Expanding Research Capacity & Accelerating HIV Vaccine Development in Asia

WHO Satellite Meeting

Expanding Capacity and Promoting Regional Networking to accelerate HIV Vaccine Development in Developing Countries

AIDS Vaccine 07, 20 August 2007, Seattle, WA, USA

Dr. Jean-Louis Excler
Senior Medical Director
International AIDS Vaccine Initiative, India
Pathway

Pattern and evolution of the epidemic in Asia
  ➡️ Implications for AIDS Vaccine Development

AIDS Vaccine Development in Asia
  ➡️ Efforts
  ➡️ Challenges
  ➡️ Missed opportunities
  ➡️ AIDS Vaccine Asian Network
Adults and children estimated to be living with HIV in Asia and Pacific, 2006

Total: 8.6 (6 - 13) million
Dynamic of Asian HIV epidemics

- Concentrated epidemic
- Risk is focused (IDU, FSW, clients, MSM)
- Spread limited and slow

Adapted from T. Brown, UNAIDS Collaborating Centre at the East-West Centre
Mode of Transmission Among Reported AIDS Cases* in Selected South-East Asian Countries, 2005

*Cumulative AIDS cases; **Reported HIV infections

Source: National AIDS Programme, 2005

HIV continues to remain high or sharply increasing or among injecting drug users

Source: WHO-SEARO and National AIDS Programme, 2005
Trends of HIV Prevalence among IDUs and FSWs Vietnam, 2005

Source: Ministry of Health
HIV Prevalence Among Men Who Have Sex With Men in Selected Countries in South-East Asia, 2003–5

<table>
<thead>
<tr>
<th>City/State</th>
<th>Year</th>
<th>HIV Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chennai (2004) - India</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>Mumbai (2004) - India</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>Mumbai (2004) - India</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>Andhra Pradesh (2004) - India</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Andhra Pradesh (2005) - India</td>
<td>18.2</td>
<td></td>
</tr>
<tr>
<td>Kathmandu (2005) - Nepal</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>Phuket (2005) - Thailand</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td>Chiang Mai (2005) - Thailand</td>
<td>15.3</td>
<td></td>
</tr>
<tr>
<td>Bangkok (2003) - Thailand</td>
<td>17.3</td>
<td></td>
</tr>
<tr>
<td>Bangkok (2005) - Thailand</td>
<td>28.3</td>
<td></td>
</tr>
</tbody>
</table>

Source: National AIDS Programme, 2005

High HIV transmission among MSM
HIV Subtypes in Asia

HIV-1 B’, C, A/E
HIV-1 A/E, B’
HIV-1 C, B, A

Recombinants
B/C
A/C
A/E
A/E/B

Source: Francine McCutchan, USMHRP
Geographic Distribution of HIV Subtypes in China

- Subtype B and B’ HIV-1
- Subtype A/E HIV-1
- Subtype A D F and G HIV-1 and HIV-2 in China
- Subtype C and B’/C recombinant HIV-1
Responses adapt over time as the epidemic evolves

Source: Thailand A² Team
Responses do correlate with prevalence

HIV prevalence trends among pregnant women in major cities in Cambodia, Myanmar and Thailand, 1990–2004

Sources: Cambodia National Center for HIV/AIDS, Dermatology and STDs (Phnom Penh); Myanmar Ministry of Health (Mandalay and Yangon); Thailand Ministry of Public Health (Bangkok), 2005.
## Examples of HIV incidence in Asian countries

<table>
<thead>
<tr>
<th>Country</th>
<th>IDU</th>
<th>CSW</th>
<th>STD patients</th>
<th>MSM</th>
<th>General Pop</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>China</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yunnan 1994</td>
<td>0 - 25%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2005</td>
<td>4%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>3.8% (spouses)</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guangxi 1999</td>
<td>2.38 - 6.86%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2005</td>
<td>3.1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sichuan 2002</td>
<td>3.17%</td>
<td>NA</td>
<td></td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Xinjiang</td>
<td>7-8.8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>India</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pune 1993-04</td>
<td>NA</td>
<td>3.7%</td>
<td>F 16.6 – M 6.8</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Pune 2000-02</td>
<td>3.6%</td>
<td></td>
<td>F 5.6 – M 2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thailand</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>5.8 - 7.3%</td>
<td>12.8%</td>
<td>4.92 - 5.2 %</td>
<td>Pending</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>2002-04</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Cambodia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>NA</td>
<td>13.9%</td>
<td>NA</td>
<td>NA</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>2002</td>
<td>6.45%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Summary of the HIV Epidemic Patterns in Asia

