Summary of CEPI Scientific Advisory Committee (SAC) meeting

Teleconference, roundtable discussion 07.02.2019

Committee members

Present

- Helen Rees (Chair)
- James Robinson (co-chair)
- Connie Schmaljohn
- John Edmunds
- Michel De Wilde
- Peter Smith
- Stanley Plotkin
- Daniel Brasseur
- Paula Bryant
- Penny Heaton
- Phil Krause
- Alan D Barret
- Josie Golding
- Tom Kariuki

Apologies

- Alash'le Abimiku
- Charlie Weller
- Christian Bréchot
- Christian Happi
- Delese Mimi Darko
- Dong Xiaoping
- Inger Damon
- Kathleen Neuzil
- Kenji Shibuya
- Myron Levine
- Yves Lévy
- Ralf Clemens

CEPI Secretariat

- Richard Hatchett
- Gunnstein Norheim
- Melanie Saville
- Frederik Kristensen
- Nora Indrehus
- Allison Adele Bettis
- Raul Gomez Roman
- Arun Kumar
- Solomon Abebe Yimer
- Johan Holst
- Trygve Danielsen
- Neil George Cherian
- Raimonda Viburiene
- Stig Tollefsen

Non-voting members

- Vaseeharan Sathiyamoorthy, WHO
- Kathrin Jansen, Pfizer
- Ali Alloueche, Takeda
- Jean Lang, Sanofi
- Johan van Hoof, J&J

Notes to readers

- Pre-read slides for the teleconference were shared ahead of the meeting. Slides are found here. Apologies for late posting of slides.
- Meeting rapporteurs: Raimonda Viburiene and Stig Tollefsen, CEPI Secretariat

1. Welcome and objectives for the day.

Helen Reese and Richard Hatchett opened the 1st SAC meeting in 2019.
This meeting was a telecon with three main themes; 1) Update on Lassa fever program and summary from NCDC Lassa conference and JCG meeting in Nigeria; 2) CFP3 Advice on RVF, and 3) SAC Terms of Reference (ToR) updates and the role of SAC in the annual portfolio review and Stage Gate Review Committees.

2. Lassa fever program update

Melanie Saville gave the update on the recent CEPI's Lassa vaccine portfolio and Gunnstein Norheim presented latest news on progress in enabling science studies planned on Lassa. In connection with the international Lassa conference in Abuja, 16-17 January 2019, CEPI also arranged a epidemiology protocol harmonization workshop (15th January) and a JCG meeting (18th January).

During the following discussion several issues were brought up.

- There was a consensus that there is a need and importance to improve the understanding of biomarkers associated with survival and protection against diseases in humans (i.e. whether it is cellular and/or Ab-based), as well as the impact the disease in pregnant women. Proposed actions were to add studies among survivors in the planned epi studies, and potentially look to other similar diseases to understand what confers protection. It was suggested that this will be set up in the coming years.
- There was a concern that research groups engaged in Biological standards were mostly located in the northern hemisphere. However, the applicants for these projects were recruited through open calls and investigators from affected countries are central in the successful partnerships (BNITM/ISTH in Nigeria and Tulane/Redeemers/Kenema hospital).
- It was discussed when to start building the vaccine stockpiles and questions on the estimates for size. In general, 100 000 doses should be manufactured. However, Lassa epidemiology studies will be conducted in affected countries to evaluate the feasibility of conducting efficacy trials and prophylactic use, and the epidemiology data from the consortia should be advisory on the size of a stockpile needed.
- WHO has pointed out that the successful vaccine should be given prophylactically in a risk population and not only for emergency use. As commented by Vaseeharan, the WHO TPP will focus on preventive use.
- In the last years, the number of Lassa cases has increased in Nigeria and thus there is a desire to accelerate Phase 1/2 studies as well as Phase 3 efficacy trials. These trials are feasible to do, given the current epidemiological. The developers should work with the affected countries and their regulatory agencies to ensure appropriate phase II design, whereas WHO should bring everyone in consensus on protocols.
- Richard Hatchett had discussions with GAVI during the summit in Davos (January 2019), and was asked to share with GAVI, what will be the natural end-point for CEPI in the Lassa project.

