More than a Decade Shaping Treatment Supply
Global Drug Facility

November 2012

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Executive Summary

This paper shows the accomplishments of the Global Drug Facility (GDF) over the 12 years since it was established and how it is meeting its mandate to expand the access and availability of quality assured tuberculosis (TB) drugs to facilitate the expansion of DOTS, as stated in the GDF prospectus of 2000 (1).

Today, quality-assured first-line drugs (FLDs) and second-line drugs (SLDS) are available from reliable sources at very good prices when compared to market competitors of the same level of quality. In addition, GDF extended its activities to provide diagnostic materials and novel diagnostic technology at affordable prices such as the GeneXpert.

The value of GDF is remarkable since its products and services cover the wide spectrum of medicines and diagnostics for TB control and should be considered by the national TB programs (NTPs) as "a one-stop shop", taking into consideration the following reasons:

- *Pooled procurement*: GDF is able to aggregate demand for anti-TB products for more timely and simplified procurement
- *Attracting suppliers*: GDF accepts bids only from prequalified manufacturers, but when none are available, GDF conducts workshops and visits manufacturing sites to get commitment from suppliers to become prequalified
- *Pricing*: GDF conducts international bidding regularly in order to achieve competitive, transparent pricing for medicines and diagnostics
- *Quantification & forecasting*: GDF assists countries in identifying their needs in a timely manner
- *Quality assurance*: GDF's policy is aligned with that of the Global Fund
- *Country focus*: GDF aligns staff at headquarters and in the field to assure that clients receive the technical assistance they need through: annual monitoring missions; calculation of medicine and diagnostic needs; and identification of their drum management (DM) challenges
- *Coordinating PSM activities*: GDF coordinates provision of technical assistance to NTPs by other stakeholders and Stop TB partners
- *Customer satisfaction*: Responses from both NTPs and technical partners show that the work of GDF has been pivotal in providing TB medicines and diagnostics in markets where no one else was able to act, either because of funding or technical problems. An analysis of customer response shows that the satisfaction rate is high, 87 – 90% for diagnostics and TB medicines, respectively
- *Innovative tools and quick response*: NTPs and technical partners appreciate the existence of GDF and wish it could respond even quicker to their needs. The facility has always supported NTPs' accurate planning for order placement through constant individual contact,

technical assistance by headquarters staff, field-based staff, in country monitoring and by trying to expedite late orders to avoid stockouts. With donor support continuing, GDF plans to implement preventative and solving measures: (a) in collaboration with technical partners, GDF will be collecting data to forecast and prevent potential stockout situations in client countries, to notify all stakeholders and trigger a quick response; (b) GDF will implement a rotating stockpile of FLDs and SLDs and (c) GDF will establish a flexible procurement fund to support the quick response and solve the potential stockout situations without delay.

As of mid-2012, GDF has provided more than 21 million patient treatments for susceptible TB and approximately 90,000 patient treatments for multidrug-resistant-TB (MDR-TB). The value of diagnostics supplied has reached about 29 million USD as of June 2012. GDF has worked in more than 100 countries in all WHO regions, conducted 44 NTP monitoring missions in 2011 and simultaneously provided technical assistance. Five workshops on TB pharmaceutical management were facilitated by GDF in 2010—2012. The number of pre-qualified suppliers has increased tremendously for both FLDs and SLDs, which goes a long way in avoiding stockouts caused by supplier problems.

GDF has had an impact on FLD and SLD markets. While nominal prices have increased for some medicines, others have decreased. However, when adjusted for inflation, the evidence shows that prices have decreased every year as GDF's market share increased: to 40% of the public market since 2005 for FLDs; and to 15% of notified cases for SLDs since 2007. With GDF's market influence, the number of prequalified manufacturers has increased from one per product to two to three for both FLDs and SLDs.

Stockouts caused by problems in countries were analyzed by GDF and partners during 2012. There were multiple reasons for the stockouts, but the greatest frequency was caused by technical proposals to the Global Fund needing various reviews over several months before funds were released for medicines. An exceptional remedy would be to have donors fund a revolving global strategic stockpile (GSS) and flexible procurement fund (FPF) to pay suppliers upfront. With these two tools in place, GDF will be able to make an even bigger impact on market shaping in the future: on price reduction, regimen standardization, technical assistance, information sharing, tremendous reductions in order lead times and of course, avoidance of stockouts.

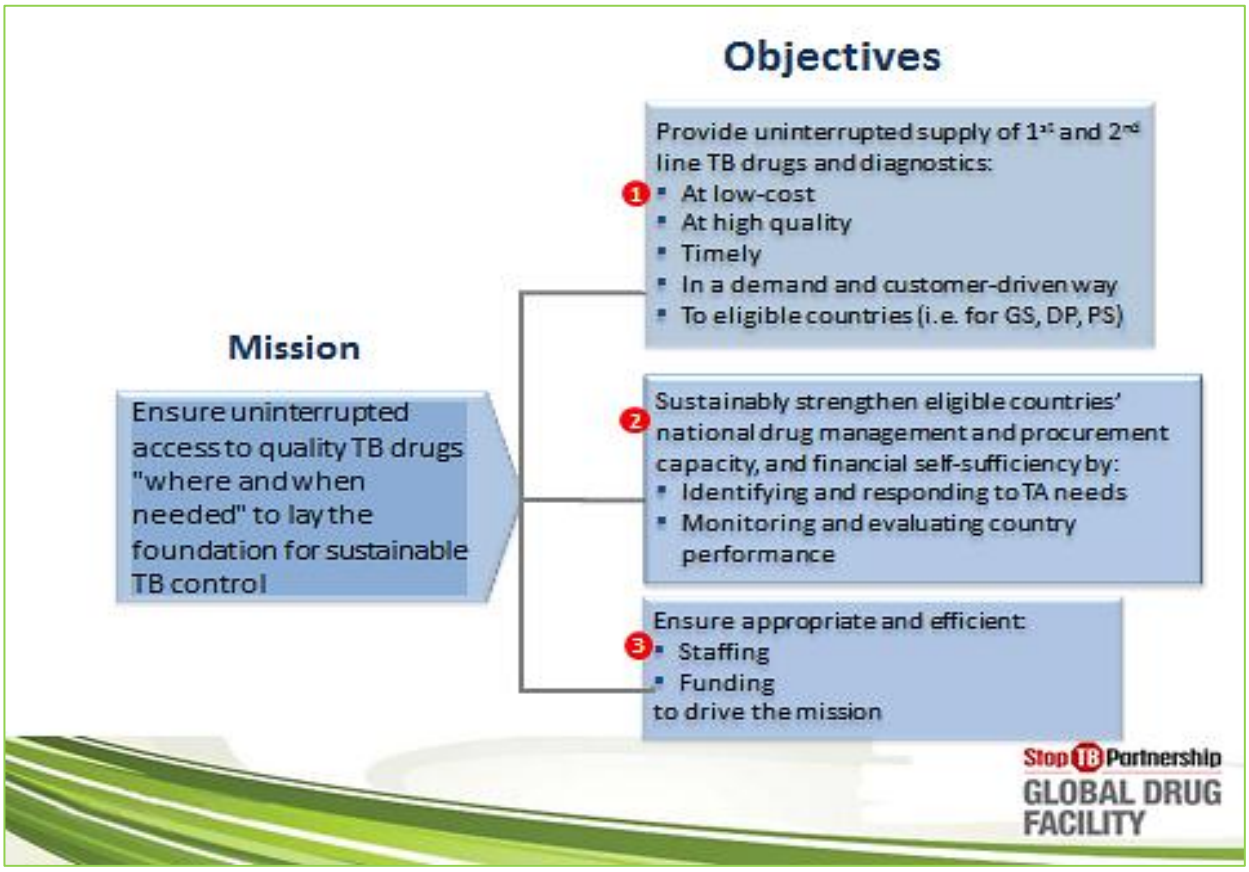
The intention of this paper is to summarize the work of GDF in the last decade and illustrate its achievements based on objective evidence supporting the fact that the facility has been a true asset to global TB control.

TB Landscape in 2001

There had been significant progress in combating the global tuberculosis epidemic when the Stop TB Initiative began discussing the possibility of a Global Drug Facility (GDF) in 1999—2000. However, progress was offset by increases in HIV and by widespread emergence of multidrug–resistant strains of TB. The problems were complicated by frequent and serious shortage of TB medicines caused by ineffective procurement, short-term political, managerial, logistic and financial crises all worsened by failures of health system management.

In May 2000, the 53rd World Health Assembly endorsed the Stop TB Initiative proposal for a GDF. They believed that GDF would expand access to, and availability of, high quality TB medicines and thereby facilitate DOTS expansion. DOTS is the comprehensive public health strategy to control tuberculosis.

GDF was established on World TB day, 24 March 24 2001 and was envisaged to rapidly turn around the situation over the next 10-15 years, when it was expected that the number of patients requiring TB treatment would decrease (1). Functionally the GDF is part of the Stop TB Partnership housed at the World Health Organization in Geneva, Switzerland with a clear vision and objectives as illustrated below.

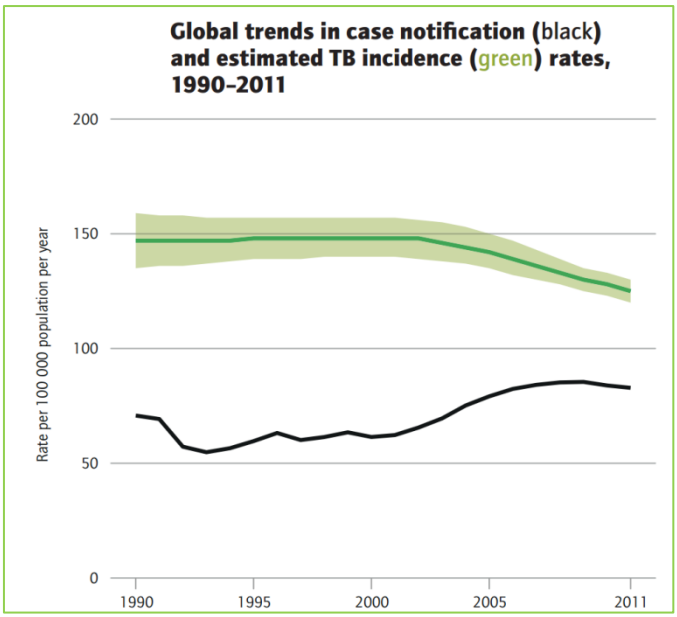


Donors fund the work of GDF including TB medicine grants. Over the years the major donors have been USAID, CIDA, DFID (for India), Novartis (for Tanzania and Sri Lanka), UNITAID grants for SLDs and pediatrics and smaller contributions from other donors.

Reasons for this paper

This paper was written based on evidence collected by GDF over its existence including: data from monitoring missions to countries, data entered into the GDF order management system (OMS) and other documents describing GDF activities, such as white papers and external audits. The paper contains information and graphical depictions of accomplishments of the facility and is being used as a basis for strategy reformulation in 2012.

After more than a decade of activities, the data show that GDF is accomplishing its mandate: "to expand access to, and availability of, high-quality TB medicines and thereby facilitate DOTS expansion". While several countries have shown a moderation in the rate of incidence of TB cases, few have been able to show a decline in the number of TB cases to date, likely due to needed DOTS expansion and improve capacity to diagnose more TB cases in the population. DOTS expansion in countries during the first 12 years of GDF activities has expanded tremendously and case finding and treatment success rates shown later in this document will support that. The below graph is taken from the 2012 WHO World TB Surveillance Report (8).



