova		EUR
Rwanda		AFR
Tajikistan		EUR
Uganda	√	AFR
Tanzania	√	AFR
Uzbekistan		EUR

[a] AFR – Africa Region
AMR – Americas Region
EMR – Eastern Mediterranean region
EUR – European Region
SEA – Southeast Asia Region
WPR – Western Pacific Region