General Picture

• Each day, 8,000 people die of AIDS in the developing world.

• The reasons for the lack of access to essential medicines are manifold…but

• In many cases high drug prices are the main barrier to needed treatments.

• Prohibitive drug prices are often the result of strong intellectual property protection.
General Picture

• WTO/TRIPS Flexibilities reinforced by Doha but
• Doha is denied and dismantled
• Pressure on Governments in developing countries that attempt to bring down the price of medicines
• Examples:
  – in 2001, 39 drug companies took the South African government to court over its medicines act.
  – More recently, Guatemala has come under pressure to implement "TRIPS-plus" data protection rules.
  – In Brazil, pressure on Patent Office to grant patents for mere “me-too”drugs.
Innovation in France between 1981 and 2001

- Major Therapeutic innovation in an area where previously no treatment was available (7)
- Product is an important therapeutic innovation but has certain limitations (69)
- Product has some value but does not fundamentally change the present therapeutic practice (203)
- Product has minimal additional value, and should not change prescribing habits except in rare circumstances (414)
- Product may be a new molecule but is superfluous because it does not add to the clinical possibilities offered by previous products available. In most cases it concerns a me-too product (1584)
- Product without evident benefit but with potential or real disadvantages (67)
- Editors postpone their judgements until better data and a more thorough evaluation of the drug is available (116)
Effects of Generic Competition on ARV Prices

May 2000-April 2004

- Originator $10,439
- Brasil $2,767
- Cipla $350
- Aurobindo $209
- Hetero $201
- Originator $562
- Hetero $168
### Second Line treatment prices: The challenge for the next few years

<table>
<thead>
<tr>
<th>Triple Therapy/price</th>
<th>3TC/d4T/NVP (1st line)</th>
<th>TDF+ddI+LPV/r (2nd line)</th>
<th>2nd line vs 1st line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western Countries</td>
<td>US $ 8.773/year</td>
<td>US$ 13.151/year</td>
<td>1.5 times more expensive</td>
</tr>
<tr>
<td>Developing Countries</td>
<td>US$ 154/year Cipla Triomune</td>
<td>US 3.950/year Originator’s products</td>
<td>26 times more expensive</td>
</tr>
<tr>
<td>Reduction</td>
<td>-98 %</td>
<td>- 70 %</td>
<td></td>
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</tbody>
</table>
reduction negotiated by the Brazilian Government under threat of CL at the end of 2003
Price of LPV/r (Kaletra) in Brazil and best international price

<table>
<thead>
<tr>
<th>Year</th>
<th>Price Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>$4,000</td>
</tr>
<tr>
<td>2003</td>
<td>$3,000</td>
</tr>
<tr>
<td>2004</td>
<td>$2,000</td>
</tr>
</tbody>
</table>

LPV/r
Why doesn’t Brazil use CL

• Fear of retaliations from developed countries
• CL still felt like “breaking the patent….violating informal agreements
• Reverse engineering not complete in Brazil
  – Low R&D capabilities in public sector
  – Lack of trust from the private sector
• No pre-qualified alternatives in India for second line treatment. Equal to pos 2005.
Post 2005 Situation

• Following the full implementation TRIPS in India, access to new drugs is expected to become more difficult.
  – For example, most of the ARVs currently available at affordable prices come from India. Successful AIDS programmes such as those of Brazil and Thailand were possible because key pharmaceuticals where not patent-protected and could be produced locally at much lower costs.
Post 2005

- **TRIPS implementation will affect both producers**  
  - in key manufacturing countries and  
  - In countries that are dependent on these manufacturers for raw materials
- **Prices will be kept high** – Less access
- **Generic producers will also be blocked from developing fixed dose combinations** until the relevant patents on the individual components of the combinations expire.
- In other words, access to essential medicines could become dramatically more difficult in the coming years if no further action is taken.
Post 2005+ FTAs

- Linkage of registration with patent
- Data exclusivity for 5 to 10 years
- Reduction of CL grounds
- Patents for second use

- INCREASE MONOPOLIES
- REDUCE ACCESS
Patents and Innovation – R&D

- imbalance between rights and obligations:

  - stimulus for innovation, but no mechanism for directing that innovation, and as a result many diseases (and patients) are totally ignored.

  - Drug research and development, which is almost exclusively confined to the private sector, is skewed towards areas that promise a profitable return.
What are “neglected diseases”? 

Global Diseases 

Most Neglected Diseases 

Neglected Diseases 

World pharmaceutical market 
> $400 bn in 2002
Most neglected diseases attract negligible R&D

- A significant medical need exists for human African trypanosomiasis, leishmaniasis, Chagas disease, Buruli ulcer… and even aids when in comes to poor-resource settings.