Mortality and incidence rates are falling in all of WHO's six regions and in most of the 22 high-burden countries that account for over 80% of the world's TB cases (8). Between 1995 and 2011, 51 million people were successfully treated for TB in countries that had adopted the WHO strategy, saving 20 million lives (8). In 2011, 5.8 million newly diagnosed cases were notified to national TB control programmes (NTPs) and reported to WHO, up from 3.4 million in 1995 but still only two thirds of the estimated total of 8.7 million people who fell ill with TB in 2011. Notifications of TB cases have stagnated in recent years (8).

"Globally, treatment success rates have been maintained at high levels for several years. In 2010 (the latest year for which treatment outcome data are available), the treatment success rate among all newly-diagnosed cases was 85% and 87% among patients with smear-positive pulmonary TB (the most infectious cases)." (8)

GDF role in the fight against TB

At the start of its activities in 2001, GDF provided first line drugs (FLDs) to treat susceptible TB, but due to an increasing need: (1) added second-line drugs (SLDs) to its portfolio in 2004 in order to treat MDR-TB; (2) developed innovative products like the Stop TB patient kit, and (3) fixed dose combination (FDC) packaging in 2006; and procured diagnostic products and new technology such as GeneXpert to facilitate the quick diagnosis of TB cases from 2008.

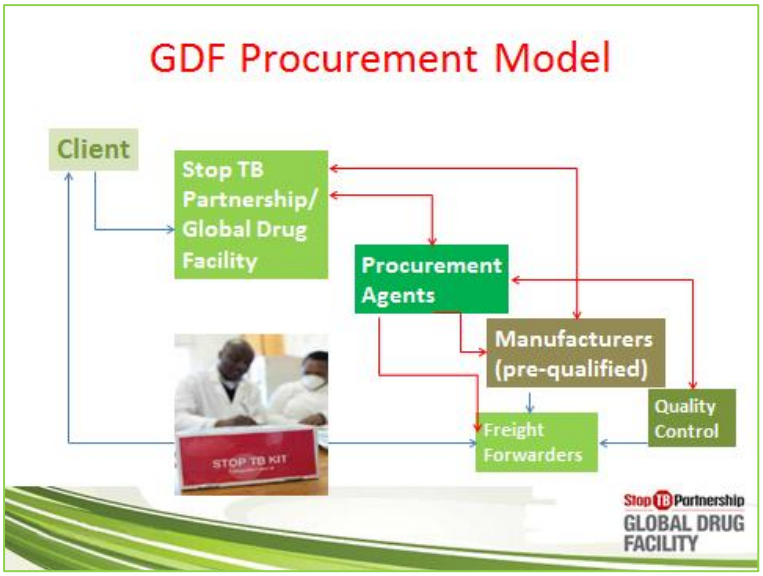
The 4-drug fixed dose combination tablet for treating susceptible TB came off clinical trial as GDF was ramping up its products and services. As a result, the 2, 3 and 4-drug FDCs for adults and 2, 3 FDCs for pediatrics were promoted seriously by GDF and today most of the national TB programmes (NTPs) have incorporated them into their treatment regimens. Using FDCs allows NTPs to simplify the number of products they need to quantify, store and administer to the patient. From the patient point of view, this measure reduces the pill burden from 7-9 tablets to 2-3 tablets per day depending on their body weight. The result is better drug management and adherence to treatment by NTPs while improving patients compliance and reducing the risk of drug-resistance.

Additionally, GDF conducts monitoring missions to countries and provides onsite technical assistance to help improve the drug management aspect of national TB control programmes, a requirement for good procurement and supply systems.

Stop TB Patient Kit ©WHO, 2004

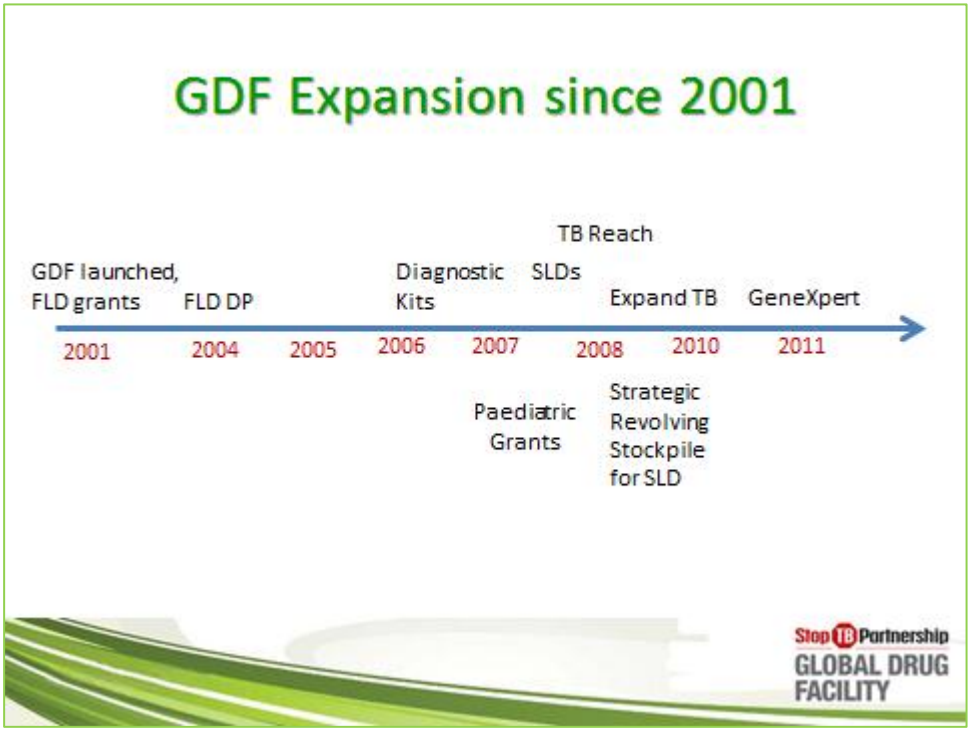
GeneXpert

GDF developed a procurement model to satisfy the needs of its clients. Today, GDF continues to be a totally donor-funded organization whereby some products that meet donor requirements are provided as grants for medicines and diagnostics. The staff and activities required to carry out GDF functions are fully reliant on donor funding since GDF does not currently charge a fee for its services. As the time line indicates below, GDF introduced other services providing FLDs and SLDs to NTPs that had their own funds but lack the capacity to carry out proper procurement practices. GDF refers to this as direct procurement (DP) services.



The timeline pictured here shows when GDF introduced the various products and services, all of which continue today. *Expand TB* is a project supported by UNITAID that provides technical assistance and funding to establish reference labs, diagnostic agents and equipment. With this support countries can more readily diagnose TB cases.

TBReach is a program supported by CIDA which provides support for diagnosing cases in hard-to-reach populations.

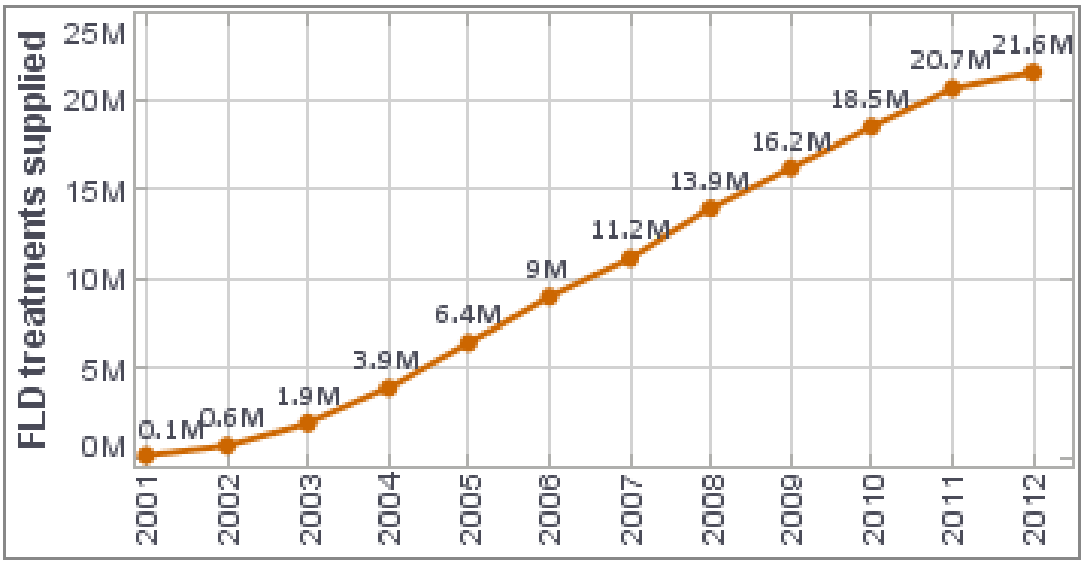


The other terms depicted on the timeline are described elsewhere in this paper. GDF continues to respond to global needs for TB control adding products and services following public demand.

Number of patients treated

Over the 12 years of GDF existence, more than 21 million FLDs patient treatments have been delivered. The graph shows the cumulative supply of adult FLDs.

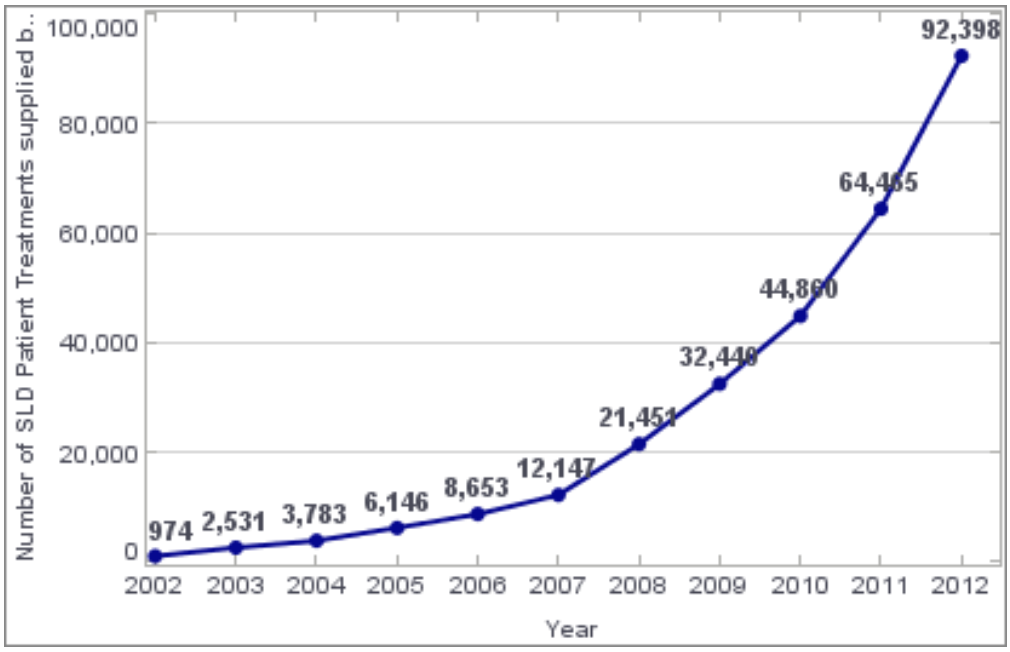
FLD Patient Treatments Supplied Running Total



By 2010-2011 GDF was supplying 40% of the public market for FLDs. From the beginning, GDF promoted standardization of treatment regimens based on the World Health Organization (WHO)'s recommendations. As a result, the FLD orders from GDF today are mainly the 4-FDC tablet for the 2-month intensive phase treatment (average 3 tablets per daily dose), and the 2-FDC tablet for the 4-month continuation phase of treatment (average of 3 tablets per daily dose). As a result, the daily pill burden from 7-9 tablets has been reduced to 3, simplifying the number of individual products that the health system must manage in terms of quantification, distribution, storage and patient administration.

