



## Malaria Vaccines For Africa, Experience Of AMANET R&D



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# Objectives



- To give a snapshot of activities within the AMANET malaria vaccine portfolio
- Highlight on current portfolio & clinical development plans
- Experiences in sponsoring clinical trials by an African Organisation.
- Lessons from characterization ➡ evaluation sites development ➡ actual vaccine trials.



# AMANET



- Not for profit organization founded 2002 (Previously as AMVTN)
- Mission: To promote capacity strengthening of African Malaria Research Institutions
- key objective: clinical development of candidate malaria vaccines through sponsorship of clinical trials in Africa
- Competing for publicly available grants, providing sub-grants for capacity development & preparing sites for vaccine trials.



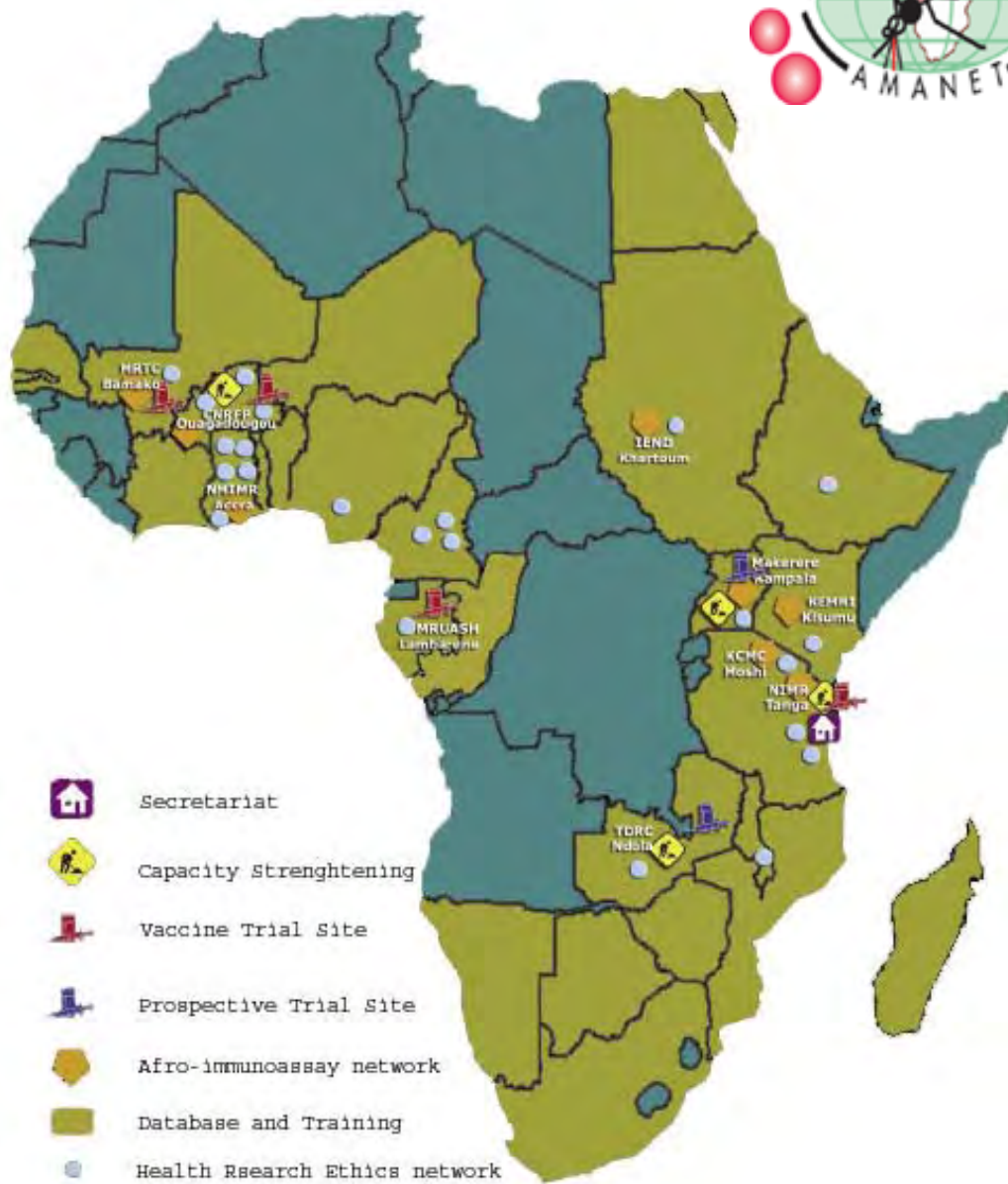
## Holistic approach

□ 3 potential malaria vaccines undergoing field testing (AMA1, MSP3 & GMZ2)

