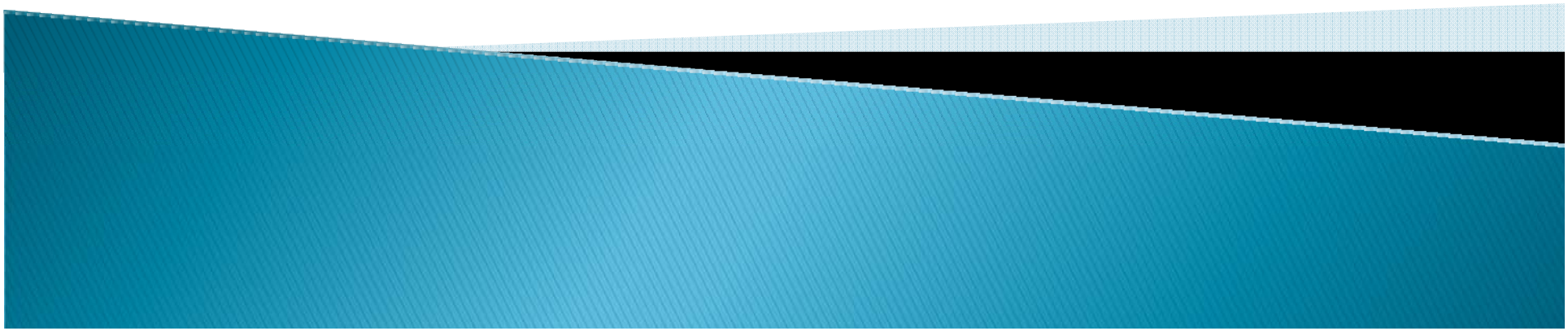
Challenges of ethical and regulatory review for malaria vaccine trials in Africa

Clinical Trials Coordinator
African Malaria Network Trust
Dar es Salaam, Tanzania

Roma Chilengi
Oxford/KEMRI-Wellcome Trust
Clinical Trials Facility
Kilifi, Kenya



Discourse

- Background –R & D in general
- Background – AMANET
- Relevant AMANET work
- General thoughts about malaria vaccines
- Status review of related ECs & RAs
- General ethical challenges
- General regulatory authority challenges
- Potentially progressive strategies

Increased Research Activities

- Increased advocacy and awareness on diseases of poverty
- Increased funding for R&D on the diseases
- Increased “non traditional” players and partnerships emerging
- Increased research activities in the field
- Increased pressure on Ethical and Regulatory mechanisms

AMANET Work

- African NGO in supporting capacity development and malaria R&D
- Based in Tanzania, access to global expertise
- Accelerating malaria vaccine development

- Support to potential trial site
- Continent wide training in research related fields
- Supports the Afroimmunoassay network of 8 sites
- Six clinical trials evaluating candidate malaria vaccines

AMANET Sponsored Studies

- Phase Ib trial of AMA1vaccine in Bandiagara, Mali (adults)
- Phase Ib trial of MSP3 vaccine in Balonghin, Burkina Faso (children 1-2 years)
- Phase Ib trial of MSP3 in Korogwe, Tanzania (children 1-2 years)
- Phase Ib trial of GMZ2 in Lambarene, Gabon (adults)
- Phase Ib trial of GMZ2 in Lambarene Gabon (Children 1-4 years)
- Phase Ib trial of MSP3vaccine in Sotouba, Mali (adults)

Afroimmunoassay network studies in Burkina Faso, Ghana, Kenya, Mali, Sudan, Tanzania, & Uganda

Malaria Vaccine Special Issues

- Malaria is a fatal disease affecting mainly poor communities
- It is a chronic disease whose natural immunity develops after repeated exposure
- Immunity to malaria is known to be temporal (unlike many immunizable diseases)
- Vaccine efforts targeting children
- Unlikely to be developed and registered the “traditional way” (in developed countries first)
- Has to be given to healthy individuals

Clinical Trial Process Experiences

Ethical Review

- Framework:
  - Existing in all cases
- Requirements:
  - Mostly standardized based on WHO guideline
- Time required:
  - Widely varied from 1 month to 4 months
- Feedbacks/interactions:
  - Ranges from "ICH GCP" acceptable to totally unacceptable"
- Oversight:
  - None so far

Regulatory CTA Review

- Frameworks:
  - From non existent to fairly good ones
- Requirements:
  - From non existent to nearly "too rigid" ones.
- Time required:
  - Widely varied from 1 month to 8 months
- Feedbacks/interactions:
  - Ranges from "ICH GCP" acceptable to totally unacceptable"
- Safety Follow Up:
  - Note clear how SAE reports, and other requirements are handled

General Challenges- Ethical

- National Legal Frameworks:
  - Rudimentary in most cases. Exists from research driven demand and not firmly rooted in the local structures
- Capacity:
  - Largely weak as reflected in the composition, procedures and kind of feedback on trials
- Written informed consent $\neq$ ethical study
  - Due diligence ought to be demonstrated to show that fundamental ethical principles are respected
- Parental consent versus participant Ascent:
  - Difficult to resolve especially when older children participate
- Eventual delivery in poor health systems:
  - There are potential problems related to cost, maintenance of cold-chain, human resources etc to deliver even the most effective vaccine.

General Challenges- Regulatory

- Still uncertain what regulatory pathway a vaccine for malaria should take:
  - Licensure in non formalized ICH regions
  - Mechanism for registration
  - Acceptability & marketing authorization across "colonial lines"
  - Ensuring pharmacovigilance for new vaccines with potential of wide spread sole use in developing world
- Implementation and enforcing of GCP
- Human resources needed to handle IND applications in Africa

Progressive Strategies

- African governments involvement:
  - Need for investment of resources by Africa
  - Need for practical legislature
  - Health systems improvement

- Coordinated efforts:
  - Share expertise i.e. ongoing joint RA review for phase III RTS,S
  - Involvement of WHO
  - Support to efforts like AVAREF
  - Coordination of capacity development efforts i.e. AMANET interaction with SIDCER for ethics committees

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