



# Summary of CEPI Scientific Advisory Committee (SAC) meeting

Teleconference, 31.01.2020

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## Committee members

### Present

- Connie Schmaljohn
- Daniel Brasseur
- Helen Rees (Chair)
- James Robinson (Vice chair)
- Michel De Wilde
- Myron Levin
- Paula Bryant
- Penny Heaton
- Peter Smith
- Phil Krause
- Ralf Clemens
- Stanley Plotkin
- Yves Levy (YL)

### Non-voting members

- Ali Allouche (AA)
- Jean Lang
- Johan Van Hoof (JVH)
- Josie Golding (JG)

## CEPI Secretariat

- Richard Hatchett
- Melanie Saville
- Nick Jackson
- Mike Whelan
- Nicole Lurie
- Svein Rune Andersen
- Deb Yeskey
- Raúl Gómez Román
- Gautam Sanyal
- Alan Liss
- Raimonda Viburiene
- Stig Tollefsen
- Valentina Bernasconi (VB)
- Sonja Henne
- Arun Kumar
- Celine Gurry
- Per Etholm

## Invitees

- Anna-Maria Henao Restrepo WHO
- Sue I. Gerber CDC
- Charlie Weller (CW)
- Stacy Wooden
- Peggy Hamburg JCG

## Meeting minutes

Richard Hatchett opened the meeting. Melanie Saville presented the content of the meeting and the meeting objectives:

- Update SAC on the 2019-nCoV outbreak
- Inform SAC of current CEPI investments
- Seek SAC advice on further investments taking into account the evolution of the epidemic
- Request SAC expert review of incoming vaccine development proposals

Helen Rees chaired the meeting.

*Please note, information provided within this meeting summary is correct as of 31 January 2020. Epidemiological information provided may change as the COVID-19 outbreak progresses.*

## WHO epi update

Ana Maria Henao Restrepo gave a brief overview of the epidemiological situation.

- As of **31 January 2020**, the World Health Organization (WHO) had registered 9832 cases, of which 9720 were confirmed, and 15238 suspected<sup>1</sup>.
- In China 31 provinces are affected. There are 1525 severe cases registered in China
- At a global level 102 cases in 19 countries.
- Handful of cases with no travel history to China.
- Based on the epidemiological data WHO has declared a Public Health Emergency of International Concern (PHEIC)

Local and globally there has been introduced

- Travel and commercial restrictions.
- Public Health global and local collaborative efforts put in motion to respond to the outbreak.

### WHO focus:

Vaccines:

- WHO support different groups and have a landscape of vaccine candidates, also supported by CEPI.
- CEPI will support 4 candidate vaccines, DNA, RNA and protein-based strategies.
- WHO will do a prioritisation of vaccines. Looking into more the background data for the various vaccine candidates.

### Vaccine protocol:

- Master protocol for trial vaccination is under development.
- Vaccines will be an important tool, but now main focus will be on therapeutics.
- The effort is comprehensive, and the WHO is seeking to have the right investment balance for research preparedness and response with development in several countries.
- Active collaborative group looking at cross reactivity for vaccines against other known coronavirus.

### Disease:

- The disease seems to be asymptomatic for several days. It appears to take a week or a little more to develop symptoms.

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<sup>1</sup> Information correct as of 31 January 2020, see [WHO Novel Coronavirus \(2019-nCoV\) Situation Report-11, Friday 31 January 2020](#)

- Portion of cases in children very low, 1% in 1-10 year age group. Majority of cases in the elderly.
- Mortality seem to affect cases with underlying other disease conditions. Not possible to conclude currently and provisional observations suggest that 1 of 5 patients will die after severe disease.

#### **The virus**

- Genome genetic variation seems to be low, and different clusters of virus seem to appear.
- Virus sequence differences from MERS and SARS but cross reactivity with antibodies is being actively investigated. Importantly, the question of whether antibodies against the Receptor Binding Domain (RBD) on the S protein cross neutralize needs to be examined. See below for more details.
- The sequence for the viral polymerase is highly conserved in 2019-nCoV compared to MERS and SARS and could be a good target for common therapeutics

#### **CDC update on the 2019-nCoV**

Sue I Gerber gave an update from CDC USA.

- Epidemiology in the US has registered 6 cases, originating from one family member.
- CDC has grown the virus from the first case registered in the US in Vero cells.
- Will be deposited in the [BEI Resources repository](#) and be shared broadly. CDC is working on amplifying the virus for sharing.
- Sequences will be uploaded in the gene bank, seem to be similar to the other reported nucleotide sequences.
- CDC is working on diagnostics, focusing on the nucleocapsid region.
- A protocol for 2019-nCoV RT-PCR assay is published on CDC web page.
- Working on antibody assays against spike protein
- Working with US colleagues to distribute diagnostics to other public health labs.
- There are similarities in spike proteins between SARS and 2019-nCoV?
- CDC plan to test old sera against from SARS patients to check if binds to 2019-nCoV.
- CDC is also testing assays against other known corona viruses.

