EUROPEAN MALARIA VACCINE INITIATIVE

Progress Towards a Malaria Vaccine
A European Concerted Effort

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EDCTP Stakeholder Meeting, Copenhagen 31/01/2007
EMVI background

- Mid-1990s, INCO-DC Programme, invited international concerted action projects, and two concerted actions were approved,
  - AMVTN (now AMANET) &
  - VINCOMAL, (12 malaria vaccine research institutions/groups in Europe & 4 from Africa, Asia and South America).

- After 2 years concertation, VINCOMAL led to the establishment of the European Malaria Vaccine Initiative (EMVI).

- EMVI officially commenced operations in March 1998.
EMVI background

- EMVI is part of the European Community’s effort to combat poverty via improving the health of populations in resource-constrained countries, (EMVI is therefore directly contributing to what later became the Millennium Development Goals).

- The mandate given to EMVI by the European Commission was to provide:
  - A mechanism to facilitate concertation between a European Commission core activity and Union Member States’ investments, and
  - A mechanism to facilitate the process of bringing promising research results, i.e. Experimental malaria vaccines, via limited industrial production, to clinical evaluation in European volunteers, and subsequent clinical evaluation in Africa, in close collaboration with AMANET
EMVI mission

- To contribute to the global efforts to control malaria by:
  - providing a mechanism for accelerated development of malaria vaccines in Europe and Developing Countries
  - promoting affordability and accessibility of malaria vaccines in Developing Countries
EMVI is legally established at Statens Serum Institut (Copenhagen DK)

EMVI has set-up a

- Quality assurance system to ensure
  - Good Clinical Practices (GCP Directive 2001/20/CE)
  - Good Manufacturing Practices (appendix 13 Eudralex vol 4)
  - Good Laboratory Practices (WHO guidelines)
  - Good Statistical Practices (PSI guidelines)

EMVI acts as **Sponsor**, thus responsible and liable for

- Clinical Trials Insurance
EMVI is a partnership of 4 European Member States and receives public funds only, mostly for Development Aid agencies:
- Sweden (SIDA/SAREC)
- Ireland (Irish Aid)
- Danemark (DANIDA) and
- The Netherlands (DGIS)

EMVI is the coordinator of the EU Integrated Project – EMVDA- 5 year project

EMVI is the coordinator of a EU Specific Supported Action – EURHAVAC-
Organisation of EMVI Projects

Product development team
- Product Leader
- Quality Control
- Pharmaco-toxicology

EMVI
- Inventor
- Regulatory

Clinical development team
- Principal Investigator
- Clinical investigator
- Immunologist
- Monitor
- Data Manager
- Statistician
Project Organisation

- Each project team commonly
  - defines and
  - agrees on
  - project objectives,
  - responsibilities
  - planning
  - & deliverables

- EMVI
  - focal point and
  - project manager
EMVI portfolio

Projects in Clinical Development
Vaccine Development

Pharmaceutical development / vaccine production

Clinical development

Antigen Discovery Validation

cGMP Manufacture/Formulation

Toxicology Stability Potency

Industrial Scale Up

Europe

Phase 1 Safety/Immunogenicity

Europe

Phase 2a Human Challenge

Africa

Phase 1b

Africa

Phase 2b

Licensure
Vaccine Development

Pharmaceutical development / vaccine production

EMVI

ANTIGEN DISCOVERY VALIDATION
cGMP MANUFACTURE/FORMULATION
TOXICOLOGY STABILITY POTENCY
INDUSTRIAL SCALE UP

EUROPE
PHASE 1
SAFETY/
IMMUNOGENICITY

AFRICA
Phase Ib

EUROPE
Phase 2a
HUMAN CHALLENGE

AFRICA
Phase 2b

AFRICA
Phase 3

Clinical development

Licensure
EMVI partnerships

Clinical Networks
(ECRIN, EDCTP, AMANET…)

Industry & SMEs

International Organisations
(WHO…)

Malaria Vaccine Scientific Community

USA Stakeholders
(MVI, NIH, USAID…)

Donors Funders

EMVI
EMVI Partnership

- EMVI is part of the Malaria Vaccine Funders group, under IVR WHO umbrella
- Several Memoranda of Understanding or of Intent (USAID, MVI, WHO)
- EMVI took part in the malaria vaccine technology road map
Levels of collaboration

- Separate programming and resourcing, post facto reporting with emphasis on exchange of information.
- Separate programming and resourcing, early coordination of effort and enhanced collaboration on: seminars/workshops, mutual representation, exchange and discussion of pre-clinical and clinical trial results, design of clinical trials, especially in malaria endemic areas and connected training.
- Joint programming, separate resourcing with enhanced co-ordination of: strategic planning, work planning, reviews.
- Joint programming, pooled resourcing with enhanced co-ordination of funding.

Specific collaborations with other stakeholders (like immuno-assay standardisation, comparison of immune results in clinical trial – eg. AMA1)
Adults 18-40 yrs

- Phase Ia ≠ Adjuvants ≠ dosages
- Phase Ib 1 formulation
- Phase IIa 1 formulation

Clinical Plan Strategy
Paris Workshop 2004

Toddlers 1-2 yrs

- Phase Ib 1 formulation
- Phase IIb dose-ranging
- No go

Infants 2-12 mos

- Phase Ib 1 formulation
- Phase IIb 1 formulation
- Phase III
  - Efficacy
  - Lot consistency
  - Large-scale efficacy

- Boosting
- Interactions

E.M.V.I.
Clinical Plan Strategy

**Adults 18-40 yrs**

1. Phase Ia
   - ≠ Adjuvants
   - ≠ dosages

2. Phase Ib
   - 1 formulation

3. Phase IIa
   - 1 formulation

**Toddlers 1-2 yrs**

- Phase Ib
  - 1 formulation

**E.M.V.I.**

NO GO: one of the following:

- Safety stopping rules: *Any SAE related to vaccination* or *50% subjects had Grade 3 ARs persisting at Grade 3 for > 48 hours during the 14 follow-up days*

- Immunogenicity stopping rules: < 60% seroconversion or AB not recognizing native parasite protein in IFA or AB non functional (validated assay)

**AMANET**

NO GO: Safety stopping rules: *Any SAE related to vaccination* or *50% subjects had Grade 3 ARs persisting at Grade 3 for > 48 hours during the 14 follow-up days*
EMVI Completed Trials

- Phase 1a trials of GLURP (LSP) – Nimegen – Accepted for publication Vaccine
- Phase 1b trials of MSP3 (LSP) – Burkina Faso 2003 – 2004 - Submitted
### Planned Clinical Trials 2006 – 2007 (AMANET)

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Conclusions

- EMVI’s niche focuses on a bottom-up approach, facilitating the demonstration and validation of malaria vaccine candidates in close collaboration with inventors and scientists,

- To properly address the pipeline concept, EMVI is developing privileged partnership(s) with the other actors in the field
Many Thanks for your attention

Very warm and special thanks to Dr Soren Jepsen.

His visionary approach has been instrumental in the development and the success of EMVI, raising the awareness of the malaria disease and vaccines in the world, and he is the best advocate for mobilising resources to fight malaria and other PRD