GDF began the supply of SLDs through the Green Light Committee (GLC) mechanism in 2007. By 2011 the GLC transitioned from a small patient-cohort-oriented service to a regional-based technical programme partner for NTPs. This change allowed NTPs to place their SLD orders directly with GDF rather than waiting for GLC approval.

Since 2009 the global TB community has talked about the need to scale up treatment of MDR-TB; however, a corresponding increase in SLD orders have not occurred as originally projected by the TB community due to slow uptake by NTPs. The graph on the next page shows the number of SLD patient treatments delivered by GDF from 2007 to the current year.

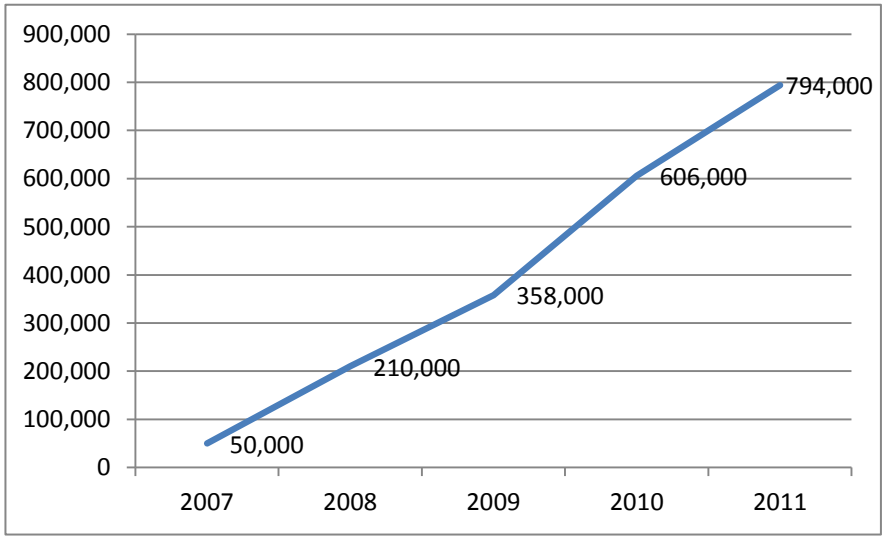


Note: The 2011 update of the WHO's guidelines for MDR-TB treatment recommends to prolong the use of injectable drugs from six to eight months. Therefore, the current calculation algorithm for the 2012 is based on the 6 months regimen and may need to be revisited in 2013 based on the evidence (treatment regimens reported by the countries).

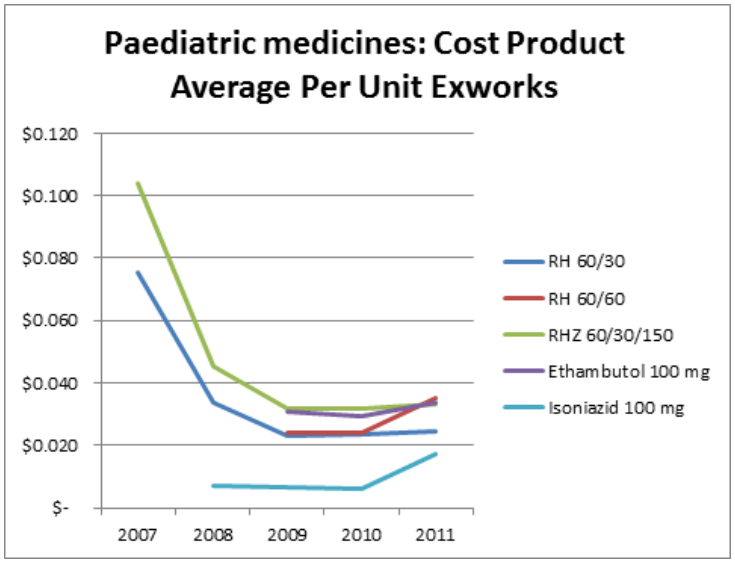
In anticipation of a larger scale-up of MDR-TB treatment, GDF has discussed with its current quality-approved suppliers and concluded that scale-up can be doubled without having any impact on their capacity to meet the demand. In the months to come, GDF will be working with stakeholders to forecast the need of current and potential new GDF clients year by year to share this information with suppliers so they can increase their production capacity as needed. This is an important step that shows how GDF continues to shape the TB market as it anticipates the demands of its clients.

Pediatric TB medicines: GDF received few requests for pediatric medicines until UNITAID awarded GDF a grant to focus on pediatric TB and to take the initiative in shaping the market; so that medicines would be prescribed with the WHO recommended dosing. Since 2007 when GDF began this endeavor until 2011, about 794,000 pediatric treatments (curative and prophylactic) have been delivered to the countries as shown in this slide. These were supported by monitoring missions to verify quantities needed and local compliance with guidelines and procedures.

Number of Pediatric Treatments Supplied by Year



GDF has been able to influence the pediatric market as shown below. Medicine prices immediately declined and have stabilized in the last couple of years. During this period, two studies conducted by WHO and technical partners prompted the revision of the pediatric guidelines. The first study resulted in modifying the treatment regimen with higher doses of FLDs. The second study is still on-going.

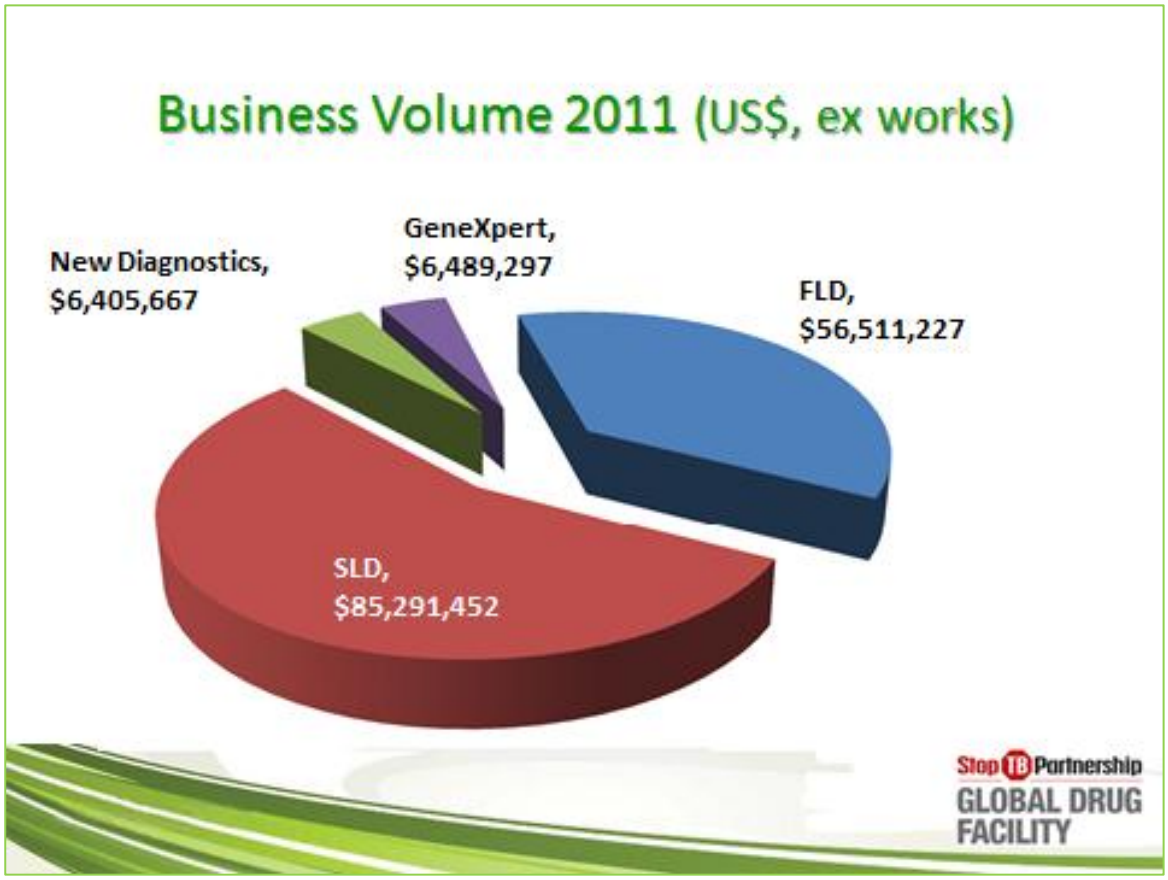


GDF had approached manufacturers about considering changes in the production and validation of procedures for higher fixed dose combination (FDC) of pediatric medicines. However, these changes will be delayed until the second clinical trial is completed. In the interim, GDF has worked with TB partners to promote interim guidelines allowing NTPs to use the higher doses from the 1st clinical trial.

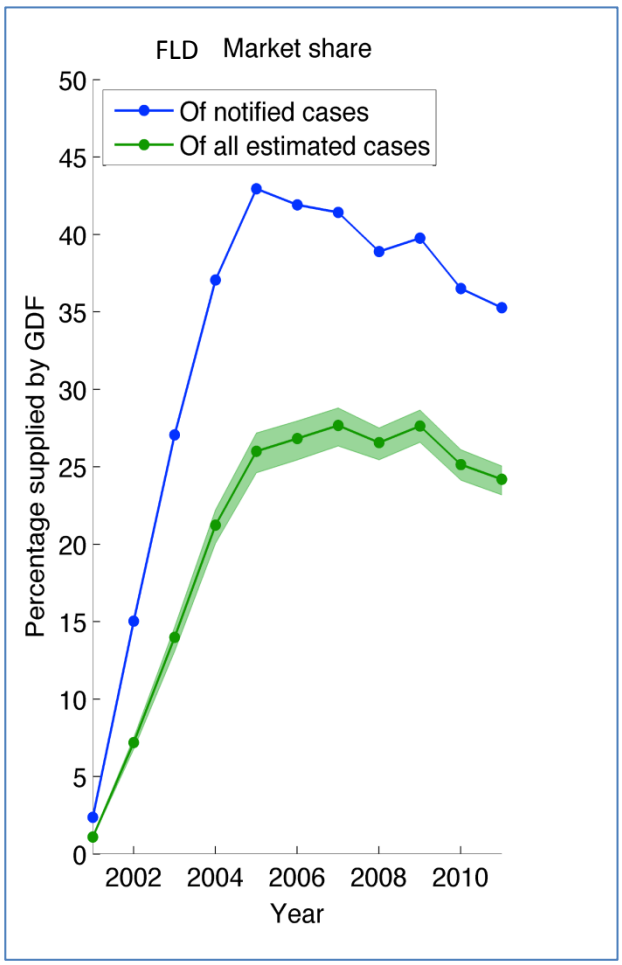
Value of diagnostics and diagnostic equipment delivered and market shaping

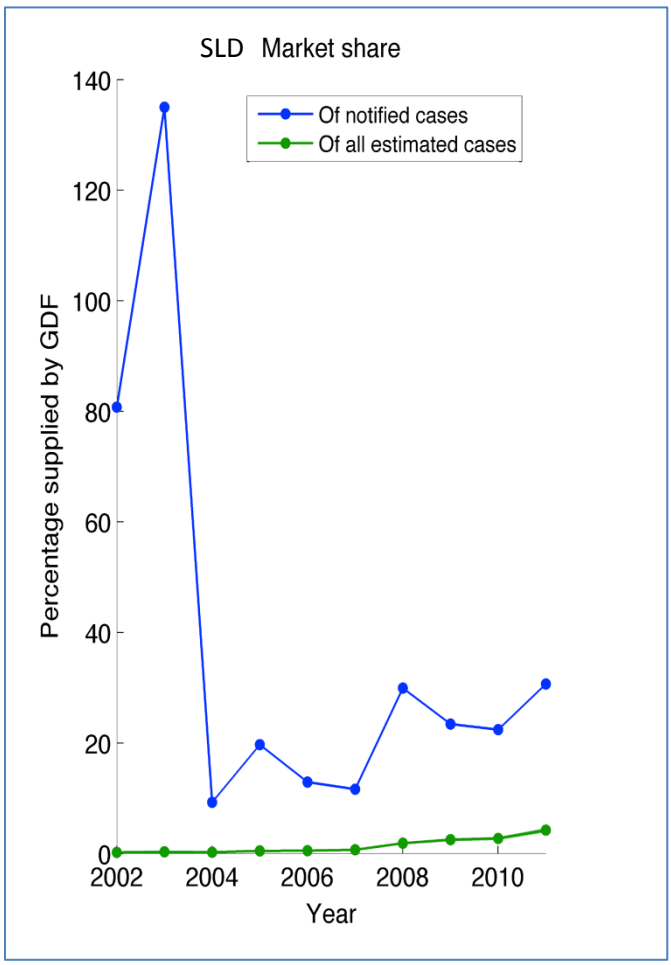
GDF's contribution to TB diagnostics started with the development of diagnostic kits, which contain bright-field or LED microscopes, slides and reagents that NTPs need to carry out the recommended smear microscopy for TB diagnosis. This service was expanded in 2009 to include the "new diagnostics" financed through the Expand-TB project, the line probe assay method for quicker diagnosis and the GeneXpert to quickly identify MDR-TB in patients.

