

## JCG Nipah Meeting Summary

### Singapore

### December 11, 2019

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#### Attendees (Alphabetical by Last Name)

- Peggy Hamburg (JCG Chair)
- Vernon Lee (JCG Co-Chair, Ministry of Health, Singapore)

#### Member Institutions Represented By

- Ana Maria Henao Restrepo (WHO)
- Robin Levis (FDA)
- Isabelle Bekerredjian-Ding (PEI for EMA)
- Diadie Maiga (WHO/AVAREF)
- Robin Nandy (UNICEF)
- Aurelia Nguyen (GAVI)
- Mark Page (NIBSC)
- Marie-Pierre Preziosi (WHO)

#### Working Groups Represented By

- Daniel Brasseur (Regulatory WG)
- Francois-Xavier Lery (Assays and Standards WG)

#### Vaccine Developers

- Hilde Depraetere (EVI)
- Sarah Gilbert (Janssen/Oxford)
- Gray Heppner (PHV/Crozet BioPharma)
- Chieko Kai (University of Tokyo)
- Abdi Naficy (PATH)
- Rong Xu (Profectus Biosciences)

#### Nipah Affected Country Representatives

- S. Eswara Reddy (India)
- Mandvi Bharadwaj (Australia)
- Tarun Bhatnagar (India)
- Raul Destura (Philippines)
- Meerjady Sabrina Flora (Bangladesh)
- John Lim (Singapore)
- Hui Ming Chua (Malaysia)
- Carmencita Padilla (Philippines)

- Anuradha Poonepalli (Singapore)
- Md. Mahbubur Rahman (Bangladesh)
- Linfa Wang (Singapore)
- K. Zaman (Bangladesh)

#### CEPI Secretariat

- Jakob Cramer
- Richard Hatchett
- Frederik Kristensen
- Paul Kristiansen
- Nicole Lurie
- Dawn O'Connell
- Melanie Saville
- Nadia Tornieporth
- Debra Yeskey

#### Observers

Svein Rune Andersen (CEPI)  
Robert Chen (Brighton Collaboration)  
Elen Hoeg (CEPI)  
Arun Kumar (CEPI)  
Yee Sin Leo (Singapore)  
Giada Mattiuzzo (NIBSC)  
Shannon Quinlan (CEPI)  
Mahmudur Rahman (Bangladesh)  
Raul Gomez Roman (CEPI)

## Participants

The meeting was co-chaired by Peggy Hamburg, JCG Chair, and Vernon Lee, Director of Communicable Diseases, Ministry of Health, Singapore. The meeting followed a 2-day scientific conference on Nipah, and much of the agenda was focused on Nipah vaccines.

## JCG Ongoing Work

### CEPI's proposed new endpoints:

Richard Hatchett, CEPI CEO, discussed plans for CEPI's evolution. Originally CEPI committed to developing its vaccines through Phase 2a during its first 5 years, but CEPI is now hearing from stakeholders about the need to take some vaccines through licensure. As a result, CEPI is contemplating extending that commitment from Phase 2a to licensure during its second five years.

### Regulatory Steering Committee:

Daniel Brasseur, Chair of the JCG Regulatory Steering Committee and Svein Rune Anderson, CEPI's Head of Regulatory--Europe, updated the group on the work of the Regulatory Steering Committee. CEPI will sponsor a workshop on regulatory lessons from animal and human vaccine trials in March, with a goal of identifying potential for regulatory innovation around vaccine platforms. Subsequent discussion (see below) focused on forming a region-wide regulatory work group to address anticipated issues related to regulation of Nipah vaccines and their use.

### Response Plan:

Nicki Lurie, Strategic Advisor to the CEPI CEO, and Richard Hatchett described CEPI's outbreak response planning both inside the CEPI Secretariat and with the broader eco-system. They requested that the JCG reactivate the Stockpiling Work Group to recommend a governance system and standard operating procedures for use of investigational vaccines that CEPI will maintain in reserve (stockpile). They requested that WHO chair such a group, which the CEPI Secretariat would staff. There was broad endorsement of the need for such a governance and decision-making system to be agreed to in advance of an outbreak.

- **OUTCOME:** JCG will re-form the Stockpiling Working Group to focus on governance and use of stockpiled investigational vaccines. WHO will be asked to chair the group, with CEPI providing support staffing.
- **NEXT STEPS:** A 6-month timeframe for completion of the work was proposed. CEPI will draft and circulate Terms of Reference for the group to review and edit by January 6, 2020.

### Sustainable Manufacturing Working Group:

Melanie Saville, head of CEPI Vaccine R&D, updated the group on the current efforts of the JCG Sustainable Manufacturing Working Group, which already engages JCG members, particularly GAVI, WHO and UNICEF.

- **OUTCOME:** The Sustainable Manufacturing Work Group will convene relevant JCG Members to obtain additional input regarding the work around predicting needed supply and identifying capacity for manufacturing. Estimated time frame, March 2020.
- **NEXT STEPS:** CEPI will continue to reach out to relevant JCG partners (GAVI, UNICEF, MSF, WHO) to get input on outstanding questions.

### Assays and Standards Working Group:

Francois-Xavier Lery of WHO and Paul Kristiansen of CEPI, reviewed ongoing work and progress made by the Assays and Standards Working Groups and discussed plans and timelines for developing a Nipah standard.

## NIPAH: Foundational Overview

Linfu Wang, Scientific Co-Chair of the Nipah@20 Conference, summarized issues discussed at the scientific conference, and Melanie Saville provided an overview of the 4 candidates in CEPI's Nipah vaccine portfolio and the expected timelines for development. [See slides.].

