# Summary of CEPI Joint Coordination Group meeting #5

## Philadelphia, 22 March 2019

### Representatives of JCG members

- Ana Maria Henao Restrepo (WHO)
- Aurelia Nguyen (GAVI)
- Charlie Weller (Wellcome Trust)
- Els Torreele (MSF)
- Emanuele Capobianco (IFRC)
- Heather Deehan (UNICEF)
- Marion Gruber (FDA)
- Mark Feinberg
- Shanelle Hall (UNICEF)
- Emer Cooke (WHO)
- Marco Cavaleri (EMA)

### Working group members represented by

- Daniel Brasseur (Regulatory WG)
- Murray Lumpkin (Regulatory WG)

### Ebola lessons learned presenters

- Anant Shah (Merck)
- Helen Mao (CanSino)
- Jayanthi Wolf (Merck)
- Johan Van Hoof (J&J)
- Julie Spencer (Merck)
- Macaya Douoguih (J&J)
- Shoubai Chao (CanSino)
- Xuefeng Yu (CanSino)

### Other observers

- Jim Robinson (CEPI SAC)
- Alain Alsalhani (MSF)

### CEPI Secretariat

- Ole Kristian Aars
- Richard Hatchett
- Nicole Lurie
- Gunnstein Norheim
- Dawn O'Connell
- Melanie Saville
- Joseph Simmonds-Issler
- Nadia Tornieporth
- Debra Yeskey

## Opening remarks

- Peggy Hamburg (Chair of the JCG) and Richard Hatchett (CEO) welcomed the JCG meeting participants.
- Both underscored that this meeting served as an important opportunity to learn first-hand from the experiences of companies developing Ebola vaccines.

## WHO - Ebola in the DRC

**Presentation by WHO**

- Ana Maria Henao Restrepo gave a status report on the Ebola situation in DRC and WHO's work, highlighting progress that has been made, and the effectiveness of ring vaccination.
- She presented the epidemic curve of the outbreak, showing that the concentration of new cases has shifted from North Kivu to the Ituri province. The age distribution showed that the entire population is affected, but women more so than men.
- Security concerns and lack of infrastructure have greatly complicated the response. Substantial resources are required, including to ensure safety and security. The WHO field staff are primarily Congolese nationals.
- It was also noted by CEPI that there will be an upcoming meeting in Kinshasa with Congolese authorities and international responders where a potential trial of a second vaccine will be discussed, including its design, logistics, and governance.
- And further that there is an upcoming SAGE meeting at which progress will be reviewed and additional recommendations will be considered.

## Merck, J&J, and CanSino - Ebola Vaccine Lessons Learned

**Presentation by Merck**

- Representatives from Merck gave an outline of lessons learned from developing V920, an investigational Ebola vaccine.
- 24 lessons were presented in the areas of clinical, regulatory, manufacturing, logistics and supply-demand dynamics. Together, these lessons could be grouped into four fundamental categories: (1) The pros and cons of public-private partnerships; (2) the challenges of different countries having different regulations; (3) the uncertainty around the outbreak; and (4) the economics of developing and sustainably manufacturing the vaccine.
- Merck will publish these lessons, so that the global community can use them when developing the next generation of vaccines for emerging epidemics.

**Presentation by J&J**

- Representatives from J&J gave an outline of their lessons learned from developing Ebola vaccine.
- Vaccine development is highly complex in regard to capacity building, process qualification, logistics and more. J&J also highlighted that although opportunity costs were high, taking on the Ebola vaccine was a good fit with the company's global public health focus.

**Presentation by CanSino**

- Representatives from CanSino gave an overview of the status of clinical studies of their recombinant Ebola vaccine.
- Three trials have been conducted, the latest in Sierra Leone. While the vaccine has been approved by Chinese regulators, and CanSino has received feedback from WHO, it is not recommended for use outside of a clinical study.