Because of its mandate to follow the directives of TB stakeholders, GDF continuously works with its suppliers, sharing estimates of annual product needs to obtain the most economical high quality products available. Once sufficient quality suppliers have been approved for a given type of TB product (e.g. FLDs), GDF then conducts competitive procurement methods and awards business to those suppliers with the best price and delivery services. The graph below shows the value of products supplied by GDF in 2011. The term "ex works" means the price GDF has to pay for the medicines before shipment and related costs are added.



Market shaping: For FLDs, GDF has been able to reach about 35-45% of those cases diagnosed and reported with TB (notified cases) and between 20-25% of estimated cases from 2004 and 2011 as seen in the figure below. For SLDs, GDF has taken a smaller market share (about 30% of notified cases and approximately 5% of the estimated cases) mainly due to funding availability and diagnostic capacity in the countries. To contribute to case detection, GDF started to supply new diagnostic tools for Expand TB and TBReach, activities that represent 4% of GDF supply in value as shown in the Business Volume slide above. GDF's impact on pricing is described in the section on *Prices of Medicines*.

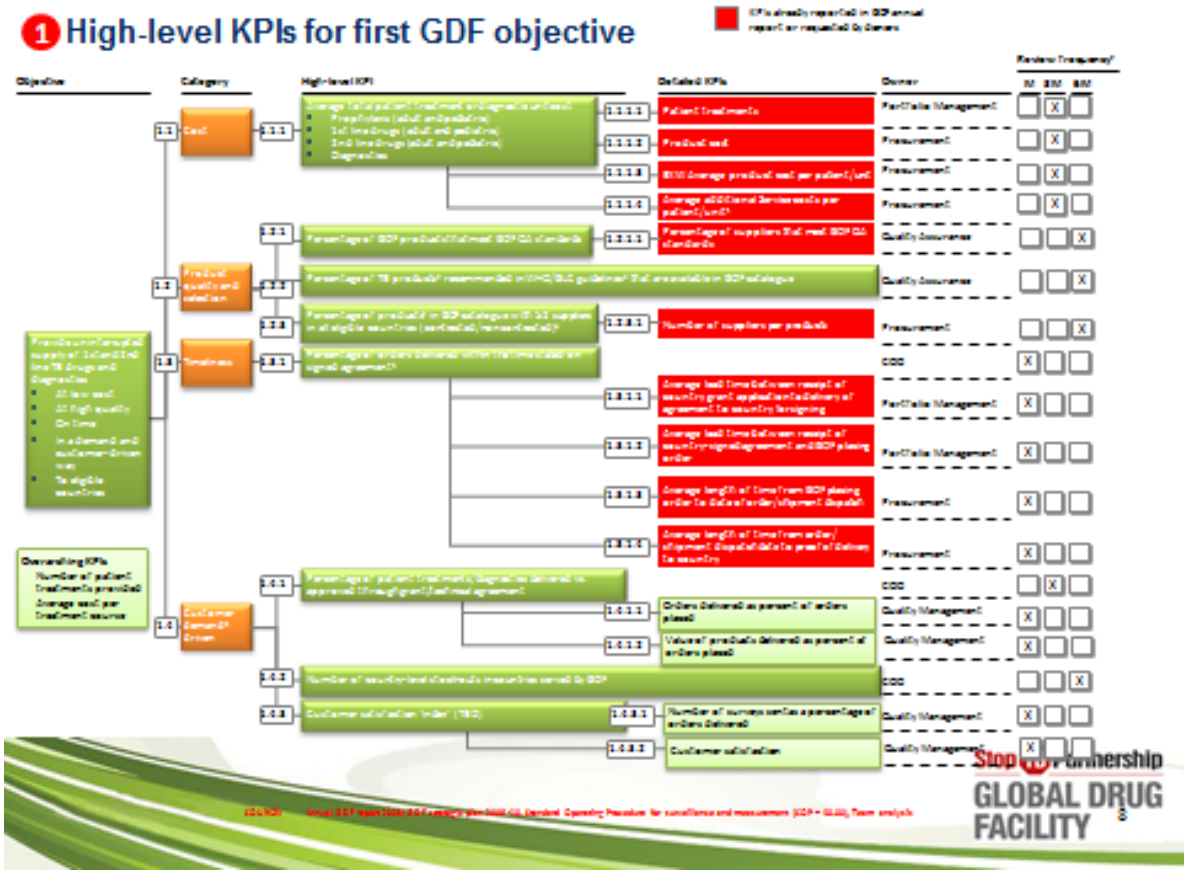




Quality management system and product quality assurance

Quality management system: Only one country received GDF support in 2001, the year it was established, but since then more than 100 countries have procured their TB medicines and diagnostics through GDF. Being a global entity, GDF saw the need in 2004 to set up a comprehensive quality management system (QMS). GDF received the ISO 9001 certification from Quality Systems Engineering – Switzerland after meeting the qualifications. Certification involves an annual inspection to see that the requirements for certification continue to be met. GDF also conducts an internal audit to verify that procedures are being followed as described in approved standard operating procedures (SOPs). GDF's QMS follows the private sector standards of performance management.

In addition to SOPs that show each GDF process, GDF has developed more than 40 key performance indicators (KPIs). For each KPI there are numerous dashboards that allow GDF staff members to monitor their work as well as that of its agents and clients. The dashboards allow live performance measurement and analysis. Recently, GDF placed a selection of the KPIs on its website (2). See sample picture below of the high level KPIs. For readability purposes, please see description of the KPIs in the GDF 2011 Annual Report, Annex 1 (3).



Product quality assurance: While the quality management system is for managing GDF staff performance and practices, product quality assurance is a separate system to assure that only quality medicines and diagnostics are supplied to clients. GDF has embraced a quality policy for manufacturer and product approvals to assure they meet international quality assurance standards for medicines. This policy requires that manufacturers of each product supplied to GDF must have met stringent regulatory approval by organizations and countries like the United States, the European Union and Japan. Otherwise, a manufacturer can apply to the WHO Prequalification Programme (WHO-PQP) (4), which involves an approval process of the medicine production site, ingredients used in manufacture, production process, stability studies and bioavailability studies of the finished product. GDF was instrumental in catalyzing the WHO-PQ and expert review panel (ERP) mechanisms in order to stimulate the market.

The WHO-PQP approval process can be long (as much as 24 months or longer). For that reason, the GDF quality assurance (QA) policy allows for a risk-based approval of manufacturers' when there are not enough products on the market either approved by stringent regulatory authorities or the WHO-PQP. This risk-based approach is called ERP whereby much of the required information is available and shared by the manufacturer, a site visit reveals that the manufacturer follows good manufacturing practices as prescribed by WHO and the experts reviewing the data think there is minimal risk to accept this product for an interim period such as 12 months, while suppliers strive to meet WHO-PQ status.

GDF delivers only high quality products at the lowest prices as shown by the "WHO survey of the quality of TB medicines circulating in selected newly independent states of the former Soviet Union" (6). From 291 samples that were collected in the survey, none of the 38 samples from WHO-prequalified products nor any of the 42 samples (14% of tested samples) supplied through GDF failed the quality testing. This supports the fact that the GDF quality assurance system is effective.

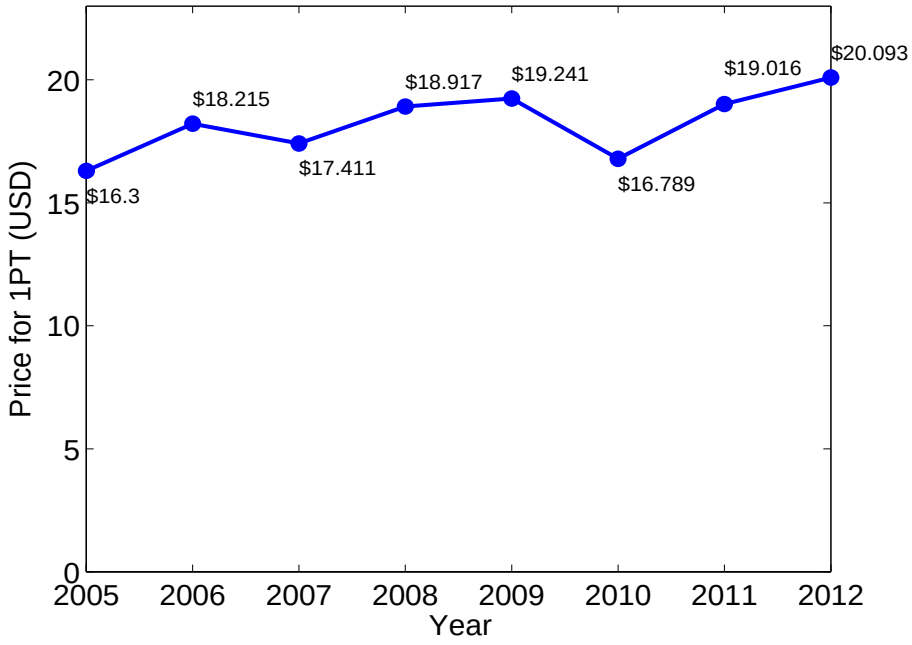
Many countries have a national drug regulatory authority that analyzes drug dossiers and tests products from manufacturers (Drug Registration) to make sure the products are safe and effective for the population. The process can take time and for that reason some national authorities issue a waiver or delay registration at first, accepting GDF products on the basis of humanitarian aid and because of GDF's strong quality assurance policy. In the WHO survey for quality, mentioned above, all of the samples supplied through GDF were either registered in the recipient country or their use was authorized as humanitarian aid.

Prices of Medicines

GDF has a positive impact on the prices of medicines. Drug supply by GDF is among the most cost-effective health interventions available and has proven to be successful in diverse low-income developing nations. A full course of the standard FLD treatment can be procured from GDF today for less than USD 21; and for an average SLD treatment, GDF can supply the medicines for less than USD 3,300.

