Therapeutics Research • Education • AIDS Training

TREATASIA

Ensuring the Sustainability of ARVs:

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

Kevin Robert Frost
Director, TREAT Asia

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

Ensuring Sustainability of ARV programs

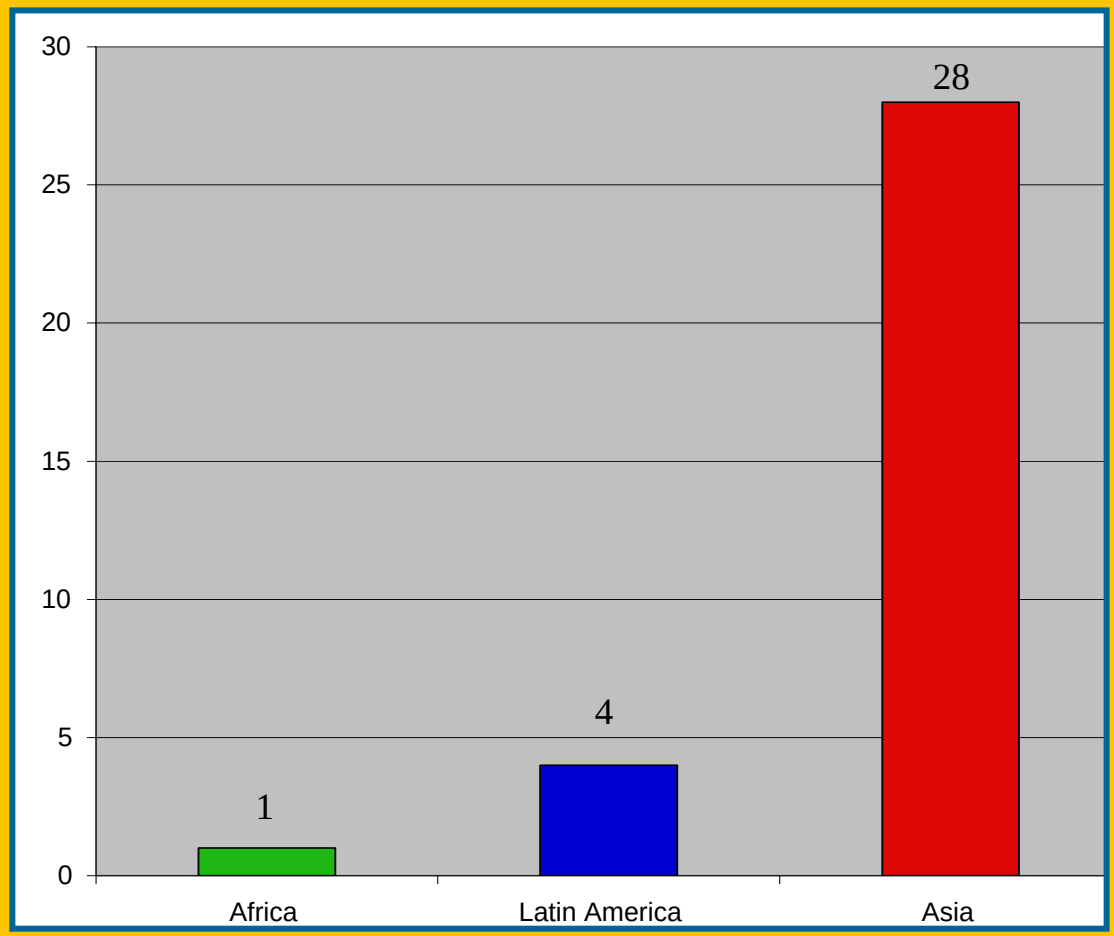
- National programs (and epidemics in Asia) are interconnected and interrelated
- Geography means little with respect to long-term success/failure of ARV treatment programs
- Drug resistance will play a critical role in success/failure of ARV treatment programs

