DEVELOPING VACCINES FOR DISEASES OF POVERTY: HOW FAR ARE WE?

Oslo, 13 September, 2011
Dr. Harry van Schooten
Presentation Outline

• Background
  – Diseases of Poverty
  – Role of Vaccines
  – Actors in Public-Private Vaccine Development

• What has been done in the last 20 years?
• European Vaccine Initiative experience
• What is needed? Vaccine future in Europe
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Diseases of Poverty

Poverty & Poor Health
- 1993 WB Report, Investing in Health
- 2001 Jeffrey Sachs, Investing in Health for Economic Development

10/90 Gap
- 1999, Global Forum For Health Research

Neglected Tropical Diseases (NTDs)
- >1 billion people living on <US$2/day are affected by at least one NTD
  (WHO, 2010)
Role of Vaccines (1/3)

‘With the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction as vaccines’

Vaccines are key assets to reduce poverty and improve human development (MDGs)……..,
Role of Vaccines (2/3)

‘With the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction as vaccines’

Vaccines are key assets to reduce poverty and improve human development (MDGs)………,

but for most diseases of poverty no vaccine exists yet!
Role of Vaccines (3/3)

Potential impact on preventable deaths

Actors in Public-Private Vaccine Development

- Academia, industry, CROs, NGOs
- Governments (local, national, EC)
- Multilateral organisations (WHO, WIPO)
- Regulatory authorities (EMEA, FDA)
- Pharmaceutical Industry (ATM Index)
- Public-Private Partnerships (IAVI, MVI, TBVI, EVI)
- Philanthropic foundations (BMGF, Wellcome)
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Global investment in R&D for neglected diseases

- **Global funding**:  
  - 2007 - 2.5 bn US$  
  - 2009 - 3.2 bn US  
  87.1% funding - public & philanthropic funders  
  73% funding for ‘big three’, .. % for drugs and diagnostics, ..% for vaccines

- **Push & Pull mechanisms**:  
  - PDPs, GFATM, GAVI,  
  - AMC, IFFim, UNITAID

*Source: G-Finder 2010, M.Moran e.a.*
Contribution of public-private partnerships

- Product development for diseases of poverty
  - 1974 – 2004: only 21 of 1556 new drugs for neglected diseases* by private sector
  - 2010: 122 new candidates in pipeline of PDPs**
    including vaccines

* T. Chirac, Global Framework on Essential Health R&D
** Cheri Grace, PDPs Lessons learned, DFID
Vaccine development for diseases of poverty

• Public-Private Vaccine Development Partnerships
  – HIV/AIDS: IAVI
  – Tuberculosis: AERAS, TBVI
  – Malaria: MVI, EVI
  – Other diseases: PATH, Sabin, IVI, EVI,…

• Funding needs:
  – HIV/AIDS - US$ 1.2 billion / year
  – Tuberculosis - US$ 1.9 billion / 5 years
  – Malaria - US$ 300-500 million / year
  – Other diseases - ??
Vaccine development for diseases of poverty

Only four on market:
- Cholera
- Pneumococcal
- Rotavirus
- Typhoid
Promise for vaccine discovery

• **Advances in vaccine development**
  
  I. Pre-genomic vaccine design /Louis Pasteur’s principles:
     - Killed micro-organism (polio, rabies)
     - Live attenuated micro-organism (polio, MMRV)
     - Subunit (Diphteria, tetanus, pertussis, Hep B)
     - Conjugated subunit (Haemophilus Influenzae, Pneumococcus)
  
  II. New & improved technologies
     - Cell culture (Rota virus, Hep A)
     - Recombinant DNA, (Hep B, pneumo, meningitis)
     - Conjugation
     - Combinations
     - New adjuvants
  
  III. Reverse vaccinology, structural and systems biology
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Evolution of EVI

- 1998 – 2009
  - Malaria focus
  - Product focus
  - Integrated in Bergen Univ., then in Staten Serum Institute

