

UNITAID

EVALUATION report

Support for MDR-TB Scale-Up Initiative

2007-2013

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The views and ideas expressed herein are those of the author(s) and do not necessarily imply or reflect the opinion of the Institute.

Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
API	Active Pharmaceutical Ingredient
EoI	Expression of Interest
ERP	Expert Review Panel
GDF	Global Drug Facility
gGLC	Global GLC
GF	Global Fund or the Global Fund to Fight AIDS, Tuberculosis and Malaria
GLC	Green Light Committee
HIV	Human Immunodeficiency Virus
KII	Key Informants Interview
LIC	Low income country
LMIC	Lower middle income country
LTA	Long-term agreement
MDR	Multi Drug Resistant (tuberculosis)
MoA	Memorandum of Arrangement
NCE	No Cost Extension
POC	Point of care
QA	Quality Assurance
QC	Quality Control
R&D	Research and Development
rGLC	Regional GLC
RR	Rifampicin Resistant
SCIH	Swiss Centre for International Health
SLD	Second-Line Drug
SRA	Stringent Regulatory Authority
SRS	Strategic Rotating Stockpile
Swiss TPH	Swiss Tropical and Public Health Institute
TB	Tuberculosis
TEC	Technical Evaluation Committee
UMIC	Upper middle-income country
USD	United States Dollar
WHO	World Health Organization

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1 Synthesis of findings, conclusions and recommendations

1.1 Grant parameters

Title	Funding of MDR TB scale-up initiative
General aim	To scale up MDR-TB control and to positively impact MDR-TB market dynamics to increase affordability of second-line anti-TB drugs.
Objectives	1) Scale-up the number of patients accessing and receiving second-line anti-TB treatment. 2) Decrease drug delivery lead times and prevent stock-outs. 3) Increase the number of quality manufacturers and products . 4) Achieve continuous price reductions of up to 20% for second-line anti TB drugs by 2010. 4.bis) Ensure cost containment per treatment by 31 December 2011 (second amendment) and 5) Subject to a sufficient number of quality-assured sources being available; and achieve price reductions of 5-25% for key second-line anti-TB drugs by 31 December 2011 (second amendment).
Time span	2007 to 2013
Beneficiary countries	Azerbaijan (LMIC), Dominican Republic (LMIC), Moldova (LMIC), Kenya (LIC), Kyrgyzstan (LIC), Uzbekistan (LIC), Burkina Faso (LIC), Cambodia (LIC), DR Congo (LIC), Guinea (LIC), Haiti (LIC), Lesotho (LMIC), Malawi (LIC), Mozambique (LIC), Myanmar (LIC), Nepal (LIC) and Timor Leste (LIC)
Partners	Green Light Committee Global Drug Facility The Global Fund to Fight AIDS, Tuberculosis and Malaria
Budget	20,818,086 USD; additional 16,842,000 USD (first amendment); up to 54,046,000 USD (third amendment)
Disbursed	51,814,447 USD (93% budget execution rate)

LIC: low income country; LMIC: lower middle-income country.

1.2 Evaluation scope

This end of grant evaluation builds on existing grant documents provided by UNITAID and on a series of online and phone interviews administered to TB programmes staff, grant partners staff and manufacturers. While facts and achievements have been already reported in other documents (and collected here as well), this evaluation builds upon the views of stakeholders who provide explanations of achievements and failures and lessons learnt to inform future decisions on how UNITAID can better support programmes along its strategic objectives. Interviews are inherently subjective and have to be interpreted with caution. The value of interviews is precisely to identify issues which escape the usual measuring, recording and reporting tools and to provide to stakeholders the opportunity of expressing their views, which could be valuable knowledge for UNITAID. Nevertheless, all reasonable efforts have been put into place in order to clearly understand responses (by means of repeated contacts by email and phone) and to verify facts where applicable.

Special statements point at potentially relevant matters which cannot be totally dismissed or supported by this evaluation; but UNITAID should be aware of them and they may warrant further investigation. They have been summarised in section 3.7.1.

Financial evaluation was explicitly not addressed in this evaluation as agreed with UNITAID.

1.3 Synthesis of findings and conclusions

1. The UNITAID grant has targeted a priority public health problem and has successfully provided treatments to 17 thousand MDR-TB patients¹ in 19 countries in almost seven years. While the grant had initially targeted 4,716 MDR treatments in 2007 in 17 countries, this treatment number has been multiplied by 3.6 at the end of the project in 2013 across 19 countries while at the same time, the budget allocated during this period has been multiplied by 2.5. This has been achieved due to reprogramming of savings during the grant cycle, allowing for more treatments provision. As could be expected in situations where multiple stakeholders coordinately intervene in the same area of work, there was lack of grant specific data on patients' treatment outcomes, impeding attribution of results to specific actions.
2. Value for money has been acknowledged by a remarkable 64% of the respondents either in terms of (i) overall reduction of prices of quality assured second-line medicines through improved negotiation with manufacturers; (ii) the use of a pooled procurement, or (iii) the ability to allocate saved governmental funding to expand care coverage or improve TB/MDR TB treatment facilities.
3. Overall, access to second-line TB treatment as a result of the grant support was considered as improved by 82% of respondents.
4. Improvements in supply seemed well documented albeit not without occasional problems, including delays and stock-outs. There were reportedly occasional problems in the types, amount and timeliness in the procurement of drugs. We could not ascertain to which extent this is compatible with the level of performance expected from partners, especially when procurement is the main mandate. It appeared that standard Global Drug Facility (GDF) lead times for back-to-back orders of 4-6 months were still considered as too long due to the issues in planning and forecasting at country level. However, good experiences also exist, such as the role of IDA which seems to have been very well valued.
5. There were reportedly remarkable price reductions for second-line treatments. This was balanced by somehow mixed effects on market dynamics with prices remain high in some instances.
6. Acknowledging the UNITAID's support does not aim at addressing the whole problem of MDR TB in the world, it may be useful to understand the scale of UNITAID support in relation to the overall MDR TB problem. The overall impact was limited due to: (i) the relatively small proportion of MDR-TB patients targeted, over the global number of cases; and (ii) its limited scope (support mainly focused on procurement).

¹ MDR-TB: TB strains resistant to the two most important TB drugs (isoniazid and rifampicin). Note that often the expression MDR-TB also includes drug-resistant cases not having MDR-TB in the strict sense (e.g. cases having resistance to rifampicin but not to isoniazid).

7. Achievements have taken place within a complex organisational environment, having to respond to and comply with very different institutional interests, regulations, mechanisms and priority settings; the institutional setting has clearly made possible the grant implementation. It has also been reported that there may have been problems in coordination and leadership: some perceptions point at the institutional credibility of UNITAID and partners, seen as 'heavy' when decisions have to be taken and not completely transparent.
8. The grant addressed disadvantaged populations to the extent that LMIC are included in the grant and that TB affects disadvantaged populations. Additional evidence on the effects of the grant in the most vulnerable populations within those countries was mentioned by some interviewees.
9. Along the life of the grant, the number of beneficiaries increased, adding more beneficiaries in initially seventeen countries over the project period 2007-2013, and incorporating two new countries (India in 2010 and Senegal in 2012). This has had implications in activities, procurement and budget. These changes suggest that there is no effective overview of global MDR-TB which can inform allocation to beneficiaries and/or that countries do not / cannot follow a systematic approach to seek for support to MDR-TB patients.
10. Over the grant implementation period, the reporting template was not standardized and for countries supported by Global Fund and UNITAID together, there was a lack of target disaggregated by donors when applicable. In the documents made available, Global Fund reporting was separated and presented as annexes rather than completely integrated into UNITAID/GDF reports.
11. Planning for a transition plan was initiated quite late in the project implementation period (2011-2012) with formal notification letters to be sent only by mid-2012 to respective countries including a request to the countries to specify the estimate number of patients to be enrolled on treatment in the upcoming years as well as the funding source for it. However no follow up on this issue could be found in any subsequent GDF reports as well as any elaboration of an exit strategy including active search by UNITAID/GDF for alternative funding before this project was completed.
12. The sustainability of grants has to be addressed by area or country and not for the whole grant. Sustainability of achievements seems limited to certain grant areas and to some countries because markets have many critical externalities beyond UNITAID's control and because organisational development and capacity building in countries may not have been deep enough. It seems that the Global Fund, at least for some countries, is expected to take over UNITAID's role in funding but also in influencing markets; on the other hand, countries becoming ineligible to Global Fund support are facing challenges to filling the financing gap while there is still a need for continuous support for MDR-TB treatments scale-up.

Sustainability has to be seen under the perspective of what is required to facilitate long term changes. In this sense, some comments seemed to suggest that hardly any investment, at least from this grant, had gone into building systems and capacity in countries to face the post-UNITAID era; and therefore, changes in market dynamics may not have continuity if countries are not able to effectively build on those issues which made the UNITAID grant successful (i.e. pooling, coordination, institutional credibility, regular funding). However, there is at least one exception (Uzbekistan).

1.4 Recommendations

MDR-TB is a complex condition which requires a global strategy and leadership to influence and gain synergies from advances in diagnostics, therapeutics, market dynamics and in public health. No single initiative (including UNITAID's support) can address every critical issue; therefore, outcomes are partial, positive but modest, or circumstantial and masked by other parts of the problem (see Annex 1).

Procurement is certainly one of the key issues, but as much as it exerts influence in market dynamics and in manufacturers, it also needs very delicate and optimal coordination with stakeholders in a context where public health priorities are not the only value, but coexist with commercial and political vested values and interests.

In this specific project, UNITAID's visibility was found as weak and more specifically in countries which benefited from simultaneous Global Fund support. This was partly due to a reporting with no data disaggregation by donors but also by the fact that UNITAID was mainly considered as a donor to GDF while the latter was procuring and performing some field visits. We strongly feel that collaboration with stakeholders has been and is critical and may need a more robust approach. Similarly, health system arrangements within countries may act as facilitators but also as barriers to access. Manufacturers and countries may need to be brought into play from the design phases of the grants up to the planning of phasing out stages to build stronger ownership and clearer rules of engagement which can only benefit grants' efficiency and efficacy.

Recommendations

1. UNITAID would benefit to better positioning itself in the area of MDR TB; including;
 - a. building a stronger evidence-informed rationale to support the scope of its actions in relation to actions carried out by other TB partners at global level with measurable objectives in order to make explicit what is the specific contribution of UNITAID to the problems of MDR TB.
 - b. working more closely with partners to strengthen the health system in general in view of the absorptive capacity of the health system being a major bottleneck in achieving universal access to treatment and care of drug-resistant TB.
2. Improve visibility of UNITAID in beneficiary countries through regular in-country visits to tighten oversight of country activities (or delegate it to an appropriate partner) through visits or with other communication means. Examples of in-country activities include:
 - annual data verification and validation exercises to verify patients detection, diagnosed, enrolled and patients outcomes;
 - support to simplified and standardised reporting across grants, aligned with current systems and global reporting requirements;
 - baseline market studies to inform strategic procurement strategies and decisions;
 - support (and building capacity if required) to short, mid and long term forecasts production;
 - build the case and advocate for strengthening health care delivery and procurement systems in conjunction with civil society.
3. Perform partner (stakeholders) engagement and ensure transition planning from the start for grant that have an element of transition using stakeholder analysis (specifically donor's mapping) for better sustainability
4. Widely disseminate and promote UNITAID's procurement guidelines while ensuring these are strictly followed as per international standards on procurement and tendering procedures
5. Assess grantees' capacity to properly forecast products and their timely use as well as the absorptive capacity of the health care system together with partners
6. UNITAID needs to decide whether 'innovation' is its added value and then consider, among others:
 - a. incentives for manufacturers, such as visibility or funding of Research and Development, invest or advocate for R&D on new TB drugs or regimens;
 - b. fostering collaborations in areas of common interest beyond the mere supply of medicine, including R&D; to incentivise innovation and risk;
 - c. strengthening supporting technical assistance for manufacturers seeking pre-qualification;
 - d. funding research positions/projects and/or partnering with research institutes.
7. UNITAID should continue:
 - a. carry out consolidated purchasing to ensure volume threshold (staircase) pricing;

- b. promote long term agreements with GDF, for the purpose of making long-term business plan;
 - c. consider flexibility in the ordering frequency;
 - d. UNITAID should ensure (or continue ensuring) that international standards on procurement and tendering are strictly followed.
8. Improve UNITAID's visibility as co-financing partner with larger public health partners such as the Global fund (e.g. in reported results donor's allocation).
 9. For future project with focus on procurement, continue stockpiling and carry out further consolidated purchasing to ensure volume threshold pricing
 10. Consider addressing equity issues to promote the access to MDR-TB drugs of especially vulnerable populations (e.g. homeless, inmates, among others).

2 Background and objectives

The estimated global TB incidence for 2013 was 9 million. In 2013, there were an estimated 480,000 new cases (range: 350,000 to 610,000) of MDR-TB worldwide and approximately 210,000 (range: 130,000–290,000) deaths from MDR-TB. Extensively drug-resistant TB (XDR-TB) has been reported by 100 countries. On average, an estimated 9% (95% CI: 6.5–11.5%) of people with MDR-TB have XDR-TB [1]. While good first-line treatment for people with drug-susceptible TB prevents the development of MDR-TB, the very high number of already existing MDR-TB cases makes it imperative to strongly promote the roll-out of internationally approved second-line treatment for the drug-resistant cases. MDR-TB is a condition much more difficult and expensive to treat than drug-susceptible TB (drug costs of approximately 20 USD for a standard 6-month course of first-line TB treatment versus several thousand USD for a 2-year course of second-line TB treatment).

Despite progress in the detection of MDR/RR-TB cases, a major diagnostic gap remains: 55% of reported TB patients estimated to have MDR-TB were not detected in 2013. The detection figures were lowest in the Eastern Mediterranean Region (22%) and the Western Pacific Region (16%).

Almost 97,000 people with MDR-TB were started on second-line treatment in 2013¹, up from 77,000 people in 2012². While the increase of 20,000 MDR-TB cases put on treatment from 2012 to 2013 is encouraging, there is still a huge number of MDR-TB patients not receiving adequate treatment: the 97,000 cases represent only 20% of the estimated 480,000 cases that developed MDR-TB in 2013. Furthermore, the currently offered treatment (commonly lasting for 20 to 24 months) is far from ideal: the global treatment success rate was only 48% (cohort of 2011)³. A so-called short MDR regimen offers some hope: this nine month treatment (in some cases up to 12 months) has so far shown treatment success rates of above 80% from several observational studies (e.g. 84% cure rate in Bangladesh among a cohort of 515 cases – only 4 cases relapsed⁴). Randomised controlled trials regarding this 9-month regimen are currently on-going⁵.

The number of TB cases detected to have MDR-TB or rifampicin-resistant TB has grown over the past few years: from 66,000 in 2011 to 111,000⁶ in 2012 to 136,000 in 2014 (many of these cases were from the European Region, from India or from South Africa)⁷. A major diagnostic gap remains: the 136,000 cases detected represented only 45% of the estimated 300,000 notified TB patients with MDR-TB in 2013.

¹ WHO Global TB Report, 2014

² WHO Global TB Report, 2013

³ WHO Global TB Report, 2014

⁴ Aung et al., IJTLD Oct. 2014.

⁵ Nunn et al., Trials 2014.

⁶ There is a lack of clarity about this figure: according to the WHO Global TB Report of 2013, the figure is 94,000 but according to the WHO Global TB Report of 2014, this figure is 111,000. It is likely that the newer figure (111,000) is more accurate.

⁷ WHO Global TB Report, 2014

In some countries, the increase in case detection has been more marked than the increase in cases put on treatment, so in these countries, gaps between numbers diagnosed and numbers started on treatment widened between 2012 and 2013. However, globally, the 'treatment gap' slightly decreased from 2012 to 2013. The ratio of enrolled to diagnosed cases was lower than 60% in 10 high MDR-TB burden countries in 2013 and lowest in Myanmar (34%), South Africa (41%), and Tajikistan (30%)¹.

The first-line TB drug market is notable for a number of characteristics. There is little innovation (no new major drugs reached the market over the last three decades – exceptions are the recently approved bedaquiline and delamanid, used for the treatment of drug-resistant cases), most drugs are not patent-protected anymore and are available from generic manufacturers, few drugs are of assured quality (e.g. demonstrated through World Health Organisation (WHO) prequalification), upward price pressure exists despite attempts at purchase pooling (e.g. by GDF) and stock-outs continue to be reported by developing countries, some caused by emergency situations beyond their control but often due to weak local forecasting and management capacities.

The advent of powerful antibiotics revolutionized TB treatment but also resulted in the selection and spread of drug-resistant strains. Current estimates suggest that globally, 5% of TB cases have MDR-TB: 3.5% (95% CI: 2.2–4.7%) of new cases and 20.5% (95%CI: 13.6–27.5%) of previously treated cases².

To treat drug-resistant TB, prolonged treatment with costly second-line drugs is necessary. Adverse reactions elicited by these drugs are also much more severe.

