The Global Crisis of Drug-Resistant Tuberculosis and the Leadership of the BRICS Countries: Challenges and Opportunities,

January 16-18, 2013
Beijing, China

Day 3, Session VI
Developing and Strengthening the Global Supply Chain for Second-Line Drugs for Multidrug-Resistant Tuberculosis
Uninterrupted supply of quality assured drugs when needed
Availability of selected medicines in public and private health facilities 2001-07

Source WHO 2008 & UN
Supply Chain Management (1)
Supply Chain

Starting Material Manufacturing → API Manufacturing → Finished Product Manufacturing → Procurement, Financing, Forecasting → Warehousing

Warehousing Level 1 → Warehousing Level 2 → Clinic
Supply Chain – Upstream Activities

0. Product R&D

1. Approval (SRAs – FDA, EMA)

2. Prequalification (WHO)
   - SRA approval and WHO PQ steps often not run in parallel

3. NRA Registration
   - NRA approval time varies for each country of delivery
   - Low-income country patients receive drugs (e.g., Ethiopia)

High-income country patients receive drugs
Pharmaceutical R&D Process

- **IND**: Investigational new drug
- **NDA**: New drug approval

**Phases**:
- **Discovery**
- **Preclinical**
- **Phase 1**
- **Phase 2**
- **Phase 3**
- **Regulatory**
- **Launch**
- **Phase 4**

**Time from start in years**:
- **0**
- **4**
- **10**
- **12**

**Phases**:
- **Research**
- **Development**
- **NDA submission**
- **Launch**
R&D Feasibility: Probability of success at each stage

<table>
<thead>
<tr>
<th>Phases</th>
<th>Time from start in years</th>
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</thead>
<tbody>
<tr>
<td>Discovery</td>
<td>0</td>
</tr>
<tr>
<td>Pre-clinical</td>
<td>1</td>
</tr>
<tr>
<td>Phase 1</td>
<td>2</td>
</tr>
<tr>
<td>Phase 2</td>
<td>3</td>
</tr>
<tr>
<td>Phase 3</td>
<td>4</td>
</tr>
<tr>
<td>Phase 4</td>
<td>12</td>
</tr>
<tr>
<td>NDA submission</td>
<td>10</td>
</tr>
<tr>
<td>Launch</td>
<td>12</td>
</tr>
</tbody>
</table>

Probabilities: Lehman Brothers

P=0.6
P=0.9
P=0.75
P=0.50
P=0.85
P=0.75
The R&D Process And Risk: Go – No Go Decisions

**R & D Stages**
- Discovery & Research
- Pre-clinical Testing
- Human Trials I
- Human Trials II
- Human Trials III
- Reg. Review & Approval

**Main Activity**
- Basic Research on Disease Process & Molecules
- Lab & Animal Testing
- Healthy Volunteer Safety Studies
- Safety And Efficacy Testing On Patients
- Large Scale Efficacy & Safety Trials
- Assemble Evidence Package

**Duration - Years**
- 2 - 10
- 1 - 1.5
- 2
- 2 - 2.5
- 1 - 2.5

**Chance Of Success**
- Less Than 1% Of Patented Pre-clinical Molecules Go Into Human Trials I
- Of Molecules Entering Human Trials, 70% Complete Phase I
- 33% Complete Phase II
- 25% Complete Phase III
- 20% Get Market Approval
Supply Chain (1)
Supply Chain Management (2)
How to achieve uninterrupted supply of quality assured drugs when needed?

Systems View
Push and pull mechanisms with enabling platforms

- Supply side incentives
- Demand creation
- Signalling

Push strategies

Institutions

Adoption system

Pull strategies

Enabling platforms

Health Systems
Empowerment
Institutionalisation
Push and pull mechanisms with enabling platforms

Push strategies
- R&D Tax breaks
- PPDPs
- Fast track approval

Pull strategies
- Global Fund; GAVI
- AMC; IFFIm; Impact bonds; volume guarantees

Institutions
- Adoption system

Enabling platforms
- Regulatory environment
- PHC/Community Care
- PPM
- Outsourcing

Atun, Knaul, Frenk, Lancet 2012
The Global Crisis of Drug-Resistant Tuberculosis and the Leadership of the BRICS Countries: Challenges and Opportunities,