  Update from NCDC Lassa Conference and JCG meeting in Nigeria was given by Richard Hatchett and Nicole Lurie. The intention of the JCG meeting in Nigeria was to help build the relationships and to introduce critical partners. CEPI takes an active role in this work. This meeting was very

successful and there was a strong presence of Nigerian stakeholders, regulators, ethics and the WHO. One of the main points to have JCG meeting in Nigeria was the possibility to bring together Lassa vaccine developers and key African vaccine development stakeholders to discuss advancement of the vaccine projects. In addition, manufacturers were present at NCDC Lassa conference to further extend their network. CEPI has an active role in fostering those relationships.

The Lassa efforts should be a template for other disease programs under development.

3. CfP3 – Advice on RVF

Gunnstein Norheim delivered a presentation about Rift Valley Fever and vaccine pipeline and asked SAC advice on three matters:

- What is the relative role of a human vaccine candidate in controlling RVFV and how can human vaccine development complement other control strategies?
- What are the preferred product characteristics for human RVF vaccines (i.e. is the vaccine intended for preventive and/or reactive use, what knowledge is critical to inform the advice for selection of criteria)?
- What additional research gaps are most critical to address to facilitate human RVFV vaccine development?

Ad human vaccine vs veterinary vaccine:
It was discussed whether vaccinating animals by developing a veterinarian vaccine would have a greater impact on human health and disease control compared with vaccination of humans. A thorough review of the existing data is necessary to answer these questions and one should await WHO view on concluding in their Target Product Profile (TPP). The SAC highlighted the One Health approach with the RVFV vaccine being considered as part of this. It was advised to reach out to the animal research community to find strategies for use of both veterinarian and human vaccines. There is a need to better connect to the animal vaccine development community to be able to find out how do they select best candidates - any difference from CEPI's? CEPI should work intensely with WHO to fill in this particular gap.

Ad preferred product characteristics for human RVF vaccines:
It was discussed how a potential vaccine should be administered, either as a prophylactic vaccine or for emergency use in case of outbreaks for population subgroups at particular risk (e.g. occupational risk such as farmers, butchers, and veterinarians). The RVF virus causes miscarriage in sheep, as one of the existing animal vaccines also can induce. How would a human vaccine potentially affect the health of pregnant women? It was agreed that it is difficult to get any conclusions without addressing the Research and Development gaps such as:

Ad research gaps critical to address:

- What is a relevant animal model? In the CFP3, one of the criteria for funding is a relevant animal model. However, the animal models used for the research reflect only partly the human disease, and none of them seem to be perfect More knowledge is needed on relevant animal model.
- What are the animal reservoirs? Wildlife animal species seems to be a reservoir for RVF, and would it then be sufficient to vaccinate stock animals in order to prevent further spread into humans?
- What human populations are affected by disease, and what affected by severe disease (i.e. CFR in newborns?). It is evident that more epidemiology studies are needed to understand the burden of disease.

- What is the contribution of mosquito transmission to the human disease burden (% of cases) as compared to transmission via animal blood transmission? Literature suggests that a small proportion of humans are infected by the mosquitos.
- What is the extent to which RVF cause abortion in women? The virus induces miscarriage in sheep as does one of the existing animal vaccines. How would a human vaccine potentially affect the health of pregnant women?
- Blindness is one of the outcomes of the disease that has never been properly defined and addressed.

CEPI will evaluate the research gaps and WHO has set out to develop an RVF vaccine TPP, expected to be available in May 2019.

4a. SAC ToR updates

- United Kingdom has announced a 10 million donation to CEPI. Prior to this announcement, the UK government ran a due diligence process. A gap in SAC's ToR was pointed out: the length of the term period for a SAC member should be defined before allowing the rotation. There will also be a review of other governance structures in CEPI as a follow up.
- SAC should work as a governance body at the annual portfolio review process.

4b. The role of SAC in the annual portfolio review and Stage Gate Review Committees

- SAC members will become part of a pool of experts to be called upon in the stage gate review committees recognizing that it is not always possible to attend each meeting.
- Call for SAC members and one committee should be established for each disease. WHO and regulators will be invited as observers. The industry has well defined milestones and approaches for stage gate reviews that also could be used in the follow up of CEPI funded projects.
- There should be a broad review of the data from the individual projects. It is also important to
- make sure that affected countries are among participants.
- An open invitation was extended for SAC members to contribute in CFP3 as reviewers, noting that this would be financially compensated.

Next SAC meeting will be held as a F2F meeting in London on 5th of April and providing a recommendation for CfP3i projects to the Investment Executive Committee will form the main part of the agenda.