□ 20 EC's are being supported

□ 8 African sites have been included into the AIA

□ Training – beyond the network sites



- Secretariat
- Capacity Strengthening
- Vaccine Trial Site
- Prospective Trial Site
- Afro-immunoassay network
- Database and Training
- Health Research Ethics network



E D C T P

# Sites & Products Development



DECISION MAKING GUIDELINES  
FOR AMANET CLINICAL DEVELOPMENT OF CANDIDATE  
MALARIA VACCINES

Funding

• Competitive Grants



Site selection

- Call for Lol – testing field sites
- Site assessment of selection

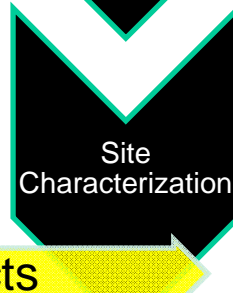


Capacity Strengthening

- Infrastructure, long and short term trainings & Standards
- Parallel supporting structures (Ethics Committees, DSMBs)

Product Search

• Call for products



Site Characterization

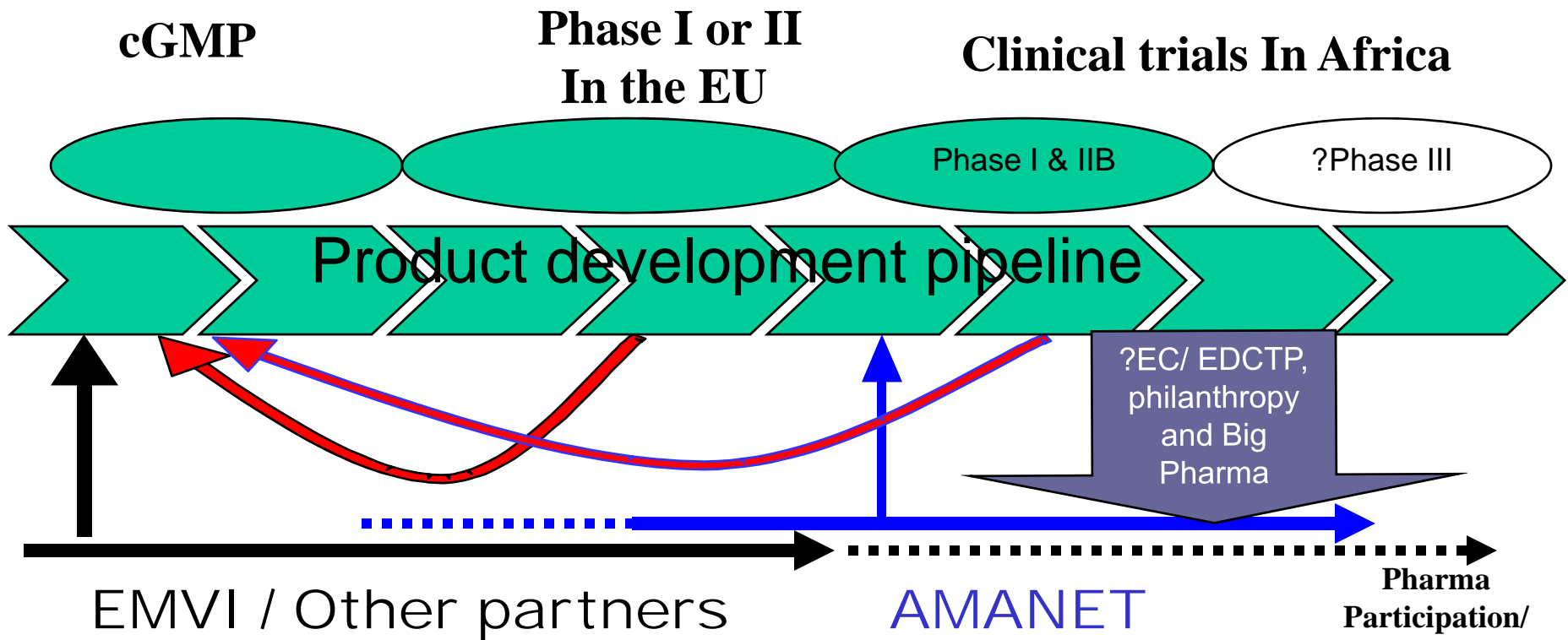
- Site assessment
- local community acceptance
- baseline malarionometric indices