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Affordable Medicines Facility – malaria

Multiple eligible ACT manufacturers

First line buyers (e.g. National Wholesalers)

Private Buyers (e.g. National Wholesalers)

Wholesalers

Retailers, private clinics and public providers

Patients

NGO Buyers (e.g. PSI, MSF)

Distributors

Central medical stores

Public Buyers (e.g. Ministry of Health)

Money

Medicines

Co-payment
Procurement and Supply Chain Support Service

**VPP:**
- **Simplifies Procurement Process**
  - Reduce timelines for ordering and deliveries
  - Ensure compliance with Quality assurance policy
  - Facilitates timely payment
  - Meet the needs of Principal Recipients

**CBS/SCMA:**
- **Addresses challenges in Supply Chain Management**
  - Through provision of Technical Support
  - To strengthen existing capacities / systems
  - Focus- Quantification, Storage, Distribution, Logistics Management Information activities
  - In collaboration with development partners

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**The Global Fund**
- Procurement Support Service

**Secretariat**
- Principal Recipients
- Participating PRs

**CBS/SCMA Technical support for in-country management and delivery of health products**

**Technical Support Providers**

**Procurement Agents**

**Consulting /TA agencies**

**Suppliers/ Manufacturers**

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**“PQR”**
- Data input

**VPP Orders / Information**

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**Procurement and Delivery of health products**

**TA Services**
Price and Quality Reporting

The Global Fund

- Principal Recipients
- General Public
- Partners

Principal Recipient

- Price
- Quality
- Delivery Conditions

Local Fund Agent

Monitor

- Price Comparison
- Quality Monitoring
- Market Information

Verify Data

Reports
Global Fund Voluntary Pooled Procurement
Core & Non Core Product Orders (2009-10)

<table>
<thead>
<tr>
<th>Proportion by</th>
<th>No. of orders</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core</td>
<td>34%</td>
<td>85%</td>
</tr>
<tr>
<td>Non Core</td>
<td>66%</td>
<td>15%</td>
</tr>
</tbody>
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No. of Orders →

Orders  All Products  Core  Non Core

461,685,267  390,770,511  70,915,442
Impact of PQR on Procured Drug Prices

- Prices at or below international references, 91%
- Prices above reference sources, 9%

- At or below international reference ranges
  - Generic products in 100 countries: 1%
  - Likely data quality issues: 0.7%
  - Branded products in add't 54 countries: 1%
  - Branded products in China: 1%
  - Branded products in Russia: 4%
  - Branded products in 10 UMI Countries: 2%
Reducing Costs of Antiretrovirals

ESTIMATES OF MEDIAN COSTS FOR COMMON FIRST-LINE ADULT ANTIRETROVIRAL REGIMENS

PRICE PER PATIENT-YEAR (US$)

2007  2008  2009  2010

TDF+FTC+EFV
TDF+FTC+NVP
AZT+3TC+EFV
d4T+3TC+EFV
AZT+3TC+NVP
d4T+3TC+NVP
Weighted index
Proposed ceiling prices to reported unit prices and trends - Efavirenz 600 mg

Points scaled by the quartile of the quantity ordered

Lowess curve f=0.2

Source: PRM and PQR reported orders as of 1 March 2009.
There are previously documented issues with the completeness and accuracy of reporting; reported orders may not be a representative sample of all orders.

Note: orders have been reported with a variety of Incoterms (freight, insurance). In general, 40% did not report the Incoterms associated with the price; of those where Incoterms were reported, the majority were inclusive of freight and insurance. To make a fairer comparison between ceiling price (ex-works) and reported orders, the ceiling price is also presented with 10% and 25% increases to provide a reasonable range for ceiling price with typical Incoterms.

Grant/country code is displayed for orders above 75th percentile for 2007 and 2008.
PQR reported Efavirenz 600mg prices compared to other price information sources

Efavirenz 600mg: Comparison of Prices Reported by GF, Other Sources, and MSF Manufacturer Survey 2004-2008YTD

USD/ppy

- GF Reported Median
- WHO Reported Median (excluding GF)
- MSF Lowest Manufacturer Reported