

EXECUTIVE SUMMARY

The meeting was convened in New Delhi, India from 29-30 August 2011. A total of 105 people registered to attend the meeting.

The objectives of the meeting were to:

1. Outline the main challenges to secure and increase global TB drug supply in the public sector;
2. Share experiences of the India TB programme;
3. Generate ideas on collaboration to enhance TB drug procurement and quality assurance, including methods for consolidating demand and providing forecasts with confirmed funding;
4. Initiate the process for development of a realistic action plan addressing the challenges on TB drug supply in the public sector.

The meeting concluded with a plenary session, highlighting the key points addressed during presentations and panel discussions as follows:

1. Demand consolidation for Active Pharmaceutical Ingredients (API) and formulations, from prequalified sources. This is critical to the continued development and ultimate sustainability of the TB drug market;
2. Steps must be taken to rapidly increase the number of patients to be put on treatment. It is anticipated that this action, in conjunction with demand consolidation, will result in reduction in the cost of treatment for MDR-TB patients with Second Line Drugs (SLD's). In particular:
 - Gaps between targets/actual enrolments;
 - Opportunity for diagnostics to change the game;
 - Engage the private sector;
 - Technical support to countries from diagnosis, implementation and treatment.
3. India's role – what is needed? Consideration to leverage the numbers of patients on MDR-TB treatment in demand consolidation, as well as potentially the large private sector market which exists, particularly for First Line Drugs (FLD's);
4. Process reforms – engaging, stimulating, streamlining, reducing barriers to entry, increasing participation, and flow of information;
5. Funding commitment – a joint meeting with all donors is highly recommended. Funding volatility is having an impact on the ability to accurately forecast demand and enable manufacturers to plan production;
6. Involvement of the regulatory authorities in setting expectations of international standards.

On 31/8/11, a short meeting was convened and attended by key stakeholders. This meeting considered the development of an action plan to address the issues outlined in the plenary session, and the establishment of a permanent working group to implement the agreed plan. A draft plan has been prepared has been circulated to the participants at this subsequent meeting, for their input. It is proposed that the key stakeholders convene a 2nd meeting in Lille, France during the Union Conference in October 2011, to endeavour to finalise the plan and circulate it to the wider audience. Further meetings will be convened in 2012 as appropriate.

1. INDIA/SEARO

Dr Ashok Kumar, Central TB Division (CTD), Government of India

- Drug resistance is challenging.
- Biggest challenge in India is treating patients with quality drugs.
- Wants to encourage more Indian manufacturers to become prequalified.

Dr Surinder Singh, Drug Controller General, India

- Global sourcing of drugs/vaccines is from India and India is making a global contribution.
- There are 169 FDA approved plants in India and the pharma sector has been growing at the rate of 14% per annum.
- A road map has been put in place to strengthen regulatory approval. Need to bridge gaps in the shortest possible time.
- Approx USD1billion earmarked to strengthen regulatory approval in next 5 years.
- Transparency/accountability are critical.
- Problems with APIs sourced from China – result is that more controls are being put in place.
- Committed to meeting international expectations on drug regulation and ensuring that consumers interests are protected.
- Development of a policy on antibiotics.

Dr Kuldeep Singh Sachdeva, CTD

- Presented statistics on India TB epidemic.
- Integrated electronic recording of TB treatment for patients is being piloted by MSH.
- Anticipate 30,000 patients on SLD's by end 2012. Concerned about cost of escalation because planned costs of USD1,600 per patient compared with actual costs now of USD2,300, reduces the number of patients that can be treated.
- RNTCP Five year plan 2012-2017 vision towards universal access to quality diagnosis and treatment of all forms of TB including DR-TB and TB/HIV. Extend RNTCP services to patients diagnosed and treated in the private sector. Target is for 90% detection and treatment of all cases of TB.
- RNTCP PMDT (programmatic management of drug resistant TB): MDR-TB services introduced in all States by 2012.
- Advocate with Indian Drug Manufacturers with Global Drug Facility (GDF) support to adhere to WHO Prequalification and GDF Quality Assurance (QA) systems.
- Extending RNTCP diagnosis and treatment of patients in the private sector
- MSF queried the outcomes of 12 month culture conversion of MDF patients using drugs from both GDF versus WB/domestic funding.
- WB/domestic funded MDR drugs cost USD800 compared with GDF cost of USD2,300. GOI claimed there was no difference in patient treatment outcomes.
- USP queried what are the differences between WB/GOI standards. Advised that the biggest message the GOI can give is to buy prequalified drugs. In response, the GOI believes that checks/balances are in place with quality testing.