The high drug costs (partly explained by the small and unattractive market) as well as the complex treatment (two years on average), compounded by the lack of MDR-TB diagnostics and resulting demands on staff training and health system performance, all contribute to a considerable shortfall in treatment delivery.

UNITAID uses innovative financing interventions to increase funding in order to improve access to treatments and diagnostics for HIV/AIDS, malaria and tuberculosis in low-income countries³. From 2007 onwards, it supported the grant to scale up MDR-TB control with the objective to positively impact MDR-TB market dynamics to increase the affordability of second-line anti-TB drugs between 2007 and 2012. In 2007, UNITAID committed 20,820,000 USD to the MDR-TB Scale-up Initiative. This project aimed at providing 4,716 MDR-TB treatment courses of 24-months to 17 LIC and LMIC countries, including six countries under Global Fund grants, within the period 2007-2011. The partners of this project were the Green Light Committee (GLC), GDF and the Global Fund (GF), and the beneficiary countries were Azerbaijan, Burkina Faso, Cambodia, Dominican Republic, Democratic Republic of Congo, Guinea, Haiti, Kenya, Kyrgyzstan, Lesotho, Malawi, Moldova, Mozambique, Myanmar, Nepal, Timor-Leste, Uzbekistan later on followed by India and Senegal with no-cost extension of the project until the end of 2013.

¹ WHO Global TB Report, 2014

² WHO Global TB Report, 2014

³ UNITAID. About UNITAID. <http://www.unitaid.eu/en/who/about-unitaid>.

The objective of this mandate is to perform an end-of-grant evaluation of the above mentioned project. During several telephone conferences and a half day meeting in Geneva (on 08/10/2014) the Swiss TPH team together with UNITAID staff refined the scope and objectives of this final evaluation. From these exchanges two key issues were emphasised:

- 1) evaluations should have the six UNITAID strategic objectives 2013-2016¹ as reference (see Annex 2) and more specifically strategic objective 5;
- 2) evaluation findings and actionable recommendations should allow UNITAID to take specific actions in grant management and/or planning for future grants of a similar type.

Based on these premises, we have produced in this document an outline of the scope and approach to the final evaluation of this grant.

This evaluation builds on the focus, approaches and methods of the mid-term evaluation carried out by the Swiss TPH as well².

¹ UNITAID Strategy 2013-2016. UNITAID April 2013.

² UNITAID – Mid-Term review. MDR-TB Scale Up Initiative 2007-2012, MDR-TB Acceleration of Access Initiative: Strategic Rotating Stockpile, First-Line Anti-TB Drugs Initiative – Final Report – Swiss TPH - 22 November 2011.

3 Findings

We report in this section the findings from the document review, from the two online questionnaires (one generic questionnaire for key informants and TB programme managers and one questionnaire for manufacturers), from the phone interviews and meetings held with relevant actors. Quantitative analyses of generic questionnaires (22 respondents) are presented in counts; when counts do not add to 22 is because there are occasional blank responses (see Annex 3 for details of counts and percentages).

3.1 Grant background

Partners to the agreement and respective role and responsibilities

The project was undertaken by UNITAID, in collaboration with the GLC, GDF and the Global Fund. UNITAID is an international drug purchase facility, established to provide long term, sustainable and predictable funding to reduce prices and increase the availability and supply of high quality drugs and diagnostics for the treatment of HIV/AIDS, malaria and tuberculosis for people in developing countries. WHO serves as the host organization for UNITAID and provides its Secretariat, Trust Fund, administrative and fiduciary support. As per the MoA, UNITAID's role was defined as follows:

- The timely provision of funds for the purchase, delivery, quality assurance and related procurement management costs of second-line anti-TB drugs for all countries covered by the Project within a budget not exceeding US\$ 20,820,000;
- An on-going review of the financial and technical progress of the Project; and
- Collaboration with the other participants to consider available actions to achieve all objectives of the Project (as set out in paragraph 3.2), most notably objectives (3) and (4) to facilitate market incentives and stimulate price reduction of second-line anti-TB drugs.

The GLC Initiative aims to increase access to preferentially priced, quality assured second-line anti-TB drugs for the treatment of drug resistant TB in resource-limited settings. Its activities are coordinated by a secretariat provided by WHO. Drug procurement for GLC approved programmes is managed and coordinated by GDF. GLC's role was defined as follows:

- Evaluate applications for access to second-line anti-TB drugs in relation to current WHO Guidelines, available evidence, and collective experience;
- Advise WHO, GDF and, in the case of programs managed under Global Fund grants, Global Fund as to the outcome of its evaluation of each application;
- Conduct on-site evaluation and monitor the operation and performance of all GLC-approved programs;
- Promote the development of the MDR TB programs' capacity to manage drug-resistant TB;
- Assist in the development of Stop TB Partners' capacity to provide to eligible MDR-TB programs expert technical assistance and consultation on drug-resistant TB; and
- Promote and participate in the analysis of programmatically-relevant research data from GLC-approved MDR-TB Programs and in the dissemination of new data-driven information on treatment of drug-resistant TB.

The GDF is an initiative of the Stop TB Partnership which ensures access to high quality anti-TB drugs at the lowest possible price for countries in need. WHO, host organization for the Stop TB Partnership, provides the Secretariat for GDF. GDF's role included:

- Coordinate and manage procurement and delivery of second-line anti-TB drugs for GLC approved MDR-TB Programs, including, but not limited to, engaging the procurement agent and maintaining a stockpile;
- Submit Interim Progress Reports and Annual Programmatic and Financial Reports to UNITAID;
- Facilitate the stimulation of price reduction of second-line anti-TB drugs;
- Work jointly with the WHO Prequalification Program to improve the quality of second-line anti-TB drugs;
- Broker technical support in drug management for beneficiaries countries of this Project; and
- Take appropriate action, in coordination with UNITAID, to suspend deliveries, upon notification from GLC or the Global Fund that a program should be terminated or suspended.

The Global Fund is a financing mechanism which was established with the aim of attracting, managing and disbursing resources to mitigate the impact of HIV/AIDS, tuberculosis and malaria. It does not implement programs directly; rather it funds programs reflecting country-led formulation and implementation. Global Fund's role consisted of:

- The determination of which Global Fund grants will receive UNITAID-funded MDR-TB contributions;
- The adjustment of the Global Fund budget and targets within the relevant grant agreement to reflect increased UNITAID-funded treatment targets agreed between the Global Fund and the Global Fund's Principal Recipient responsible for MDR-TB Scale-Up;
- The monitoring of Global Fund program results and targets relevant to MDR-TB Scale-Up;
- The determination of whether or not to approve the Principal Recipient' request for disbursement of UNITAID-financed MDR-TB drugs, based on performance; and
- The determination, at the end of the first two years of funding of a grant ("Phase I " funding), of whether Global Fund grants that are participating in the MDR-TB Scale-Up Initiative are eligible to continue to receive MDR- TB medications financed by UNITAID during the remaining years of such programs' terms (during their "Phase 2").

The objectives of the grant were adapted according to the amendments described in the following chronology:

- 1) Memorandum of Arrangement (MoA) dated 20 July 2007** (UNITAID Board resolution N°5 dated 7-9 May 2007) was signed for the funding of MDR TB Scale up initiative 2007-2011 undertaken by UNITAID in collaboration with the GLC, the GDF and the GF.

The UNITAID project (2007-2011) had four (4) objectives:

- 1) Scale-up the number of patients accessing and receiving second-line anti-TB treatment;
- 2) Decrease drug delivery lead times and prevent stock-outs;
- 3) Increase the number of quality manufacturers and products; and
- 4) Achieve price reductions of up to 20% for second-line anti-TB drugs by 2010.

UNITAID was responsible for the timely provision of funding to GDF to enable the purchase, delivery and quality assurance, together with related procurement management, of second-line anti-TB drugs for 17 low and lower middle-income beneficiary countries such as Azerbaijan (LMIC), Dominican Republic (LMIC), Moldova (LMIC), Kenya (LIC), Kyrgyzstan (LIC), Uzbekistan (LIC), Burkina Faso (LIC), Cambodia (LIC), DR Congo(LIC), Guinea (LIC), Haiti (LIC), Lesotho (LMIC), Malawi (LIC), Mozambique(LIC), Myanmar (LIC), Nepal (LIC) and Timor Leste (LIC) within a budget not exceeding **20,820,000 USD** to cover **4,716** treatments during a 24-month period (beginning Q4 2007) and, for six of the countries under Global Fund grants (Azerbaijan, Dominican Republic, Moldova, Kenya, Kyrgyzstan, and Uzbekistan) for an additional period equal to the remainder of the respective grants (from mid-2009 through 2011).

As part of Objective 2, a Rotating Stockpile of second-line anti-TB drugs of 800 patient treatments was to be created at the outset of the project for smooth implementation of Scale Up, reduction of lead-times and avoidance of stock-outs. Estimates of total cost per patient for 24 months range between 1,506.76 USD and 4,366.44 USD.

2) UNITAID Board Resolution EB7 Resolution No 3 dated 2-3 April 2008 subsequently committed **33.690,000 USD** to finance a further project with GDF: "MDR-TB Acceleration of Access Initiative 2008-2011", involving: (i) the establishment of a **Strategic Rotating Stockpile** (SRS Project) and (ii) a Strategic Revolving Fund. This SRS Project was launched to increase the stockpile from 800 patient treatments established in the Original MoA by an additional 5,000 patient treatments.

3) **First amendment of MoA in June 2009** (UNITAID Board resolution N°7 dated 2-3 July 2008) authorized the commitment of **additional funding of 16,842,000 USD** with an increased budget from 20,820,000 USD to **37,662,000 USD** due to: 1) increase of the estimated cost for a course of second-line treatment for a patient with MDR-TB in several countries due to changes in certain treatment regimens in line with GLC recommendations with substitution of Moxifloxacin 400mg (5.93 USD per tablet) or Levofloxacin 500mg (0.0862 USD per tablet) and Levofloxacin 250mg (0.0520 USD per tablet) for Ofloxacin 200mg (0.0349 USD per tablet) depending on the regimen; 2) inclusion of additional patient treatments for 3 of the 17 countries i.e. Kyrgyzstan, Lesotho, and Nepal **increasing by 1,040** the total patient treatments (from 4,716 to **5,756**); 3) increase in the unit price of two key second-line TB drugs: (i) PASER, from 48.42 USD to 59.09 USD for 30 sachets and (ii) Kanamycin, from 18.58 USD to 26.36 USD for 50 vials due to higher production costs as a result of: investments in increased production capacity, the continuing depreciation of the USD and the rising price of oil and a single quality assured source available to GDF; 4) correction of original 2007/2008 freight cost estimates for certain countries to accommodate several additional and necessary urgent partial deliveries to avoid stock-outs and 5) inclusion of a cost fluctuation buffer of 10% (products) plus 4.4% (freight). Estimates of total cost per patient for 24 months of treatment range between 1,564.12 USD and 9,134.42 USD.

4) **Second amendment of MoA in August 2010** (UNITAID Board resolution N°7 dated 12-13 May 2009) with request for increased budget from 37,662,000 USD to **54,046,000 USD** (new funding required of 16,384,000 USD for 2010-2012) to increase by three-fold from 5,756 to **15,606** (i.e. 9'850 additional treatments) the number of second-line treatments by supporting the scale up of MDR-TB treatment in **18 countries including India** during financial years 2010-2011 & 2011-2012. Extension of funding from 2007- 2012. This second amendment had five (5) objectives:

- 1) Scale-up the number of patients accessing and receiving second-line anti-TB treatment;
- 2) Decrease drug delivery lead times and prevent stock-outs;
- 3) Increase the number of quality manufacturers and products;
- 4) Ensure cost-containment per treatment by 31 December 2012; and
- 5) Subject to a sufficient number of quality assured sources being available, achieve price reductions of 5 - 25% for key second-line anti-TB drugs by 31 December 2012.

- 5) **Third amendment of MoA dated 07 August 2012** agreed to a budget reprogramming as well as that the management of the 800 patient treatments established in the Original MoA be fully transferred and integrated into the SRS Project. Under this 3rd amendment the project was amended to provide **15,657** treatments (51 additional patient treatments for Haiti) and the maximum amount was revised to **52,000,000 USD** for Project duration to 31 December 2012. The inclusion of Senegal was approved on 07 August 2012 after signature of 3rd amendment.
- 6) At the same time in August 2012, a **second amendment to the SRS project** extended the period until 31 December 2012.
- 7) **Fourth amendment of MoA in April 2013** (UNITAID Board Resolution no. 3-2013-e of March 2013) authorized a one-year no-cost extension (NCE) up to 31 December 2013 **for five (5) countries for transition:** Guinea, Kenya, Myanmar, Nepal and Kyrgyzstan with final budget of 52,000,000 USD. This NCE aimed at providing **1,152 additional** patient treatments in these countries to a value of 4,485,000 USD due to the savings gained in the duration of the Scale-Up Project. This also included the support of 30 patients for **Senegal** resulting in a total of **19 countries** supported by the project.

3.2 Relevance

3.2.1 What has been the contribution of the project to UNITAID strategic objectives?

- Consistency with UNITAID guiding principles (evaluation area 1)
- Contribution to UNITAID strategic objectives, particularly objective 5 (evaluation area 1)

The relevance of the grant is widely supported by all pieces of evidence scrutinised. First of all, from the point of view of the grant design and objectives, it shares and addresses UNITAID's strategic objective 5¹. The whole grant is designed to select countries in need of support for MDR-TB medicines and to ensure that the supply chain is made operational within a complex market and TB stakeholders environments. This can be clearly seen in the figure of page 18 of the Memorandum of Arrangement and in the text accompanying it².

This was further verified with the responses to the generic questionnaire. Most of the 22 respondents indicated that the grant is totally or mostly targeting LIC and/or LMIC and disadvantaged populations (19 and 20, respectively). Although UNITAID did not mean to target disadvantaged populations at the expense of well-off, it was indicated that disadvantaged populations were targeted to the extent that (i) the TB problem was targeted, because of the association between TB and socio-economic status; (ii) paediatric TB was addressed (i.e. children are considered as disadvantaged); (iii) retreatment patients (also seen as belonging to the most

¹ Secure supply of second-line tuberculosis medicines, and increase access to emerging medicines and regimens that will improve treatment of both drug-sensitive and MDR TB.

² Memorandum of Arrangement for the Funding of MDT TB Scale-up Initiative 2007-2011. REM-UNITAID-GEN 401447. 2007-08-08.

disadvantaged groups) were beneficiaries. Apart from children, other groups were mentioned, such as prisoners, former inmates, patients in remote areas, homeless people, HIV/AIDS co-infected people, migrants and refugees from neighbouring countries.

The grant is meant to influence market dynamics mainly through pooling and reorganising supply in order to exert some pressure onto manufacturers and intermediaries to improve availability and reduce prices and lead times. This being a reasonable approach, it does not seem clear what 'innovation' as such is for UNITAID and it is difficult to ascertain it, as it was also put by at least one of the respondents. Someone else attributed innovation to the fact of involving private providers (which, in any case, would be a country-specific policy) and beneficiaries from disadvantaged populations; another respondent to 'innovative' financing. Consistently, a relatively smaller proportion of respondents considered that the grant was applying innovative approaches (10 'yes', 1 'partially', 5 'no' and another 4 did not know).

Whether with innovative approaches or not, there was almost unanimity in considering that the grant ensured supply of second-line TB medicines (19 'yes' and 1 'partially; no one answered 'no'), and comments were positive, in general. For example, it was mentioned that "GDF was well positioned to facilitate the procurement of the drugs funded by UNITAID. Further, since the funds were held by GDF and provided as grants to countries, they could likely act faster than the regular direct procurement process (where payment is often a source of delays for order placement)". Factors mentioned included: prompt availability of funds, long-term agreements with suppliers, or forecasts for suppliers.

Slightly less considered though that access to emerging medicines and treatment regimens was ensured (16 'yes', 1 'partially and 3 'no'). Some respondents put 'access' and treatment regimens under the direct responsibility of countries rather than on the grant. However, it was also pointed out the some countries' regimens were modified as a result of the grant. It was also suggested that 'access' did not necessarily translate uptake of medicines in countries; other respondents pointed at the number of patients who seemed to have received the treatment.

3.2.2 What has been the contribution of the project and UNITAID to partners' development?

- Degree of fulfilment of partners' mission (evaluation area 1)

Although it was not part of the scope of this specific project, we have not found much evidence in relation to the capacity built in recipient countries, in terms of systems and staffing. This has been expressed by several interviewees as a missed opportunity more specifically in countries where there was no combined support by the Global Fund. It has been suggested that countries may be left without the necessary requirements to face a post-UNITAID (e.g. diagnostics, coordination and leadership, organisation, efficiency in processes, expertise). However, there are rare examples where it was felt that UNITAID helped to train staff now able to manage MDR-TB and where governments seemed prepared to take over although in a stepwise approach (e.g. Uzbekistan). It was also reported more than once that the grant helped to get Global Fund support.