Clinical Trials

- Phase Ib trials
- Phase IIb trials

# AMANET-EMVI Seamless Malaria vaccine Strategy



Pre-clinical development  
GMP production of clinical batches  
Early clinical development  
Sponsor phase I-IIa studies

Trial sites in Africa  
Human resource/equipment  
Strengthen capacity for trials  
Sponsor phase I-IIb studies  
Proof of concept



# MSP 3 – Vaccine

## [181-276] LSP



The merozoite surface © Borre M  
*et al*

### Sequence of the peptide (N to C-term)

RKTKEYAEKA KNAYEKAKNA  
YQKANQAVLK AKEASSYDYI  
LGWEFGGGVP EHKKEENMLS  
HLYVSSKDKE NISKENDDV  
L DEKEEEAEET EEEEE

Encompasses at least one B-cell epitope (MSP3-b peptide) which is the target of major protective immune responses for the human immune system and three T-cell epitopes (MSP3-a, b, c peptides).

Expressed in asexual stage

2 completed phase Ib trials 1-2 year olds in Burkina Faso and Tanzania

Ongoing phase IIb trial in Soutouba, Mali

Tested to over 500 children in Africa so far

Positive preliminary results from Burkina Faso and Tanga

Good tolerance in 1-2 yrs old with satisfactory safety profile at 2 dosages

Good immunogenicity, predominant cytophilic Abs (IgG1 & IgG3), little to none of the remaining classes; **titres rise 20-30 folds reaching protected adult levels**; strong seroconversion @ each Antigenic doses

Clinical malaria incidence from phase Ib's indicates desired effect, to be confirmed with phase IIb in Mali



# AMA 1 Vaccine

(PfAMA-1-FVO[25-545])



Expressed in asexual stage

Critical role on erythrocyte invasion

High prevalence of antibodies in endemic populations

Immune responses increase with age

Acquired antibodies inhibit P.F growth in vitro (dose dependant manner)

Degree of Allele specificity of anti-AMA1

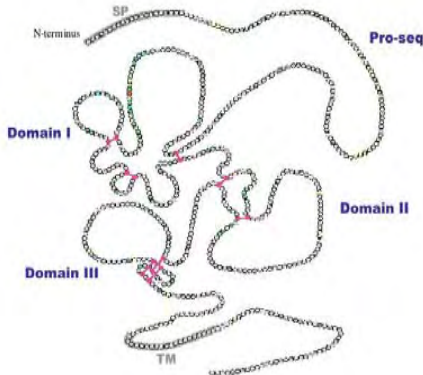
But high degree of polymorphisms in Mali [Most common haplotype 3D7; but this is only about 10% in Bandiagara]

Better immunogenicity with CPG adjuvant than Alum

Phase Ib interim results confirmed safety; immunogenicity results yet to be finalised

Current Formulation discontinued.