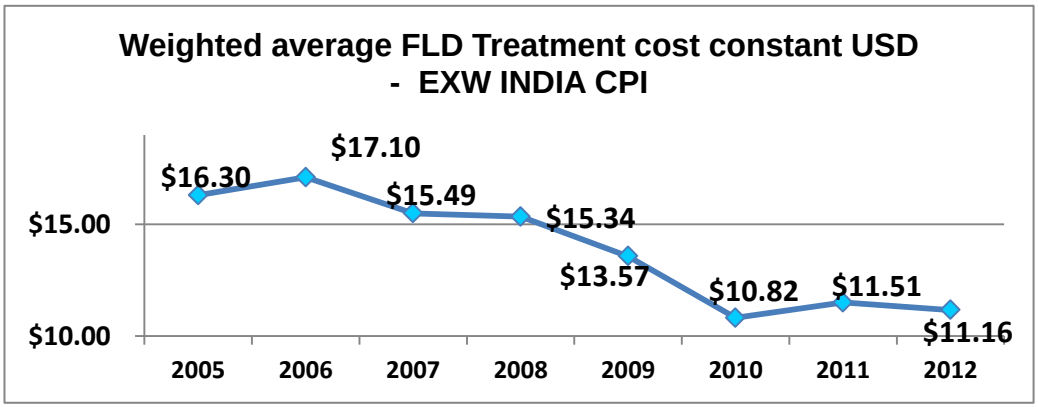
The slide below seems to show negative impact, in that the price of a FLD treatment increased by 23% over 8 years. The graph shows price per patient treatment per year.

Weighted average FLD Treatment cost in nominal USD (EXW)



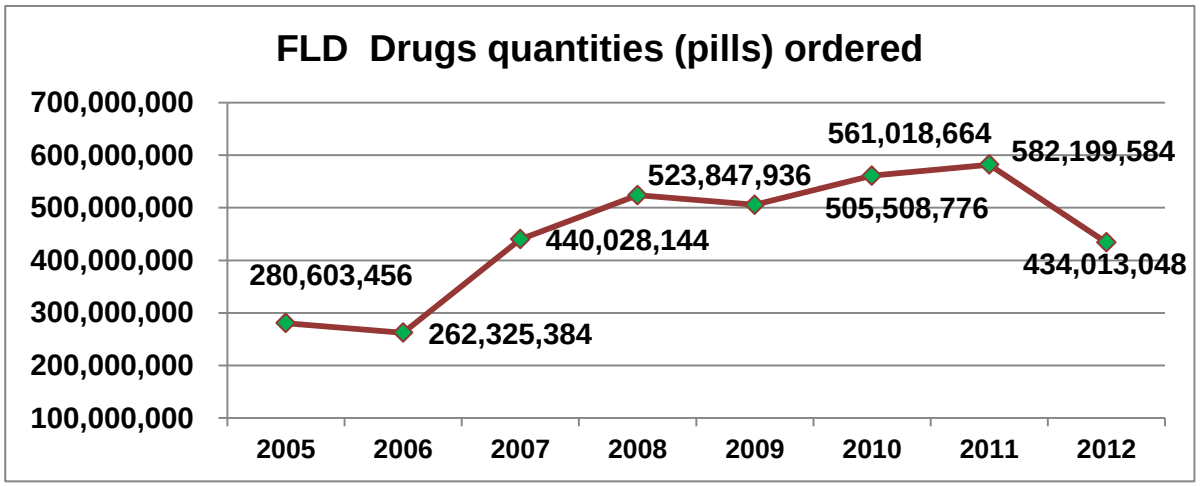
Note: EXW in the graph above means the price of the medicines used to calculate patient treatments is the price before leaving the supplier, thus excluding shipping and related costs until delivery to client. The quantity for 2012 is through the month of October

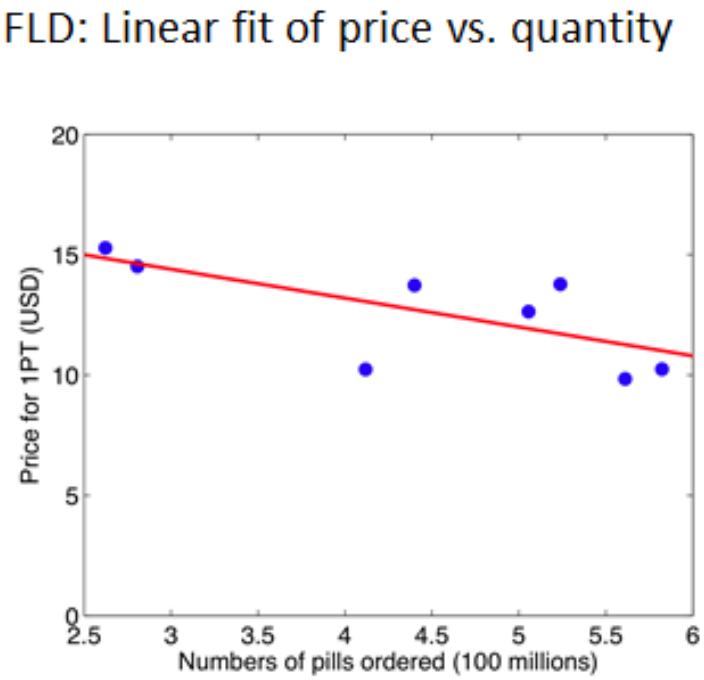
However, the following slide shows price *reduction* for a FLD patient treatment when adjusted for inflation (consumer price index in India) by 32%.



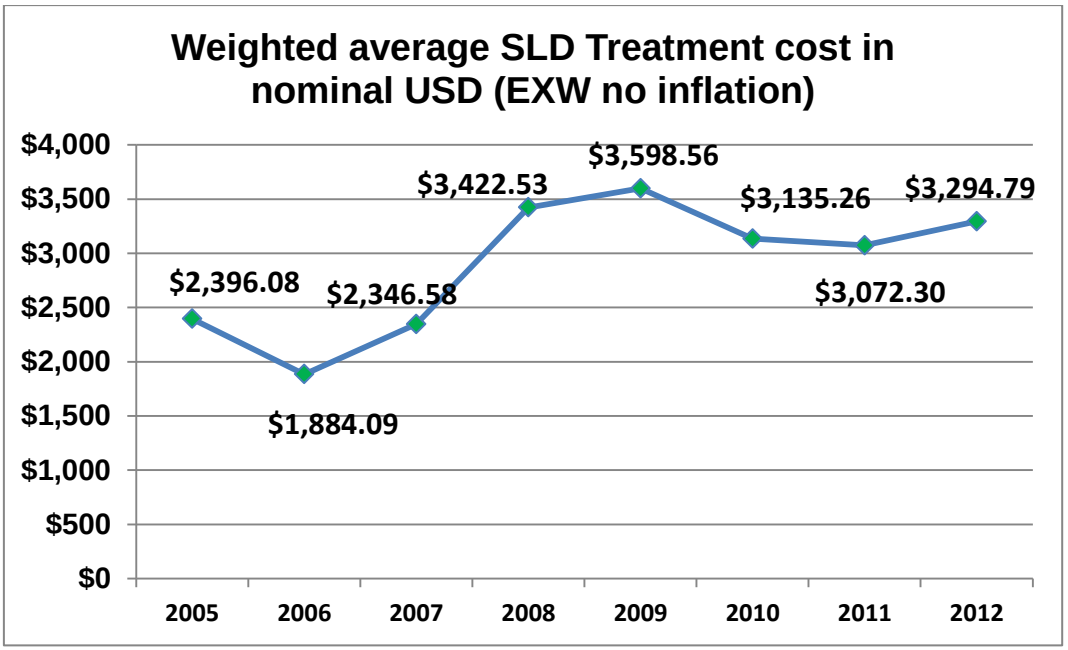
To attempt to explain the price reduction above, there seems to be a correlation between the quantities of medicines ordered by GDF and the price of patient treatments (slide below). This is explained by the statistical model which shows a strong linear correlation between prices and quantities (slide further below).

FLD quantities (pills) ordered per year

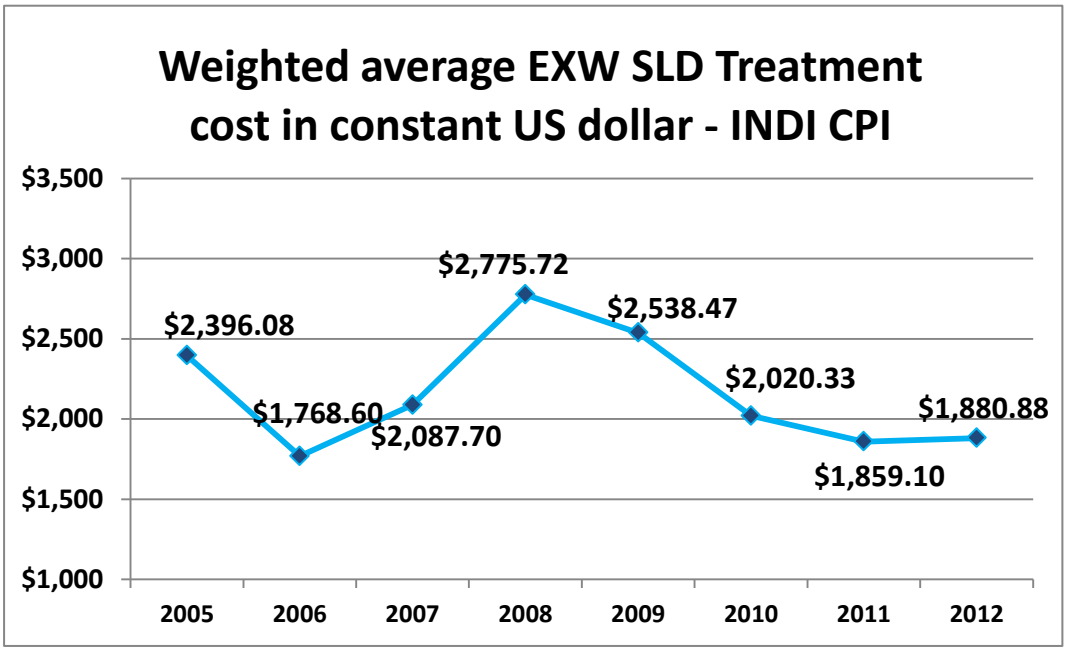




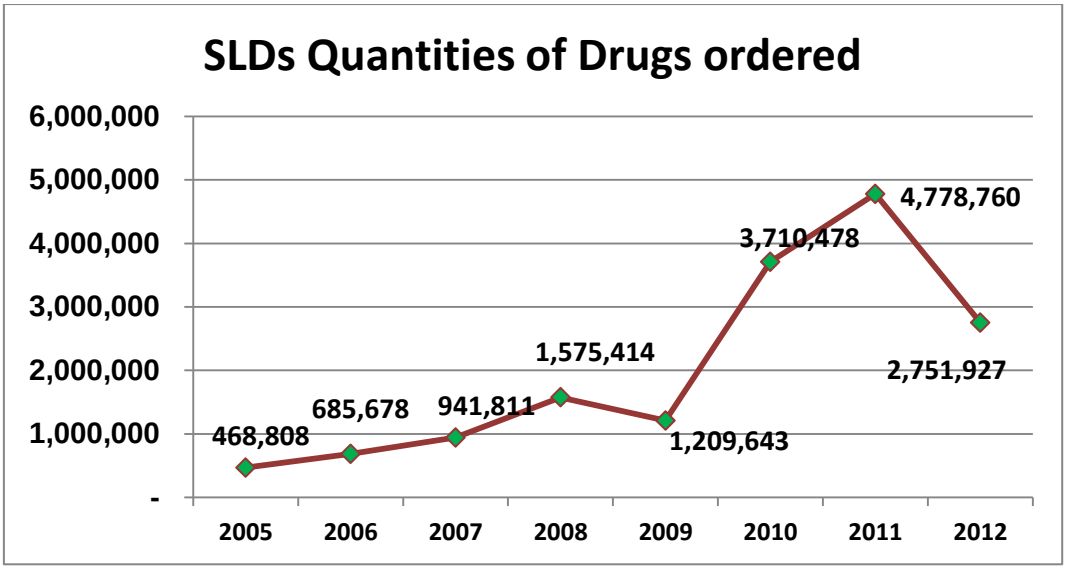
For SLDs the same story seems to be true as shown in the graph below whereby cost of one patient treatment increased by 38% from 2007 when GDF began procuring SLDs until 2012.