From the documentation, examples of collaboration are mentioned in 2010 with Global Fund and GDF synchronizing their selection processes and issuing combined Expression of Interests (Eols) for TB manufacturers every 6 months for Expert Review Panel (ERP) review as well as using the same sampling and testing services and pooling quality control testing activities with the Global Fund and partners. Another example of collaboration mentioned was with The United States Pharmacopoeia Promoting the Quality of Medicine Programme initiated in 2008 to facilitate the prequalification of MDR-TB medicines.

MDR-TB burden and country selection

Country selection can be assessed by the following three criteria:

a) MDR burden:

Russia, China and India together account for 52% of the global MDR burden, so it is reasonable that one of them (the poorest) was chosen.

b) Income level of countries (as of 2013):

Among the 19 UNITAID countries, seven are high MDR burden countries, namely Azerbaijan, DR Congo, India, Kyrgyzstan, Myanmar, Moldova and Uzbekistan (one could argue why only seven were selected). Among the 27 high burden countries, 5 are LIC and 11 are LMIC. The seven UNITAID high burden countries are as follows: 2 LIC, 4 LMIC and 1 UMIC. Among the remaining 12 UNITAID countries: 8 are LIC, 3 are LMIC and 1 is UMIC. Note that when this UNITAID project began, the income classifications were partly different, as reflected on page 1 (see also Table 1).

c) Gap between number of drug-resistant cases detected and number of cases enrolled on second-line treatment:

In most of the 27 high MDR-TB burden countries, the number of cases diagnosed with drug-resistant TB is much higher than the number of cases enrolled on second-line treatment (see Annex 1). One could argue that only countries having a large gap regarding the number of cases diagnosed versus the number of cases enrolled for treatment should have been selected for this UNITAID project. While Annex 1 does not present data as of 2007, the data presented for 2009 can be taken as proxy. Based on this, four of the seven UNITAID countries clearly had a large treatment gap while for three UNITAID countries (DR Congo, India, and Uzbekistan), the treatment gap was small.

Although UNITAID constitutional requirement is to dedicate at least 85% of its funding to LICs, the selection of beneficiary countries originally departed from that criterion so as to take into account the high MDR-TB burden also in LMICs since around 75% of such burden is in lower and middle income countries. It has also to be noted however that the World Bank revises its income groupings in June of each calendar year. To minimize the effect of “income group creep” on the UNITAID’s constitutional requirement to distribute at least 85% of its annual budget to Low Income countries, less than 10% to Lower middle income countries and less than 5% to Upper middle income countries, the income groups remain constant throughout the grant period from date of grant signature.

Based on these three criteria, the selection of the 19 countries is reasonable.

Table 1. Evolution of World Bank country classification from inception to end of project.

Country	2007 classification	2013 classification
Azerbaijan	LMIC	UMIC
Dominican Republic	LMIC	UMIC
Moldova	LMIC	LMIC
Kenya	LIC	LIC
Kyrgyzstan,	LIC	LIC
Uzbekistan	LIC	LMIC
Burkina Faso	LIC	LIC
Cambodia	LIC	LIC
DR Congo	LIC	LIC
Guinea	LIC	LIC
Haiti	LIC	LIC
Lesotho	LIC	LMIC
Malawi	LIC	LIC
Mozambique	LIC	LIC
Myanmar	LIC	LIC
Nepal	LIC	LIC
Timor Este	LIC	LMIC
India	LIC	LMIC
Senegal	LIC	LMIC

How MDR-TB is globally managed

Until 2011, there was only one GLC, based in Geneva. This GLC decided which country applications for GLC-approved MDR-TB management received green light. In late 2011, this committee was re-named into Global GLC (gGLC) and acceleration of access to MDR-TB treatment was promoted by having six regional GLCs: a rGLC for the African region, a rGLC for the American region, a rGLC for the Eastern Mediterranean region, a rGLC for the European region, a rGLC for the Southeast Asian region and a rGLC for the Western Pacific Region. By October 2012, 4 rGLCs were operational and the rGLCs in the African and in the Eastern Mediterranean region became operational during the first half of 2013. The rGLC provide technical assistance to the countries and no longer have the power to veto an MDR project. Diagnosis of MDR is being pushed and treatment as well. Scarcity of funds is an issue, and the absorptive capacity of the countries to deal with all their MDR cases is a major bottleneck; and that is why apart from GF, there is UNITAID to assist.

The grant operated in a limited number of countries and beneficiaries: approximately 17,000 patients (9,850 of them in India) in 19 countries. In these 19 countries, an estimated 32% of the global burden of multi-drug resistant TB (MDR-TB; TB strains resistant to the two most important TB drugs isoniazid and rifampicin) occurs¹. Among these 19 countries, 7 are high MDR-TB burden countries; in these seven countries, an estimated 29% of the global MDR-TB burden occurs.

¹ Calculated based on the estimated number of MDR-TB among notified pulmonary TB cases, 2013 (Source: WHO, Global TB Report 2014)

The peak year of this UNITAID project was in 2011, when 6,568 patient treatments were delivered within a year. These 6,568 patient treatments represent 12% of the 55,597 MDR-TB cases globally enrolled for second-line treatment in 2011¹.

3.3 Effectiveness

First of all, the project objectives have been slightly modified over the period 2007-2013. The MoA signed in 2007 is committing funding (up to 20,820,000 USD) for the project based on the four (4) following objectives: 1) Scale-up the number of patients accessing and receiving second-line anti-TB treatment; 2) Decrease drug delivery lead times and prevent stock-outs; 3) Increase the number of quality manufacturers and products; and 4) Achieve price reductions of up to 20% for second-line anti-TB drugs by 2010.

The second amendment signed in August 2010 with an additional funding of 16,384,000 USD including India as new beneficiary country has increased the number of objectives to five and re-defined them as follows. 1) Scale-up the number of patients accessing and receiving second-line anti-TB treatment; 2) Decrease drug delivery lead times and prevent stock-outs; 3) Increase the number of quality manufacturers and products; 4) Ensure cost-containment per treatment by 31 December 2012; and 5) Subject to a sufficient number of quality assured sources being available, achieve price reductions of 5 - 25% for key second-line anti-TB drugs by 31 December 2012.

From the project documentation, the Logframe approach seems to have been introduced only from 2011 reports onward. From the previous annual reports made available in 2008, 2009 and 2010, there is a reporting approach that includes indicators as well as actions; however some indicators were added in the 2010 report compared to the 2009 report as a result of the increased number of objectives. From 2011 onwards, a Logframe 2007-2012 has been used defining four outputs, activities and specific indicators (used for the 2011 and the 2012 reporting).

Finally, as a result of the fourth amendment signed in April 2013 related to a NCE of one year in 2013, another Logframe adjusted to the 5 countries in transition has been developed in March 2013, and later on adjusted to the then 4 countries which benefited from UNITAID support.

The reviewers are not aware if grantees and/or GDF received any directives from UNITAID related to the use of a specific reporting template and this perhaps explain why the reporting is not very standardized before 2010. The decision by UNITAID to introduce the use of the Logframe (or performance framework) is seen as one result of the 2011 mid-terms reviews recommendation.

Changing reporting structure and indicators over a project period is challenging any proper analysis of results making them not easily comparable from one year to another. The reporting has improved from 2011 but still, this reporting could be further developed through better standardization of the narrative report structure with the inclusion of lessons learnt and challenges. Simultaneously, the Logframe could be improved similarly to the Global Fund performance framework by e.g. clearly indicating targets to be achieved during a time period.

¹ WHO Global TB Report, 2013

3.3.1 Were MDR TB medicines available for purchase and distribution?

- Validation of effectiveness on MDR medicines (log frame output 1; evaluation area 1)

By the end of 2013, GDF ordered 17,054 patient treatments to 19 countries, including 745 treatments paid for and ordered during 2013 for delivery in 2014 (Table 2.). Based on GDF reporting, the target of 16,679 treatments ordered was reached (the reviewers calculated a target at 16,768 with the inclusion of 89 treatments patients initially planned for Nepal but allocated to Myanmar).

In terms of the achievements of outputs within the timeframe specified in the initial project plan 2007 – 2012: the project period has benefited from one-year NCE for 2013 focusing on initially 5 countries but reduced to 4 (as Nepal declined the application) with the delivery of 1,081 patients treatments in 2013 for the 4 countries; 527 were paid and ordered in 2013 but scheduled for delivery during 2014 in Myanmar. Over the project period 2007 – 2013, a total of 17,054 patient treatments to 19 countries were ordered while the initial target was to provide MDR TB drugs for 4,716 patient treatments in 17 countries during 2007 – 2011.

Despite some delays occurred in signing the project agreement, reprogramming of the Global Fund grants, and procuring the drugs (reported by six respondents), 17 interviewees suggested that outputs were totally or partially achieved in the expected timeline; and 14 (64% of respondents) that the grant produced 'value for money' (5 did not know and 2 left it blank). None of the respondents rejected the statement that more patients were accessing second-line TB medicines (3 did not know). Some more detailed responses are illustrated below.

Reported reasons for delays included the long time to agree and sign the project agreement, reprogramming the Global Fund grants, and procure drugs or countries' readiness¹. The example of a country which had to use alternative medicines from other sources because of lack of first choice medicines was mentioned.

¹ Even the Ebola epidemic was mentioned as a reason to have fewer patients than expected.

Table 2. MDR treatment targets and quantity of treatments ordered and delivered or pending delivery by country (based on the reviewers' calculations).

Country	Cumulative treatment target as of end 2013	Cumulative delivered as of end 2013	% completed 2013 (delivered/target)	Ordered 2013 not delivered	% ordered 2013 (ordered/target)	Total patient treatment for the project (delivered + ordered not yet delivered)
Azerbaijan	1'170	1'260	108%	0	108%	1'260
Dominican Republic	323	324	100%	0	100%	324
Moldova	150	155	103%	0	103%	155
Kenya	475	475	100%	0	100%	475
Kyrgyzstan,	818	600	73%	218	100%	818
Uzbekistan	614	614	100%	0	100%	614
Burkina Faso	60	69	115%	0	115%	69
Cambodia	200	200	100%	0	100%	200
DR Congo	550	592	108%	0	108%	592
Guinea	74	73	99%	0	99%	73
Haiti	211	233	110%	0	110%	233
Lesotho	550	640	116%	0	116%	640
Malawi	100	97	97%	0	97%	97
Mozambique	100	104	104%	0	104%	104
Myanmar	873	346	40%	527	100%	873
Nepal	600	625	104%	0	104%	625
Timor Este	20	22	110%	0	110%	22
India	9'850	9'850	100%	0	100%	9'850
Senegal	30	30	100%	0	100%	30
Total	16'768	16'309	97%	745	102%	17'054

* It should be noted that the information is related to the number of treatment delivered to the country and not the number of patients who started treatment.

Value for Money

Value for money has been acknowledged by 64% of the respondents either in terms of overall reduction of prices of quality assured second-line medicines through improved negotiation with manufacturers allowing for more patient treatments, the use of a pooled procurement, or the ability to allocate saved governmental funding to expand care and coverage or improve TB/MDR TB treatment facilities.

Limitations to increased value of money identified were mainly related to the size of UNITAID budget which could only cover a small portion of the overall MDR-TB demand as well as the scope of the grant focusing only on procurement of drugs.

While all the objectives are considered as achieved to some extent, interviewees emphasized more specifically as enabling factors the uninterrupted supply of medicines as a result of the use of stockpile to cover specific product shortages together with affordable prices for quality-assured products.

In terms of barriers jeopardizing the achievement of outcomes, several are external to the project such as those related to a challenging MDR-TB drug market with more patients needed to be treated while funding is limited, or weak national health systems with a lack of skilled human resources which do not allow proper planning as well as adequate drugs forecast.

More enabling factors and barriers to achieving the outcomes have been identified by the interviewees and are presented in Annex 10.

There were also disagreements among respondents. For example, in terms of the communication between UNITAID / GDF and national TB programs, this was judged as a positive facilitating factor by some and as a barrier (i.e. lack of communication) by others. Another point of disagreement was the availability and use of medicines forecasts (present by some and insufficient by others).

Another objective of this project was to ensure prompt delivery of MDR TB treatment. Average delivery lead time was lower than the 4 months target for the first four years of the project (2008 to 2011) and increased above 4 months in 2012 and 2013 (Table 3.). It should be noted that the delivery time is also depending on the country’s requested delivery. **The overall average lead time through the life time of this project is four months (note that the objective was a lead time of up to 4 months). It is, however, noteworthy that for the years 2012 and 2013, the lead time was approximately 5 months.**

Table 3. Average lead time (days).

2008	2009	2010	2011	2012	2013	Average (2008-2013)
113	100	102	114	164	141	122

Minimum and maximum times in bold. Statistical significance was not assessed.

In relation to lead times, manufacturers suggested that “the stock pile helped in shipping goods to patients much earlier than a back to back ordering system, which will require vendors to produce against specific orders”; and “the collaboration with IDA is perfect. The way IDA is proceeding is perfect for all. We, as suppliers, know when we have to deliver the goods and the delivery time is quite long to be able to supply the goods on time”.

Based on manufacturers’ survey results, most manufacturers agreed that the grant contributed to:

- increase the quality of second-line TB drugs (6 of 6)¹;
- increase the number of manufacturers (6 of 6);
- affect positively lead times (5 of 6);
- secure access to second-line drugs (5 of 6).

Manufacturers suggested that the grant brought larger quantities to supply and that payments were received on time; that it also served populations that otherwise manufacturers would not have had a chance to help; it produced some growth on manufacturer’s business; but had no impact on innovation.

In the manufacturers’ questionnaire, it was reported that annual estimates of product demand were calculated at inception and manufacturers arranged the production schedule accordingly. A strong increase of the number of patients enrolled on MDR treatment led to more manufacturers having stepped in, thereby increasing competition, and lowering price In the last years; the elimination of buffer stocks; and the entrance of multiple manufacturers of similar products eliminated the need for continuous production (of any given volume scale) due to direct

¹ However, a respondent also suggested that “quality is a function of policies [and that] grants can't change the policies”.

procurement (delivery to a country rather than a consolidated uniform procurement process on behalf of the countries). Early forecasting allowed minimising the risks of increasing the cost of production and facilitated preliminary agreements with the producers of raw materials and packaging materials to plan the production schedule.

Supplier Base

During this grant, the number of products and manufacturers eligible by GDF increased drastically; this shows significant progress in this area (Table 4).

Table 4. Medicines available and eligible manufacturers by year.

Year	Items available	Manufacturers eligible
2007	7	5
2009	17	10
2013	53	24

Following the bidding exercise launched in 2012 by GDF, 37 Long-Term Agreements (LTA) have been signed in 2013. This is a large achievement compared to the two LTAs signed by the end of 2010. Four new suppliers have been added in 2013 to GDF suppliers list. However, MDR-TB drugs prices still remain high.

For all products except two, there were at least two quality assured manufacturers (only Terizidone and PAS acid formulation product¹ had only one source of supplier). From two products prequalified in 2008 (Cycloserine 250 and Ethionamide 250mg), 7 new products have been either prequalified or ERP reviewed during the project period (Table 5. and Table 6.).

Nevertheless, the overall number of quality-assured sources remains limited, leaving the supply of quality-assured MDR-TB medicines vulnerable to disruption. In some cases, multiple manufacturers are relying on the same source for Active Pharmaceutical Ingredient (API), as for Cycloserine and Capreomycin.

¹ Some reservation can be made, as this is one of the PAS products if Na PAS is considered.

Table 5. List of WHO prequalified MDR TB products as of December 2013

Ref number	Products	Dosage	Manufacturer	Date of Pre Qualification
1	Amikacin (as sulfate)	500mg/2ml	Cipla Ltd	2011-Jan-14
2	Cycloserine	250mg	Macleods Pharmaceuticals Ltd	2007-Mar-23
			Aspen Pharmacare Limited	2009-Jun-19
			Biocom JSC	2013-Aug-20
			Dong-A ST Co, Ltd	2012-Nov-16
3	Ethionamide	250mg	Macleods Pharmaceuticals Ltd	2007-Dec-21
			Cipla Ltd	2011-Dec-22
			Micro Labs Limited	2012-Dec-19
			Lupin Ltd	2012-Dec-19
4	Levofloxacin	250mg	Cipla Ltd	2011-Dec-22
			Cipla Ltd	2011-Dec-22
			Micro Labs Limited	2012-Oct-03
			Apotex Inc.	2013-Jun-24
4	Levofloxacin	500mg	Micro Labs Limited	2012-Oct-03
			Apotex Inc.	2013-Jun-24
4	Levofloxacin	750mg	Apotex Inc.	2013-Jun-24
5	Moxifloxacin hydrochloride)	(as 400mg	Cipla Ltd	2010-Nov-01
			Macleods Pharmaceuticals Ltd	2012-Nov-16
			Ranbaxy Laboratories Ltd	2013-Nov-04
6	Ofloxacin	200mg	Macleods Pharmaceuticals Ltd	2012-Oct-31
			Cipla Ltd	2011-Dec-22
			Micro Labs Limited	2012-Sep-11
6	Ofloxacin	400mg	Cipla Ltd	2011-Dec-22
			Micro Labs Limited	2012-Sep-11
7	p-Aminosalicylic acid (as sodium salt) (common name)	4 g	OlainFarm JSC	2011-Mar-22
8	Prothionamide	250mg	Micro Labs Limited	2013-Feb-25

Source: WHO PQP website.