- These diseases:
  - Are of no strategic (military, security) interest
  - Have very little R&D, no drug innovation

- Patients have:
  - No purchasing power
  - No advocacy group to lobby for them
Only 1% of new drugs developed are for neglected diseases

1975-1999: **1393** new chemical entities marketed
Gaps exist in the R&D process for neglected diseases...

New knowledge on drug targets and lead compounds is published but pre-clinical research does not begin

- GAP1
  - mainly industry (in North)

- GAP2
  - mainly public sector
  - Validated candidate drugs do not enter clinical development because of strategic company choices.

- GAP3
  - New or existing drugs do not reach patients: registration problems, lack of production, high prices, or not adapted to the local conditions of use
...due to failure of the market and public policy

**Market failure**

- Drug development largely confined to the R&D-based pharmaceutical industry operating for profit
- Poorer patients are thus neglected

**Public policy failure**

- Public policy does not redress this imbalance
- Need to have a national and international public health agenda based on needs and not on market
Current responses have failed to spark drug R&D for most neglected diseases

- **WHO/UNDP/World Bank Special Programme: TDR**
  
  With a very broad mandate and few resources, TDR has developed several new treatments for tropical diseases

- **Market “push and pull” mechanisms**
  
  = Incentives to attract investment in R&D for rare diseases.

  - In Brazil, incentives to private companies for TB drug development in the 70s. Failure because of lack of guaranteed market for the drugs

**Public Private Partnerships (PPP)**

  PPPs try to use the market in richer countries to yield drugs for high volumes in disease-endemic countries, e.g. MMV, GATB, IAVI
One example: Chagas Disease
Epidemiological Situation

• There is an estimate that **16 to 18 million people are infected** in 21 countries of Latin America and Central America

• 100-120 million people exposed to the risk of infection (**1/4 of the Latin American population**)

• Around **300,000 new cases/year**

• **50,000 death/year** due to cardiological form of disease

• Prevalence in **contaminated blood** (blood bank) varies from 1.7% in São Paulo/Brazil to **53 % in Bolívia**.
Chagas Disease - Treatment

Benznidazol (ex-Roche*)

- Introduced in 1970
- Use limited to the early acute phase (1% diagnosed)
- Restrictions due to toxicity and efficacy
- Technology transfer to Brazil
- Who is going to export to other countries?
- No effective treatment for chronic phase !!!
Chagas Disease - Treatment

Nifurtimox (Donation Programme Bayer)
• Only through pressure from civil society this medicine has been produced.

Nothing new in the pipeline for Chagas !!!
• Some PPPs working on it from Scratch.
• No strong IP system succeeds in stimulating R&D for this dramatic public health problem
• Designated by WHO for elimination as a public health problem by 2010
Aids is a neglected disease?

- Children with HIV/AIDS 2.5 million in 2003. They are **neglected patients**
- 700,000 children under the age of 15 were newly infected with HIV/AIDS.
- Children represent 6% of HIV infections, but account for 17% of deaths due to AIDS.
Aids is a neglected disease?

• First, there is the problem of diagnosis. Most serological methods used to diagnose HIV are not reliable for children under 18 months.

• Virological confirmation tests are needed but these tests are expensive, need sophisticated lab facilities and thus are not available.
Aids is a neglected disease!

- **Monitoring CD4** is difficult.
  - CD4 count machines are not adapted for use in young children.

- **Lack of paediatric formulations** of ARV
  - Administering doses complex and burdensome and often leads to over- or under-dosing

- **No paediatric fixed-dose combinations.**
  - Children do not have the possibility to take one pill twice a day, like adults do
Aids is a neglected disease!

- high price of the few paediatric formulations
  - FDC of d4T/3TC/NVP for adults is US$200/patient/year and US$1,300 for children (oral solutions and syrups for a 14 kg children).

- Merck does not offer any reduced, differential price for its EFV syrup

- There are no WHO pre-qualified generic versions of d4T oral solution.
Conclusions

• High level of IP in developing countries neither promotes R&D nor favors access to life-saving medicines

• Medicines should be considered essential goods when they mean the difference between life and death

• Priorities should be driven by public sector; WHO has a huge role to play in defining strategies
Conclusions

• **Doha must be implemented** in each developing country and flexibilites should be used constantly without threat or fear.

• **Innovative tools** must be created:
  – **patent pools** amongst developing countries with systematic use of CL to create market and economy of scale for generics
  – **R&D funds** derived from royalties associated to systematic use of CL to promote targeted innovation
  – R&D treaties etc.. **Must be developed to stimulate R&D** in needed public health area in developing countries