Availability, Accessibility and Affordability

The challenge of diseases of poverty

Dr Gill Samuels
Some Definitions

- What is the medical need?
- Is it scientifically viable?
- Will it meet regulatory requirements?

- Can it reach the patients who are in need?
- Can health care professionals administer it?

- How will the R&D be funded?
- How will innovation be incentivized?
- Who can purchase and distribute?
Availability

R&D Stage
- Research & Discovery
- Preclinical development
- Phase I
- Phase II
- Phase III
- Registration
- Phase IV

Public Sector
- Basic, ‘untargeted’ research enabling further research and discovery
- Clinical development infrastructure
- Regulatory standards and drug approval processes

Specialized Companies
- Targeted research and discovery focusing on very narrow therapeutic areas
- Limited capacities to conduct large scale clinical trials
- Practically no role

Large Pharma Companies
- Main contributors to drug discovery and preclinical development
- Unique sponsors of large scale, multi-centre clinical trials
- Unique capability to produce regulatory dossiers and conduct post-marketing studies

World Health Care Congress Europe 2005
### What has the private sector done for us?

<table>
<thead>
<tr>
<th>Disease</th>
<th>Health burden (% global deaths/DALYs)</th>
<th>PS contribution to existing treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV/AIDS</td>
<td>4.9/5.7</td>
<td>All 21 drugs in 4 classes developed by PS</td>
</tr>
<tr>
<td>Respiratory infections</td>
<td>6.9/6.3</td>
<td>All recent &amp; effective antibiotics discovered and developed by PS</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>29.3/9.9</td>
<td>All drugs in 8 classes discovered and developed by PS</td>
</tr>
<tr>
<td>Cancer</td>
<td>12.5/5.1</td>
<td>All most effective in 8 classes discovered and developed by PS</td>
</tr>
</tbody>
</table>
Availability

- R&D is high cost/high risk
- 90% of drugs on WHO Essential Drugs List, and most key modern treatments, developed for human use by private sector
- Effect is significant improvements in public health
- Would not have happened without the patent system
- The patent system is a necessary, successful (but not always sufficient) incentive for pharmaceutical innovation
Availability

- >95% of drugs on WHO EML are not patented, but 30% of those who need them do not get them.
- Almost 5 million deaths p.a. are caused by TB, Malaria and diarrhoeal diseases, but drugs to treat them are not patented.
- Most antiretroviral drugs for treating AIDS are not patented in most of Africa (and where they are, most are licensed) but the vast majority of patients who need them do not get them.
- India
The evidence from India

- No patents
- Extensive and high quality generics industry
- Patients needing HAART (est. 2005) – 710,000
- Patients receiving HAART (June 2004) – 21,000
- Patients lacking access to essential drugs
  - India – 500 – 649 million - 50-65 % population
  - Africa – 267 million - < 50% population
## The access crisis

<table>
<thead>
<tr>
<th>Pathogen/Disease</th>
<th>New cases pa</th>
<th>Deaths pa</th>
<th>% in developing world</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>30 million</td>
<td>1.1 million</td>
<td>&gt;95</td>
</tr>
<tr>
<td>TB</td>
<td>8.8 million</td>
<td>1.7 million</td>
<td>84</td>
</tr>
<tr>
<td>Diarrhoeal</td>
<td>200 million</td>
<td>2 million</td>
<td>&gt;95</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>5.3 million</td>
<td>3 million</td>
<td>&gt;92</td>
</tr>
<tr>
<td>Respiratory infection</td>
<td>?</td>
<td>3.8 million</td>
<td>&gt;95</td>
</tr>
</tbody>
</table>
Improving Access

- Political will
  - prioritisation
  - allocation of resource commensurate with need
- Infrastructure development
  - systems
  - human capacity
- Role of PPPs
  - donations
  - clinics
Accessibility Is An Issue

