WHO Consultation: Beyond Phase 1 trials, what could be the clinical and regulatory pathway for Ebola vaccines? Objectives and key design elements for Phase 2 and 3 trials of Ebola vaccines.

**Background:**

Given the public health need for safe and effective Ebola interventions, it is WHO’s assessment that the expedited evaluation of all Ebola vaccines with clinical grade material is a public health priority in the framework of the WHO Ebola emergency response. Two candidate vaccines have clinical grade vials available for Phase 1 pre-licensure clinical trials. These vaccines are cAd3-ZEBOV (GSK/NIAID) and rVSV-ZEBOV(Newlink/PHAC). WHO and other partners have engaged in facilitating expedited evaluation of these vaccines in order to generate Phase 1 safety and immunogenicity data for decision-making. A series of coordinated Phase 1 trials are currently ongoing or will soon be initiated with international consortia to ensure good communication and harmonization of key design elements to allow for merging of data from different trials of the same product.

**Parallel pathways for experimental use and Phase 2 and 3 trials of Ebola candidate vaccines**

- **GMP-grade vaccine**
  - **Phase 1 safety and dose selection based on immune take, and further vaccine available**
  - **Data are expected at end Dec 2014**
  - **Offer pre-exposure under informed consent to frontline HCW based on risk**
  - Need to ensure data collection as recommended by WHO ethics consultation on August 11, 2014.

- **Phase 2 trials:**
  - Design to benefit from outcomes of this consultation: an adequate Phase 2 safety database will be required for each vaccine for possible licensure package as per selected regulatory pathway.

- **Phase 3 efficacy trials in affected countries; ethical designs considerations**
The **key outcomes** expected from the meeting are as follows:
- identification of questions to be addressed through additional Phase 1 trials (e.g. special populations)
- consensus on clinical designs and regulatory pathways that would support licensure and use in affected areas, and
- consensus on the strategy for emergency use under informed consent in front-line workers
- outline of potential population to include in broader vaccination campaigns
- consensus on data for decision-making on large scale manufacturing.

Following the meeting: agreement on key elements in discussions with regulators and ethics committee representatives at the AVAREF meeting Nov 3-7 in South Africa

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**Agenda**

**Monday 29 September**

**08:00-09:00**  *Registration*

**Session Chair:** Fred Binka

**09:00-09:10**  Welcome remarks. Marie-Paule Kieny

**09:10-09:30**  Overview of vaccine development pathway: Marie-Paule Kieny

**09:30–10:00**  Overview and key scientific questions- cAd3 Consortium perspective: Barney Graham, VRC

**10:00-10:30**  Overview and key scientific questions- VSV Consortium perspective: Nelson Michael, WRAIR

**10:30-11:00**  *Coffee*

**11:00-12:00**  Data needs from Phase 1 prior to or in parallel with Phase 2: Discussion co-chaired by Maxime Agnandji, Mahamadou Thera. Comments by Claire-Anne Siegrist, Blaise Genton, and other participants

- Safety
- Immunogenicity
- Dose selection
- Special populations (in parallel with Phase 2)

**12:00-12:45**  *Lunch (sandwiches will be served outside the conference room)*

**12:45-13:30**  Situation update, what has changed in the last month, projections: Chris Dye

Initial discussion on potential vaccine(s) role in curbing the current epidemic.

**Session Chair:** Samba Sow

**13:30-14:30**  Proposal for Phase 2 trials - to develop data package for licensure.

- Manufacturers perspective (GSK, Newlink)
- Investigators perspective: Kader Konde, Fred Binka

**14:30 – 15:10**  Ethics perspective on proposed emergency use of vaccine in affected countries in parallel with Phase 2 clinical trials: Michael Selgelid.
15:10-15:30  EMA perspective on regulatory pathways for Ebola vaccines during the current outbreak: Marco Cavaleri

15:30-16:00  Coffee

16:00-16:20  FDA perspective on regulatory pathways for Ebola vaccines during the current outbreak: Theresa Finn

16:20-16:40  Overview of regulatory perspective from AVAREF representative: Eric Karikari Boateng, Ghana NRA

16:40-17:00  Discussion and Wrap up of day 1

18:30  Cocktail reception

Tuesday 30 September

Session Chair: Brian Greenwood

0900-10:00  Phase 2 trials design: structured discussion led by Brian Greenwood

1. Who to enrol?
   • Health care workers?
   • Which age range?
   • Pregnant women
   • Immunocompromised
   • Other considerations
2. What is must-have vs nice-to-have with regard to immunogenicity?
3. Durability/boostability
4. Communication strategy

10:00-10:30  The design and analysis of Phase 2b Ebola vaccine trials: Ira Longini (15 min plus discussion)

10:30-11:00  Coffee

11:00-11:30  Methodological approaches to generation of safety and efficacy/effectiveness data under emergency use conditions-with informed consent- in frontline workers in affected countries: Matthias Egger.

11:30-12:00  Development of operational plan for emergency use -under informed consent-in affected countries once Phase 1 safety data is available: Alejandro Costa

12:00-12:30  Discussion on emergency use
   1. Informed consent
   2. Data collection, what will be feasible?
   3. Allocation with limited supply

12:30-14:00  Lunch
14:00-14:15  Post-licensure-Possible designs for further vaccine assessment: Peter Smith

14:15-14:30  Potential impact of large-scale implementation of Ebola vaccines: John Edmunds

14:30-15:00  Key target groups for vaccination outside clinical trials - considerations for 500 doses, 3,000 doses, 15,000 doses, 100,000 doses and millions of doses available. Mike Levine
  • Health care workers (definition?)
  • Others at high risk pre-exposure
  • Contacts of cases
  • Ring vaccination
  • Vaccination of communities affected

15:00-15:30  Discussion

15:30-16:00  Coffee

16:00-17:00  Walking backwards: what information would be needed, and when, to take full advantage of Ebola vaccines in the current epidemic? Structured discussion

17:00-17:30  Wrap up, next steps.