WHO-UNAIDS HIV Vaccine Initiative (HVI): Background

- In 2000, HVI was established as a joint WHO-UNAIDS HIV Vaccine Initiative (HVI). Since 2002, HVI is part of the WHO Initiative for Vaccine Research (IVR).

- Coordination of HVI's activities within WHO and UNAIDS is ensured by the WHO-UNAIDS Management and Support Committee (MSC).

- HVI is guided by the WHO-UNAIDS HIV Vaccine Advisory Committee (VAC), which provides technical advice to WHO and Member States on various aspects of HIV vaccine development and clinical trials.

- **Since October 2006**: HVI has been tasked to coordinate its activities with Malaria and TB vaccine R&D, focusing on: **Ethics**, **Policy Development**, **Regulatory Research**.
3 Areas of Strategic Advantage for IVR in the development of vaccines against HIV, TB and Malaria are in:

I. Facilitating the development of globally effective and accessible vaccines through promoting policies and strategies for public health decision making based on sound science

II. Support innovation and rapid evaluation of novel vaccines through promoting best practices and development and implementation of internationally agreed norms and standards

III. Contribute to comprehensive, integrated and sustainable clinical trial capacity strengthening in developing countries

Contributing to development of a favorable environment for HIV, TB and Malaria vaccine development & introduction in developing countries

National Capacity Building - International collaboration

- Government willingness & commitment
- Community involvement
- Regulatory & Ethical Frameworks
- Public (media) attention
- Clinical trial and laboratory expertise
- Data management
- Epidemiology
- Molecular Monitoring
- Scientific infrastructure
- Availability of cohorts
- Social behaviour expertise
- National Capacity Building
- International collaboration
Promoting the development of policies and strategies that balance public health priorities with sound scientific basis

Example:

- Initiated in 1992 in Brazil, Thailand & Uganda, now in many other countries, specifically in Africa, e.g. Tanzania 2006.
- Facilitate trials by describing policies, approval mechanisms, research priorities
- A framework for coordinated plan of capacity building and site development

Promote comprehensive and sustainable capacity strengthening in developing countries

- Launched in 2000
- Activities to be implemented through four Resource Facility Centres:
  - Biomedical sciences (laboratory and clinical).
  - Ethics, Law and Human Rights.
  - Regulatory issues
  - Communication and media
- Support to country Strategic Planning located in WHO
AAVP Framework

AAVP Work Areas

<table>
<thead>
<tr>
<th>Country-based strategic planning</th>
<th>Biomedical research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication &amp; media</td>
<td>Regulatory issues</td>
</tr>
<tr>
<td>Ethics, law and human rights</td>
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</tbody>
</table>

AAVP Strategic Directions

<table>
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<tr>
<th>Capacity Strengthening</th>
<th>Advocacy</th>
<th>Policy Development</th>
<th>Community Involvement</th>
<th>Networking</th>
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AAVP Work Areas AAVP Strategic Directions

Promoting the development of policies and strategies that anchor public health priorities in a sound scientific basis

Example: Malaria Vaccine

- Development of Country-specific malaria vaccine decision-making framework (2005-6)

Partners:
PATH, USAID, WHO HQ, WHO AFRO

Outcome
Framework Reviewed in 6 countries July-December 2006:
- Tanzania, Kenya, Mozambique, Ghana, Gabon, and Mali
- 6 Country specific DMF
- Country meeting reports & presentations available at www.malvacdecision.net
- Data to generate a robust regional decision-making framework.
### Promoting best practices and Capacity strengthening: ETHICS

- Vaccine trials must meet the requirements of international ethical guidance documents
- Vaccine trials must adhere to principles of Good Clinical Practice (ICH, WHO)
- **However, the capacity of developing countries in the area of ethical review and monitoring of vaccine trials is very limited**

- Need for **practical guidance** where novel or difficult situations arise;
- Resolving ethical dilemmas arising in specific vaccine trials provides shared experience and lessons learnt
- Documentation of shared experiences and opinions from consideration of specific ethical issues provide valuable resources for ethical decisions in future trials

### IVR Activities in Ethics

- Development of guidance documents on selected issues:
  - Provision of care and treatment in Vaccine trials;
  - Inclusion of Adolescents in HIV vaccine trials

- Strengthening institutional and regulatory framework for proper ethical review of vaccine trials

- Training and Evaluation of Institutional Ethical Committees
### Determining standards of care for specific populations and diseases in vaccine trials:

**Position paper accepted for publication in *Vaccine* in 2007**

<table>
<thead>
<tr>
<th>Populations in the community hosting the trial</th>
<th>Type of care for consideration</th>
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<tbody>
<tr>
<td></td>
<td>Target disease by the vaccine under study</td>
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<tr>
<td></td>
<td>Diseases/Conditions diagnosed as part of study design</td>
</tr>
<tr>
<td></td>
<td>Diseases/Conditions unrelated to study objectives</td>
</tr>
<tr>
<td>Trial Participants</td>
<td></td>
</tr>
<tr>
<td>Individuals considered for enrollment and excluded as a result of pre-enrollment screening</td>
<td></td>
</tr>
<tr>
<td>Others linked to the trial participants, but not considered for enrollment (family members, partners)</td>
<td></td>
</tr>
<tr>
<td>Others in the host community</td>
<td></td>
</tr>
</tbody>
</table>

Each cell opens a space for determining the standard of care applicable to particular individuals and diseases

### Ethics: Examples of Future Activities I

- **Area 1:** Development of resource or guidance documents on selected issues:
  - Revision and Update of the UNAIDS/WHO guidance documents for HIV Vaccine trials

- **Area 2:** Strengthening institutional and regulatory framework for proper ethical review of vaccine trials
  - AAVP Collaborating Center on Ethics
  - Training and Evaluation of Institutional Ethical Committees through SIDCER program: Development of an African Training Program
Promoting **best practices** and development & implementation of internationally agreed **norms** and **standards**

**Example:**

- Used by Member States as the basis of national legislation for the regulation of such products
- Provide guidance for NRAs and manufacturers on international regulatory expectations for the production & quality control, non-clinical and clinical evaluation of vaccines
- Used by WHO as the basis for pre-qualification procedure for vaccines procured by UN agencies

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**Determining which standards at what stage – a challenge for HIV, TB and Malaria Vaccine development**

Product development → Characterization of candidate vaccine → Preclinical/ Nonclinical testing → Clinical trials → Licensing → PMS → Monitoring performance → Establishment of IS/IRP
Promoting best practices and development and implementation of internationally agreed norms and standards: Regulatory Research

Why regulatory research?
Complex challenges face HIV, TB, and malaria vaccine development – need for guidance and coordination of scientific information; analysis of knowledge to generate guidance that supports innovation and rapid development of products of public health importance

What is Regulatory Research?
Research which will support critical aspects of regulatory decision making regarding novel vaccines
- Developing relevant standards and tools based on best current science in the field
- Developing and defining parameters of product evaluation i.e. assays, endpoints and build knowledge base on product characterization, safety, and efficacy
- Improving Trial design, definitions and analysis

Products of Regulatory Consensus

Identify research needs and regulatory expectations

- Prerequisites for clinical trials: preclinical, animal studies, trial design
- Endpoint definitions - immunogenicity & clinical outcomes
- GCP/GLP related research
- Production & Control specifications

Support for regulatory decision-making

- Production & Control specifications
Regulatory Research: Developing and defining parameters of product evaluation in the areas of assays and endpoints

- **HIV**
  - Network on standardization of HIV Neutralization Assay - Support to NeutNet and consultation of network, jointly convened by WHO and EU (2007)

- **Malaria**
  - Working Group on optimizing and standardizing Key Assays in Malaria Vaccine Development

- **TB**
  - Standardisation and Harmonisation of Immunological Outcomes in Novel TB Vaccine Trials: Proposed Strategy of the WHO Initiative for Vaccine Research

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Regulatory Research: Guidance on Trial Design, Clinical Endpoints and Analysis

- **HIV**
  - Definition of HIV vaccine efficacy (sterilizing immunity vs prevention of disease development), validation of surrogate markers and standardization of lab assays
  - Development of strategies for communication of efficacy trial results

- **Malaria**
  - WHO Study Group on Measures of Malaria Vaccine Efficacy
  - Guidance on clinical case definitions of Phase 3 trials endpoints

- **TB**
  - Development of New TB Vaccines: Global Perspective on Regulatory Issues
### Lessons learnt & future challenges

- We need to live up to the challenge of coordinating our activities with a growing number of international partners and new initiatives in the areas of HIV, TB and Malaria vaccines.

- We must synthesize the lessons learnt and use them to develop broad guidance/tools that would be more generally applicable for other novel vaccines.

- We should be vigilant and identify other "orphan" products that would be targeted to needs of developing countries and may require our involvement.

- We must, in a continuous and proactive way help partners to link efficiently with other components of IVB or other sectors of WHO and UNAIDS.