- Higher risk groups are mostly represented by IDU, FSW, MSM and Transgender populations
- Prevention interventions and HIV care & treatment are scaled up with growing success
- HIV incidence data are scarce and may decrease
- HIV genetic subtypes are still relatively homogeneous by geographic region, with however more and more recombinant viruses observed
AIDS Vaccine Development in Asia

1993-2007

Thailand
China
India
Japan
Australia
# AIDS Vaccine Development in Asia

<table>
<thead>
<tr>
<th>Country</th>
<th>Vaccine</th>
<th>Sponsor</th>
<th>Subtype</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>DNA + MVA China DNA + MVA DNA + Tientan replicative DNA + Tientan attenuated Anthrax-derived fusion protein DC with inactivated HIV (therapeutic)</td>
<td>China China/ADARC China/NIH China/NIH China/NIH China/France</td>
<td>B'/C C B'/C B''/C B'/C C</td>
<td>I In discussion I Preclinical Preclinical In discussion</td>
</tr>
</tbody>
</table>
# AIDS Vaccine Development in Asia

<table>
<thead>
<tr>
<th>Country</th>
<th>Vaccine</th>
<th>Sponsor</th>
<th>Subtype</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>India</strong></td>
<td>Adeno-associated virus</td>
<td>IAVI</td>
<td>C</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td>MVA</td>
<td>IAVI</td>
<td>C</td>
<td>I</td>
</tr>
<tr>
<td><strong>Australia</strong></td>
<td>DNA + fowlpox</td>
<td>NIH</td>
<td>B</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td>DNA + fowlpox</td>
<td>Australia</td>
<td>A/E</td>
<td>I</td>
</tr>
<tr>
<td><strong>Japan</strong></td>
<td>DNA + DI (attenuated vaccinia)</td>
<td>Japan</td>
<td>A/E</td>
<td>Preclinical</td>
</tr>
<tr>
<td></td>
<td>BCG</td>
<td>Japan</td>
<td>A/E</td>
<td>Preclinical</td>
</tr>
<tr>
<td></td>
<td>Replicative Sendai</td>
<td>DNAVEC/IAVI</td>
<td>A</td>
<td>Preclinical</td>
</tr>
</tbody>
</table>
Challenges of efficacy trials in Asia

- HIV incidence in general population is low
- HIV incidence may lower in higher risk groups
  - More targeted interventions
  - Access to Care and Treatment will increase
Challenges of efficacy trials in Asia

- Sample size needs will also balloon as 1st partially-effective vaccine or other prevention method sets new bar & becomes comparison group or additional intervention

- Vaccine efficacy trials may compete for access to volunteers with efficacy trials of non-vaccine HIV prevention technologies
Are efficacy trials in Asia still feasible?

**China:** likely if stable HIV incidence
  ➤ Yunnan, Guangxi, Sichuan, Xinjiang

**India:** Still unknown
  ➤ Recent estimates less than half of previous ones
  ➤ Feasibility studies needed in high risk groups
  ➤ Investment and time

**Thailand:** Yes - MSMs and IDUs

**Vietnam, Indonesia, Cambodia, Myanmar, others?**
  ➤ Possibly - Need thorough assessment

This situation ‘snapshot’ will likely evolve over time
Implications for AIDS Vaccine Development in Asia

- Bring and develop new vaccines for Asia
- Prioritize AIDS vaccines for efficacy trials
  - Design test of concept trials to screen vaccine candidates
- Prioritize prevention interventions for efficacy trials
- Expand capacity to conduct clinical trials
  - Tremendous capacity and (missed) opportunities
  - Document HIV incidence in different settings
  - Develop new sites for clinical trials
South East Asia Assets 1

- Thailand has developed a wonderful and efficient technical platform for AIDS vaccine clinical development and has now high risk cohorts necessary for advanced clinical development.

- Subtype E or A vaccines in early human trials (MVA), monkey trials (Ad35, Japanese BCG, Sendai).