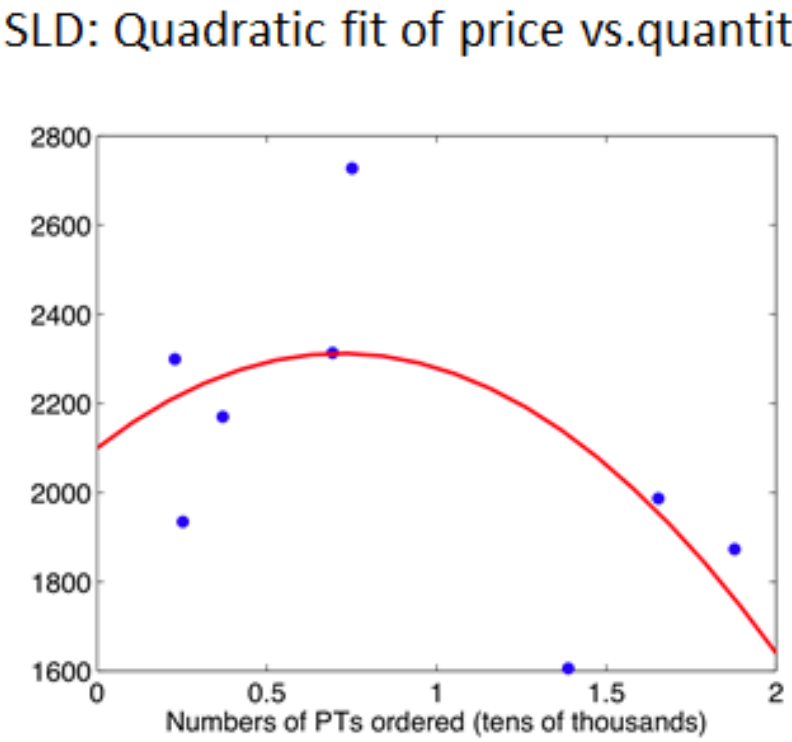
However, the following slide shows price *reduction* for SLDs when adjusted for inflation by 22%.



As for FLDs, an explanation for the price reduction adjusted for inflation in SLDs is the same – it shows a correlation between the quantities of medicines ordered by GDF and the price of patient treatments (slide below).



The trend of increase in quantities delivered affects a reduction in price is explained by the statistical model which shows a good *quadratic* correlation between prices and quantities (slide further below).



Note: PT = patient treatments

Lead times

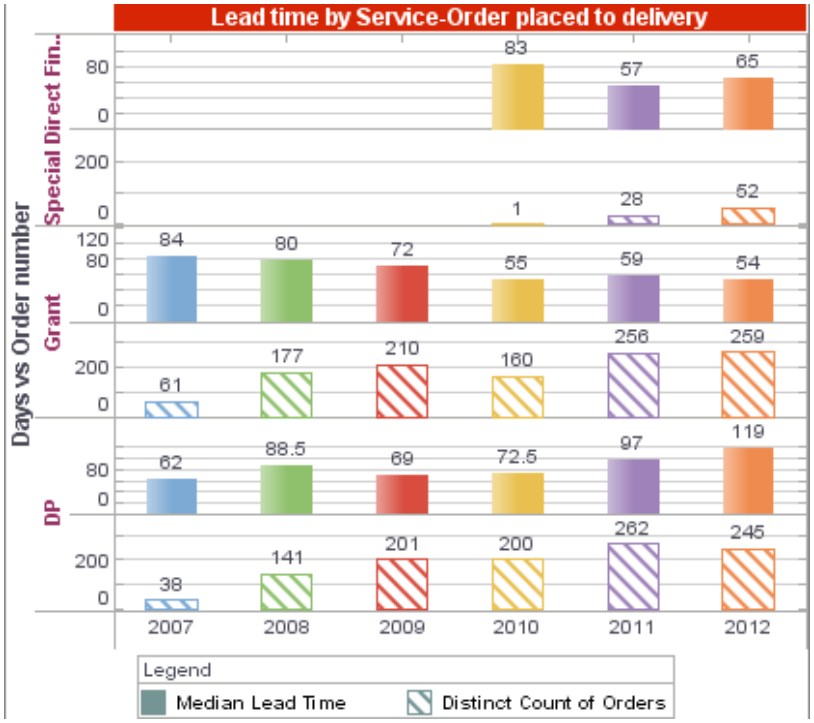
When procuring medicines and other products, the lead times can be broken up into smaller units so as to measure where bottlenecks might be occurring. For example, procurement lead time is the time when an NTP first contacts GDF about wanting to place an order until they actually receive the medicines or diagnostics. This can be broken down into time subunits such as: obtaining signature on technical agreement between GDF and country and verifying quantities of each item needed, getting price quote for the order, getting money secured to pay for medicines, placing the order with suppliers, getting quality assurance done on the finished product, shipping of the products and port clearance in the recipient country.

Below are some graphs showing how GDF has performed, using KPIs to measure procurement activities. GDF shares several of these lead times on its webpage (2).

The Order Lead Time, defined as: "date order placed to date of delivery in country", is the area that GDF and its suppliers mostly impact the supply chain from the date the order was first requested by NTP until the order is delivered in the country. Earlier lead times such as: (1) "date quantities requested by NTP until date order placed by GDF with supplier", are very much in the hands of NTP, since NTP must obtain authorized signatures for the price quote and agreement form for GDF (containing quantities and medicines desired, as well as cost to manufacture and deliver to the country); likewise, (2) the payment of funds upfront are required before orders can be placed with suppliers. Both of these lead times "1" and "2" are almost totally within the hands of NTP and are a major reason for overall long lead times to deliver medicines to countries (4-6 months on average).

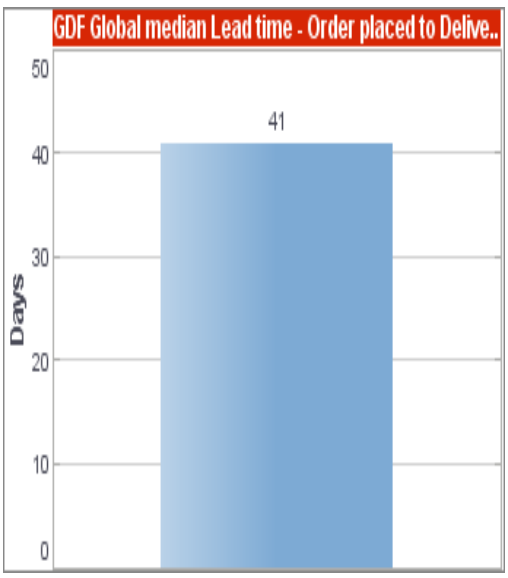
Using KPI data the graph below, called "Lead Time by Service Order placed to Delivery" shows the median "Order Lead Time" per year disaggregated for grants versus DP. The striped bars show the number of orders and the solid bars show the media number of days lead time for the orders. As can be seen, GDF grant orders decreased from 84 days in 2007 to 55 days in 2012 (a savings of 29 days in the process).

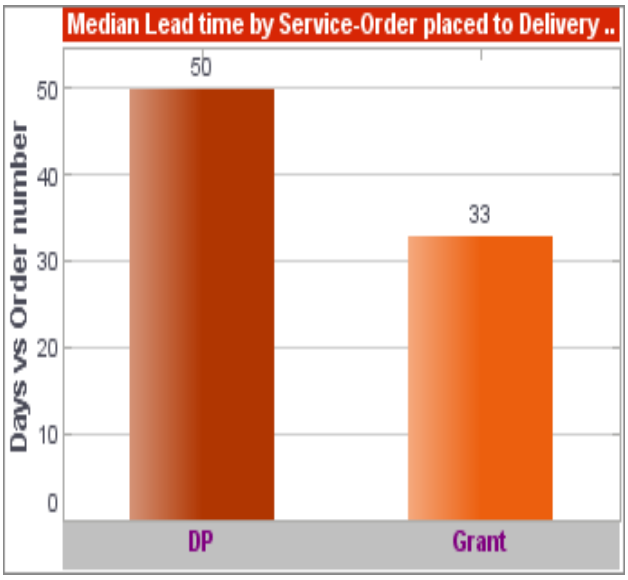
Direct procurement (DP) orders increased from 62 days in 2007 to 119 in 2012 (an addition of 57 days). The best explanation for DP order lead time increasing over the years is that more NTPs are having problems getting funds released from either country budgets or from donor grants such as the Global Fund. The difference in lead time cannot be related to the number of orders which are very similar: 264 versus 268 respectively.



GDF has a limited-quantity stockpile supported by UNITAID, which allows the shipment of product as soon as the paperwork and monies are delivered by NTP to GDF. The stockpile is used for emergency orders and to rotate medicines from the stockpile relative to their shelf life which are used to complete regular orders.

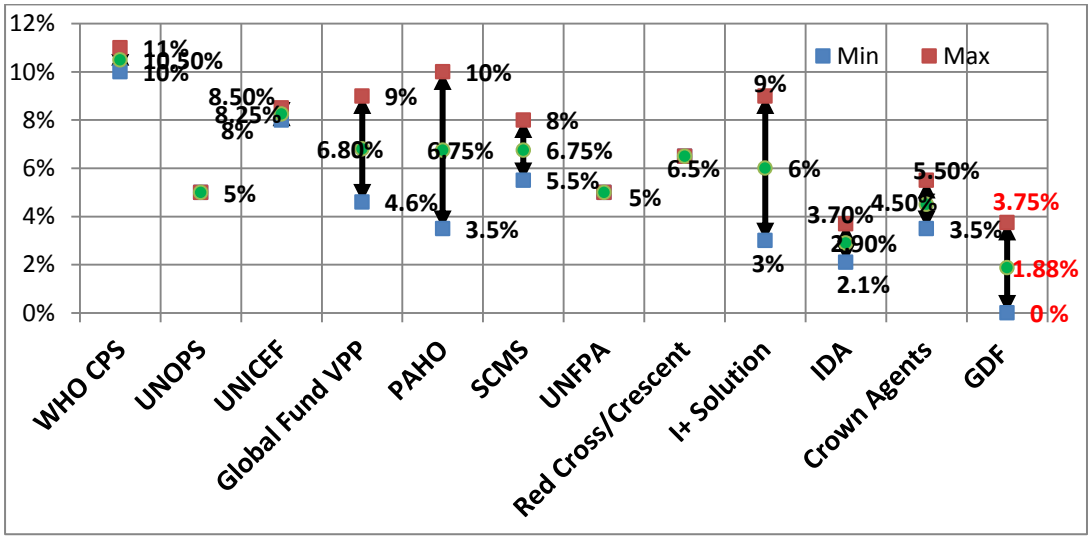
The blue bar below shows the median *Order Lead Time* when SLDs are delivered as *accelerated* orders from the stockpile; these data are for the years January 2007 to October 2012. The orange bars shows the median *Order Lead Time* by type of service, that is a grant (GDF has the funds) or DP (NTP must pay with its own funds). This supports very graphically that having a stockpile and funds in-house to advance pay for the medicines, the lead time reduces dramatically.





Procurement fees

GDF's procurement fees are less than any of its peers. The slide below based on a survey done by GDF, shows that GDF's fees range from 0% to 3.75 depending on the line item. GDF may take advantage of the 0% currently charged for two of its projects and earn a small fee to help defray costs of its operations currently funded only by donors. The other fees go directly to the external procurement agent.