- GOI is open to inclusion of SLD's on schedule H (i.e. restricted sale drugs) with sound justification. Want a recommendation to come to the GOI including non utilization of sero diagnostics.
- A policy is being formulated for over the counter treatment. Problem: 600,000 pharmaceutical retail outlets in India and the manpower to enforce the prevention of sale of drugs without prescription is insufficient.

Nigor Muzafarova, WHO SEARO

- There have been no stock outs of FLD's in SEARO in the past 2 years, but this trend is not evident in other regions.
- Support to regional countries/capacity building on TB drug management: Progress of countries adapting to WHO treatment recommendations i.e. use of FDC, quality-assured medicines, use of pediatric formulations and improvement planning and quantifying and storing TB medicines.
- A number of challenges/problems remain:
 - 1) delays in fund disbursement - disbursement is linked to grant implementation, performance and submission of reports to the Global Fund (GF). Long term planning, budgeting and annual procurement is required;
 - 2) Poor infrastructure including warehouses, racking, air circulation/ventilation, staff training and retention, automated stock recording;
 - 3) Delays in shipment deliveries;
 - 4) Customs clearance timeframe is often excessive and reduces the product shelf life and utilization by the consumer.

2. PROCUREMENT

Dr Michael Kimmerling, Bill & Melinda Gates Foundation

- New BMGF strategy 2011 to accelerate the reduction in global TB incidence.
- TB community is generally conservative, while the epidemic is evolving: New approaches. We need to be game changers.
- Further emphasis is needed on FLD's/preventing resistance and availability of new drugs.
- The future is about new drug regimens for first line therapy. Recognizing where and why we are not functioning well is critical to the future introduction of any new drugs.
- Sub-optimal competition: limited pool of prequalified suppliers.
- GDF was praised for bringing quality to the market.
- Noted that the price of FLD's has continued to increase over time. Increased production costs (energy and APIs) .
- Some countries i.e. China and Brazil are changing their policies and moving towards WHO treatment and regulatory recommendations.
- Concerned that GDF has played a limited role in the public market (approximately a 14% share) and no impact on the private market, which is an important market. Little known about use and quality of TB drugs in the private sector.
- For the future, we must look critically at ourselves, plan, identify barriers, work urgently and consider the private sector.
- The correlation between price and quality needs to be understood, including the factors impacting on quality assured APIs.
- Increased prices to recover investment on prequalification.
- Manufacturers called for a 2nd level of handholding to give incentives/guide them to prequalification – this will increase competition and ultimately reduce pricing if it is accompanied by a consolidation of demand.

Caroline Bogren, Global Drug Facility

- GDF is responsible for public sector procurement of TB drugs, together with technical assistance by way of monitoring missions.
- TB drug market is categorised as high risk, with insufficient number of quality assured products/limited number of manufacturers.
- Competition is limited.
- 2011 price increases of FLD's attributable to increased cost of rifampacin/fuel.
- 2011 price maintenance of SLD's and no major reduction despite increased volumes.
- Sustainability of high priced SLD's is questionable.
- Market fragmentation.
- Potential interventions – improved forecasting/reduced order volatility; coordinated procurement/consolidated demand; firm funding commitments/revolving credit; guaranteed volumes; increased emphasis on the importance of quality; political/partner commitment to improve basic infrastructure in countries.