**HIV/AIDS**
- Not Treated
- Treated

**Lower Respiratory Infections (LRI)**
- ~30-40%

**Diarrheal diseases**
- ~25-35%

**Malaria**
- 15-35%

**TB**
- 35-40%

**STDs**
- Lymphatic filariasis
- Intestinal infections
- Leishmaniasis
- Trachoma
- Schistosomiasis
- Trypanosomiasis
- Onchocerciasis
- Dengue
- Chagas
- Leprosy

Key:
- Treatment not available, but pipeline exists
- Treatment exists but not accessible
- Treated with drug therapies

Next Slide
Availability: Meeting Medical Need

- Leishmaniasis
- Trachoma
- Schistosomiasis
- African Trypanosomiasis
- Dengue
- Chagas
- Leprosy
- Onchocerciasis

Key:
- Treatment not available, but pipeline exists
- Treatment exists but not accessible
- Treated with drug therapies
R&D PIPELINE FOR DDW

Inadequacy of current treatment

- Dengue Fever
- Chagas Disease

African Trypanosomiasis

10

6

4

2

Global disease burden (million DALYs)

HIV

127

Lower Respiratory Infections

42

Diarrhoeal Diseases

5

TB

26

Malaria

26

Leishmaniasis

5

Leprosy

2

Schistosomiasis

10

STDs

Trachoma

Onchocerciasis

Intestinal Nematodes

Source: WHO GBD 2002; MSF/DND Working Group; Pharmaprojects; IOWH; DNDi; Towse

Circle size represents expected yield of current pipeline

= ~7 therapeutics (by 2015)

Number of compounds in pipeline
40 Preclinical Development Candidates

20 Clinical Development Candidates

3 Phase 3 Candidates

1-2 Medicines

Prospective Medicines

Scientific ideas

Reasons for Failure:
- Early safety issues
- Complicated dosing
- Drug to drug interactions
- Impractical to manufacture
- Efficacy issues
- Side effects
- Lack of medical benefit
Regulatory Approval Process
From Submission to Launch Industry
Failure Rate around 20%

Compilation of Data → Submission of Application → Review by Regulatory Agency → Questions to Company

Review by Expert Committee → Outcome → Approval

Double Arrow:
Review by Regulatory Agency → Appeal

Reasons for failure:
- Trial design
- Choice of endpoints
- Robustness of data
- Clinical significance of data
- Risk: benefit

EMEA 2004
More incentives for DDW R&D are needed

- Encourage new R&D
- Speed up existing R&D
- Improve regulatory capacity
- Enable faster manufacturing scale up
- Accelerate sustainable access to patients

- PUSH – reduce cost, time risk of R&D
- PULL - create markets, reduce unpredictability
Affordability: Mechanisms Are Needed

- Public-Private Partnerships
- Advanced Purchasing Commitments
- A Global Fund for Tropical Diseases
- Tropical Diseases Drug Act

WHO ‘BIG THREE’ HAVE MULTIPLE PIPELINE COMPOUNDS AND COMMITTED RESOURCES ACROSS INDUSTRY AND NON-PROFITS

Activities Within Each Disease

- **HIV:**
  - 127 compounds in development from multiple companies
  - hundreds of non-profit programs/partnerships across industry, NGOs, MLOs, and governments

- **Malaria:**
  - 30 compounds in development from multiple companies and partnerships
  - disease institutes:
    - GSK Tres Cantos Center
  - active PPPs include:
    - Medicines for Malaria Venture
    - Lapdap Antimalarial Product Development
    - Malaria Vaccine Initiative
    - European Malaria Vaccine Initiative
    - Japanese Pharmaceutical, Ministry of Health, WHO Malaria Drug Partnership

- **TB:**
  - 22 compounds in development from multiple companies and partnerships
  - disease institutes:
    - AstraZeneca Bangalore Research Institute
    - Novartis Institute for Tropical Diseases
  - active PPPs include:
    - Global Alliance for TB Drug Development
    - Global TB Vaccine Foundation
    - Foundation for Innovative New Diagnostics