- The relative homogeneity of subtype E in SEA facilitates both genetically matched and mismatched trials.

- Post-infection Viral Load and CD4 count are extremely well defined for subtype E and will therefore be most useful in planning for surrogate endpoints (without much confounding by the presence of other subtype effects on progression).

- The availability of ARV and adherence to standardized guidelines for initiation will enhance data precision around clinical surrogate endpoints.
South East Asia Assets 2

Major sponsors already present in Thailand have unfortunately not expressed a renewed interest in SEA as a site for short-term HIV vaccine development (next 3 years).

Finally the relatively strong public health infrastructure means that uptake and utilization of an effective vaccine will be greater in SEA than other regions.

- Dressed up to dance… Desperately needs partners and funding to advance vaccines to trials in SEA.
## AIDS Vaccine Development Capacity in selected Asian countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Advocacy</th>
<th>Applied Research</th>
<th>Feasibility studies</th>
<th>Clinical Trials</th>
<th>Manufacturing</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Ph I to III</td>
<td>Yes</td>
</tr>
<tr>
<td>India</td>
<td>Yes</td>
<td>Possibly</td>
<td>Possibly</td>
<td>Phase I</td>
<td>Yes</td>
</tr>
<tr>
<td>Thailand</td>
<td>Yes</td>
<td>Possibly</td>
<td>Yes</td>
<td>Ph I to III</td>
<td>Limited</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Yes</td>
<td>Assess</td>
<td>Assess</td>
<td>Ph I to ?</td>
<td>Yes</td>
</tr>
<tr>
<td>Vietnam</td>
<td>Yes</td>
<td>Assess</td>
<td>Assess</td>
<td>Ph I to ?</td>
<td>Limited</td>
</tr>
<tr>
<td>Japan</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Australia</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Phase I</td>
<td>Yes</td>
</tr>
</tbody>
</table>
What should be done for and in Asia?

- Engage other Asian countries
- Engage sponsors and donors for and in Asia
- Bring and develop new AIDS vaccines
- Different countries: different capacity and skills
- Think regional
  - Multi site
  - Multi country
- Foster and facilitate alliances and networks
First and next steps


- Expanding Research Capacity and Accelerating HIV Vaccine Development in Asia - WHO-UNAIDS regional consultation in Sapporo, Japan, 30 October – 1 November 2006
  - Rationale and recommendation for an AIDS Vaccine Asian Network at the WHO VAC Meeting – March 19, Milano
  - Publication of the Proceedings (in preparation)
  - Constitution of the Asian AIDS Vaccine Network

- Regional visits: advocacy, gathering information on willingness, epidemiological situation, capacity, gaps and needs, approval process
Acknowledgements

UNAIDS
Initiative for Vaccine Research, WHO Geneva
WHO Regional Office for South East Asia
WHO Regional Office for West Pacific
Chinese Center for Disease Control and Prevention
Division of AIDS, NIAID, NIH
Tim Brown, East – West Centre, Hawaii U
Asian Development Bank, Manila
HIV Vaccine Trial Network
IAVI Team
IAVI gratefully acknowledges the generous support provided by the following major donors:

- Alfred P. Sloan Foundation
- Basque Autonomous Government
- Becton, Dickinson and Company (BD)
- Bill & Melinda Gates Foundation
- Broadway Cares/Equity Fights AIDS
- Canadian International Development Agency
- Continental Airlines
- Crusaid
- Deutsche AIDS-Stiftung
- European Union
- Google Inc.
- The Haas Trust
- Irish Aid
- The John D. Evans Foundation
- Kathy Bole & Paul Klingenstein
- Merck & Co., Inc.
- The Netherlands Ministry of Foreign Affairs
- The New York Community Trust
- Norwegian Royal Ministry of Foreign Affairs
- Pfizer Inc.
- The Rockefeller Foundation
- Royal Danish Ministry of Foreign Affairs
- The Starr Foundation
- Swedish International Development Agency
- Swedish Ministry of Foreign Affairs
- U.K. Department for International Development
- Until There’s a Cure Foundation
- The U.S. President’s Emergency Plan for AIDS Relief through the U.S. Agency for International Development
- The World Bank/Global Forum for Health Research

And many other generous individuals and organizations from around the world.

* As of 11/06