- 2009 -
  - Legal entity: EEIG
  - Stockholm Univ., Heidelberg Univ., Jenner Institute, RCSI, NVI/RIVM, BPRC

- Diseases of Poverty focus
- Vaccine R&D focus
- Infrastructure focus
  - federation, harmonisation, standards
EVI mission and mandate (1/2)

- To contribute to the global efforts to control diseases of poverty by:
  - Creating the environment conducive to accelerating the development and clinical assessment of vaccines for diseases of poverty
  - Promoting affordability and accessibility of vaccines for diseases of poverty in low income population;
EVI mission and mandate (1/2)

- Aligning all major stakeholders and acting as a focal point in order to ensure successful development of vaccines for diseases of poverty in low income population;

- Communicating to the stakeholders and the general public the importance of the Initiative’s mission, goals, and progress towards the deployment of affordable and efficacious poverty-related diseases vaccines.
EVI partnership

- 50 partners, Academic institutions in Europe, DC – Africa
- Other PdPs TBVI, MVI

> 30 partners, big pharma, SMEs, DCVMN

International Organisations (WHO...)

Vaccine Scientific Community

Clinical Networks (ECRIN, EDC-TP,...)

USA Stakeholders (NIH, USAID...)

Industry & SMEs

Donors Funders

Malaria Vaccine Funders Group

Brighton Collaboration, ICGEB
Strong R&D environment:
Scientific network (EC funded projects), clinical trial networks (EDCTP, AMANET), other PDPs

Governance structure
efficient, pro-active, transparent

Very well defined decision process, recognised quality standards

Strong policy and political environment:
Regulatory Agencies (EU, EMEA, AVAREF), Malaria Vaccine Funders Group, EC support, WHO
EVI Scope

Early phase vaccine development

Pharmaceutical development / vaccine production

Licensure

EVI

EUROPE

PHASE 1
SAFETY/IMMUNOGENICITY

AFRICA
Phase 1b

AFRICA
Phase 2b

EUROPE
Phase 2a
HUMAN CHALLENGE

AFRICA
Phase 3

ANTIGEN DISCOVERY VALIDATION

cGMP MANUFACTURE/FORMULATION
TOXICOLOGY STABILITY POTENCY

INDUSTRIAL SCALE UP

Clinical development
Prime Focus on Malaria

- 881,000 annual deaths
- 91% of deaths in Africa
- 85% of deaths in children under 5
- 10,000 pregnant women die every year from malaria in Africa
Prime Focus on Malaria

• 881,000 annual deaths
• 91% of deaths in Africa
• 85% of deaths in children under 5
• 10,000 pregnant women die every year from malaria in Africa

1 child every 45 second
Societal impact of a 90% efficacious malaria vaccine

- Prevents yearly 5,482 deaths / 100,000 children vaccinated
- 66% reduction in malaria deaths worldwide
- Save 193,926 DALYs
- At a cost of US$ 14 / DALY*

* WHO guidelines: US$25-30/year=highly attractive
EVI key accomplishments 2000-2010

• Contributing to the development of 24 malaria antigens in 29 vaccine formulations
• Advancing 10 vaccine candidates into phase I clinical trials, three of which have been transitioned to partners for further development in Africa
• Taking a leadership role in efforts to standardise and harmonise vaccine development efforts in Europe
Cycle of *Plasmodium*

**Sporogonic Cycle**
- Oocyst
- Release of sporozoites
- Ruptured oocyst
- Mosquito takes a blood meal (injects sporozoites)
- Liver cell
- Infected liver cell

**Mosquito Stages**
- Ookinete
- Macrogametocyte
- Microgamete entering macrogamete
- Exflagellated microgametocyte

**Exo-erythrocytic Cycle**
- Ruptured schizont
- Schizont

**Erythrocytic Cycle**
- Immature trophozoite (ring stage)
- Mature trophozoite
- Gametocytes

**Human Liver Stages**
- Ruptured schizont
- Schizont

**Human Blood Stages**
- *P. falciparum*
- *P. vivax*
- *P. ovale*
- *P. malariae*
### EVI FUNDED PROJECTS AND STATUS AT THE END OF 2010