Table 6. List of ERP reviewed MDR TB products as of December 2014

Ref.No	Products	Strength/ Dose	Dosage form	Manufacturer
1	Capreomycin	1g	Powder for Injection	Macleods
2	Cycloserine	250mg	Capsule	Microlabs
				Cipla
3	Levofloxacin	750mg	Tablet	IPCA

Source: Global Fund website

Five of six manufacturers suggested that the grant contributed positively to the number of second-line drugs; and that it increased the number of generic versions only and not innovative drugs.

The questionnaire to manufacturers provided some additional insights which suggested that market dynamics are even more complex. For example, a manufacturer suggested that the grant “removed to some extent the incentives for companies to invest in research and to bring products to market given the lack of financial recovery even over a long time horizon. A company, for

example, has a very strong pipeline of wonderful compounds but knowing that a large [foreign] company will copy those compounds provides a lack of incentive to bring them to market. ... programmes should support the innovators of the compounds and not the compounds themselves. Pharmaceutical companies will be reluctant to offer pricing which is affordable in the long term but will be forced to sell at high (exorbitant) pricing during periods of exclusivity. This is the wrong approach from an ethical and public health perspective [...] [The grant contributed to the increase in the number of manufacturers] at the expense of the innovators [who would] have long-term impact on pharmaceutical companies' incentives to bring new drugs to market”.

Reasons provided on why there is reluctance by manufacturers in investing in better second-line TB products were mainly summarized around a very narrow market with a weak long-term commitment by donors or programmes which could not allow for solid investments and innovation.

Price

As reported in the 2012 Annual report, under Activity A1.2, four major Second-Line Drugs (SLDs) contribute to 80% of a standard regimen and the costs of it [PAS products combined (sodium and acid formulations), Cycloserine, Kanamycin and Capreomycin]. It is to be noted that while prices of kanamycin remain unchanged for 2013, price reductions were achieved for PAS products, Capreomycin and, most importantly, Cycloserine (-37% price reduction from current supplier Macleods, and up to 45% reduction for Lupin ERP product versus 2012 GDF price).

Overall cost for the current regimen: 8 Cm Pto Cs Mxf PAS / 12 Pto Cs Mfx PAS has decreased, from 7'890.60 USD in 2011 to 5'351.04 USD in 2014 (-32.2%). Likewise, the overall cost for the regimen: 8 Am Eto Cs Lfx / 16 Eto Cs Lfx has also decreased, from 2'069.90 USD in 2011, to 1'471.25 USD in 2014 (-28.9%).

Cost of GDF Unit Price for several products (in USD) are available in Table 7 for 2007, 2011 and 2013 which show some major decrease of prices especially between 2011 and 2013. In 2010, stringent GDF Quality Assurance (QA) policy was introduced, in full alignment with QA policy of the Global Fund. Therefore, the prices before 2010 are not necessarily directly comparable with the prices of products as per GDF stringent QA policy from 2010 onwards. GDF used year 2011 as a baseline for its price comparison.

Manufacturers' responses related to the prices

Four out of six manufacturers suggested that UNITAID/GDF contributed to a decrease of MDR TB prices by tenders processing and increasing volumes. However several comments recognized that UNITAID/GDF had a limited contribution on further price reduction emphasizing the contradiction between the need of significant investments to develop new drugs so as to increase competition, and the requirements to lower prices to win a tender.

Table 7. Evolution of unit price (USD) for seven MDR products in 2007, 2011 and 2013.

Product	Dosage	Pack size	Cost per unit 2007*	Cost per unit 2010 (\$) **	Cost per unit 2013 (\$) ***	Difference 2013 - 2010
Capreomycin	1g	1	3.21	4.25	3.96	-6.82%
Cycloserine	250 mg	100	50.25	65.70	43.00	-34.55%
Kanamycin	1g	1	0.37	2.77	2.58	-6.93%
Ofloxacin	200mg	100	3.49	6.64	4.80	-27.71%
PASER	4g	30	48.36	55.98	46.00	-17.83%
Prothionamide	250mg	100	13.03	15.27	19.80	29.67%
Ethionamide	250mg	100	10.21	10.13	7.50	-25.96%

Source: * MDR TB Scale-up Project Outline 20 July 2007; ** GDF Report 2010, p.26 *** GDF Report 2012, Annex A.1.2 and 2.

3.3.2 Are MDR TB medicines available for purchase and distribution now that UNITAID support has ended?

- Access to MDR medicines (evaluation area 2)
- Enablers and barriers of observed changes (evaluation area 4)

Access to second-line TB treatment

Overall, access to second-line TB treatment as a result of the grant support was considered as improved by 82% of respondents while also recognizing some limitations.

Enabling access factors identified were mainly related to the availability of UNITAID funding as a complement to Global Fund support for improving drug availability free of charge, as well as a better procurement system in general including the stockpile.

Further enabling factors for access to treatments are included in Annex 10.

Some factors identified as hampering access were internal to the grant but also external to the project and mainly related to challenges of TB diagnosis as well as capacity limitation at country level in terms of human resources skills, planning and logistics (transport for drugs but for patient care as well) combined with a weak coordination between national and international stakeholders.

Further barriers to access to treatments are included in Annex 10.

3.3.3 What is the market situation once UNITAID support has ended?

- Effects on the market space (evaluation area 3)
- Enablers and barriers of observed changes (evaluation area 4)

Based on the project documentation, in order to proactively identify suppliers, the GDF launched an invitation of Expression of Interest (Eoi) for second-line drugs in September 2008. The list of eligible products included: Amikacin, Amoxicillin + Clavunavic acid, Capreomycin, Clofazimine, Cycloserine, Ethionamide, Kanamycin, Levofloxacin, Linezolid, Moxifloxacin, Ofloxacin, Prothionamide, PAS Acid, PAS Sodium, Terizidone, Thioacetazone. In total, 53 dossiers were received to be screened in Q1 2009 for acceptability by a GDF-appointed Technical Evaluation Committee (TEC) comprising pharmacists from GDF and key Stop TB Partners. However, in 2009 it was decided by GDF not to launch a tender process but rather to enter into price negotiations with suppliers of the GDF approved products facilitated by the establishment of a Task Force on Price Negotiation. From the project documentation (annual report 2009), the GDF seems to mainly have relied on few suppliers. From the documentation made available for the review, it is not clear to the reviewers why a competitive tendering which should have been published and open to more suppliers for bidding and therefore better prices for drugs, has been cancelled and replaced by restricted negotiations or invitations published by the Global Fund for ERP.

Similarly, the project document does not mention any market research or survey conducted e.g. using pharmaceutical databases which could have allowed for the identification of more potential suppliers.

Market

In terms of market situation now that the UNITAID support has ended, 55% of the 20 interviewees' responses considered it as "better" or "equally good" while only one response reported it as "worse" mentioning that "the increased needs of putting more patients on treatment cannot be achieved due to limited funding available from other donors or government".

It was reported that there were more quality-assured MDR-TB suppliers, more affordable prices and more stable supply.

However, the lack of funding (from other donors or funding sources) after UNITAID withdraw allegedly limits the number of patients to be put on treatment. Interestingly, a respondent pointed out the fact that lack of country planning remained the same, as well as other 'underlying' problems. There did not seem to be preparations to substitute UNITAID funding, to the extent that several respondents pointed at this issue as a negative influence in post-UNITAID market landscape. There was also at least one example of a country reporting that they were more prepared to manage MDR-TB treatments, with continuous good quality support from regional WHO. In several cases, it was stated that funding was taken over by the Global Fund, although we could not ascertain whether this was done in continuity or there were treatment interruptions.

In any case, it was recognised that markets have a lot of externalities and are very complex environments, and that it may not be reasonable to expect larger and/or durable changes.

Several factors were reported to improve the market situation (although responses do not necessarily point at 'permanent' market improvements but rather at circumstantial improvements as a result of the grant implementation): a more stable demand and supply, a better pricing of some regimens. Most of the responses who rated the market as "better" linked the improvement to the Global Fund financing without relating it directly to UNITAID support.

Further enablers for market situation improvement are presented in Annex 10.

Factors identified by respondents with a lack of progress or which could jeopardise progress in terms of the market situation were mainly related to a market still at an early stage of development with limited incentives and interests for manufacturers despite funding support combined with a weak stakeholder coordination, limitations in diagnostics, and poor country capacity to sustain scale-up with domestic resources.

Further factors related to a lack of progress are presented in Annex 10.

Note that these comments provide some indication that the question about "market situation" was not fully understood.

Two main factors that contributed to maintaining or improving the good aspects of the market situation once UNITAID support had ended were identified by respondents: the decrease of prices for SLD as well as funding from the Global Fund (either existing or new funding).

Effectiveness of procurement processes

Most respondents perceived that procurement processes were effective in accomplishing the project' objectives (price reduction of products, increasing access to treatment, making effective use of the existing supplier base, and encouraging new suppliers to enter the market): only one gave a 'No' as answer to this question with no further comments, though. Three felt there was partial success and eleven felt 'yes', there was success. Two respondents did not know what answer would be appropriate.

Manufacturers pointed at certain **challenges when the grant ended**; most were linked to the limited financial resources to tackle MDR-TB resulting in potential drug shortage in the absence of stockpile, a decreased treatment access with longer waiting lists for diagnosed patients as well as a decrease in the quality of medicines or drug management leading to increased resistance and therefore higher TB prevalence.

Further challenges related to the completion of the grant are presented in Annex 10.

3.4 Efficiency

One aspect to take into account is how market issues were approached. We did not attempt to obtain a complete reconstruction of how this was carried out. However, a respondent provided interesting insights which are worthwhile to report. An initial point is whether there was sufficient

market research to identify all potential medicines suppliers in order to maximise competition among suppliers. It has been reported that there were no calls for EoIs published till early 2008¹. Then, from 2009 onwards, the main approach used was invitations issued by the Global Fund for the ERP review and temporary acceptance of products. However, it seems that these were not necessarily directed to manufacturers with Stringent Regulatory Authority (SRA) products from certain countries such as Canada or USA. There was also no formally communicated mechanism to attract and handle spontaneous SRA manufacturer applications for consideration in tenders.

3.4.1 Were medicines management and procurement optimised and funding sources identified?

- Validation of findings on efficiency (log frame output 2 or 4 (depending on period); evaluation area 1)

Drug stocks during grant implementation

To the question whether drug stocks were appropriate to avoid stock-outs and facilitate access during grant implementation, 81% responded positively.

Lead time during grant implementation

Similarly, to the question whether lead times were appropriate to avoid stock-outs and facilitate access during grant implementation, 81% also responded positively despite some bottlenecks (around Kanamycin) and as long as planning and forecasting were adequate. One respondent however responded negatively mentioning that “most orders were supplied from the Strategic Rotating Stockpile.

Order processes during grant implementation

To the question whether order’s dynamics or processes were appropriate to avoid stock-outs and facilitate access during grant implementation, 80% responded positively. There were, however, some concerns expressed related to a competitive process for orders not always optimized.

Comments on this subject are presented in Annex 10.

Prices during grant implementation

To the question whether prices were appropriate to avoid stock-outs and facilitate access during grant implementation, 60% responded positively although some limitations were mentioned, mainly related to the fact that prices for MDR-TB drugs still remain high.

As a summary, medicines management and procurement were felt as optimised by the interviewees in terms of drug stocks, lead times, order’s processes and prices during the implementation of the grant.

- Validation of findings on long term funding (log frame output 3; evaluation area 1)

In terms of long terms funding, a transition plan has been made available; it was, however, requested quite late in the project implementation period (2011-2012). Formal notification letters

¹ Note that GDF involvement in the project did not start till late 2007.

were planned to be sent only by mid-2012 to respective countries including a request to the countries to specify the estimate number of patients to be enrolled on treatment in the upcoming years as well as the funding source for it. The selected countries were mainly relying on Global Fund support, and GDF was mentioning the Global Fund funding changes with the introduction of the transitional funding mechanism.

However the reviewers did not identify any follow up on this issue in any subsequent GDF reports.

3.4.2 Is the project's procurement model still in place? (transition)

- Procurement model and functioning (evaluation area 2)

To the similar questions on whether current prices, current drugs stocks and lead times are appropriate to avoid stock-outs and facilitate access now that the grant has ended, a majority of survey recipients answered positively (average of 66.7% of 21 survey answers for the three questions).

Interviewees added the following comments regarding blocking points:

- In terms of prices: most of the comments emphasized that despite some decrease, MDR-TB drugs prices still remain very high and therefore representing a barrier to treatment scale-up
- In terms of drug stocks and orders' dynamics: concerns were expressed on the challenges faced by some national entities related to GDF requirement of pre-payment orders.

Comments on procurement model limitations are presented in Annex 10.

Procurement processes efficiency

Most respondents (66.7% of 21) replied that procurement processes have been efficient (or partially efficient) in accomplishing the Projects' objectives, notably achieving price reduction of products, increasing access to treatment, making effective use of the existing supplier base, and encouraging new suppliers to enter the market. However some reserves were expressed on the strategic choice of the support i.e. procurement of drugs to countries versus more innovative approaches suggesting more flexibility to make long term commitments to manufacturers against a binding forecast or other more innovative procurement techniques (e.g., engagement with API manufacturers).

Further comments on procurement process efficiency limitations are presented in Annex 10.

Survey recipients had expressed different views concerning the use of the supplier base to encourage competition in the market. Some interviewees will continue to use GDF mechanism to procure medicines (2 responses), some of them will perform competitive tendering amongst prequalified suppliers, and one reply was that MDR medicines are supplied from manufacturers who registered their drugs within the country.

Regarding the question related to, when there are multiple manufacturers of the same quality assured product, what is the split of the business (quantities, costs, etc.) between them and how is it determined, the few respondents mainly related the split to the tendering process.

Comments of interviewees on this subject are presented in Annex 10.

The same survey recipients expressed some quality issues regarding one medicine Cycloserine (“power inside the capsule was solidified”) and one consumable i.e. syringes (“failed QC test done by the country”).

- Funding alternatives (evaluation area 3)

As mentioned previously, there is no evidence of active search by UNITAID/GDF for alternative funding besides the late transition plan elaborated in 2012 and with no available follow-up.

3.5 Impact

3.5.1 Are changes of KPI plausibly attributable to UNITAID support?

- Validation of access to MDR medicines (evaluation area 1)

A total of 19 survey recipients (TB managers, UNITAID, Global Fund, GDF, ex-GDF) responded to the question if there were changes (positive or negative) observed during the grant unit; 74% (14) perceived there were changes and only one did not perceive any changes. In addition, four did not know if changes could be observed. A total of 26% respondents (5) perceived (clearly or partially) that issues which did not go well were attributable to UNITAID, and 58% (11) denied this.

Most of the positive changes mentioned were related to increased access to treatment with reduced prices together with an improved quality assurance for SLD.

Comments of interviewees on changes are presented in Annex 10.

Most respondents who did not perceive that there were problematic issues attributable to UNITAID did not comment. One commented that after UNITAID left, problems/challenges grew.

A total of 63% of the respondents (12 out of 19) perceived (clearly or partially) that improvements in the supply of medicines were attributable to UNITAID. Four stated that it was not attributable to UNITAID and three did not know.

Similarly, 74% of the respondents (14 out of 19) perceived (clearly or partially) that improvements in the access of medicines were attributable to UNITAID. Three stated that it was not attributable to UNITAID and two did not know.

Comments regarding the supply of and access to medicines are presented in Annex 10:

Only 18 survey recipients responded to the question on whether improvements in prices were attributable to UNITAID. A total of 56% of the respondents (10 out of 18) agreed with this statement (clearly or partially). Four did not perceive that improvements in prices were attributable to UNITAID and four did not know. A pooled procurement with large quantities of drugs under UNITAID project was identified by interviewees as the main reason leading to improvement in prices in terms of reduction.

As a summary related to the access to MDR medicines, approximately two-thirds of the respondents stated that there was an improvement due to UNITAID in terms of the supply of and access to medicines and 56% of the respondents stated that price reductions were attributable to UNITAID.

From manufacturers' point of view, to the question on whether the grant had an impact on the way they are doing business, different answers were provided. One was mentioning a negative impact as a result of grant implementation as it hampered innovation through increased competition (and copy-cat of drugs).

All manufacturers' responses confirmed that the market landscape had changed during the period 2007-2013. Such changes were sometimes attributed to the grant, however not always. Changes identified were related mainly to an increased market size with more manufacturers and therefore increased competition leading to reduced prices. This translated into an increased number of patients treated. One interviewee felt, however, more specifically that the entrance of more manufacturers in the market eliminated the need for continuous drug production for some manufacturers as there were less concrete orders of significant volume.