Reformulation work at BPRC

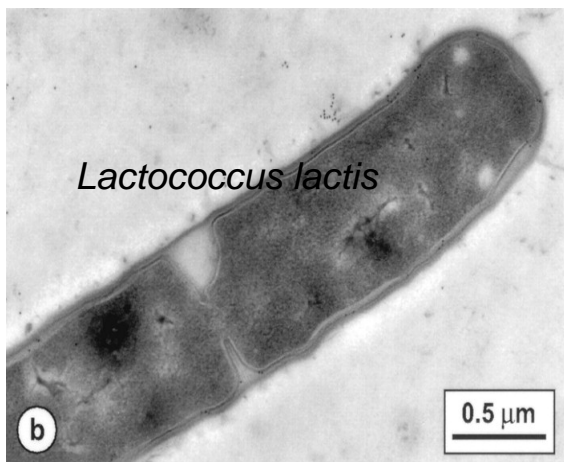




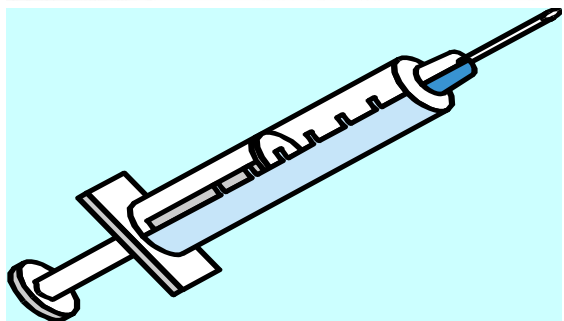
Medical Research Council



# GMZ 2 Vaccine [GLURP<sub>25-514</sub> and MSP3<sub>212-380</sub>]



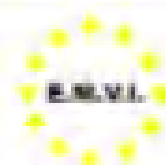
- Recombinant hybrid protein [GLURP and MSP3 ]
- Expressed in *L. lactis* expression system.
- Safe in humans as G/positives do not produce endotoxins
- GMZ2 100µg selected for trials in Africa;
- Ib adult trial shows safety.



Pre-filled syringes for EPI

## GMZ2 Consortium

- Funded by the **EDCTP**
- Cofounding from 2 member states
- Phase Ib paediatric ongoing
- Baseline study (Gabon, The Gambia, Burkina Faso and Uganda)
- Phase IIb study to start 2<sup>nd</sup> quarter 2010