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

Generic Manufacturers by Region

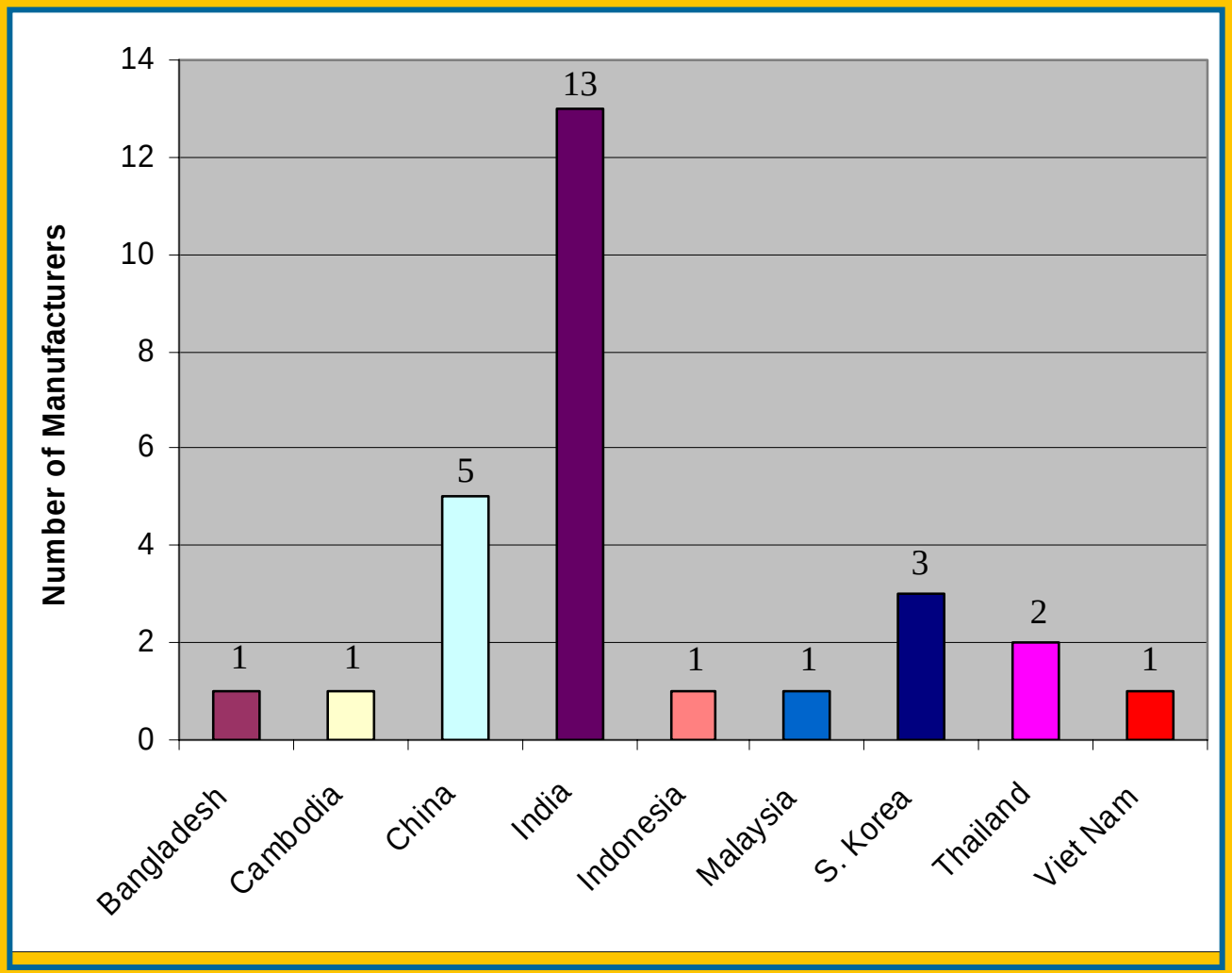


amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

Generic Antiretroviral Manufacturers in Asia



amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

China

First Line Regimen

D4T+DDI+NVP

Second Line Regimen

???

