The Global Crisis of MDR-TB

Barriers, Needs and Potential Solutions For the Second Line Drug Supply Chain

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The Law of Systems

• Every system is perfectly designed to produce the results it achieves

• If we want a greater level of achievement, we must change the system

• Not all change is improvement, but all improvement is change

Donald Berwick
Institute for Healthcare Improvement
The Law of Darwinian Selection

• If you treat only drug-susceptible TB, you will select for expansion of MDR-TB
Achievements: 1995-2010

- TB Patients treated: 55 million
- Patients Cured: 46 million, 84% success rate
- Mortality: Reduced by > 33%
- Lives saved: ~7 million
- Lives that could be saved: 5 million, incl. 2m women and kids

WHO Stop TB
Developing and Strengthening the Global Supply Chain for Second-Line Drugs for Multidrug-Resistant Tuberculosis

WORKSHOP SUMMARY

INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMIES
Supply Chains for Pharmaceutical Products Are Complicated

Chart 1: Actors in the value chain for pharmaceutical products in developing countries

Prashant Yadav
Two Levels of the TB Supply Chain

P. Yadav, IOM workshop on Developing and Strengthening the Global Supply Chain for Second-Line Drugs for Multidrug-Resistant Tuberculosis.
For MDR TB - Multiple Drugs, Limited Producers

<table>
<thead>
<tr>
<th>Drug Description</th>
<th>Number of Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethionamide 250 mg</td>
<td>1</td>
</tr>
<tr>
<td>Prothionamide 250 mg</td>
<td>1</td>
</tr>
<tr>
<td>Cycloserine 250 mg</td>
<td>3</td>
</tr>
<tr>
<td>Ciprofloxacin 250 mg</td>
<td>1</td>
</tr>
<tr>
<td>Ciprofloxacin 500 mg</td>
<td>3</td>
</tr>
<tr>
<td>Amikacin 500 mg/2ml inj</td>
<td>1</td>
</tr>
<tr>
<td>Kanamycin 1 gram inj</td>
<td>1</td>
</tr>
<tr>
<td>Levofloxacin 250 mg</td>
<td>1</td>
</tr>
<tr>
<td>Levofloxacin 500 mg</td>
<td>1</td>
</tr>
<tr>
<td>Ofloxacin 200 mg</td>
<td>3</td>
</tr>
<tr>
<td>Ofloxacin 400 mg</td>
<td>2</td>
</tr>
<tr>
<td>Moxifloxacin 400 mg</td>
<td>1</td>
</tr>
<tr>
<td>PAS granules</td>
<td>2</td>
</tr>
<tr>
<td>Capreomycin 1 gram inj</td>
<td>1</td>
</tr>
</tbody>
</table>

Except for FQ, the only market is for MDR-TB

>80% of TB APIs are made in China

Source: IDA Foundation, August 2009
The Need is Not Being Met

10 YEAR PICTURE
(2000-2009)

~5 million cases

3.5 million patients
No treatment reported.

Some treatment probably obtained, quality unknown.
Continued transmission

0.5%

Treated in GLC approved programmes

1.5 million patients – DEAD

Photo: James Nachtwey, XDRTB.org
Origins of the WHO/Stop TB Green Light Committee and Global Drug Facility

Conceived of as a Pilot Project

• To Enable Dots-Plus strategy for both TB and MDR-TB
• To enable access to SLD at lower cost
• To review projects and facilitate better treatment of MDR-TB
• Stipulation: “all procurement of medications to treat MDR-TB must be conducted through the Green Light Committee (GLC)”.

• Global Drug Facility has made significant changes in past year. Seeking to increase suppliers, reducing order delays, negotiating for reducing prices.
Flow Through the GLC Initiative

GLC Secretariat → Expert committee → Country/Project → GDF: Procurement Agent

Rx SITES → REG/CUSTOMS → Country/Project → FUNDS

WHO: Technical Support / M&E

Salmaan Kesavjee. IOM workshop on Developing and Strengthening the Global Supply Chain for Second-Line Drugs for Multidrug-Resistant Tuberculosis.
Barriers and Bottlenecks

- Diagnostics
- Production
- Forecasting
- Financing
- Quality Assurance and Regulation
- System organization and leadership
Supply Chain Problems

- The overall market for SLDs is small, partly due to limited diagnostic capacity at the country level and singular usage (except FQ).
- Forecasting is inadequate, failing to meet needs of patients or producers; Latent demand for products far exceeds the actual demand.
- Information Systems are lacking or inadequate.
- Little demand from countries for drugs for MDR-TB
- Markets are opaque, contracting mechanisms are archaic, with high barriers to entry deterring producers, lack of financing up-front, guarantees.
- MDR TB drugs carry high prices (~$4,000/treated case) due to low volume and lack of competition; some have short shelf lives, and prices had been increasing.
Supply Chain Problems [2]

• Varying Quality of APIs and FPP drugs
• Varying Regulatory processes, quality standards, and treatment regimens between countries.
• Market for fake and substandard drugs.
• Once drugs are ordered, there are lengthy time lines to reach the country.
• <60 percent of the available funds were actually used by countries for MDR TB treatment regimens.
Forecasting

Demand forecasts require:

• reliable data on pace of enrollment, consumption, and real number of patients being treated
• Informing orders, lead times, production, and shipment schedules, buffers and emergency supplies
• Information systems are essential to developing early-warning stock-out systems.
• Ideally, should be 80 percent accurate 2 months into the future, and projecting at least 24 months
Proposed Solutions to Solving the SLD TB Problems

- Improved demand forecasting and predictability could help to attract new manufacturers to the market and improve competition.
- Functional information systems, possibly linking with existing systems (HIV, Malaria).
- Pooled or aggregated procurement and flexible contracting from QA manufacturers, based on forecast-driven purchasing.
- Linking, bundling and bargaining with existing supply chains for malaria and HIV.
- A working capital fund or APC to assure up-front payment and motivate suppliers to place full-batch orders to bring prices down;
Proposed Solutions [2]

• A revolving stockpile to expedite delivery to countries and provide flexibility to countries for scale-up;
• Bar coding or G10 coding of key parameters, drug, expiry date, batch.
• In-country training and capacity building in Supply Mgt, QA, regulation,
• Incentives to countries, esp BRICS, to procure QA medicines, support domestic QA manufacturing and pharmacovigilence.
• Create a Public-Private Partnership(s) to do what neither the public nor the private sector can do alone.
Longer Term Solutions to the Problem

- A new mechanism to engage private sector manufacturers, distributors, governments, donors to improve efficiency, especially for new drug combinations. e.g. distribution hubs, SMS forecasting,
- Regional regulatory harmonization and expediting regulatory processes
- Innovative financing mechanisms, incl. split tenders to increase producers and reduce price, APC, initial guarantees, tiered pricing, AMFm negotiation and subsidy model.
- Strong and visionary leadership - globally and in countries
Where We are Now

Who will get it done?

From Marcel Tanner