3.6 Learning and risk mitigation

The following findings are the results of the generic survey responses.

To the question "Have lessons learnt been documented and widely disseminated by or to you as grantee?" 28% of respondents selected either 'Yes' or 'Partially' but a large majority answered either 'No' (45%), Don't know or left the question blank (28%).

One reason suggested was related to the fact that the project "Logframe was created mid-way through the project for better accountability but reporting by the grantee was very poor towards the end of the grant". A Logframe describing the goal, purpose and 4 outcomes of the project as well as identifying the specific indicators to be reported on by grantees is indeed only included in reports from 2011 onwards (following mid-term evaluation recommendations). Such Logframe seems to have facilitated later on the structure of the (annual) report by GDF/GLC/Global Fund while such structure is less obvious in the annual reports made available for the years 2008, 2009 and 2010.

Another respondent pointed out more specifically the potential lack of visibility of UNITAID given that the funding is channelled through GDF. It was reported that "It is important for the dissemination of this information. Many countries are not even aware where the support originates from. These medicines are always confused to come from the GDF". It is noted that in the six (6) countries (Azerbaijan, Dominican Republic, Moldova, Kenya, Kyrgyzstan, and Uzbekistan) where UNITAID/GDF/GLC has been providing support together with the Global Fund for an additional period equal to the remainder of the respective grants (from mid-2009 through 2011), there is no mention of funding support in the Global Fund performance framework while targets are combined for one specific indicator.

In addition, while e.g. the 'Annex 6 of the annual GDF/GLC/Global Fund report 2011 - Global Fund specific reporting on the seven Global Fund grants supported through the project in 2011'¹ includes under 'annex 2' some comments regarding Progress to date mentioning data/targets for support, these do not seem to be tracked individually. Targets are rather combined with Global Fund targets which also sometimes (e.g. grant treatment targets) "can be linked to National Program targets and therefore may also include the provision of MDR-TB drugs from funding sources other than Global Fund". There is, therefore, a lack of target disaggregated by donors when applicable.

Feedback on this question was quite divergent. While a respondent almost regretted not to have done a better documentation stating "Unfortunately NO. It was a mistake not to document this important experience for increased access to treatment in our country", another one felt that the need for such documentation was not necessary as the "project was strictly for the deliveries on agreed number of patient treatments. This has been successfully ... there is no need to document any lessons, as either the treatments are delivered as agreed, or no, and this has been done".

At the question "Have you documented and widely disseminated lessons learnt as grantees?", only one third of respondent selected 'Yes' (9%) or 'partially' (23%) while the remaining majority either responded 'No' (41%) or Don't know / blank (28%). Those who responded positively mentioned sharing information with the Government so as to show the project's contribution to TB control, the intention to organize a dissemination platform, or having documented lessons learnt in donors' reports including success story. On the contrary, one respondent did not consider this activity as part of the work "No to be honest. We received grant, ordered medicines and distributed them; that was our work".

Feedback provided on both questions seems to indicate a need for improved communication as well as information sharing between donors / grantees. In future projects, it may be worthwhile to identify the dissemination of lessons' learnt as output with established indicators for reporting, and include it in the Logframe.

Regarding the issue on whether programmatic and financial risks have been identified and tracked over the course of grant implementation, we note the following strengths and weaknesses:

Strengths

Disbursements of UNITAID to GDF / GLC as of 31 December 2013 amount to 51'814'865 USD (leading an outstanding amount of 1'519 USD compared to the revised approved budget of 51'816'384 USD) for a total of 17'054 patients treated.

As of 31 December 2013, GDF spent a total of 48'169'482 USD distributed as follows:

- Payment of orders for a total of 46'168'044 USD
- GDF Procurement-Related Management Costs for 2'001'438 USD

¹ Annex 6 – UNITAID MDR-TB Scale-up Initiative – Annual Progress Report for 2011. The Global Fund.

This leads to **93% budget execution rate which is quite satisfactory**. In addition, GDF committed 3'197'013 USD (orders placed but not paid), leading to a cash balance end of period of + 448'370 USD.

As of 31 December 2013, countries reported expenses paid for 46'615'996 USD (exceeding by 447'952 USD disbursements reported by GDF) and commitments for 3'197'013 USD. It is likely that this excess of USD 447'952 has been financed from bank interests earned.

The agreed disbursement schedule has ensured a positive cash flow at the level of GDF over the course of the project implementation and sufficient funds available as of 31 December 2013 to pay commitments.

In 2013, a high degree of flexibility of UNITAID and GDF allowed for a swift reprogramming of the project by using unspent funds to partially mitigate the risk of treatment interruption and decrease the gap between planned enrolment and funds available. GDF has also demonstrated flexibility by providing urgent delivery to Senegal based on UNITAID urgent request and advances of some of the deliveries based on countries requests.

Weaknesses

As mid-2012 (toward the end of the project), UNITAID requested each recipient to provide a transition plan, including an estimate number of patients to be enrolled on treatment in the upcoming years as well as the funding source (other funding sources and their own governments). Such transition plan should have been negotiated and agreed at the beginning of the project, to ensure more sustainability of gains seen under the project.

The accuracy of estimated Funding Gaps provided by recipients to GDF cannot be verified due to the absence of a comprehensive information and detailed donor mapping per country. From the documentation made available by UNITAID, there was no evidence on whether countries had secured alternative sources of funding for MDR TB products following UNITAID support or not.

We note a lack of diversification of resources to fund MDR treatments from January 2014 onwards, the countries relying essentially on Global Fund current and upcoming grants while Governments contributions remain low.

UNITAID did not consider before the inception of the project any possible re-classification by the World Bank of beneficiary recipients based on the evolution of their incomes and contractual implications (i.e. Uzbekistan, Lesotho, Timor-Leste, Azerbaijan, and Dominican Republic).

UNITAID has no leverage on the programmatic management fully owned by the recipients whose capacities are often limited.

In the completeness checklist for reporting (semi-annual and annual report), there is no mention on the reporting / use of bank interests, follow-up of commitments, delays of payments, criteria to assess the eligibility of expenses, tracking of other funds supporting MDR patients, accruals, etc.

The absence of standardized reporting templates linking programmatic and financial information and reflecting cumulative achievements at recipients and GDF levels makes the follow-up of the project and the process of decision making by UNITAID complicated.

To the specific question on whether the findings and recommendations of mid-term evaluations or audits (where relevant) have been used to improve grant performance, half of the respondents answered positively ('Yes' or 'Partially') to this question while the remaining answers were evenly spread between 'No'/'Don't know'/blank. Some reasons suggested related to the fact that while a Logframe had been established mid-way through the project to better facilitate reporting, "the quality of the reports was still poor with little information". From the responses provided, it seems that there was "No noticeable change with regard to procurement and supply chain management". Several grantees mentioned not having, or remembering any mid-term evaluation taking place but some GDF missions every two years.

When requested to answer on whether MDR TB medicines availability was a concern or problem during the project, 41% of the respondents answered positively ('Yes' 32% and 'Partially' 9%) while approximately the same proportion of respondents felt the other way ('No' for 45% of them), others either 'Did not know' or did not provide any answer. Overall this concern is less expressed by grantees than by GDF staff. However, there does not seem to be any difference among respondents regarding such concern whether countries were also supported by the Global Fund together with UNITAID or not.

When asked a similar question now that the project has ended, almost 2/3 of respondents expressed such concern ('Yes' for 41% or 'Partially' for 23%) while 32% did not see this issue as a concern ('No' at 31%).

Responses to the question on whether the market situation is a concern / problem now that the project has ended resulted in 46% of the respondents expressing the existence of such concern ('Yes' at 23%, 'Partially' at 23%) while one third ('No' at 32%) did not.

Almost two-thirds (59%) of the respondents did not consider that there was any concern related to medicine management and procurement during the project. Some who provided comments related the concern to the limited scope of the UNITAID grant (procurement) addressing mainly the supply side of drug while other challenges remain on the demand side in a market still in an evolutionary stage where all needed drugs are still not available.

The same question asked now that support has ended resulted in an increase of concern related to medicine management and procurement from 31% in the previous question to 45% among same respondents.

Among the very few recommendations expressed by respondents besides their interest for applying to another project or "should continue their project to fill the gap or back up of SLD for the program", some suggestions and limitations were expressed and related to further in-country capacity building, more dissemination of lessons learnt from grant implementation (e.g. establishing a platform for discussion and exchanges of experience) while demonstrating more flexibility and less involvement in implementation, or considering funding activities which go beyond HIV, TB and Malaria in other health areas as e.g. smoking, diabetes, depression based on burden of diseases.

Some recommendations expressed by interviewees are reported in Annex 10.

Specific recommendations from manufacturers were related to maintaining stockpiles, ensuring annual forecasts to manufacturers as well as performing consolidated purchasing so as to ensure better efficiency and better pricing, or entering in long-term agreements with GDF so as to establish long-term business plans.

Specific recommendations expressed by manufacturers are reported in Annex 10.

Besides the seeming need for more flexibility of the model and its implementation (note that flexibility is one of the guiding principle), the above comments and recommendations from respondents seem to be more related to the length of the project as well as the size of the support (some countries received one off support for very few patients e.g. Timor Leste while more than half of the patients treatments was provided to only one country, namely India). The issues of capacity building of grantees as well as the need for better information and experience sharing are also emphasised.

As a summary of lessons learnt, the project support has been recognized as useful by many respondents with advocacy for benefiting from such support in the future. However, given that the total budget ceiling commitment to the project was 52,000,000 USD allocated to 19 countries over a period of five years, focusing on procurement of drugs with support moreover channelled through another agency (GDF), **there is a concern for visibility and sustainability** (one of the guiding principles) expressed by several respondents who suggested **an improved communication** between all parties involved (UNITAID, GDF, Global Fund), **a stronger coordination with other partners** and the **establishment of co-financing mechanisms with Governments and others partners** (although for countries supported by Global Fund grants, Global Fund is also requesting Government for co-financing of activities and programs for the last two years more specifically during assessments of Phase 2 of the grants).

Although the current strategy is to remain focussed on product markets for the diagnosis and treatment of HIV, TB and malaria, as well as prevention commodities, co-morbidities and co-infections significant to these three diseases i.e. adopting market-based approach for increased impact, some respondents suggested the need to support more capacity building activities (e.g. forecasting) for grantees so as to be more visible “on the ground”.

In terms of project documents, the final GDF annual report¹ emphasises some limitations of the project acknowledging that “objectives 3 and 4 of the Project cannot be optimally achieved under this Project Plan alone. The number of beneficiary countries supported by and other donors would need to be substantially increased in order to provide the required market incentive for adequate numbers of manufacturers to (i) be motivated to participate in the WHO Prequalification Program and (ii) allow for effective competition, negotiation and market commitments to reduce prices by the targeted level”.

¹ Final report on GDF/UNITAID MDR-TB Scale-Up Initiative 2007-2013. GDF

For the six countries which benefited from support from both and Global Fund, there is no analysis of the added value of such partnership. The Global Fund part of the reports is not completely included in the overall annual UNITAID/GDF report but rather added as an annex.

Out of the five initial countries in transition (Guinea, Kenya, Myanmar, Nepal and Kyrgyzstan), only four have benefited from support in 2013 (Nepal having withdrawn his application), and only three have provided responses to the questionnaire. Although being the most significant beneficiary of the no-cost extension support in 2013 with 673 additional treatments provided, Myanmar did not provide any information to the questionnaire. The 2013 annual GDF/ report¹ however mentioned “currently 600 patients’ gap is identified by Myanmar. It is likely that government funds will be used for this procurement. There is currently no gap information from other 3 supported countries”. For Myanmar more specifically, the Global Fund is still significantly supporting the TB national program for the period 2013-2016.

3.6.1 Are changes of KPI plausibly attributable to support?

- Follow up of previous recommendations (evaluation area 5)
- Capacity to draw lessons from project documentation (evaluation area 5)

The following Table 8 below summarises the recommendations as well as the follow-up from the mid-term review 2011².

¹ Annual Report on GDF/UNITAID MDR-TB Scale-Up Project – January-December 2013. GDF

² UNITAD mid-term review - MDR-TB Scale-Up Initiative 2007-2012, MDR-TB Acceleration of Access Initiative: Strategic Rotating Stockpile, First-Line Anti-TB Drugs Initiative. Alexei Sitruk, Svenja Weiss, Peter Steinmann, Bruno Clary, Dominique Guinot, Xavier Bosch-Capblanch. Swiss TPH, November 2011.

Table 8. Mid-term review 2011 recommendations

	Conclusion	Recommendation	Status	Follow up / comments
	Project specific findings			
1	GDF does not publish prices of MDR TB drugs, preventing countries from using this information to negotiate better prices when carrying out their own procurement.	GDF should publish on its website the price it pays for second-line drugs. GDF could negotiate with suppliers to extend negotiated/bid prices to countries (similar to CHAI consortium) that conduct drug procurement on their own (outside GDF).	Completed	At the beginning of the project the prices were available upon request as reference prices for planning purposes only. This was due to the fact that suppliers base was changing due to ERP approval mechanisms that were time limited. As of 2011, the prices have been published online and available to everyone: prices for 2 nd line TB medicines on GDF website ¹ .
2	Accelerated access to treatment under the project could not be clearly demonstrated.	Now that the GLC approval is no longer required for a country to procure MDR TB drugs, UNITAID should consider extending its project to additional countries.	Partially	Following the endorsement by the Stop TB Partnership Coordinating Board and the WHO TB Strategic Technical Advisory Group, the implementation of the New Global Framework to support expansion of MDR-TB services and care started on 1 July 2011. Therefore no GLC approvals were required after that date. However, budget was not increased and stayed static. NOTE, that based on GDF savings, we were able to supply additional treatments to In 2010 amendment, the project was extended to India for 9'850 additional treatments therefore before the waiver of GLC approval. Senegal was added as beneficiary country later on. The budget was not increased to take on more countries but saving allowed the supply of additional treatments to 4 countries in 2013 resulting in a total of 19 countries supported by UNITAID/GDF instead of 17 initially planned in 2007.
3	Although countries report to have enrolled patients, the gap between GLC approved patients and patients being actually treated remains substantial.	2- UNITAID should ensure that funding for technical support to heavy burdened countries to increase diagnosis and treatment is available concomitantly to UNITAID support for anti TB drugs and diagnostics.	Not completed	For this specific project, funding was allocated for procurement mainly.
4	No concrete actions have been taken towards the objective of stimulating the development of new MDR TB drugs.	3-. UNITAID should favour the development of new drugs. Incentives could include advanced purchase commitments to facilitate new product market entries. Similarly, a link should be established between scale up access projects and TB alliance (Global Alliance for TB drugs development http://www.tballiance.org/) or any initiative aiming at making new treatments available.	Not completed	This was not one of the objectives of this specific MDR-TB Scale Up Initiative project. Note that based on the manufacturers survey responses, the aim of decreasing prices is done at the expense of innovators and does not provide incentives for companies to invest in research and expose products to the market that would then be copied.

¹ <http://www.stoptb.org/assets/documents/gdf/drugsupply/katalog2014web.pdf>

	Conclusion	Recommendation	Status	Follow up / comments
	Common findings			
7	Only a small portion of TB drugs procurement is channelled through GDF; therefore the majority of patients are treated with non QA products. Local manufacturers of high burdened countries do not submit their products for pre-qualification.	<p>Considering that UNITAID supports both the GDF and WHO PQP, in the context of a new project, UNITAID should put an emphasis on the need for partners (GDF and WHO) to consider Prequalification of local supplier products a priority.</p> <p>This could result in the development of a UNITAID list of priority products (please refer to WHO PQP MTR report¹) taking into account whether these products are produced in high burden country and the provision of financial incentives and technical support with collaboration of USP. This would support synergies across UNITAID portfolio and potentially increase UNITAID projects impact.</p>	On-going	<p>GDF is the largest TB related procurement mechanism for public sector worldwide, and works under stringent Quality Assurance policy, aligned with UNITAID and Global Fund</p> <p>However, this recommendation is not relevant to patient treatment deliveries under this project</p>
8	Supply of TB drugs will remain vulnerable to disruption unless quality of forecasting improves and some level of order pooling is facilitated with the aim to provide manufacturers with increased predictability of country needs.	Quarterly orders and granting access to some features of the OMS should facilitate order pooling and assist manufacturers in production planning. .	Don't know	OMS data is connected to GDF forecasting activities. Pooling of orders is standard practice.
9	The definitions of performance framework indicators evolved and were not always sensitive enough to accurately reflect GDF performance and open to different interpretations.	Partners should work together on the development of a performance framework featuring clearly defined performance indicators and targets consistent with the most up to date LoAs and MoAs.	Partially	In relation with the MDR-TB Scale up project, a Logframe has been established and used from 2011 but it could still be improved e.g. clearly stating updated yearly targets if applicable. For projects implemented in countries together with Global Fund, the support from UNITAID should be clearly mentioned in the Global Fund performance framework and results attributable to UNITAID support clearly demonstrated.