## Common Lessons Learned:

- Partnerships are critically important and the key is to have the right partners with experience and credibility. Even when you do, there are lots of transaction costs and complications that are difficult to anticipate. Respect between partners is critical for success.
- Regulators, especially FDA, EMA, and the African Vaccines Regulatory Forum (AVAREF) have been consistently responsive and helpful.
- Recombinant vaccines containing genes from Ebola Virus are considered dual-use agents and are subject to export control laws requiring licenses that take a long time to secure and are burdensome.
- Many countries regulate GMO products in different ways. Vaccines are included in these regulations. It may be difficult and time consuming to comply with each country's different GMO regulations.
- BSL-classification is not standardized across countries, so differences in BSL regulations as applied to supply chain for development, manufacturing, testing, and distribution can limit options for support in rapid response.
- Development and agreement on protocols in advance for Ebola vaccine trials would have saved time.
- Pathways and protocols for investigational use of vaccine candidates to be used for outbreak response need to be determined in advance, and to be usable/supported in LMICs, especially in Africa.
- Joint scientific advice and review by multiple regulatory authorities throughout the development and licensure process is extremely helpful, including harmonized expectations of data required for approval.
- Nuances of labeling requirements, which are different in each country, add time to the process. Standardization and flexibility on the label (and other artwork) may save time and complexity.
- A global infrastructure is needed to support stockpile maintenance and deployment, including for investigational vaccines.
- Sustainable manufacturing and business models for unique, non-routine, often lower volume vaccines such as those specific to outbreak-prone diseases need to be developed.
- Knowledge sharing across different vaccines should be promoted, including on animal models; assays; immunobridging methodology; validation requirements. Standardization of animal models should be promoted early in the event that non-traditional regulatory pathways are needed.
- Transfer of clinical trial data to the Marketing Authorization Holder (medicinal product manufacturer) can be complex and time-consuming and is best addressed proactively with the end goal of supporting regulatory submissions in mind.
- Manufacturing site selection is exceptionally complex; many items need to be factored (space, technical expertise, facility infrastructure) and therefore options may be limited. Speed of manufacturing and optimal site location might be at odds with rapid outbreak response; the global community might have to plan in advance.
- Important to understand shipment logistics in advance (full cold chain, permits, capacity).
- Using the same manufacturing site to produce clinical and commercial supplies might reduce the overall time taken to obtain an approved product; tradeoffs in the decision to do so, or to select a different manufacturing site need to be weighed carefully and planned for completely. The issues may be different when considering the need to have vaccine supplies ready to support outbreaks.

## MSF - Lessons Learned in Deployment of Ebola Vaccine

**Presentation by MSF**

- Els Torreele presented on the many challenges that result from using an unregistered vaccine, observing that the need for informed consent and other ethical considerations require a high volume of staff and therefore the distribution of the vaccine is slow. Given the challenges in implementing the currently recommended protocol (contacts and contacts' contacts etc) and the evolution of the epidemic (not quite under control), alternatives should be explored.
- The exclusion of pregnant and lactating women and women of child bearing age from the protocol and the distrust that exists in the community towards the Ebola response, including some times the vaccination campaign (people do not understand why some people receive a vaccine, and not everybody) created very challenging situations.
- Els noted, "There was a lack of urgency to find an adequate regulatory solution to register VSV in affected countries. Existing early approval mechanisms (USFDA & EMA) were not used for VSV and the WHO EUAL process delivered no opinion on any of the three Ebola vaccines dossiers submitted".
- MSF called for greater transparency on pricing, availability and stockpiling vaccine and on data sharing, in addition to the collective decision making, when summarising what could have been done differently.

## GAVI – Assessment of Vaccine Investments for Epidemic Preparedness and Response

**Presentation by GAVI**

- Aurelia Nguyen provided an overview of Gavi's Vaccine Investment Strategy, and how it drives prioritisations, including for vaccines for epidemic preparedness and response.
- Criteria for Gavi procurement of vaccines for endemic diseases do not fully translate into those for epidemic diseases as the public health goal of the vaccine investment is different.
- The decision to make investments into epidemic diseases is informed by three different aspects: WHO policy guidance; major public health need; and an identified pathway to licensure in the short term (which presupposes that preliminary safety and immunogenicity data are available).
- Before an Ebola vaccine is licensed, Gavi's engagement in Ebola is two-fold:
    - Gavi has entered into an Advance Purchase Commitment with MSD, the manufacturer of the rVSV-ZEBOV vaccine currently used in DRC, for the procurement of licensed vaccines as of when a vaccine will be licensed, and one of the condition of the agreement was for the manufacturer to create and maintain a stockpile of investigational vaccines;
    - Gavi has also provided funding to WHO to support vaccination operational costs for both the Equateur and North Kivu outbreaks. Gavi has also provided funding in 2015 for health system recovery in Guinea, Liberia and Sierra Leone.
- Once a vaccine will be licensed, Gavi's Ebola engagement will include the funding of a stockpile of licensed and recommended vaccines, as well as vaccination operational costs during outbreaks. As licensure of an Ebola vaccine nears, a detailed work plan is being put together to ensure the Gavi Alliance can procure the vaccine as soon as it is licensed and recommended.

## Open Discussion

- There needs to be a better platform for problem solving in the pre-competitive space, with CEPI facilitation of studies to arrive at correlates of protection when clinical efficacy studies are challenging being one example. Advances have been made – including through the JCG – but CEPI should consider how it can play a larger part in driving development.
- It was suggested that there is a need for better mechanisms to support collective decision making and related accountability. The role CEPI could play in facilitating this deserves further consideration.
- It was pointed out that CEPI can do more to involve affected countries in the JCG. As was clear from the Nigerian participants at the last JCG, they would like to be co-developers – not just recipients of what others develop for them.
- A suggestion was made for the Secretariat, working with relevant companies, to identify priority challenges to tackle. Some, but not all, may be addressed through the regulatory working group.
- A suggestion was made for CEPI to report back on follow up of JCG recommendations, as well as the progress of the regulatory and manufacturing working groups to the rest of the JCG.
- It was noted that following the National Academy of Medicine meeting in March 2017 there were several outstanding issues identified that still need to be done to get to a licensed Ebola vaccine. CEPI is conducting a review of that list and if it is substantial, will likely reconvene a scientific meeting and also support additional scientific work.