## NIPAH: Endemic-Country Expectations for Phase 1 and Phase 2 Clinical Trials and Additional Regulatory Issues

The first part of the discussion was facilitated by K Zaman of icddr, Meerjady Sabrina Flora of Bangladesh's Institute of Epidemiology, Disease Control and Research, and Jakob Cramer, Head of Clinical for CEPI's Vaccine R&D office. The second part was facilitated by John Lim, head of Centre of Regulatory Excellence in Singapore, and Debra Yeskey, CEPI's head of Regulatory Affairs for North America. K Zaman reviewed the process for starting clinical trials in Bangladesh [see slides]. A number of issues were discussed:

- Currently, most of CEPI's Nipah vaccine developers are planning to conduct their clinical trials in Bangladesh. To which Tarun Bhatnagar of India's Council on Medical Research, offered that ICMR has significant experience doing Phase 1/Phase 2 studies in India as well.
- Participants called attention to a presentation at the Nipah@20 Scientific Conference, indicating that with current Nipah epidemiology, it would take over 500 years to conduct an individual randomized controlled trial, so developers and regulators will need to consider the kinds of data that otherwise would be needed for emergency use in an outbreak.
- Whether regulators in a given country would accept data from Phase 1 and Phase 2 trials conducted in another country was discussed. S. Eswara Reddy of India's Regulatory agency said India would perform a gap analysis to determine if additional clinical data would be needed before moving forward with emergency use in India.
- Carmencita Padilla Chancellor of the University of Philippines Manila observed that both the Philippines and Thailand, which have never had Nipah outbreaks, could benefit from the training of their PI's by countries like India and Bangladesh who have had outbreaks.
- Robin Levis of US FDA raised the issue of using an animal model to license Nipah products and asked what data would be required for a post-licensure commitment. Since there is no animal rule in the impacted-countries, it was suggested that this might be an issue a Nipah-focused regulatory working group could take on
- Regardless of where clinical trials take place CEPI's vaccines will be made accessible to all impacted countries should an outbreak occur—not just those countries in which the trials took place. However, the country regulatory agency will need to authorize their use.
- Hence, a framework for data sharing across the impacted countries will be needed, as was discussed at a regulatory roundtable meeting of Nipah-impacted countries the day before. Robin Levis, of US FDA offered FDA and the EMA would like to support that work.
- The group discussed the concept of forming an AVAREF-like arrangement for joint review and data sharing across the Nipah-impacted countries. Since the countries occupy different regions in the WHO construct (ASEAN and SEARO)—there would not be a regional designation to the working group, rather a "Nipah-Impacted" designation. In addition, the group would only focus on Nipah issues and not try to branch out into other pathogens at this time.
- **OUTCOME:** The Nipah-impacted country regulators as well as WHO and FDA agreed to establish a Nipah-focused regulatory working group to facilitate data sharing and joint review of Nipah vaccine candidates. It was agreed that the regional working

group would: (1) be Nipah-product specific; (2) use WHO's AVAREF model; (3) be initially coordinated by CEPI staff; (4) FDA/EMA will support along the way.

- NEXT STEPS: The CEPI regulatory team will convene a conference call in 3 months and an in-person meeting in 6 months to advance the organization and development of this Nipah regulators group. Ideally, this group would develop the capability to harmonize workflows; establish ways to communicate/collaborate; decide when special populations should be brought into clinical studies; create a framework for clinical trial protocols and how to address animal models; and emerging science.

## NIPAH: Special Populations

Robin Nandy of UNICEF and Tarun Bhatnagar of India's Council of Medical Research led this discussion, which was framed in terms of providing equitable access to our Nipah vaccines and the harm of excluding vulnerable populations during an outbreak. It was noted that pregnant women are more likely to die from Nipah than others. The data does not suggest a difference in Nipah impact, however, across age groups in outbreak conditions. So pregnant women became the focus of the JCG discussion. There was an unspoken acknowledgement that thinking on this issue has evolved in recent years to lean in favor of including special populations in outbreak response efforts under expanded access programs. Several meeting participants said to otherwise exclude vulnerable populations would be discriminatory, but there was not agreement about when in the development process pregnancy-related issues should be addressed.

- OUTCOME: The newly formed Nipah-focused regulatory working group was encouraged to analyze the current data available regarding the impact of Nipah on special populations and possibly generate different recommendations regarding both trials and outbreak use for different situations.
- NEXT STEPS: The CEPI regulatory team will figure out how and when to feed this into the work of the newly formed Nipah-focused regulatory working group.

## NIPAH: Community Engagement

The meeting's final session dealt with the importance of community engagement in vaccine development and delivery. Carmencita Padilla Chancellor of the University of Philippines Manila and Aurelia Nguyen of GAVI led this discussion. Dr. Padilla shared Philippine's lessons learned regarding recent challenges with a dengue vaccine campaign. Ms. Nguyen shared the fundamentals of good community engagement: do have social mobilization programs that create higher demand; don't politicize the program; do have civil society involved in governance and don't underestimate the value of private sector partners. Marie-Pierre Preziosi of WHO shared the critical elements of communication plan: (1) be prepared; (2) be reactive; (3) be aligned.

- OUTCOME: A proposal was made that CEPI's website serve as an information hub for disseminating information to the community about CEPI vaccines. This would provide a systematic way of getting standardized information out in a timely manner.
- NEXT STEPS: CEPI's communications team, in conjunction with the vaccine developers, will discuss whether this makes sense and if so how to implement.

## OPEN DISCUSSION AND CLOSING REMARKS

The meeting ended with an open discussion and wrap-up led by the Chairs. Universally, it was agreed that the establishment of the new Nipah-focused regulatory working group was the most significant and potentially impactful outcome of the meeting.