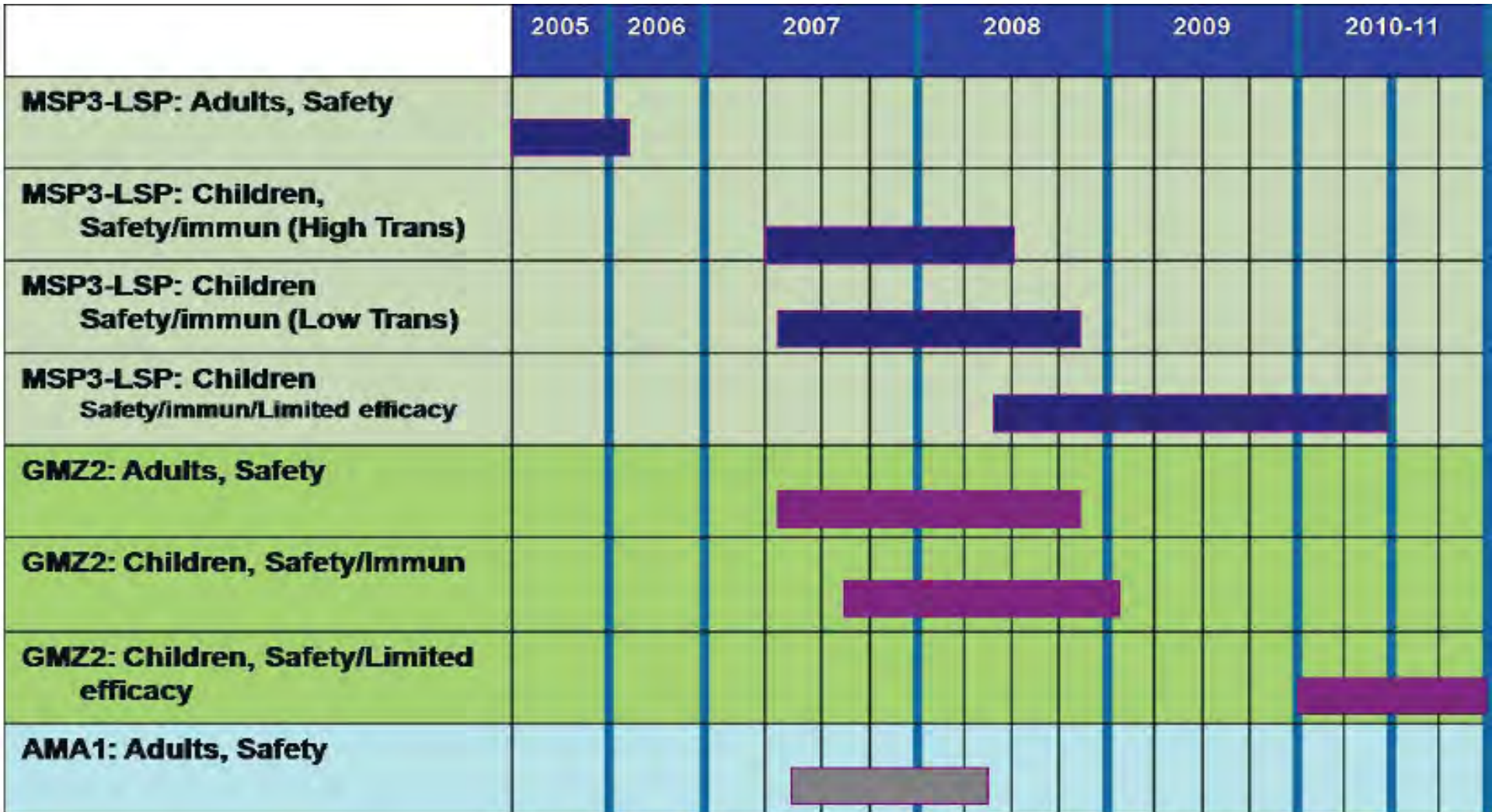




# Field trials



## AMANET Vaccine Trial Matrices





# Challenges



- Speed of developing a site in Africa quite multi-factorial:  
(internal socio-political centre environment, local leadership, existing infrastructure +/- external collaborators)
- Sites easily stretched (professional training & mass dev. of clinical trialist - critical)
- Hidden costs e.g. new clinical batches & product reformulations costs etc
- Decreasing Malaria transmission
- Supporting capacities e.g. Evolving ECs/ RAs, CRAs, CROs, Insurance & Indemnity rarely existed in Africa before
- Support between trials/grants



# Future perspectives



- Increased research: potentially, at least 10 separate clinical trials envisioned within next 5 years
- As supported sites get stronger – attract further funding/collaborators
- Need to move to creation of new sites, meanwhile continue to include the supported sites in other initiatives
- Expansion of operationally able sites for Clinical trials
- Complementing collaborations in Africa



# Conclusion



- AMANET has successfully demonstrated capacity of the pan African network in;
  - supporting previously weak institutions to develop and be able to conduct vaccine trials at required international standards.
  - taking the role of sponsorship of GCP trials and effectively accelerate development of malaria vaccines
- N-S Networking is absolutely essential  
(inputs required from northern & southern researchers, African research participants, African Governments, donor agencies, NGOs, private sector -all of which is indispensable)
- In between grants or trials support needs funders consideration



# Acknowledgements



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