

## Workshop “Efficacy trials of ZIKV Vaccines: endpoints, trial design, site selection”

June 1-2, 2017

Hotel Royal Manotel, Geneva

### Final Agenda

#### Proposed objectives:

To discuss detailed points for consideration to move forward the evaluation of Zika candidate vaccines to Phase 3 efficacy trials.

#### Expected outputs:

- Outline of suitable primary, secondary and exploratory endpoints.
- Outline on trial designs that can be used (including alternative designs with immunological endpoints)
- Considerations for identification of suitable sites for trials
- Identification of key research gaps to inform efficacy evaluation and product development.

**Meeting Chair: Peter Smith**

#### Day 1- June 1, 2017

Time	Title	Proposed presenter
9:00	Introduction and objectives of the meeting (15 min)	AM Henao-Restrepo
9:15	<b>Part I Context</b>  Bringing Zika vaccines to licensure – Zika vaccine and study designs (15 min)  WHO/UNICEF Zika Vaccine TPP and vaccine landscape (15 min)  A review of conclusions from prior Zika vaccine consultations – (15 min)  What do we know (or don't know) about Zika incidence and geographic spread that is critical for planning vaccine trials? (15 mins)  What are the lessons learned from evaluating other flavivirus vaccines in the field that are relevant to Zika ? (15 min)  <b>Points of Discussion</b> (20 min) - What are some implications of Zika epidemiology and pathogenesis on trial design and endpoints selection? - How should Zika efficacy trials be designed differently in light of the experience with dengue efficacy trials?	I. Longini  K. Vannice  J. Hombach  L. Rodrigues  L. Villar

Time	Title	Proposed presenter
	<p>- When will we have clinical data to inform whether there are dengue/Zika interactions? What are the key data that should be collected in the context of an efficacy trials?</p> <p>- What are the key research gaps that limit our ability to plan and design efficacy trials? Are there studies ongoing that will inform the discussion and when will they be available?</p>	
10:50	Coffee break	
11:10	<p>WHO Blueprint - Overview of options in design for current and future Zika Vaccine Trials (40 mins)</p> <ul style="list-style-type: none"> <li>Target population, end point selection, comparator, randomization unit</li> </ul>	Plenary discussion Introduction by R. Eggo
11:50	<p><b>Part II – Considerations for immunological endpoints in trials of Zika vaccines</b></p> <p>Implications of Zika PCR and serological tests for clinical and immunological endpoints selections (15 min)</p> <p>The role of prior flavi-immunity on Zika infection: what are the implications on trial design? (15 min)</p> <p>Dengue experience to establish a CoP. (15 min)</p> <p>Points of Discussion (35 min):</p> <p>What are the best approaches to establish prior infection with Zika and other Flaviviruses to inform trial results?</p> <p>What are the most likely approaches to inform serological endpoints and what value do we give them ?</p> <p>What are the prospects to differentiate vaccine induce immunity and post vaccination infections?</p> <p>How do we minimize cross-reactivity in measuring immunological endpoints?</p> <p>How do we interpret immunogenicity in the context of pre-existing flavivirus immunity?</p>	<p>M. Fischer</p> <p>E. Harris</p> <p>S. Thomas</p>
13:10	<b>Lunch- break</b>	
14:10	<p><b>Part III – Considerations for clinical endpoints in trials of Zika vaccines</b></p> <p>What are the options for efficacy endpoints? – (15 min)</p>	S. Thomas

<b>Time</b>	<b>Title</b>	<b>Proposed presenter</b>
	<p>How can definitions and data from surveillance clinical case definitions for Zika illness, complications and manifestations help inform trial designs ? (15 min)</p> <p>Points of Discussion (20 min)</p> <p>Are there any challenges in using current case definitions in vaccine trials?</p> <p>What clinical endpoints are ‘best suited’ for vaccine trials?</p> <p>What endpoints are the most informative? The most feasible? What should be the primary endpoint? Secondary/exploratory endpoints?</p>	T. Jaenisch
	<b>Coffee-break</b>	
15:00	<p><b>WHO Blueprint - Considerations for Zika Vaccine Efficacy Trial Design (cont)</b> (60 min)</p> <p>Other key questions to inform design decisions:</p> <ul style="list-style-type: none"> <li>• Designing a trial in an epidemic vs endemic state</li> <li>• Perspectives of testing several vaccines at the same time</li> <li>• Accumulating evidence across sites/outbreaks/trials</li> <li>• Framework for a preselection of most promising candidates</li> </ul>	Plenary discussion facilitated by E. Halloran
16:00	<b>Summing up on consensus reached today</b>	Plenary discussion
17:30	<b>Cocktail</b>	

## Day 2- June 2, 2017

Time	Title	Proposed presenter
09:00	<b>Part V – Alternative Studies and endpoints</b>  What is the role of a human challenge model in vaccine evaluation ? (15 min)  What is the role of animal models in studying protective titres and the need for establishing surrogates/correlates of protection ? (15 min)  What are the options to develop correlates and surrogates? (15 min)  Points of Discussion (45 min)  If surrogates or correlates are used, what are the implications for study designs?	A. Durbin  A. Barrett  K. Modjarrad
10:30	Coffee-break	
11:00	<b>Part IV - Site Selection</b>  Zika projections in 2017 and the future – Potential for site selection (15 min)	A. Vespignani
11:15	Points for discussion (45 mins) <ul style="list-style-type: none"> <li>• Rationale for trial sites selection</li> <li>• Will transmission behaves differently in other continents ? Implications for trials ?</li> <li>• Pathogenesis/Epidemiological data needed to inform models in the future</li> <li>• Possibility of planning trials for future transmission waves</li> <li>• Responsiveness of trial designs</li> </ul>	Plenary
12:00	Lunch Break	
13:00	Protocol for multi-candidate vaccine efficacy trial (10 min + 5 min questions)	B. Walker
13:15	<b>Revisit generic protocol elements for Phase 2b or 3</b> <ul style="list-style-type: none"> <li>- Study design</li> <li>- Study endpoints</li> <li>- Study procedure and schedule</li> </ul>	Plenary
15:00	Coffee break	
15:30	<b>Next Steps –</b>	
16:00	<b>Closure</b>	