#### **Cross reactivity between SARS and 2019 nCoV**

William Dowling gave an update.

- The Spike protein has 76% aa identity with SARS (Lu et al 2020)
- There is evidence that both viruses use the same Receptor - ACE2
  - Structural predictions (Wan et al 2020, GSAID)
  - Laboratory studies (Zhao et al 2020, Letko et al 2020)
- There is some experimental evidence of limited cross-reactivity, but more definitive experiments are in progress by multiple groups
  - nCov is neutralized by an anti-SARS equine hyperimmune serum (Zhao et al 2020)
    - Caveat – it unclear if this neutralization was as potent as against SARS – it was tested at a 1:80 dilution but it was reported that this serum neutralizes SARS at a 1:100,000 dilution (LinFa Wang personal communication)
  - nCov purified S protein was recognized by a SARS mAb (Tian et al 2020)
    - However, two other potent anti-SARS mAbs that target the S protein ACE2 binding site do not bind to nCoV
- Sequence divergence from MERS-CoV, especially in the RBD, make it highly unlikely to have any significant cross-reactivity
- nCoV and MERS-CoV likely use different cell receptors for entry (ACE2 vs CD26/DPP4)

#### **CEPI investment in vaccine development**

Update by Melanie Saville

CEPI has decided to invest in 4 platform technologies, total investment 19–20 mUSD.

- Moderna Therapeutics, mRNA
- The university of Queensland, Molecular clamp (protein)
- Inovio: DNA plasmid delivered with electroporation
- Curevac: RNA

Investment in enabling Sciences

- AAHL Australia developing a ferret animal model

In addition, CEPI has launched a call for proven vaccine technologies applicable for large scale manufacturing for rapid response against the novel coronavirus has been developed

- Call was launched 30 January 2020
- 14 days open call; review starts immediately after reception of applications
- SAC members were requested to take active part in the vaccine call review process.
  - Industry, vaccine development expertise is needed.
- SAC should recruit Corona virus experts on an ad hoc level in the first round to assist the review process. Plotkin will share names of experts.

**Question to SAC;** should CEPI consider other technologies and manufacturers for investment?

It was discussed if CEPI should invest in immune monoclonal antibody technologies and if it should be part of the newly developed call. It was agreed that CEPI should focus on the vaccines at this stage. CEPI should monitor the development of antibodies for therapeutic or immunoprophylactic use.

As an important part of CEPI's endeavor, we should develop

- Standardized tools to be able to compare the vaccine candidates.
- CEPI should continue to invest in enabling sciences, standards and assays animal models. Vaccine candidates need all these tools, and will help the down selection of candidates

As part of the new call one of the criteria is the description of how the vaccine production will occur, where are we going to produce the vaccine in large quantities?

- It should be determined at an early stage to be able to support the strategy for equal access also taking geopolitical aspects into the consideration.
- CEPI will stick to its objective of developing vaccines with equitable access in vulnerable areas.
- Through the call CEPI aim to globalize the manufacturing and under the current circumstances CEPI will invest substantially up front.

How many candidates should CEPI invest in?

- Decide what assays that are the most critical to determine which vaccine will offer the highest efficacy.
- CEPI should work with WHO commitment on the down selection process that to ensure it is transparent and sound.
- Until epidemiology situation clarifies CEPI need to think about speed and scalability of the potential vaccine candidates, and not narrow down too early.
- CEPI should utilize the work of other organizations and funders and consider what is being developed in totality, potentially for CEPI to step in to support the development.
  - CEPI should follow candidates supported by US government funding and look at the possibility collaborate for activities outside their US investment.

Is this investment sufficient for now?

- CEPI should rapidly and critically review the applications that come in and decide if one needs to “throw the net wider”.

- WHO has produced guidelines for what to expect for a vaccine against disease X. This needs some tailoring to this epidemic specifically but can be regarded as a Target Product Profile. The WHO TPP might be ready Tuesday February 4.
- It will be useful for CEPI to have access to this in the development of new vaccines, looking at safety data, number of doses before we expand the pool of vaccines.
- CEPI suggest bringing in the WHO TPP as part of the review criteria.
- The call will need to get data on a variety on candidates and review the production capacity, the regulatory approaches and other bottle necks before and investment.

### **Adjourn**

Helen Rees closed the meeting, wishing CEPI good luck in further development of vaccines. SAC members were thanked for their fruitful contribution and reminded to sign up for help in the review process of the incoming applications in the 2019-nCoV call for vaccine development.