- Lamivudine†
- Zidovudine
- Stavudine
- Nevirapine
- Didanosine
- Indinavir

APIs

东北制药总厂
NORTHEAST GENERAL PHARMACEUTICAL FACTORY

DESANO

MCHEM

华海药业
HUAHAI PHARMACEUTICAL

amfAR
AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

India

First Line Regimen

???

Second Line Regimen

???

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

APIs

**WHO Prequalification*

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

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

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

Pediatric Formulations

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

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

Who will ensure drug safety and efficacy?

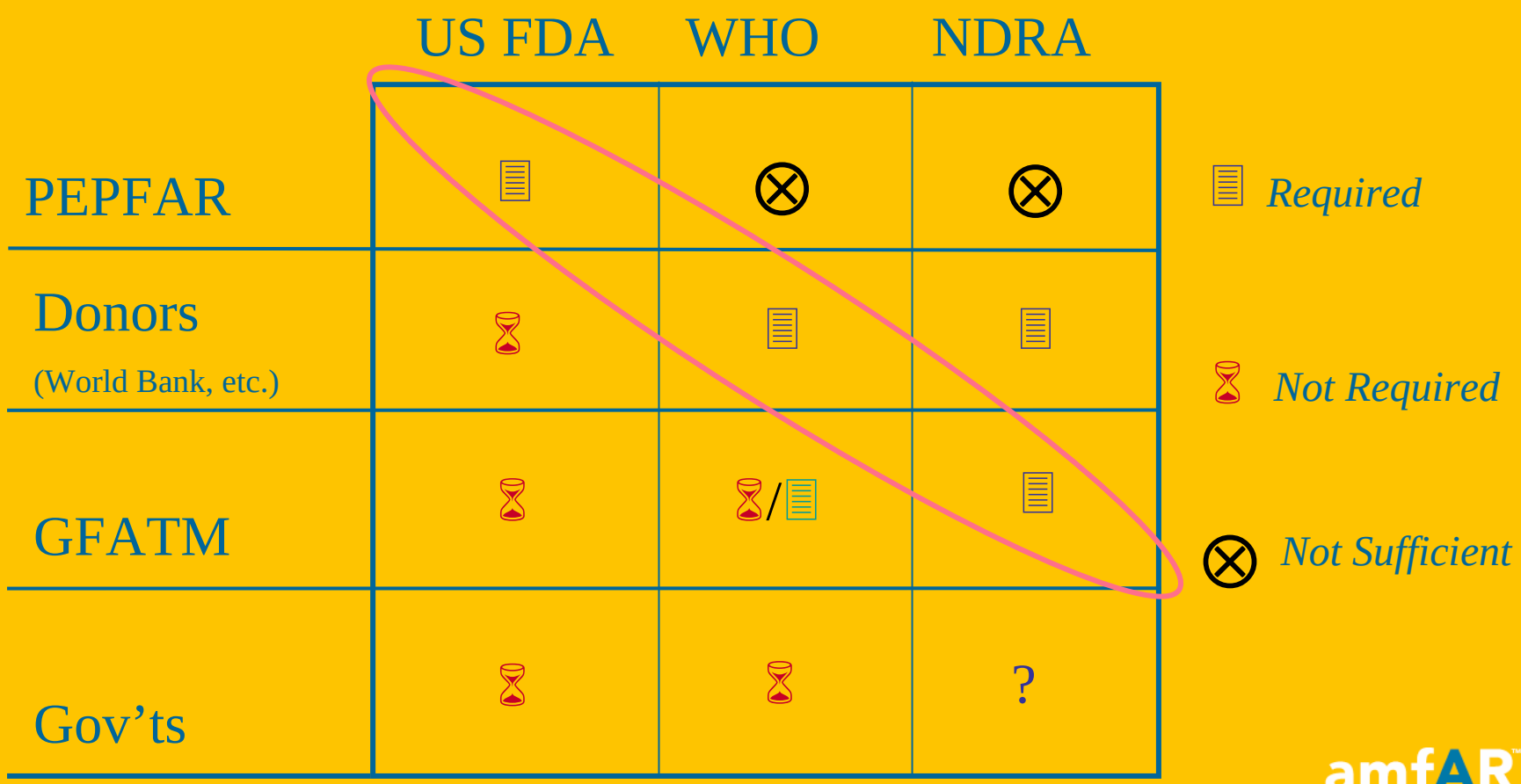
- US Food and Drug Administration??
- WHO Prequalification Project??
- National Drug Regulatory Agencies??
- Other??