<table>
<thead>
<tr>
<th>EVI Projects</th>
<th>Process Development</th>
<th>Preclinical Stage</th>
<th>PBE Technology transfer</th>
<th>GMP batch production</th>
<th>Preclinical Stage</th>
<th>Phase Ia</th>
<th>Phase Ib</th>
<th>Phase II</th>
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* EMVDA funded project
** EDCTP funded project

- Principles of operation:
  - Preclinical stage: Projects in this stage are not yet ready for human trials.
  - Clinical stage: Projects in this stage are ready for human trials.
  - Projects terminated: Projects are no longer under development.
  - Projects transferred: Projects have been transferred to other funding bodies.

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Vaccine R&D in Europe

Half of global industry R&D investment in Europe in 2008

<table>
<thead>
<tr>
<th>Region</th>
<th>2008 R&amp;D Investment</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Europe</td>
<td>€1,062 million</td>
<td>49,3%</td>
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<tr>
<td>North America</td>
<td>€462 million</td>
<td>22%</td>
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<tr>
<td>Asia (including Japan)</td>
<td>€262 million</td>
<td>1,3%</td>
</tr>
<tr>
<td>Others</td>
<td>€39 million</td>
<td>1,7%</td>
</tr>
</tbody>
</table>

Total R&D investment: €2,124 million

Half of global industry R&D sites are located in Europe in 2008

<table>
<thead>
<tr>
<th>R&amp;D sites*</th>
<th>Sites</th>
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<tbody>
<tr>
<td>Austria</td>
<td>2</td>
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<tr>
<td>Belgium</td>
<td>4</td>
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<tr>
<td>France</td>
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<td>Germany</td>
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<td>Hungary</td>
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<td>Italy</td>
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<td>Netherlands</td>
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<td>Switzerland</td>
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<td>U.K.</td>
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TOTAL Europe       | 22    |

<table>
<thead>
<tr>
<th>TOTAL outside Europe</th>
<th>21</th>
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<tbody>
<tr>
<td>USA</td>
<td>17</td>
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<td>Canada</td>
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<tr>
<td>Japan</td>
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</tbody>
</table>

Source: European Vaccine Manufacturers survey 2008
Public funding of vaccine R&D by Industry

*Funding of survey participants’ R&D projects
Source: EVM survey 2008
Why an European Vaccine Initiative?

• Infections are global
• Industry is global
• In Europe, National Vaccine Institutes disappear
• In Europe, public funding for Vaccine R&D has declined
• Governments increasingly dependent on private sector advice
European Vaccine Landscape

- Fragmentation of Public-funded Vaccine R&D in Europe:
  - Lack of common strategy and coordination in the public sector.
  - EU Member States Public sector provides limited countervailing power.
  - Too limited collaboration/cooperation with Private sector
Added value of a European Vaccine Initiative

- A focal point for vaccine development in Europe:
  - Federation of institutions/organisations involved in EU vaccine R&D
  - Network that provides knowledge based, development expertise and facilities that enable follow-up on an European vaccine agenda (EU research valorisation).
  - Network with other stakeholders, including in developing countries (e.g. DCVMN)
  - Synergy with Private sector
  - Focal point for Global collaboration
Priorities for Europe

• Malaria and other NTDs should be high on the research and development agenda in Europe
• To manage a globally established vaccine portfolio
• To foster European Efforts for a global impact
• To maintain and strengthen European Infrastructure
• To develop capacities in low income populations, including technology transfer supported by a fair and strong IP policy
EVI priorities

- Keeping the pipeline filled!
- Coordination
- Harmonisation
- Tech Transfer
- Training and education in vaccinology
Many thanks for your attention