Note: CPS = WHO procurement service; SCMS = Supply Chain Management System

Avoiding stockouts

Increasingly NTPs are asking GDF for emergency FLD and SLD orders because of problems with local funding. The problem may be with government budget allocations, but many times the problems are related to Global Fund grant policy. Other reasons are listed below this paragraph. The Global Fund requires that technical plans are in place including the one for procurement and supply management. Until those plans are approved by the Global Fund, the monies are not released to the principal recipient of countries. This delay continues until the plans are technically correct according to Global Fund procedures which can take weeks and even months causing many countries to approach or reach stockout status of FLDs and SLDs.

While GDF has some funding today for grants, these monies will decrease greatly over the next couple of years as donors decrease their support for FLDs, believing this is what the Global Fund was established to do. As a result, GDF is asked by the affected NTPs to quickly supply medicines. While GDF is glad to do this as long as it fits the requirements, mandate and resources, GDF is not an emergency order agency at this time. Placed orders take 4-6 months to be delivered to countries because of manufacturing requirements. GDF does have a limited-quantity stockpile of SLDs funded by UNITAID, but have indicated that support will end soon. There is no stockpile for FLDs. This

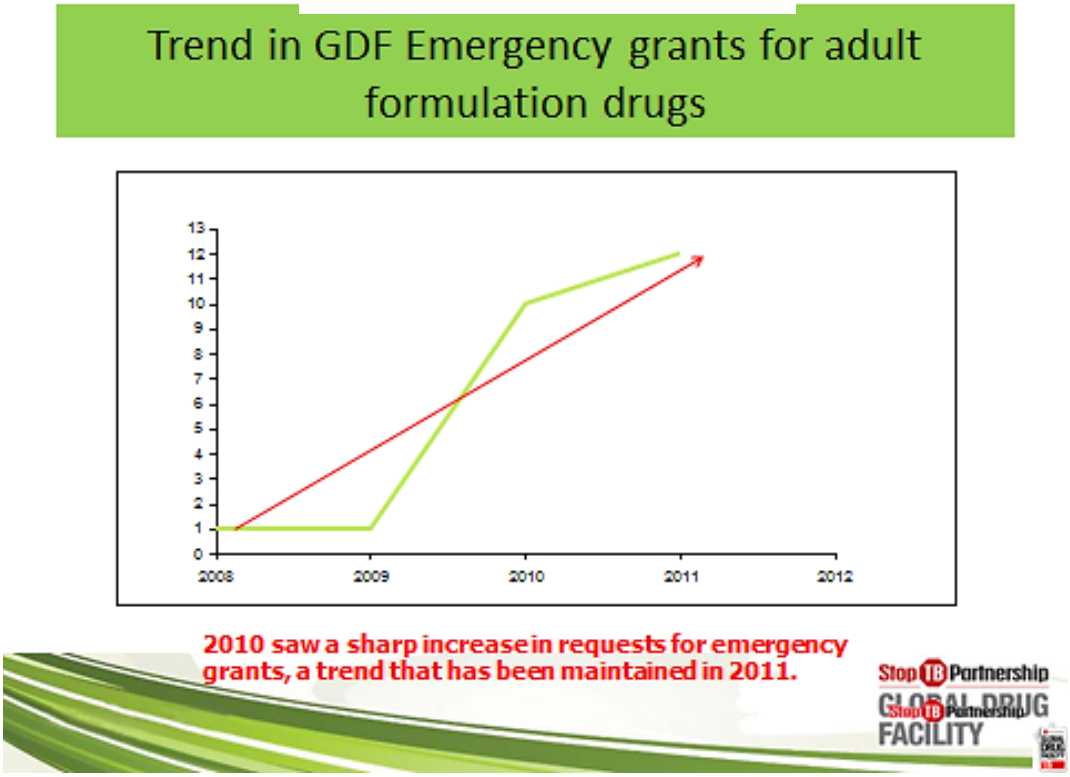
means that GDF has to scramble to see if orders intended for other NTPs can be delayed to shipment to the NTP facing potential stock out.

Examples of reasons for emergency orders are:

- Shortfall in Government budget or transitioning to Government funding (Iraq, Senegal, Mali, Burkina Faso in 2010; and Egypt in 2011)
- Humanitarian (2011) Pakistan, Libya.
- Delay in release of Global Fund funding (2010) Mauritania, Djibouti.
- Delay in signing the grant agreement ((2008) Yemen, (2009) Haiti, (2010) Mozambique, Madagascar, Guinea Bissau, (2011) Central African Republic and Cambodia).
- Not adequate funding under GFATM grant (Democratic People's Republic of Korea provincial grant and Niger).
- Program suspension (2011) Mauritania).
- Global Fund moved support to Malaria and HIV; country did not do necessary to cover the gap.
- Quality assured streptomycin supplier lost approval causing delay in delivery by GDF agents.
- Late disbursement of funds by Global Fund.
- Poor drug management.
- Inadequate funding availability.
- Late delivery on the part of GDF due to supplier delay.
- Solution for some countries: redistributed existing drugs or procured from the local market.
- Lack of buffer stock in some DP orders funded by GF leading to stock outs.
- Specific type of contracts (bilingual, plus additional non-standard clauses) required by EURO countries.
- Change of consignee's name when products have been packed and inspected.
- Requests from countries for additional shipping documents after the inspection has taken place.
- Requests to ship all products at the same time due to complicated custom clearance procedures. In these cases, the medicines which have been produced on time or faster have to wait for the medicines with longer production lead time (e.g. Streptomycin).
- Registration not done promptly.

The graph below shows the number of countries requesting emergency orders for FLDs which are increasing every year due to problems at the country level, very often related to funding as mentioned above.

Number of Emergency Grants by Year



Mitigating stockouts: There are two mechanisms that would reduce or practically eliminate stockouts: a global strategic stockpile (GSS) and funds for advance order placement, a flexible procurement fund (FPF) for both FLDs and SLDs. With the GSS and FPF tools in place, GDF could alleviate most of the stockout problems if it were to be supported by donors. There would be striking reductions in lead time. For example, the manufacturers only order the medicine ingredients and plan production of the medicines of a GDF order when they receive the money in advance, called production to order. With strategic funding, GDF could both: 1) pay for orders while waiting for NTPs to organize paperwork and funding from Global Fund or national budgets; and 2) issue medicines from the stockpile. Based on the small stockpile that GDF has for SLDs, the order lead time could be reduced from 4-6 months to 4-6 *weeks*. This is discussed in more detail in the last section of this paper.

Impact of GDF on national TB programmes

GDF has an impact far beyond drug prices and quality assurance. With GDF support, NTPs are able to:

- Become more effective,
- treat more patients,
- receive only drugs approved according to international standards,
- perform better

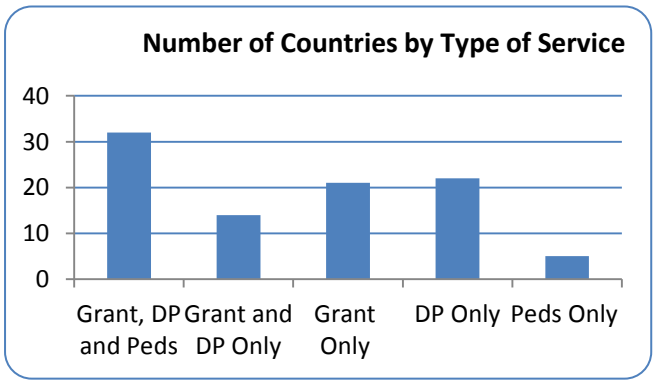
Where GDF has worked: GDF has worked in more than 100 countries since 2001, ranked by WHO Region. It is notable that the largest number of countries served by GDF is in the AFRO region and the smallest in AMRO. Some countries have only been recipients of GDF grants for adult and pediatric medicines. Some have procured TB medicines through GDF using government or donor funds organized by them.

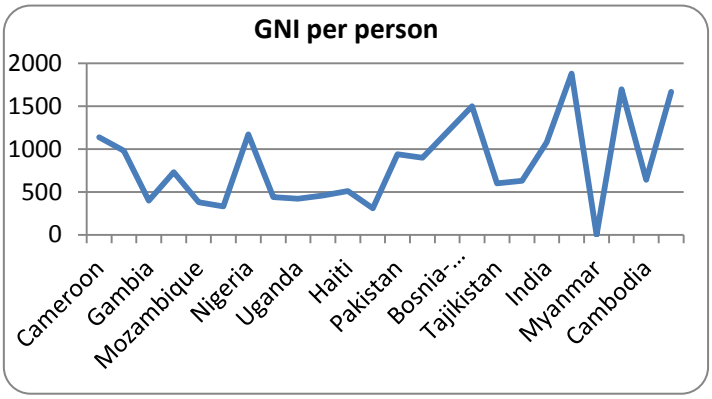
Some countries have procured only diagnostic products through GDF. Others have received all of these services. This is due mainly to gross national income (GNI) of the countries (see picture below), where low income countries are targeted more than middle income ones, but also, many of the AMRO countries either have their own funding and/or require that medicines are procured from local sources (5). The other picture below shows the number of countries by type of GDF service with respect to TB medicines.

Countries where we work

WHO Region	Number of Countries
AFRO	39
EMRO	17
AMRO	5
SEARO	10
WPRO	13
EURO	17
Total	101

All are low income countries if receiving grants (is GDF criteria) and low to low-middle income countries if NTP orders by direct procurement





These boxes show comments from satisfied GDF clients.

See more on customer feedback in that section later in the paper.

"Keep up the good work. Particularly these consignments were great and exceptional services."

- Uganda

"Comment from Bangladesh: "The Xpert cartridges arrived very quickly and were in perfect working order."

The picture to the right shows a small sample of GDF clients and the types of services they require of GDF. To clarify, the information under the "DP" column, this means that countries paid for the medicines procured through GDF using either their own government funds, that of the Global Fund or both. (6).

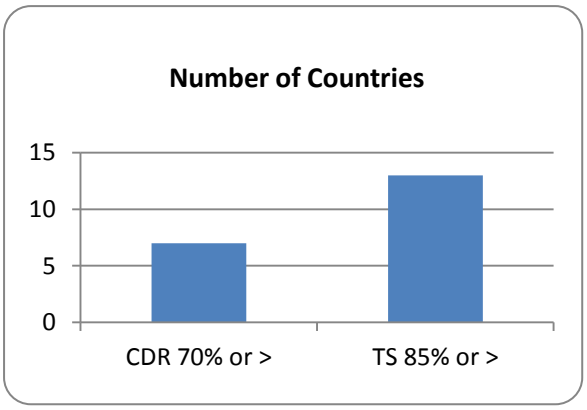
Examples of Countries we service

• Includes grants and paid orders by NTPs

Country	FLDs		SLDs	Diagnostics
	Grants	DP		
Mozambique	√	√ GF	√	√
Nigeria	√	√ GF	√	√
Azerbaijan	X	√ GF+ Own	√	X
Uzbekistan	√	√	√	√
Cambodia	√	√ GF	√	√

Diagnostics through Expand-TB project

National TB Programme Indicators: 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 programme is expanding to detect the needs of the TB population in the country. The treatment success rate (TS) is made up of two components, 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 above 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, consequently NTPs still have much work to do in that regard.