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

Who will ensure drug safety and efficacy?



amfAR
AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

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*

amfAR AIDS RESEARCH

HIV Drug Regimen Selection

NRTI	NNRTI	PI
FTC	NVP	TPV
AZT	EFV	IDV
3TC	DLV	SQV
ABC		LPV
DDC		FPV
DDI		RTV
TDF		ATZ
D4T		NFV
		APV

Therapeutics Research • Education • AIDS Training

TREATASIA

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

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

Second Line Tx Regimens in Asia

??????

DDI, NFV, IDV

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

Viet Nam

First Line Regimen

???

Second Line Regimen

???

STADA Vietnam J.V. Ltd.
Stada Arzneimittel AG
Khuong Duy Pharmaceutical Company Ltd.

AZT + 3TC

3TC

D4T

NVP

IDV

DDI

EFV

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

HIV Drug Resistance

What is drug resistance:

HIV drug resistance is the 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.

amfAR AIDS RESEARCH

HIV Drug Resistance

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

Therapeutics Research • Education • AIDS Training

TREATASIA

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

amfAR AIDS RESEARCH

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

Therapeutics Research • Education • AIDS Training

TREATASIA

HIV-1 drug resistance in Thailand: Before and after National Access to Antiretroviral Program

542 HIV-1 infected subjects who received ARV therapy in 1999 and 2001-2003 and perinatal chemoprophylaxis in 1998 and 2000.

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.

J Clin Virol. 2005 Dec;34(4):272-6. Epub 2005 Apr 15.

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

YRG Centre for AIDS
Research and Education
VHS Campusm,Taramani
Chennai 600113
India

Virology Unit
Institut Pasteur du Cambodge
5, boulevard Monivong,
Phnom Penh, Cambodge

Pasteur Institute in Ho Chi Minh City
167 Pasteur Street
District 3, Ho Chi Minh City
Viet Nam

Division of Research on Virology and Immunology
National Center for AIDS/STD Control and Prevention (NCAIDS)
Chinese Center for Disease Control and Prevention
27 Nanwei Street, Xuanwu District
Beijing 100050 China

Laboratory of Therapeutic Research and Clinical Science
AIDS Research Center
National Institute of Infectious Diseases
4-7-1 Gakuenn Musashimurayama
Tokyo 2080011 Japan

Agarkar Research Institute
Han Ul Medizin Pvt. Ltd.
C-4 Hermes House
1989 Convent Street
Pune 411001
India

AIDS Prevention and Research Center
National Yang-Ming University
155, Li-Noun Street, Sec. 2, Peitou
Taipei, Taiwan

Department of Medicine, Faculty of Medicine Chulalongkorn University
Thai Red Cross AIDS Research Centre
Rama 4 Road
Bangkok 10330 Thailand

The University of Hong Kong
Department of Microbiology
Queen Mary Hospital
Hong Kong SAR, China

Infectious Diseases Unit
Faculty of Medicine
University of Malaya Medical Center
50603 Kuala Lumpur
Malaysia

Infectious Diseases Research Laboratory
Level 2
Tan Tock Seng Hospital
Medical Centre
11 Jalan Tan Tock Seng
Singapore 308433

Department of Microbiology
Faculty of Medicine
University of Udayana
Jln. P.B. Sudiman
Denpasar, Bali
Indonesia

Research Institute for Tropical Medicine
Filinvest Compound, Alabang
Muntinlupa City
Philippines

Therapeutics Research • Education • AIDS Training

TREATASIA

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

amfAR AIDS RESEARCH

Therapeutics Research • Education • AIDS Training

TREATASIA

amfAR™
AIDS RESEARCH