	Conclusion	Recommendation	Status	Follow up / comments
10	Reporting practices have several pitfalls (e.g. delayed responses to GDF clarification requests) and reports have missing information (e.g. absence of report submission dates, interest earned not consistently reported, non-cumulative reporting).	Partners should convene regular meetings in order to develop and enforce clear, timely and commonly agreed processes on reporting and feedback. Partners are advised to draft and use a reporting template based on performance framework indicators and targets, linking programmatic and financial information and reflecting cumulative achievements. Interest earned should be systematically and formally reported	Not completed Not completed	As part of documentation made available by UNITAID, there is no reporting template linking actual and cumulative programmatic and financial results submitted by recipients and GDF. It seems that the programmatic reporting has continued to be separated from the financial reporting between 2011 and 2013. The financial report as of 31 December 2013 does not refer to bank interest revenues earned by GDF and the use of these additional funds.
	The number of patients actually treated with UNITAID funded drugs is not deemed sufficiently accurate/reliable	UNITAID and partners should agree on a methodology to estimate the number of patients actually treated with UNITAID funded drugs. The numbers reported should cross checked during in country monitoring visits and against WHO latest estimate.	Partially	The methodology was reported by GDF to UNITAID before and agreed upon and did not change over the course of the project.

Management

In terms of staffing related to volume of activities: the project budget comprised the annual costs from 2007 - 2011 (5 years) of 1 full-time P3 level (WHO classification) professional staff and 1 full time G4 level (WHO classification) administrative support staff, with annual cost estimates based on WHO-HQ (Geneva) projected staff costs for the 2008-2009 biennium.

GDF final report mentions that GDF hired two additional staff in late December 2008: a procurement officer dedicated to the MDR and Paediatric Projects and a Business Services Officer responsible for, among other things, coordinating GDF donor reporting, work planning and financial transaction monitoring.

According to GDF, human resources costs were exclusively for GDF staff and were considered highly instrumental to the success of the project. It has been “considered adequate, however on lower side”.

3.7 Additional findings

3.7.1 Special responses

Some responses were especially critical with the way some activities were carried out, containing severe statements about what happened. A lack of transparency related to tender evaluations as well as internal reluctance for change or flexibility were more particularly mentioned. These

statements, even if produced by a limited number of respondents, merited to be explicitly mentioned. On the other hand, the reviewers did not have the capacity during the current evaluation to fully elucidate the evidence supporting those statements and are certainly bound to respect anonymity. In the following paragraphs the reviewers report on what was judged to be especially critical responses. While acknowledging that some statements may not be completely clear, the reviewers are not in a position to endorse any of those except for the fact reported in previous sections.

However, instead of being completely discarded, such suggestions may encourage the organization to have regular internal / external audits as done in many projects.

Some of those specific comments are reported in Annex 10.

3.7.2 Other

There is a significant issue of approximation of number of patient treatments delivered as an extrapolation based on the quantities of medicine delivered in a country. Moreover translating quantities of medicines delivered into a number of patient treatment will not reflect the number of patients treated in a country as per target due to changes in treatment regimens related e.g. to drug resistance patterns, defaulters, patients who die, etc. With reference to the extrapolation underlying the principle for conversion from delivered medicines into patient treatments, GDF mentioned that a deviation of 30% from the UNITAID treatment target should be considered acceptable.

4 Methodology

Following conversations with UNITAID staff members in Geneva, the scope of the evaluation was defined around the following five evaluation areas:

- Evaluation area 1: validation of the impact evaluation already carried out by UNITAID.
- Evaluation area 2 (transition): what is happening now in countries which stopped UNITAID funds; this will be sought in terms of effectiveness and efficiency.
- Evaluation area 3 (sustainability): what is the impact in the market space and to which extent this impact remains intact or progressing.
- Evaluation area 4: this is a cross-sectional area where players, funding, processes, enablers and barriers will be identified and their plausible effect on outcome described;
- Evaluation area 5: this area will present the conclusions and recommendations to assist future decision making (e.g. what should be done in the future to scale up in order to ensure access; in relation to the market and public health issues).

These evaluation areas were approached using the DAC evaluation criteria¹ adapted to the purposes of this evaluation in order to properly cover all evaluation areas: relevance, effectiveness, efficiency, impact, learning and risk mitigation including sustainability and transition issues.

Annex 4 presents an outline of the evaluation matrix.

The current methods outline was presented and discussed to obtain a final evaluation matrix with details on the approaches to follow for each evaluation area, criteria and indicator.

The following approaches were used:

- 1) documents review: this informed other approaches (e.g. Key Informants Interviews -KII) and provided information to estimate certain indicators;
- 2) KII (see Annex 5 and Annex 6): with a generic questionnaire (Annex 8) this was addressed to people suggested by partners, recipients, procurement agents, staff, countries partners and other stakeholders; and another questionnaire specific for manufacturers (see Annex 9). KII helped to identify factual errors, assisted in the interpretation of evaluation findings and provided views about certain issues as detailed in the evaluation matrix. Three types of interviews were implemented:
 - a. an online questionnaire with a common module and specific modules for each stakeholder or group of stakeholders. The questionnaire had an online format and provided the essential facts and views on the different evaluation areas;
 - b. face-to-face interviews to the most relevant actors to deepen on the findings of the online questionnaires or to address additional issues;
 - c. phone interviews where face-to-face interviews were not feasible.

¹ DAC Criteria for evaluating development assistance.

The formula of using generic online interviews followed by focused phone interviews proved to be an efficient way to access information. Interestingly, some interviewees were more prone to phone interviews even if these may eventually last longer, partially as well due to the technical limitations in some settings¹.

The generic questionnaire was sent to the responsible managers of the 19 countries under review based on contact details provided by GDF followed by 10 phone discussions, 4 GDF staff, 3 former GDF staff, 2 Global Fund staff and 6 UNITAID staff. Out of a total of 34 invitations sent for the generic questionnaire, a total of 20 responded completely while 2 did only partially (65% respondents).

Out of the 19 TB managers contacted, 14 completed the survey (74% respondents). Those who responded were the ones in charge of the implementation of the grant in their respective countries even when few managers had changed positions or left the project.

The manufacturer's questionnaire was sent to 15 manufacturers' contacts persons as well as two contacts for the procurement agent. Only manufacturers responded with a total of 7 complete questionnaires submitted (47% respondents).

- 3) Quantitative analyses was carried out in a limited manner, only where this was required to understand or inform evaluation statements and where these analyses have not been already done;
- 4) Qualitative analyses identified the key issues in each evaluation area and criteria and provided the narrative of the evaluation findings, conclusions and recommendations. The qualitative analyses described the project architecture and log frame.

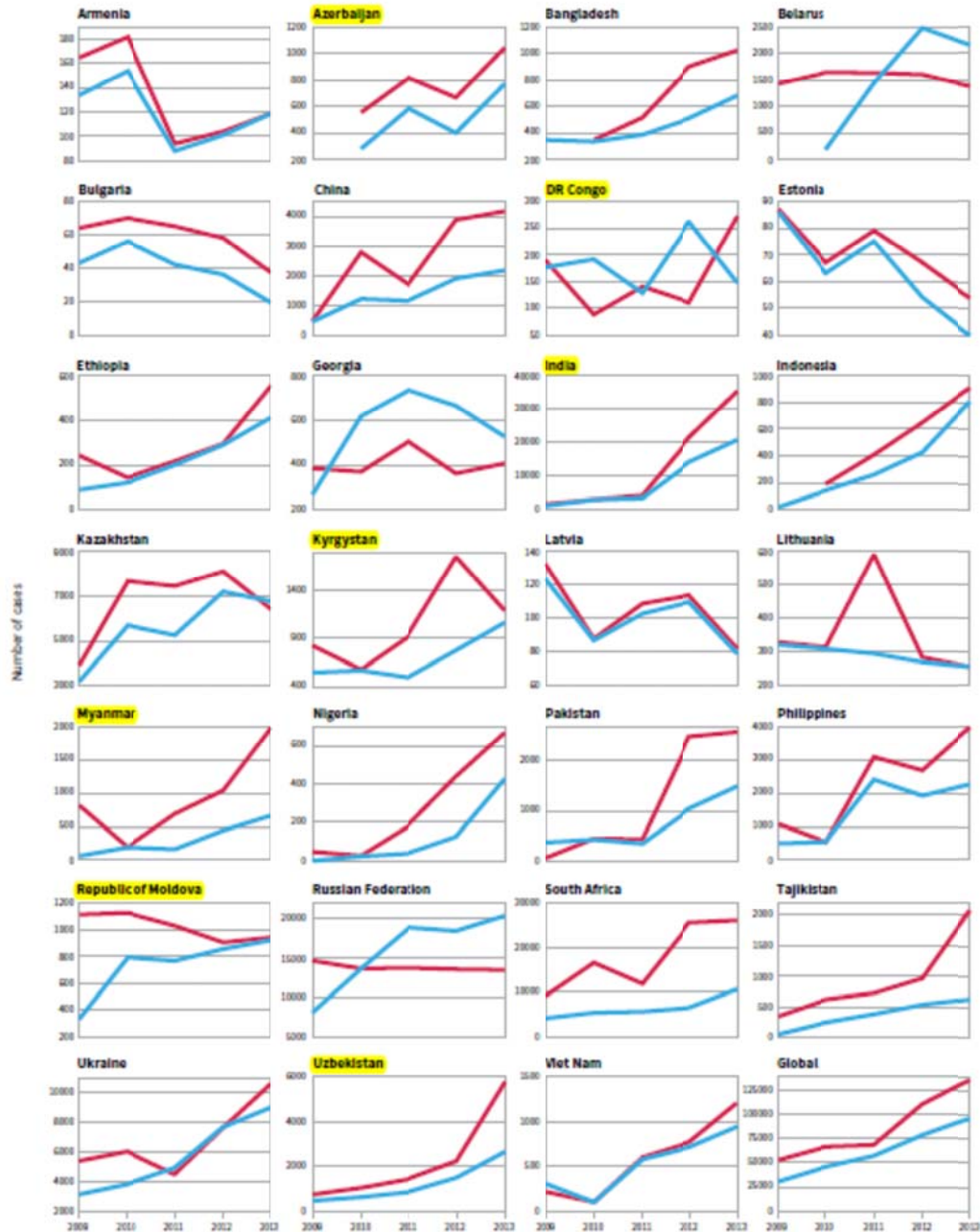
Note that, in agreement with UNITAID, finances were not evaluated.

¹ As one interviewee commented by email later on: "it was indeed so nice to talk to [name of interviewer] for the interview yesterday [...] I felt so delighted as I was able to sit for interview for almost one hour which was not possible through online as I would not have got that much time to spend on someone's computer (as I do not have internet access in our building)".

ANNEXES

Annex 1. Gap between drug-resistant cases detected and enrolled on appropriate treatment

MDR-TB cases and additional rifampicin-resistant TB cases detected (red) compared with TB cases enrolled on MDR-TB treatment (blue), global trend and trend in 27 high MDR-TB burden countries, 2009–2013



Countries receiving UNITAID support coloured yellow.

Source: WHO Global TB Report, 2014 (Figure 5.7).

We can consider that a given situation worsens when MDR-TB patients remain undetected, or when diagnosed patients are not treated or treated with delay, or when real incidence increases (detected or not). In this regard, of the seven UNITAID high-burden MDR-TB countries, only

Moldova and may be Kyrgyzstan clearly improved; and Azerbaijan showed no worsening. This situation cannot be fully attributed to UNITAID; however, it stresses the need to seriously strengthen approaches to fight MDR-TB in all fronts.

Table A - 1. Number of patients and proportion addressed by UNITAID.

	Total patient treatments for the project	Expected to be treated in 2008	Number of drug-resistant cases started on MDR treatment					Total (2008-2013)	% UNITAID over total
			2009	2010	2011	2012	2013		
Azerbaijan	1260		no data	286	592	406	771	2055	61.3%
DR Congo	592	523	176	191	128	179	147	1344	44.0%
India	9850	450	1136	2967	3384	14,143	20,763	42,843	23.0%
Kyrgyzstan	818	no data	545	566	492	790	1064	3457	23.7%
Myanmar	873	125	64	192	163	442	667	1653	52.8%
Moldova	155	466	334	791	765	853	931	4140	3.7%
Uzbekistan	614	334	464	628	855	1491	2647	6419	9.6%
Total	14,162*	1898	2719	5621	6379	18,304	26,990	61,911	22.9%

* 83% of the total of 17'054 patient treatments delivered

Annex 2. UNITAID Strategic Objectives

1. Increase access to simple, POC diagnostics for HIV/AIDS, Tb and malaria.
2. Increase access to affordable, paediatric medicines to treat HIV/AIDS, Tb and malaria.
3. Increase access to emerging medicines and/or regimens as well as new formulations, dosage forms, or strengths of existing medicines that will improve the treatment of HIV/AIDS and co-infections such as viral hepatitis.
4. Increase access to artemisinin-based combination therapies (ACTs) and emerging medicines, which, in combination with appropriate diagnostic testing, will improve the treatment of malaria.
5. **Secure supply of second-line tuberculosis medicines, and increase access to emerging medicines and regimens that will improve treatment of both drug-sensitive and MDR TB.**
6. Increase access to products for the prevention of HIV, Tb, and malaria, notably to improve the availability of devices for male circumcision and of microbicides, once they are approved; and to increase access to vector control tools to prevent malaria transmission.

Annex 3. Overview of the quantitative analysis of codified responses to the generic questionnaire.

Table A - 2. Overview of the quantitative results of generic questionnaire

Questions	Yes	Partially	No	Don't know	Blank	Total	Yes	Partially	No	Don't know	Blank	Total
1) Is the grant targeting developing countries?	17	2	1	1	1	22	77%	9%	5%	5%	5%	100%
2) Is the grant targeting disadvantaged populations?	17	3	0	0	2	22	77%	14%	0%	0%	9%	100%
3) Is the grant applying innovative market approaches?	10	1	5	4	2	22	45%	5%	23%	18%	9%	100%
4) Has the grant ensured supply of second-line TB medicines?	19	1	0	1	1	22	86%	5%	0%	5%	5%	100%
5) Has the grant increased access to emerging medicines and treatment regimens?	16	1	3	1	1	22	73%	5%	14%	5%	5%	100%
8) Were outputs achieved in the expected timeline?	11	6	0	3	2	22	50%	27%	0%	14%	9%	100%
9) Has the grant produced "value for money" in their outputs?	11	3	1	5	2	22	50%	14%	5%	23%	9%	100%
12) Are more patients accessing second-line TB medicines as a result of the grant?	15	3	0	3	1	22	68%	14%	0%	14%	5%	100%
15) How is the market situation once support has ended compared with when the grant was active?	7	8	1	4	2	22	32%	36%	5%	18%	9%	100%
19) Were drug stocks during the grant implementation appropriate to avoid stock-outs and facilitate access?	15	2	1	3	1	22	68%	9%	5%	14%	5%	100%
20) Were lead times during the grant implementation appropriate to avoid stock-outs and facilitate access?	14	3	1	3	1	22	64%	14%	5%	14%	5%	100%
21) Were orders' dynamics or processes during the grant implementation appropriate to avoid stock-outs and facilitate access?	15	1	2	2	2	22	68%	5%	9%	9%	9%	100%
22) Were prices during the grant implementation appropriate to avoid stock-outs and facilitate access?	12	0	3	6	1	22	55%	0%	14%	27%	5%	100%
23) Are current prices now that the grant has ended appropriate to avoid stock-outs and facilitate access?	12	1	2	6	1	22	55%	5%	9%	27%	5%	100%
24) Are current drug stocks now that the grant has ended appropriate to avoid stock-outs and facilitate access?	12	3	1	5	1	22	55%	14%	5%	23%	5%	100%
25) Are current lead times now that the grant has ended appropriate to avoid stock-outs and facilitate access?	13	1	1	6	1	22	59%	5%	5%	27%	5%	100%
26) Are current orders' dynamics or processes now that the grant has ended appropriate to avoid stock-outs and facilitate access?	12	1	1	7	1	22	55%	5%	5%	32%	5%	100%
30) To your knowledge, was there any issue related to potential diversion of products, counterfeit or quality?	1	0	12	7	2	22	5%	0%	55%	32%	9%	100%
31) Are any changes (positive or negative) observed during this grant period?	14	0	1	4	3	22	64%	0%	5%	18%	14%	100%
32) Are issues which do not go so well attributable to ?	3	2	11	3	3	22	14%	9%	50%	14%	14%	100%