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(1) Includes companies with therapeutics only, not those with vaccines
Source: WHO GBD 2002; MSF/DND Working Group; Pharmaprojects; IOWH; DNDi; Towe
## Gaps exist where treatment is poor, pipelines are thin, and resources are limited

<table>
<thead>
<tr>
<th>Neglected Diseases</th>
<th>African Trypanosomiasis (HAT)</th>
<th>Chagas Disease</th>
<th>Leishmaniasis</th>
<th>Dengue Fever</th>
<th>Malaria</th>
<th>TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Burden (in DALYs)</td>
<td>2.1 M</td>
<td>.7 M</td>
<td>2 M</td>
<td>.5 M</td>
<td>45 M</td>
<td>33 M</td>
</tr>
<tr>
<td>Current Therapy</td>
<td>Suramin, pentamidine, melarsoprol, eflornithine</td>
<td>Nifurtimox, benznidazole</td>
<td>Miltefosine <em>(new approval)</em>, amphotericin B, pentamidine, etc.</td>
<td>None</td>
<td>Multiple- e.g. chlorquine, primaquine, coartem, etc.</td>
<td>DOTS with rifampin, ethambutol, isoniazid, etc.</td>
</tr>
<tr>
<td>Limitations</td>
<td>Resistance, serious adverse events, not oral, affordability</td>
<td>Does not treat all stages (only early)</td>
<td>Resistance, compliance, only one oral drug</td>
<td>N.A.</td>
<td>Resistance, affordability, compliance, side effects</td>
<td>Resistance, compliance, side effects</td>
</tr>
</tbody>
</table>
| Current Pipeline | Preclinical: 3  
Phase I: 1  
Phase II: 1  
Phase III: 0  
Total: 5 | Preclinical: 7  
Phase I: 0  
Phase II: 0  
Phase III: 0  
Total: 7 | Preclinical: 3  
Phase I: 0  
Phase II: 1  
Phase III: 2  
Total: 6 | Preclinical: 5  
Phase I: 2  
Phase II: 1  
Phase III: 0  
Total: 8 | Preclinical: 21  
Phase I: 1  
Phase II: 3  
Phase III: 5  
Total: 30 | Preclinical: 18  
Phase I: 2  
Phase II: 2  
Phase III: 0  
Total: 22 |
| PPP | DNDi*(1)* | DNDi*(1)*, Institute for One World Health | DNDi*(1)*, Institute for One World Health | None | Medicines for Malaria venture, MVI | Global TB alliance, Aeras*(2)* |
| Industry Research Institute | None | None | None | Novartis | GSK | AstraZeneeca, Novartis, GSK |

*(1)* Drugs for Neglected Diseases Initiative  
*(2)* Global TB Vaccine Foundation
Ideas for Industry R&D Solutions

Form a consortium across industry to deal with truly neglected diseases (i.e. poor/absent therapy, weak pipelines, few committed resources)

<table>
<thead>
<tr>
<th>Chagas Disease</th>
<th>Dengue Fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Trypanosomiasis</td>
<td>Schistosomiasis</td>
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Leveraging the WHO-Tropical Disease Research Group (TDR) as a third party ‘discovery’ broker for screening compounds from multiple companies

Building a standalone PPP institute or virtual network across companies for discovery efforts or to develop promising compounds

Creating a noncompetitive market to out-license most promising compounds which are suitable for development to ‘non-profit’ pharmaceutical development companies (e.g. Institute for One World Health or organizations such as the Bill and Melinda Gates Foundation).
The way forward

- Recognise problems of development and access are complex and multi-faceted
- Avoid simplistic solutions and the ‘blame game’
- Approach in a co-ordinated manner using resources and expertise of key stakeholders
- Recognise vital role of private sector R&D and the need to incentivise it