Technical assistance to NTPs: In-country monitoring missions are conducted annually for all grants and some direct procurements. The purpose of this visit is to carry out the GDF mandate that countries can show evidence they know how to manage TB medicines, an expensive commodity where donor funds are used to buy

GDF provided Technical Assistance

In country TA missions conducted annually for all grants and some direct procurements

TA team consists fo 2 experts: TB program and PSM

Number of country missions	
Year	Number
2005	51
2006	59
2007	57
2008	76
2009	88
2010	52
2011	44
2012 (estimated)	65

Longer term TA provided ad hoc

*Number of PSM workshops - 5 during 2010-2012

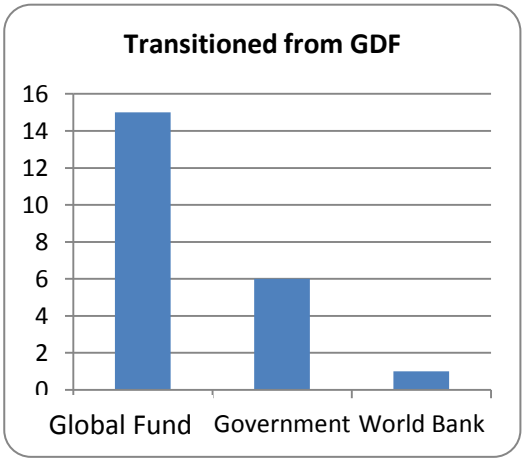
the medicines. GDF collects this information on a standard template and for grants asks the GDF Technical Review Committee to make a decision on the capacity of the country to receive the medicines free of charge. During these missions, two GDF consultants (one programme and one drug management consultant) assess country drug management capacity by reviewing documents, visiting warehouses and treatment centers, interviewing stakeholders and promoting best practices. During the mission, GDF consultants also provide on-the-spot technical assistance (TA) to help programmes with tools to quantify, store, deliver and use TB medicines and diagnostics appropriately.

Another area of technical assistance Is TB drug management capacity-building workshops. GDF facilitates these workshops with its TB technical partner, SIAPS and five were conducted during 2010 to 2012. These are held in various WHO regions and are attended by one NTP and one drug management person in each country of the region that wishes to participate. The workshops are partially didactic, but always involve a practical approach with visits to warehouse and treatment centers to use evaluation tools that measure the appropriateness of TB drug management in TB programmes. The quantification component requires that participants use data from their own NTPs to calculate TB medicine needs for the next year. The rational use component of the evaluation involves interviewing patients and health workers alike about what information must be given or is provided so patient will better understand their TB treatment and thereby improve adherence to the TB medicine regimens

Sustainability of TB control programmes: By supplying uninterrupted access to quality TB medicines and diagnostics and provision of technical assistance to qualifying DOTS and MDR-TB programmes, GDF and partners contribute to the success of NTPs by stimulating political and popular support for effective, publicly funded TB control. Several countries had transitioned from GDF support by 2010 as shown in the slide below. This is because a requirement for GDF included the need to improve local funding of their medicine needs as GDF provided grants.

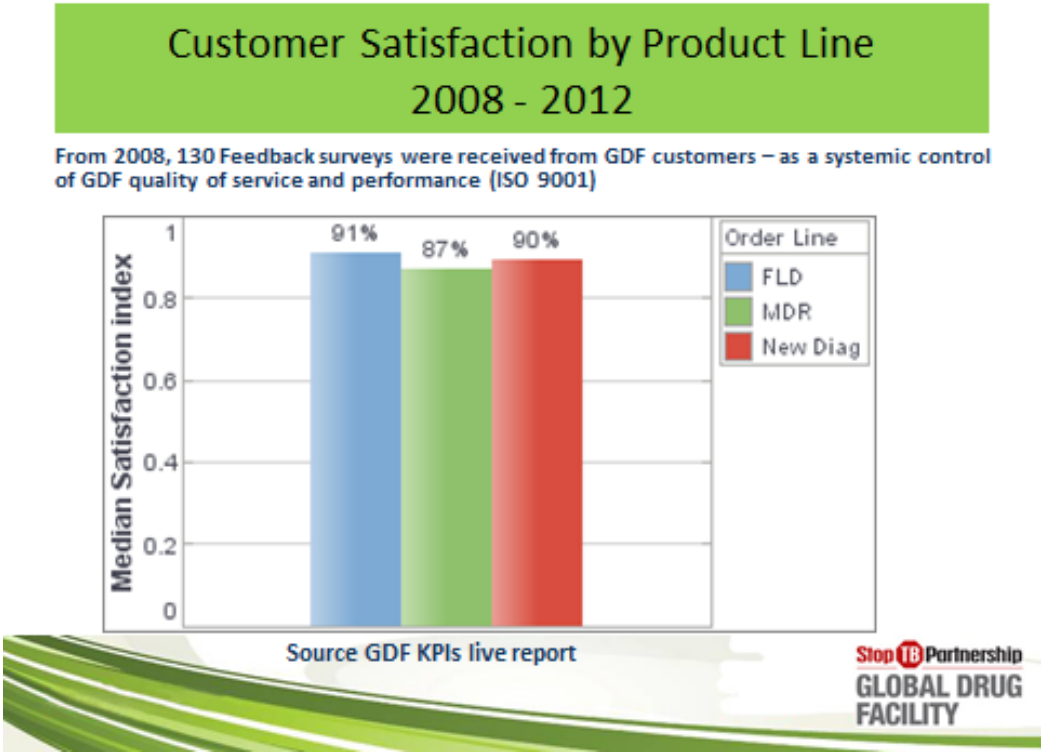
The slide below shows the number of countries that transitioned from GDF to other sources for their TB medicines. And the table below shows the range of funding countries were able to provide as GDF encouraged them to do, during grant support over the decade.

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



How countries rate GDF services

GDF service is highly rated. GDF sends customer feedback forms systematically with each order delivery. It is very interesting to note that GDF only receives One or two complaints per year compared to an average 494 of orders per year; this represents a rate of 0.4%. Below, the graph shows KPIs from the GDF order management system from 2008 – 2012, showing percent satisfaction by line item.



The boxes below show comments that GDF has received from NTP managers and partner organizations.

"We are happy with SLD procurement for MDR-TB Management project from GDF"

- Myanmar

"From my experience with GDF, it plays a crucial role towards provision of reliable products for the elimination of most of the diseases of public health importance around the world. I strongly recommend GDF to all organizations around the world."

- Nigeria

"Because in general the service is excellent. The problems we are facing are more in the nature that sometimes projects are ordering and expecting a very short lead time."

-MSF The Netherlands

GDF's Future

GDF is meeting its mandate as stated in the prospectus of 2000 (1). Quality assured FLDs and SLDS are available from reliable sources at very good prices when compared to market prices of the same level of quality. NTPs and technical partners appreciate the existence of GDF and wish it could respond even quicker to their needs. GDF has always tried to expedite orders for countries to avoid stockouts by supporting good planning by NTPs for order placement through constant individual contact, technical assistance by headquarters staff, field-based staff and in-country monitoring and provision of technical assistance.

GDF has proposed a way to show considerably quicker response through the use of a global strategic stockpile (GSS) and a flexible procurement fund (FPF). Today ordering through the GDF requires that payments are in the hands of suppliers before they will begin production of the medicines and processing of diagnostics. Thus understandably, the suppliers will not take risks that orders are later cancelled or modified in some way at the whim of the NTPs. Waiting for funds from NTP can cause big delays which are mostly due to: in-country approval procedure; and donor requirements that delay funding approvals (e.g. Global Fund grants). For a country's pending stockout situation this is very problematic.

Being a donor-funded organization that is currently receiving no fee for services, GDF will continue to grow as donors continue to support GDF's work activities. At the same time, GDF will look for other ways to fund its operations such as charge a small fee for order placement. The data presented in this paper show the many accomplishments made by GDF including the amount of market shaping that has gone on in such an environment where no specific funds were provided for that purpose.

GDF and its partners have developed a reshaped strategy for GDF which would make it an even more valuable tool for TB control in the future.

Under the reshaped strategy, GDF will continue to provide FLDs and SLDs. However, funds for grants of FLDs to GDF are diminishing and donors expect the Global Fund or country budgets to fill this gap. Grants to GDF for SLDs will continue on a small scale, with expectations that the Global Fund or country budgets will pick up this tab for most patient treatments. Based on these factors GDF will move toward becoming a provider of FLDs, SLDs and diagnostics that are funded by NTPs directly, called direct procurement (DP) by GDF.

DP through GDF works well as long as the planning cycle is adhered to by NTPs who must do their part to know the quantities needed and actively secure the funds at least one year in advance. With an order cycle of 4-6 months for FLDs and SLDs, and about 2 months for diagnostics, planning ahead one year gives plenty of time for the entire GDF procurement cycle to take place and medicines and diagnostics arrive in country when they are needed.

As the global and local TB communities know, the situation in the paragraph above is not the norm. For example, some countries try to do procurement themselves which is great for capacity building and giving total control to NTPs. However, procurement is not an easy thing to do because of the many factors involved, such as, funding availability, knowing exact quantities of products needed,

shelf life of products, quality control of products, supplier production scheduling, efficient shipping (sea vs. air to cost less), port handling and clearance, to name a few. In many other situations, the funder's technical requirements for receiving grants frequently delay medicine order placement.

GDF believes it has a very viable solution, but would need more support from donors for the GSS and FPF mentioned above. The GSS and FPF would include revolving stocks and funds to maintain them viable at all times; they would work as proposed below:

1. The GSS would consist of a 6-month supply for FLDs and SLDs for clients procuring through GDF or about:
    - 300,000 patient treatments for FLDs and
    - 16,000 patient treatments for SLDs.
    - When orders come in, GDF would ship needed quantities to NTP from the stockpile.
    - Order placement lead time would be cut by 75% - from 4-6 months to 4-6 *weeks.*
    - Annually GDF would study the forecast needed for the stockpile based on consumption data from the past year and expected case finding by client countries.
    - Information on expected cases and enrollment rates would come from multiple sources:
        - the *WHO TB Global Surveillance* reports;
        - early warning system being piloted in Africa by GDF's technical partner, SIAPS;
        - GDF reports from in-country monitoring missions.

2. The FPF is needed in tandem with the GSS to alleviate the problem of funding availability to suppliers so that the production of the medicines can begin at the earliest.
    - The FPF allows immediate replacement of the GSS (stockpile) for the order quantities being shipped to NTPs.
    - In the interim, NTPs would continue to organize the needed funds and transfer the monies as soon as possible to GDF to refill the FPF.
    - The fund would need to be equal to about 300,000 patient treatments worth

With these two tools in place, GDF will be able to make an even bigger impact on market shaping in the future: on price reduction, regimen standardization, technical assistance, and information sharing. GDF will also serve as the data recipient of the Early Warning System of stockouts (SIAPS). These data would be used to identify constant bottlenecks and be a clearinghouse to warn all stakeholders of pending stockouts in individual countries, and if immediate action needed to resolve the problem.

If the MDR-TB scale-up moves forward as expected by TB technical partners, GDF will be able to supply the needed quantities. For example, after discussions with current suppliers, they indicated they could double the quantity of medicines they are producing today – this without making any major changes to their scheduling or processes. Should the market ramp up beyond this, the

suppliers indicate they would make appropriate modifications internally to assure that demand can be met, such as adding another production shift or even enlarging batch sizes, which today are a problem for SLD suppliers because of the small quantities being requested by NTPs.

Some technical partners have criticized GDF as being not very transparent. This is a perception issue as GDF has presented in fact lots of data at global and regional conferences throughout the years. It regularly holds conferences with suppliers and other agencies involved in procurement to update them on the upcoming requirements of GDF in TB control. Through annual reports, which are available on GDF's website (2), data on prices, product catalogue, patient treatments and advances in number of prequalified suppliers is provided. In 2012 GDF has added some KPIs to the website. Also in 2012 GDF is working with a consultant firm to develop ways to better communicate the mandate of GDF and its accomplishments, as they are happening.

As shown in the evidence in this paper, and continuing its current and future planned activities, GDF is convinced it can meet all the demands of its TB clients for the next three years. This will mean that multiple prequalified suppliers will be ready to supply FLDs, SLDs and diagnostics in quantities needed by GDF and its clients. There would be no active pharmaceutical ingredient or finished product interruptions and no registration bottlenecks. Through donor funding of the GSS and FPF, there would be no stockout issues for GDF clients. Then in 2015, GDF will assess what it has done and in collaboration with its stakeholders determine its place in the TB control world for the longer future.

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