Dr Paul Nunn, WHO

- MDR-TB represents 3.6% of all TB cases but is more difficult and expensive to treat than drug susceptible TB.
- Incidence rates in China/India are 7/8 out of 100,000, but the size of the population is a concern.
- The highest incidence of MDR-TB exists in eastern Europe – Belarus, Russia.
- Beijing Meeting in 2009 outlined why so few cases are diagnosed/treated – political commitment translated into funding (gap for 2011 is approx USD1 billion), financial barriers to patients, engaging all care providers, optimizing management and care, addressing laboratory crisis, prioritizing infection control.
- In 2009/2010, countries treated virtually all patients planned. However, the problem is that not all patients who needed to be treated, were in the plans. 39,129 enrolled patients in 2010. The target for 2011 is 132,000.
- No large country plan exceeds 1/3 of estimated incidence of MDR-TB before 2016.
- Global Fund (GF) is vital to progress but conditions for funding increasingly strict, with some unpredictable consequences.
- Drugs remain extremely expensive.
- Gene Xpert: impact from 2010 an unknown magnitude (in terms of increase number of patients on treatment).
- **Russia** exceeded planned requirements in 2010, but the problem is the Government refused to allow funding of USD126 million to be accepted from the Global Fund. GLC anticipates that the treatment target of 11,400 patients for 2011 will be met, but we have no knowledge of the quality of drugs used as they are not procured by GDF.
- **China** planned to treat 3,201 patients in 2010 but actually treated just 1,000. The GF grant was suspended in May 2011 and enrolment stopped. Funding resumed 23 August 2011 and enrolment will follow. China is scheduled for an inspection by the GF Inspector General and the outcome of this may impact on continued GF funding.
- **India** planned for 1,420 patients in 2009 and treated 1,136. 8,000 were planned for 2010 and 2,927 ultimately treated.
- What will assist in meeting forecasts? Gene Xpert, public sector working with private sector by providing drugs in return for data to WHO.
- Manufacturers requested access to information as to patient numbers planned/enrolled and this is available from the GLC. The problem is that funding to back the planning is not always in place.

Neeraj Mohan, CHAI

- CHAI has engaged in TB drugs because the market is clearly dysfunctional.
- The key question is what is a “reasonable price”.
- Manufacturers have a stake in a well functioning market.
- Demand consolidation in favor of PQ drugs is critical to ensure sustainability of PQ drug market in the long term: 1) More patients treated overall with the same mix of funds; 2) Price difference coming down significantly with higher volumes; 3) Manufacturers able to recover investments in high quality plants and drugs. A well-functioning SLD

market requires approximately 30,000 patients on treatment, but the volumes at this state are insufficient to encourage manufacturers to enter.

- If there is no alignment, the market will revert to where it has been historically – i.e. non- prequalified drugs. Need to get traction on this issue
- Critical to evaluate which options we have/coordinated action needed to render the market functional.
- Onus on manufacturers to demonstrate what can be done to impact on pricing.
- Need to innovate to have all parties commit to getting the market to a functional stage.
- Potential interventions include:
 1. Consolidating the API market/providing subsidies;
 2. Increasing competition at API level as well as at formulation level;
 3. Addressing the risk/uncertainty in the market.

Lisa Hedman, WHO/EMP

- Guidelines for pediatric dosing were revised in 2009 and recommendation to use Fixed Dose Combinations (FDC's).
- Problem in 2011 is that we do not have a product which corresponds to the appropriate dosing levels.
- Expert consultation convened by WHO in July 2011 to identify gaps/solutions. Pharmacokinetic studies are being undertaken.
- Need to continue with existing pediatric drugs until new formulations are available.
- Pediatric market assessment work continues
- Disease burden in children is currently difficult to ascertain due to problems with diagnostic capacity.

3. QUALITY ASSURANCE

Vimal Sachdeva/EMP

- TB dossiers submitted to WHO prequalification have a number of concerns:
 - Immature/incomplete submissions;
 - Lack of motivation from applicants;
 - Lack of new innovator products;
 - Quality (i.e. specs/stability data) part of the dossier can be incomplete;
 - Poor clinical, safety and efficacy data.
- A total of 141 products are prequalified from India.
- Unannounced inspections have sometimes resulted in problems with data verification/authenticity.
- Issues with sterility/endotoxins in kanamycin and capreomycin.
- Technical assistance is provided to manufacturers and is done separately from prequalification. Highlights the gap analysis and increases understanding of international requirements.
- PQ status of SLD's is very limited but the demand for PQ drugs is increasing.
- The PQ team is actively working to increase the pool of QA drugs.
- Noted that many API manufacturers are not willing to be inspected and that this impacts on FPP – joint effort required by partners to address this key issue and potential intervention for an API bank.