Questions	Yes	Partially	No	Don't know	Blank	Total	Yes	Partially	No	Don't know	Blank	Total
33) If applicable, are any improvements in supply of medicines attributable to?	8	4	4	3	3	22	36%	18%	18%	14%	14%	100%
34) If applicable, are any improvements in access to medicines attributable to?	13	1	3	2	3	22	59%	5%	14%	9%	14%	100%
35) If applicable, are any improvements in prices attributable to ?	8	2	4	4	4	22	36%	9%	18%	18%	18%	100%
36) Have lessons learnt been documented and widely disseminated by or to you as grantees?	3	3	10	3	3	22	14%	14%	45%	14%	14%	100%
37) Have you documented and widely disseminated lessons learnt as grantees?	2	5	9	3	3	22	9%	23%	41%	14%	14%	100%
38) Have programmatic and financial risks been identified and tracked over the course of grant implementation?	6	2	8	3	3	22	27%	9%	36%	14%	14%	100%
39) Have the findings and recommendations of mid-term evaluations or audits (where relevant) been used to improve grant performance?	9	1	4	4	4	22	41%	5%	18%	18%	18%	100%
40) In your opinion a) Was MDR TB medicines availability a concern / problem during the project?	7	2	10	0	3	22	32%	9%	45%	0%	14%	100%
40) In your opinion b) Is MDR TB medicines availability a concern / problem now that the project has ended?	9	4	5	1	3	22	41%	18%	23%	5%	14%	100%
40) In your opinion c) Is the market situation a concern / problem now that the project has ended?	5	5	7	2	3	22	23%	23%	32%	9%	14%	100%
40) In your opinion d) Were medicine management and procurement of concern/problem during project?	5	1	13	0	3	22	23%	5%	59%	0%	14%	100%
40) In your opinion e) Are medicine management and procurement of concern/problem now that the project has ended?	6	4	8	1	3	22	27%	18%	36%	5%	14%	100%

Annex 4. Outline of evaluation matrix

Table A - 3. Evaluation matrix

Area / question	Criteria	Sources	Methods
Relevance			
1 What has been the contribution of the project to UNITAID strategic objectives?			
1-1	Consistency with UNITAID guiding principles (evaluation area 1)	Exemplification of guiding principles in project processes and outputs	- Project documentation - KII Qualitative analyses
1-2	Contribution to UNITAID strategic objectives, particularly objective 5 (evaluation area 1)	Outputs matched with strategic objectives	- Project documentation - Previous evaluations Quantification of effects against strategic objectives
2 What has been the contribution of the project and UNITAID to partners development?			
2-1	Degree of fulfilment of partners' mission (evaluation area 1)	Exemplification of synergies	- Project documentation - Previous evaluations - KII Qualitative analyses
Effectiveness			
3 Were MDR TB medicines available for purchase and distribution?			
3-1	Validation of effectiveness on MDR medicines (log frame output 1; evaluation area 1)	1. Price 2. Availability 3. Accessibility	- http://www.unitaid.eu/en/mdr-tb-scale-up/16-home/963-multi-drug-resistant-tuberculosis-mdr-tb-scale-up - UNITAID KPI 2013 Data mining; completeness of data; interpretation
4 Are MDR TB medicines available for purchase and distribution now that UNITAID support has ended?			
4-1	Access to MDR medicines (evaluation area 2)	1. Price 2. Availability 3. Accessibility	- KII - Data from countries - Project documentation Quantitative description of current indicators on price, availability and access
4-2	Enablers and barriers of observed changes (evaluation area 4)	Delays in chain of events, perceived or objective	- KII - Data from countries - Project documentation Log frame analyses, chain of events and "theory of change"
5 What is the market situation once UNITAD support has ended?			
5-1	Effects on the market space (evaluation area 3)	1. Market price 2. Quality of medicines 3. Availability of medicines	- Data at global, regional and national levels - Project documentation Quantitative description of procurement indicators
5-2	Enablers and barriers of observed changes (evaluation area 4)	Delays in chain of events, perceived or objective	- KII (manufacturers) - Data at global, regional and national levels Log frame analyses, chain of events and "theory of change"
Efficiency			
6 Were medicines management and procurement optimised and funding sources identified?			
6-1	Validation of findings on efficiency (log frame output 2 or 4 (depending on period); evaluation area 1)	1. Access to stockpile 2. Lead times 3. Orders' dynamics 4. Cost per capita	- http://www.unitaid.eu/en/mdr-tb-scale-up/16-home/963-multi-drug-resistant-tuberculosis-mdr-tb-scale-up - UNITAID KPI 2013 Data mining; completeness of data; interpretation
6-2	Validation of findings on long term funding (log frame output 3; evaluation area 1)	1. Alternative funding sources	- http://www.unitaid.eu/en/mdr-tb-scale-up/16-home/963-multi-drug-resistant-tuberculosis-mdr-tb-scale-up - UNITAID KPI 2013 Data mining; completeness of data; interpretation
7 Is the project's procurement model still in place? (transition)			
7-1	Procurement model and functioning (evaluation area 2)	1. Access to stockpile 2. Lead times 3. Orders' dynamics 4. Capacity of grantees	- KII - Data from countries - Project documentation Quantitative description of procurement indicators
7-2	Funding alternatives (evaluation area 3)	1. Alternative funding sources 2. Increase in project efficiency	- KII - Data from countries - Project documentation Quantitative description of financial indicators
Impact			
8 Are changes of KPI plausibly attributable to UNITAID support?			
8-1	Validation of access to MDR medicines (evaluation area 1)	1. Patients effectively treated	- Data from countries - Project documentation Data mining; completeness of data; interpretation
8-2	Validation of UNITAD findings on impact evaluation and KPI, where project specific data exists (evaluation area 3)	1. Quality of data used 2. Appropriateness of analyses 3. Balanced interpretation	- http://www.unitaid.eu/en/mdr-tb-scale-up/16-home/963-multi-drug-resistant-tuberculosis-mdr-tb-scale-up - UNITAID KPI 2013 Data mining; completeness of data; interpretation
Learning and risk mitigation			
9 Are changes of KPI plausibly attributable to UNITAID support?			
9-1	Follow up of previous recommendations (evaluation area 5)	1. Applicability of recommendations 2. Follow up of recommendations by time frame	- KII - Project documentation Qualitative tracking of recommendations
9-2	Capacity to draw lessons from project documentation (evaluation area 5)	1. Scope of evidence, availability, presentation 2. Use of available evidence 3. UNITAID visibility	- KII - Project documentation Qualitative analysis of significance of evidence

Annex 5. List of key people contacted

- Joel Keravic (GDF)
- Kaspars Lunte (GDF)
- Fabienne Jouberton (GDF)
- Thierry Cordier – Lassale (GDF)
- John Loeber (Former GDF, now UNHRC-Hungary)
- Maria Sarquella (Former GDF, now Global Fund)
- Louise Dann (Former GDF, now Global Fund)
- Silas Holland (Former GDF, now Global Fund)
- Tala Jallow (Global Fund)
- Lorenzo Witherspoon (UNITAID)
- National TB programs representatives in selected countries
- Robert Matiru (Former GDF, now UNITAID)
- Manufacturers (sampling of the list Annex 7)

Annex 6. List of TB managers – national focal points

1) Azerbaijan

Prof Eljan Mammadbayov - Director

Scientific Research Institute of Lung Diseases of the MoH

2514 mehelle, E Suleymanov Str

Baku - AZ1118 - Azerbaijan

2) Dominican Republic

Dr Belkys Marcelino - Directora Programa Nacional de Control de la Tuberculosis

Ministerio de Salud Publica y Asistencia Social

Avenida Hector Romero Hernandez, esquina Tiradentes

Santo Domingo

10129 - Dominican Republic

3) Moldova

Mr Ion Mosenet - Procurement Specialist

PI "CIMU HSRP"

18-A Toma Ciorba str.,

Chisinau - MD 2004 - Republic of Moldova

4) Kenya

Dr Richard Muthoka

5) Kyrgyzstan

Zhyldyz Ysykeeva - Project HOPE Drug Management Specialist

6) Uzbekistan

Dr Gulnoz Uzakova - Manager of PIU

15, Sh. Rustaveli st., Tashkent, 100070, Uzbekistan

7) Burkina Faso

Dr P. Serge Diagbouga - Coordonnateur
Programme National de Lutte Antituberculeuse
Ministere de la Sante- PNLT
01 BP 6632 Ouagadougou - Burkina Faso

8) Cambodia

Dr Mao Tan Eang - Director
National Center for Tuberculosis and Leprosy Control - Cambodia

9) DR Congo

Dr André Ndongosieme – Directeur
Georges, Bakaswa - Programme National de lutte contre la Tuberculose " PNLT" -
Ministère de la Santé / Programme National de Lutte
Avenue KABINDA, en face de la RTNC - Commune LINGWALA - Ville de Kinshasa -
Democratic Republic of the Congo

10) Guinea

MISSION PHILAFRICAINE – Eric Bafende and Dr Stefan Strahm
BP 214 - Conakry 1 - République de Guinée

11) Haiti

GHESKIO project - Drs Leandre and Pape

12) Lesotho

Dr L. B Maama-Maime - National TB Programme Manager

13) Malawi

Dr. James Mpunga - Program Manager

14) Mozambique

TB-Program Manager: Dr Ivan Manhica (ivanmca2004@yahoo.com.br)

15) Myanmar

Dr. Si Thu Aung

16) Nepal

Ajudey Shrestha - PSM focal point

17) Timor-Leste

Mr Costantino Lopes - NTP Manager

18) India

Dr. K.S. Sachdeva,

MoHFW, New Delhi, India

19) Senegal

Dr Talla Diop, pharmacien - Responsable des approvisionnements

Programme National de lutte contre la Tuberculose (PNT)

Dakar - Senegal

Annex 7. List of manufacturers

Supplier
Medochemie
Vianex
Microlabs
Akorn
Macleods
Dong-A
Cipla
Meiji
Panpharma
Jacobus
Olainfarm
Fatol
Cadila
Labesfal
Hindustan

Annex 8. Generic questionnaire**End of project TB scale up initiative evaluation****RELEVANCE**

- 1) Is the grant targeting developing countries? If answer is Yes or Partially, please provide an example
- 2) Is the grant targeting disadvantaged populations? If answer is Yes or Partially, please provide an example
- 3) Is the grant applying innovative market approaches? If answer is Yes or Partially, please provide an example
- 4) Has the grant ensured supply of second-line TB medicines? Please comment if possible
- 5) Has the grant increased access to emerging medicines and treatment regimens? Please comment if possible

EFFECTIVENESS

- 6) What have been the facilitating factors contributing to the achievement of outcomes?
- 7) What have been the barriers jeopardizing the achievement of outcomes?
- 8) Were outputs achieved in the expected timeline? If delays (some or severe) were noted, please provide some comments on the reasons
- 9) Has the grant produced "value for money" in their outputs? If Yes, please provide an example. If No or Partially, please provide some reasons.
- 10) What factors have facilitated the value for money?
- 11) What factors have jeopardized the value for money?
- 12) Are more patients accessing second-line TB medicines as a result of the grant? If No or Partially, please provide some comments
- 13) What factors have facilitated access?
- 14) What factors have jeopardized access?
- 15) How is the market situation once support has ended compared with when the grant was active? Except if the answer is "Don't know", please provide comments for the rating you chose
- 16) What factors have contributed to maintain or improve the good aspects of the market situation once support has ended?
- 17) What factors have jeopardized the market situation once support has ended?
- 18) Have procurement processes been effective in accomplishing the Projects' objectives, notably achieving price reduction of products, increasing access to treatment, making effective use of the existing supplier base, and encouraging new suppliers to enter the market?

EFFICIENCY

- 19) Were drug stocks during the grant implementation appropriate to avoid stock-outs and facilitate access? If No or Partially, please provide some comments

- 20) Were lead times during the grant implementation appropriate to avoid stock-outs and facilitate access? If No or Partially, please provide some comments
- 21) Were orders' dynamics or processes during the grant implementation appropriate to avoid stock-outs and facilitate access? If No or Partially, please provide some comments
- 22) Were prices during the grant implementation appropriate to avoid stock-outs and facilitate access? If No or Partially, please provide some comments
- 23) Are current prices now that the grant has ended appropriate to avoid stock-outs and facilitate access? If No or Partially, please provide some comments
- 24) Are current drug stocks now that the grant has ended appropriate to avoid stock-outs and facilitate access? If No or Partially, please provide some comments
- 25) Are current lead times now that the grant has ended appropriate to avoid stock-outs and facilitate access? If No or Partially, please provide some comments
- 26) Are current orders' dynamics or processes now that the grant has ended appropriate to avoid stock-outs and facilitate access? If No or Partially, please provide some comments
- 27) Have procurement processes been efficient in accomplishing the Projects' objectives, notably achieving price reduction of products, increasing access to treatment, making effective use of the existing supplier base, and encouraging new suppliers to enter the market?
- 28) How did you optimize the use of the supplier base to encourage competition in the market? Please provide examples
- 29) When there are multiple manufacturers of the same quality assured product, what is the split of the business (quantities, costs, etc.) between them and how is it determined?
- 30) To your knowledge, was there any issue related to potential diversion of products, counterfeit or quality? If Yes , please indicate if the issue related to diversion of products and/or counterfeit drugs and/or quality of drugs and provide some comments

IMPACT

- 31) Are any changes (positive or negative) observed during this grant period? If No, please provide some comments. If Yes , please provide some comments on positive or negative changes related to price/supply quality / access / others
- 32) Are issues which do not go so well attributable to ? Except for answer "Don't know", please provide some comments and/or examples if possible
- 33) If applicable, are any improvements in supply of medicines attributable to ? Except for answer "Don't know", please provide some comments and/or examples if possible
- 34) If applicable, are any improvements in access to medicines attributable to ? Except for answer "Don't know", please provide some comments and/or examples if possible
- 35) If applicable, are any improvements in prices attributable to ? Except for answer "Don't know", please provide some comments and/or examples if possible

LEARNING AND RISK MITIGATION

- 36) Have lessons learnt been documented and widely disseminated by or to you as grantees? If Yes, please provide examples if possible. If No or Partially, please provide some comments on the reasons why.

- 37) Have you documented and widely disseminated lessons learnt as grantees? If Yes, please provide examples if possible. If No or Partially, please provide some comments on the reasons why.
- 38) Have programmatic and financial risks been identified and tracked over the course of grant implementation? If Yes, please provide examples if possible. If No or Partially, please provide some comments on the reasons why.
- 39) Have the findings and recommendations of mid-term evaluations or audits (where relevant) been used to improve grant performance? If No or Partially, please provide some comments on the reasons why
- 40) In your opinion
- a) Was MDR TB medicines availability a concern / problem during the project?
 - b) Is MDR TB medicines availability a concern / problem now that the project has ended?
 - c) Is the market situation a concern / problem now that the project has ended?
 - d) Were medicine management and procurement of concern/problem during project?
 - e) Are medicine management and procurement of concern/problem now that the project has ended?
- 41) Please kindly write recommendations for those items a-e of question 40 that you have rated as "Yes" or "partially"
- 42) What is your general assessment of the mechanism / model and what would you recommend to and other partners for improvement?
- 43) Contact - Name- Surname - Position - Country

Annex 9. Questionnaire for manufacturers

UNITAID strategic objective 5: Secure supply of second-line tuberculosis medicines, and increase access to emerging medicines and regimens that will improve treatment of both drug-sensitive and MDR TB

- 1) In your opinion, did the /GDF /GDF grant contribute to decreasing second-line TB drugs' prices? If yes, how? If no, what is hampering lower prices for second-lines TB drugs?
- 2) In your opinion, did the /GDF /GDF grant contribute to increasing the number of new second-line TB drugs? If yes, how? If no, why?
- 3) In your opinion, did the /GDF /GDF grant contribute to increasing the quality of second-line TB drugs? If yes, how? If no, why?
- 4) In your opinion, did the /GDF /GDF grant contribute to increasing the number of manufacturers? If yes, how? If no, why?
- 5) In your opinion, did the /GDF grant contribute to increasing the access to second-line TB drugs? If yes, how? If no, why?
- 6) In your opinion, did the /GDF support affect the lead times of the second-line TB drugs? If yes how and what were the reasons for this?
- 7) In your opinion, did the /GDF grant contribute to securing supply of second-line TB drugs? If yes, how? If no, why?
- 8) What are the key reasons why there is reluctance for manufacturers in investing in better second-line TB products?
- 9) In your opinion, what will be the challenges faced in a given country once the /GDF grant has ended?
- 10) In your opinion, what was the impact of the /GDF grant on the way manufacturers have done business?
- 11) In your opinion, has the market landscape changed during the period 2007-2013? If no, why? If yes, what kind of changes are considered and would you attribute them to /GDF grant?
- 12) In your opinion, how is the market situation now that the /GDF support has ended compared with when /GDF grant was active?
- 13) In your opinion, what factors have contributed to maintain or improve the good aspects of the market situation now that the /GDF support has ended?
- 14) In your opinion, what factors have jeopardised the market situation once /GDF support has ended?
- 15) What are the lessons learnt as manufacturers or procurement agent and what would you recommend to /GDF regarding its business model?

