Ensuring the Sustainability of ARVs:

Critical Issues in the Success of National ARV Treatment Programs in Asia

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Ensuring Sustainability of ARV programs

- National programs (and epidemics in Asia) are interconnected and interrelated

- Geography means little with respect to long-term success/failure of ARV treatment programs

- Drug resistance will play a critical role in success/failure of ARV treatment programs
Generic Manufacturers by Region

- Africa: 1
- Latin America: 4
- Asia: 28
Generic Antiretroviral Manufacturers in Asia

- Bangladesh: 1
- Cambodia: 1
- China: 5
- India: 13
- Indonesia: 1
- Malaysia: 1
- S. Korea: 3
- Thailand: 2
- Viet Nam: 1

The diagram above illustrates the number of generic antiretroviral manufacturers in various Asian countries, with India having the highest number at 13.
China

First Line Regimen
D4T+DDI+NVP

Second Line Regimen

• Lamivudine†
• Zidovudine
• Stavudine
• Nevirapine
• Didanosine
• Indinavir

APIs
India

**First Line Regimen**

- Zidovudine
- Lamivudine*
- Didanosine
- Stavudine
- Zidovudine/Lamivudine*
- Stavudine/Lamivudine
- Zidovudine/Lamivudine/Nevirapine
- Stavudine/Lamivudine/Nevirapine*
- Indinavir
- Nelfinavir
- Saquinavir
- Nevirapine*
- Efavirenz

**Second Line Regimen**

- Zidovudine
- Lamivudine*
- Didanosine
- Stavudine
- Zidovudine/Lamivudine*
- Stavudine/Lamivudine
- Zidovudine/Lamivudine/Nevirapine
- Stavudine/Lamivudine/Nevirapine*
- Indinavir
- Nelfinavir
- Saquinavir
- Nevirapine*
- Efavirenz

*WHO Prequalification
Thailand

First Line Regimen
D4T+3TC+NVP (GPOvir)

Second Line Regimen

Thai Government Pharmaceutical Organization

AZT
NVP
D4T
D4T+3TC+NVP
Nelfinavir
AZT + 3TC
DDI
Pediatric ARV formulations:

- 11 of the 18 drugs (brand name) used to treat adults' HIV infection have a pediatric labeling
- No Fixed Dose Combinations (FDCs) available in pediatric formulations
Who will ensure drug safety and efficacy?

- US Food and Drug Administration??
- WHO Prequalification Project??
- National Drug Regulatory Agencies??
- Other??
**Who will ensure drug safety and efficacy?**

<table>
<thead>
<tr>
<th></th>
<th>US FDA</th>
<th>WHO</th>
<th>NDRA</th>
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<tbody>
<tr>
<td><strong>PEPFAR</strong></td>
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<td>✗️</td>
<td>✗️</td>
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<tr>
<td><strong>Donors</strong> (World Bank, etc.)</td>
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<td><strong>GFATM</strong></td>
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<td><strong>Gov’ts</strong></td>
<td>☐️</td>
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</tbody>
</table>

- ☐️ Required
- ✗️ Not Required
- ☒️ Not Sufficient
Selection of ARV Treatment Regimens

- Efficacy
- Toxicity
- Adherence/Resistance
- Price*
- Availability*

• *Human resources, more than price, is likely to be the rate limiting step for treatment scale-up programs in Asia*
## HIV Drug Regimen Selection

<table>
<thead>
<tr>
<th>NRTI</th>
<th>NNRTI</th>
<th>PI</th>
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<tbody>
<tr>
<td>FTC</td>
<td>NVP</td>
<td>TPV</td>
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<tr>
<td>AZT</td>
<td>EFV</td>
<td>IDV</td>
</tr>
<tr>
<td>3TC</td>
<td>DLV</td>
<td>SQV</td>
</tr>
<tr>
<td>ABC</td>
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<td>LPV</td>
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<td>ATZ</td>
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<tr>
<td>D4T</td>
<td></td>
<td>NFV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>APV</td>
</tr>
</tbody>
</table>
First Line Tx Regimens in Asia

AZT, D4T, 3TC, NVP, EFV

 AZT+3TC+NVP
 AZT+3TC+EFV
 D4T+3TC+NVP
 D4T+3TC+EFV

= 1 First Line Regimen
Second Line Tx Regimens in Asia

DDI, NFV, IDV
## Viet Nam

### First Line Regimen

<table>
<thead>
<tr>
<th>Drug</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT  + 3TC</td>
<td>STADA Vietnam J.V. Ltd.</td>
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</table>

### Second Line Regimen

<table>
<thead>
<tr>
<th>Drug</th>
<th>Company</th>
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<tbody>
<tr>
<td>3TC</td>
<td>Stada Arzneimittel AG</td>
</tr>
<tr>
<td>D4T</td>
<td>Khuong Duy Pharmaceutical Company Ltd.</td>
</tr>
</tbody>
</table>

**Note:** The company names and drug information are provided as a reference. For the most current and accurate information, please consult the latest official sources.
What is drug resistance:

HIV drug resistance is defined by the ability of the HIV virus to replicate in the presence of antiretroviral drugs. Drug resistance can be measured either genotypically or phenotypically. Genetic resistance is the presence of at least one major mutation associated with resistance to one or more drugs.
What causes HIV drug resistance:

- Some resistance occurs naturally in HIV replication cycle
- Lack of Adherence
- Lack of Absorption
- Lack of potency of the regimen
HIV Drug Resistance

How frequently does HIV drug resistance occur?:

• In the US, it’s estimated that 12% of patients are infected with a strain of HIV already resistant to one drug
• 6% are infected with a strain already resistant to two or more drugs
• In patients receiving antiretroviral treatment, 78% are resistant to one drug
• 51% are resistant to two or more drugs
HIV Drug Resistance

How do we reduce the risk of HIV drug resistance:

• Appropriate patient education treatment programs should be an integral and vital part of any treatment program.

• Understand that treatment is only one part of a continuum of care (others include exercise, nutrition, hygiene, etc.).

• Select the most appropriate and potent regimens for treatment programs.

• Monitor patients appropriately to allow for changing drugs in the event resistance develops.
HIV-1 drug resistance in Thailand: Before and after National Access to Antiretroviral Program


The percentage of drug resistant detection from the ARV therapy group in 1999 and 2001-2003 were:

- 1999: 12.14% (34/280)
- 2001-2003: 10.23% (9/88)

Perinatal:

- 1999: 86.96% (20/23)
- 2001-2003: 57.55% (61/106)

CONCLUSION: Thailand may need more appropriate monitoring of drug resistance in the free ARV therapy program to protect the future usage of drugs by minimizing the emergence of drug resistance.

Ensuring Sustainability of ARV programs

- ARV Treatment Programs (and Asia's HIV/AIDS epidemics in general) are connected and related
- The safety and efficacy of generic ARVs from many manufacturers are largely unproven
- Human resource capacity will be the rate limiting step for treatment access in the region
- Optimum regimen selection is critical for reducing the risk of drug resistance
- Drug resistance will likely be a long term predictor of success and durability of ARV treatment programs