Paloma Marroquin Lerga, Global Drug Facility

- Last revision of GDF QA policy and procedures in 2010.
- Harmonization of policies and synchronization of qualification process i.e. Expert Review Panel (ERP) with GF.
- Need to ensure all major financiers and/or buyers subscribe to a common QA standard: e.g. WHO STB & EMP, GF, UNITAID, UNICEF, MSF are aligning on GF standards; currently GOI. and World Bank (WB) are not aligned.
- Quality standards are set by The WHO Expert Committee on Specifications for Pharmaceutical Preparations.
- GDF collaborates with many partners to promote the use of quality assured TB drugs and aims to achieve the goal of consolidated demand.
- Increase of quality-assured oral TB formulations/manufacturers since 2009.
- To date, there is only one quality assured source for the injectables streptomycin, kanamycin, and capreomycin.
- Quality/availability of the APIs is a major impediment to increasing the number of quality assured finished formulations.
- In 2011, 104 dossiers submitted for ERP review; 96 eligible for review; 44 recommended for supply; 52 not recommended for procurement.
- 13 ERP recommended TB medicines for procurement became prequalified since 2009.

Dr Patrick Lukulay, USP

- USP aim to increase the demand and supply of quality assured drugs.
- No manufacturer will submit to an inspection unless there is regulation enforcing it.
- Quality Assurance is the totality of all processes to ensure that a product's quality is maintained from production to use by the patient.
- Quality Control is the specific tests done to determine the quality attributes against compendia standards.
- A poor quality product can compromise disease treatment and lead to drug resistance.
- USP provides free support to manufacturers who seek prequalification of their products, with priority given to those products identified by the Global Fund/GDF where there are no/few quality assured products available.
- Universal level of drug quality - this is WHO recognized international standards. The debate should be how to achieve this.

4. MANUFACTURERS DISCUSSION PANEL

Rajiv Alex, Strides

- Major problem for new entrants: Cost of obtaining prequalification is very high (approx USD2.5 million) and time consuming (approx 2 years to submit for approval).
- No guarantee of return on investment.
- Major problems with monopoly API supply and reluctance of API manufacturers to provide the requisite quality assurance documentation.
- Unlikely that many more manufacturers will enter the TB market. Need to consider how to engage manufacturers to remain in this business.

Shrikant Kulkarni, Lupin

- Capacity planning and the timeframe required, requires investment. What is the return and what is the risk?
- Key product is rifampacin, which requires investment in infrastructure. Because it requires fermentation, it is energy intensive and fuel costs therefore impact on the FPP price
- Manufacturers support PQP and commitment to manufacture quality assured drugs.

Tejasvi Sharma, Sandoz

- Endorsed comments as already made.
- Noted that Novartis/Sandoz is fully committed to neglected diseases but is concerned that the demand for TB SLD's seems very small and this impacts on the decision to invest in this market.

Vijay Aggarwal, Macleods

- Concerned about repeated bidding, lack of forecasts and no commitment on purchase orders.
- Concerned about processes for FLD's with delays incurred on pre shipment inspection, clean reports of finding etc. and would prefer to have the same processes as for SLD's.
- Concerned about financial costs incurred by manufacturers with advance payment required for the supply of APIs, but no payment made by GDF/GIZ until approximately 180 days after Macleods have incurred expense.
- Concerned about low dollar value orders and would prefer to see consolidation of requirements to maximize batch quantities.

Raul Lande, Cipla

- Limited commercial market for TB drugs.
- Strong preference from countries to buy from domestic manufacturers and therefore no incentive for Indian generic manufacturers to enter the market.
- Demand forecast is at the epicenter of the problems.
- Problem with quality of API/commitment to procure APIs but API manufacturers are unwilling to invest in PQ of their products because they believe that the quantity requirements are low.

- Questionable market sustainability.

Iain Richardson, Eli Lilly

- 4 major issues with the TB market:
 1. The volume of product required is very small and not economically sustainable – issue of scale up. For example, 430,000 patients not enrolled in TB programmes creates an opportunity;
 2. In 2003, Eli Lilly's goal was to transfer technology to manufacturers in developing countries;
 3. Volume will drive improvement with respect to price/competition – market dynamics;
 4. Regulatory process – Strict Regulatory Authority (SRA)/PQ process is 1 aspect, but in addition, countries have their own internal requirements
- PQ allows access to the WHO process but it does not guarantee business. Contrast this with licensing access to improve delivery of drugs to markets.
- Transparency of process – PQ/SRA process is cumbersome/rules developed over time. Concern as to lack of transparency on bidding process.
- Need to address patient enrolment issue in order to sustain manufacturers business – this requires funding commitment.
- Concern about ability to forecast – depends on what countries are able to commit with respect to patient enrolment.
- If countries can count on including the private sector, whereby public sector can provide drugs to the private sector, this could make a difference.
- Potential for an API bank to make a difference in ensuring accessibility of supply.