Annex 10. Comments extracted from survey

Value for Money

The following factors were mentioned as facilitators of value for money:

- the grant allowed presenting a precise forecast of the needs with committed money, and, therefore, engaging the manufacturers;
- investment in TB treatment was a positive guiding principle;
- use of existing systems;
- pooled procurement, long-term agreements, supplier engagement, stockpile, additional GDF free services as training in drug management, GDF participations in country M&E mission;
- negotiations with manufacturers on reduced prices for procured products;
- monies saving (state budget fund was used for improvement of TB/MDR TB treatment facilities such as renovation of national and regional TB facilities including infection control measures)
- GDF proactive engagement with suppliers, widening the suppliers base, usage of stockpile, additional GDF free services as training in drug management
- GDF participations in country M&E missions
- partner support and political commitment enhanced value for money

Some comments on limitations of value for money were as follows:

- this is only support for drugs. Support for diagnosis, hospital management and other tests are needed simultaneously while there is no clarity on how the money for other items will come.
- lack of forecasts, absence of kits, paediatric formulations
- no standardized forecasting tools

Achievement of objectives

The following was mentioned in terms of the reasons which could have positively affected the achievement of objectives:

- the uninterrupted supply of the medicines;
- the good communication between GDF and National TB programs;
- fast and staggered deliveries with optimal shelf life;
- proactive follow up for GDF side, use of stockpile to cover specific products shortages;
- affordable prices and quality assured products.

More barriers were identified below by respondents to the survey:

- slow reaction of the donor and to implement changes in the budget such as number of treatment regimens, increase number of countries on the grant due to efficiencies in the budget;
- absence of kits; absence of paediatric formulations and molecular methods for rapid diagnostics¹;
- difficulty of providing supply forecasts due to varying regimens;
- several players attempting to gain a market share in the provision of MDR-TB medicines, leading to uncoordinated efforts, market fragmentation and high price perpetuation;
- The following opinion was expressed: a risk-based system on determining appropriateness of

¹ Although some of the reported issues may be out of the scope of the project, it is worthwhile mentioning them in order to have a more complete landscape of factors enabling or jeopardising project's objectives.

country sources, combined with rigorous quality control, would have been far superior and achieved much greater market impact;

- Another opinion was: “partially lack of clarity on purchase prices”;
- Also reported was a “lack of some essential medicines in sufficient quantities, as well as a sustainable and transparent access strategy”;
- lack of planning in NTPs, varying differential capacity of health systems in different states, unavailability of sufficient numbers of skilled human resources are key constraints.
- weak link between advanced diagnostics deployment and MDR TB medicines requirements;
- irregular demand of third-tier medicines;
- the sourcing of medicines is solely supported through the Global Fund. The government is yet to allocate funds for procurement of second-line TB medicines;
- lack of funding to support the facilitating factors meant that the organisations and staff working on this grant needed to find additional funding and/or incentives to apply this grant and request extra work from all participants in the distribution chain.

Reasons for reluctance in investing in better second-line TB products given by manufacturers were:

- global support programmes do not invest enough in innovators;
- global market place is only concerned with price rather than collaboration;
- the market is narrow and consumption in the private sector is too low;
- lack of appropriate commitment by programmes for a certain period in order to justify a big investment;
- manufacturers need to be confident about the relevance of the product during a long enough period of time;
- programmes are reluctant to accepting new drugs due to lack of safety evidence and lack of clinical experience.

Access to treatment

Informants mentioned the following comments as enabling factors for access to treatments:

- easier access to treatment and on time delivery
- large amount of new funding
- use of existing systems
- treatment/care and medicines for MDR-TB patients available and free of charge
- strong technical support from WHO and UNITAID
- reasonable delivery lead times
- fast TB diagnostics through DOTS corners of rural health facilities
- wide mass media campaign (elaboration of special thematic movies)
- availability of qualitative second-line TB drugs distributed through network of DOTS corners located in general health care facilities
- clear ordering systems and tracking mechanisms consistency in supplies regulated cost continued support through regional GLC, providing oversight of the PMDT
- national programs that do not have sufficient budget could receive second-line drugs.
- stockpiles system of procurement
- good cooperation between GDF and UNITAID.

Further barriers to access were as follows:

- patients died before initiating SLD due to delay diagnostic (solid culture) - long time required for conventional diagnosis
- inequitable use of supplier base and procurement strategy
- poor planning at the country level
- weak logistic system (transportation of drugs)
- low capacity of TB doctors and general practitioners
- lack of coordination between national and international stakeholders
- lack of funding for facilitating factors
- problems receiving the size of needles desired by the country (GDF / IDA provided needles having a different size)
- sometimes long enlistment process
- lack of capacity to deal with side effects
- the reluctance of some patients
- distance of the hospital from other parts of the country.
- delays in procurement

Market

Enablers for market situation improvement are as followed:

- GDF coordination for purchases;
- more stable demand and supply;
- UNITAID stimulated market dynamics by scaling up treatments, incentivising manufacturers and increase production or new entrants;
- on-going Global Fund rounds and support;
- the country obtained new Global Fund grants for procurement of SLD TB drugs and since 2013 the Government has started the procurement of SLD TB drugs for the first 100 MDR TB patients;
- after and during the grant, funding from the Global Fund happened;
- SLD prices have decreased and became more available for most low-income countries;
- Better pricing for some regimens.

Factors related to a lack of progress are presented below:

- interestingly, it was pointed out the even after UNITAID, the market for second-line anti-TB drugs is still in its very early stages;
- poor stakeholders coordination;
- delays in Global Fund funding; lack of funding for GDF and Stop-TB partnership;
- risk to stop pooling;
- still the MDR-TB market is very small compared to others and the interest of the manufacturers is limited, therefore can be a challenge to maintain a stable supply;
- a treatment gap between funding from other donors and diagnosed patients remains; on the other hand, it has been pointed out that if support for advanced diagnostics laboratories ends, there will be fewer patients diagnosed;
- lack of capacity of countries to sustain the scale up with 'domestic' resources;
- lack of country level planning;
- new products might be a challenge for consumers;
- additionally, new products may pose bigger challenges in the future;
- perception that the quality of products was poor.

Some comments on the challenges related to the completion of the grants identified by interviewees are as follows:

- lack of financial resources. Economic growth of the country is crucial;
- access to MDR TB treatment will likely decrease, leading to a creation of waiting lists among patients;
- risk of shortage of products as there will be no stockpile;
- risk of TB rate will increase;
- quality of medicines will decrease;
- there will need to be on-going public health surveillance regarding both diagnosis and treatment and funds to support the public health care workers and drugs and diagnostics. I think the world has seen from the Ebola outbreak in West Africa (as well as NYC in the early 1990s) that infectious disease can go from bad (misinformation and fear) to worse (resistance and lack of local response) very quickly. There is the additional concern that if treatment (drugs) is not managed with care resistance will very quickly develop and will spoil the few effective drugs available. Pharmaceutical companies will not be willing to invest millions of dollars in the development of a drug if it will be rendered ineffective almost immediately due to poor oversight and use. Companies may develop drugs but they will be reserved for single wealthy payers not the underserved.

Order processes during grant implementation

Among the different comments on the subject:

- orders were not always the outcome of a competitive tender, and supplies were considered "resold" from the SRS
- there were additional and new processes created to incorporate this grant into the Global Fund framework, so more people were involved in each order which slowed the process for order
- IDA mostly performed well. Though customers mostly did not have much choice in terms of shelf life of medicines provided, delivery times and had to accept what was offered, for lack of other sources
- order processing was quick.

Procurement processes efficiency

Different comments have been made in terms of efficiency limitations:

- GDF's procurement probably could have been more efficient. The UNITAID funds were used to provide grants of drugs to countries. However, they might have been better spent if there had been more flexibility to make long term commitments to manufacturers against a binding forecast - or other more innovative procurement techniques (e.g., engagement with API manufacturers).
- GDF processes remain the same before and after the UNITAID project.
- It was also reported that "procurement had only been partially effective (issues in regard to sourcing (2009 WHO Resolution, ICH/PICS outsourcing), award criteria/evaluations, forecasts, flawed supplier negotiations, shipments via Amsterdam)"
- limited suppliers for MDR TB, no large differences in prices
- GDF/IDA good assistance to respond to emergency orders.

Project's procurement model

Interviewees' comments on procurement model limitations are described below:

Prices:

- although prices have come down generally over the life of the project, the prices of MDR-TB drugs remain very high and price remains a barrier to MDR-TB scale-up.
- price of Linezolid was very high, now it has come down a lot.
- it was reported that "prices are still very high. In domestic market drugs are available at about 40 % of cost as against GDF prices"¹.

Drug stocks:

- difficulties in the process of acquisition by prepayments and national procurement processes;
- continuation of provision of treatment by other sources

Lead times:

- still very long delay

Orders' dynamics:

- GDF requirement of pre-payment orders, which introduces delay compared to the UNITAID grant-funded orders;
- a generic statement that "GDF process needs to be more efficient" was also reported
- grantee has not reported how it has facilitated the handover of procurement processes to country

Regarding the question related to when there are multiple manufacturers of the same quality assured product, what is the split of the business (quantities, costs, etc.) between them and how is it determined, the following comments were made:

- it is determined according to several factors such as production capacity, lead times, prices, etc. All those are mentioned in the bidding documents and determined during the awards and signing of the long term agreements.
- dedicated market share is allocated between eligible suppliers based on the tender evaluation
- quality of the products: referring to the products with WHO pre-qualification. Price of the products: referring to the products with lower price. Form of the products: referring to end user requirements a) can store in normal temperature, b) form: Ampoule is better than Powder Vial, and blister is better than Jar
- this depends on the offers made (price, lead time, shelf life etc.). Depending on the ranking, awards were split e.g. 65 % / 35 % or 40 % / 30 % / 30 % (?) of anticipated market for that product.
- orders are segregated into different schedules as per the estimates of capacity of each manufacturer to supply within a stipulated delivery period. Competition takes care of the rest.

¹ Note that the respondent did not make any reference about the comparability of drugs with the domestic market.

Changes of KPI plausibly attributable to UNITAID support

Comments regarding changes were:

- many MDR-TB-patients started treatment and were cured.
- prices have apparently come down, and suppliers' product portfolios have partially enlarged.
- the actual government activity doesn't relate to the UNITAID 2007 grant in (country)
- changes were reported in terms of "1. Capacity building 2. Logistic system improvement 3. Improvement of TB epidemiology situation 4. Patient/population satisfaction increased"
- there was no need to worry about the finances
- access to second-line TB medicines
- access created demand for services and goodwill for the programme
- quality assurance for SLD.

Comments regarding the supply of and access to medicines were:

- better prices, more supplies
- UNITAID is only providing funding
- UNITAID provided the funds for the grant, so can claim the project improvements
- strong UNITAID engagement at donor/supply chain partner conferences, trade fairs, meetings. Good presence and visibility, substantive contributions, discussion (facilitation)
- improved access and generated goodwill for the programme
- without funding from UNITAID, agency in (country) would not be able to offer second-line drugs
- UNITAID funded treatments were delivered to beneficiary countries / Without UNITAID support, these treatments would not have been delivered
- support of WHO Prequalification Programme. Via the UNITAID grant, more patients have received medicines. Publications have attracted attention to grant impact
- at least MDR-TB are available in the country
- many low/middle income countries now have supplies for DRTB medicines for all their patients.

Comments on whether improvements in prices were attributable to UNITAID were as follows:

- UNITAID's funding was leveraged to influence the behaviour of prices
- the funding has enabled tendering for large procurement volumes, leading to improved prices, lead times, shelf lives
- bulky/pooled procurement has resulted in lowering of prices
- only marginal reduction in prices
- the grantee negotiated for reduced prices for products funded by UNITAID.

Market landscape

Comments on market changes were as follows:

- the "landscape" has changed completely. Historically, at the inception of the program we were afforded annual estimates of product demand and we would arrange our production schedule accordingly. In the last several years, the elimination of buffer stock and the entrance of multiple manufacturers of similar products has eliminated the need for continuous production (of any given volume scale)... some of this is a change in the programme ship to country specific procurement rather than a consolidated uniform procurement process on behalf of the countries. To ensure both steady quality production manufactures must be supported with concrete orders of a volume which will allow lowest possible pricing per dose.
- the market size has increased. In 2009, there were less than 500 patients on treatment in xxx. This has increased to 12000 in 2014. More manufacturers have stepped in, thereby increasing competition, and lowering prices.
- the number of patients who received second-line TB drugs was increased and the therapy was better for them and this has to be attributed to UNITAID/GDF Grant.
- a lot of patients of MDR TB could receive the treatment, who never had a chance in the past without the grant. In addition, the introduction of diagnostic for MDR TB created a bigger chances for the patients for receiving proper treatments
- the market landscape has essentially changed during the last years An early forecasting allows minimizing the risks of increasing the cost of production. There is a possibility preliminary agreements with the producers of raw material and packaging materials, plan the production schedule.

Comments from interviewees who considered that there were some concerns related to medicine management and procurement during project were as follows:

- there are many challenges in the MDR-TB market - on both the demand and supply sides. While the funding for additional MDR-TB treatments was helpful in addressing funding-related constraints to MDR-TB scale up, the other challenges remained.
- access to MDR-TB medicines have been and will always be a problem.
- market development and procurement and supply management processes are still in evolutionary stage and not all required drugs are still available.
- with increased investment in diagnosis of TB patients being funded by UNITAID (Expand TB Diagnostic grant and GeneXpert grant), providing appropriate treatments is critical. Smooth procurement and supply mechanisms including no delays at customs along with functional health systems would be needed.
- beyond the on-going round 8 TB grant, supply of MDR-TB medicines might be a concern. The manufacturing to meet the demand might be a challenge in the future, as evidenced by the current trends where there are queues for e.g. clofazimine.

Some recommendations expressed by interviewees are reported below:

- further reinforce/sustain country capacity. Review system of categorisation of medicines sources (ICH/PICS). Address link between advanced diagnostics and medicines supply. Disseminate knowledge gained / lessons learned from grant implementation.
- the QUANT-TB is different from what we use. I am afraid that drugs will expire; especially when we have a lower number of DR-TB patients (lower than expected). It is 75% less than according to our PMDT expansion plan. We need to be educated on QUANT-TB. 2) We need to be better informed on IDA, GDF (we need to be better informed on the "outside world").
- should mobilize the resource to continue their activities in order to assure the quality of SLD and accessibility for patients suffering from drug resistant TB
- should continue its grants for countries such as (country). So could serve as a back-up for the GF
- is willing to invest in new mechanisms that are often unattractive to traditional donors. However, they are relatively inflexible and too heavily involved in implementation.
- another respondent also commented in that direction with "allow for more flexibility"
- has a tight, but well defined objective of market impact. I would recommend going beyond HIV, TB and malaria and examining other health areas, e.g. smoking, diabetes, depression, car accidents which have many more losses/fatalities than the 3 big diseases.
- need for accompanying a country in the quantification process - Responsiveness in order processing - Assessment of on-going grants
- establishment of a platform for discussion and exchanges of experiences
- strengthened capacity of responsible pharmacists purchases of health programs and levels of central purchasing countries
- periodic publication of the list of pre-qualified suppliers
- periodic publication of unit prices ExWork
- encourage recipient countries to the development of pharmacovigilance systems and the establishment of quality assurance system
- facilitate through WHO for domestic or regional manufacturing in the most affected countries or regions and build capacity in good manufacturing practices for good quality assured medicines
- need for advocacy to countries receiving support from UNITAID. Involvement of countries to participate in the financing
- since this project was in the country for a short time and only for few patient dosages for MDR-TB patients, we have no elaborated comments.
- it was helpful but still has miles to go.
- I would recommend that the grants have long-term basis.
- I would encourage all partners to ask for an incremental commitment/contribution by governments and in-country partners so that as the project ends, the country should be able to sustain the initiative. Absence of approaches like these makes countries continuously dependent. Otherwise, well done for the support during the life of the grant.

Specific recommendations from manufacturers are as follows:

- ensure that annual predictions are given to manufactures so they can be most efficient;
- continue the stockpile;
- use the buffer stock to hedge against unforeseen logistics problems;
- perform consolidated purchasing to ensure volume threshold (staircase) pricing;
- support companies who are innovators which take risk to invest;
- No support to copy-cat drugs manufacturers;
- have a long-term supply agreement with GDF For the purpose of making long-term business plan;
- use more flexible approach to supply schedule (more frequent order with adjustment of amounts of drugs and type of drugs).

Special critical responses are reported below:

- it was reported that “there seemed to be some lack of transparency with some tender evaluations and breach of regulation may have happened in some instances”;
- it was reported that “there were also internal problems/disagreements and vested interests in resisting change seemed to have brought some difficulties”;
- it was reported that “internal regulations might not have been followed all the time”;
- it was reported that “none of the organizations involved (UNITAID, GDF, Global Fund, GLC) are known for their speed or flexibility”

Annex 11. List of documents consulted

List of reference documents besides all documents made available on Sharepoint by UNITAID

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