5. DONORS PANEL DISCUSSION

Dr Igor Oliynyk, Global Fund

- GF has invested USD3.6 billion in TB programmes in 116 countries
- GF is concerned to obtain best value for money and to ensure that there is additionality in funding.
- GF is concerned to avoid stockouts/overstocking of drugs and a feasibility study is currently being done for regional storage depots.

Dr Patrick Mullen, World Bank

- WB has loaned USD270 million to the GOI since 1997 to finance its TB programme. This funding ends March 2012.
- GOI emphasis on universal access means much greater resources will be needed and bulk of this will be financed by the GOI.
- WB's future strategy for 2012-2017 will be technical support, e.g. Joint Monitoring Missions. Role of international partners will also move in this direction.
- Scale up will require new ways of doing business, for example how to reach patients in the private sector.

Lorenzo Witherspoon, UNITAID

- UNITAID has been innovative from inception.
- Out of the box thinking is required to address the issues of increasing the numbers of patients on treatment, consolidating demand for drugs and ultimately impacting on price in order that the market remains sustainable.

Hemachandren, USAID

- USAID is committed to TB and has spent USD545 million to date, 11% of which has been allocated to the procurement of drugs.
- USAID is a major donor to GDF and provides USD15 million per annum for drug procurement.

Sabina Bindra Barnes, DFID

- USD44 million spent by DFID on TB drug procurement in India but this funding ends December 2011.
- Emphasis on 2 supply lines for FLD's (i.e. GDF and domestic) has resulted in no stock outs and quality assured drugs procured by GDF.
- Instrumental in India in establishment of the Empowered Procurement Wing.
- Working with CHAI on access to medicines, predominantly ARV's/ACT's and since the end of 2010, involvement in TB for the next 3-4 years.
- Need to look at an operationalised strategy.

Dr Peter Small, Bill & Melinda Gates Foundation (BMGF)

- BMGF has committed approximately USD1 billion in the past 10 years – 75% of which has gone to product development.
- Clarification that the focus is not on paying for procurement, but instead on innovation.
- Looking at where assistance can be given to counteract the catch 22 situation that exists with pricing/delivery/patient treatment.
- Focus on a new regimen being implemented.

6. CIVIL SOCIETY PANEL DISCUSSION

Blessi Kumar

- “Nothing for us without us”. Patient perspectives are so important.
- Civil society provides the last mile connection – increasing patients enrolled.
- Quality is priceless – the patient deserves the best.

Dr Subbanna Jonnalagada, TB Care & Control in India

- 90 partners within the partnership.
- Demand for FDC’s and pediatric formulations.
- Supply chain, logistics and operational issues.
- Increase capacity of drug stores.
- Stringent enforcement of schedule H drugs (FLD’s and SLD’s).

Cecile Mace, The Union

- Provides technical assistance to national programmes.
- Stock outs exist in regions such as AFRO and Latin America due to non alignment of procurement and finance cycles.
- Problems in these countries in getting proper service from GDF.
- GDF needs to improve its services - communication, delivery, procurement agents.
- Need to look at transport costs – concern that they are very high.
- Clients need confidence that GDF service is useful.
- Need to look at other procurers of TB drugs.
- Need a stockpile of FLD’s.
- Need longer shelf life on products.
- Need fast track registration of products prequalified by WHO.

Dr Tido von Schoenangerer, MSF

- MSF treated 30,000 TB patients in 2010/29 countries (3,000 paediatrics/1,000 MDR).
- Scale up of treatment for MDR is too slow but pleased to hear about ambitious plan in India.
- MSF want healthy competition and healthy business. Want to improve supply security with minimum 2 API sources for each drug and at least 2-3 FPP.
- MSF wants to drive volumes to PQ products to benefit from economies of scale.
- Would like to encourage private sector to buy from GDF.
- Keen to explore whether an API pool could work and suggests to start doing this with 1 drug.
- Lack of sufficient availability of Class 5 drugs to treat XDR-TB.
- Research to consider what the new MDR regimen will look like/transparency to manufacturers.