Summary of CEPI Scientific Advisory Committee (SAC) meeting

Teleconference, 13.05.2020

Attendees

Voting SAC members	CEPI Secretariat
• Alan D. Barrett • Alash´le Abimiku • Christian Bréchot • Christian Happi • Connie Schmaljohn • Daniel Brasseur • Delese Mimi Darko • Helen Rees (Chair) • Inger Damon • James Robinson (Vice chair) • John Edmunds • Michel De Wilde • Myron Levin • Penny Heaton • Peter Smith • Phil Krause • Ralf Clemens • Stanley Plotkin • Tom Kariuki • Yves Levy	• Richard Hatchett • Frederik Kristensen • Melanie Saville • Nick Jackson • Raimonda Viburiene • Stig Tollefsen • Ingrid Kromann • Bill Dowling • Jakob Cramer • Debra Yeskey • Svein Rune Andersen • Gabrielle Breugelmans • Paul Kristiansen • Amy C. Shurtleff • Other CEPI staff as observers
Non-voting members	Invitees
• Ali Alloueche • Jean Lang • Johan Van Hoof • Josie Golding • Vaseeharan Sathiyamoorthy, WHO	• Anna-Maria Henao Restrepo, WHO • Simon Funnell, PHE • Charlie Weller Wellcome Trust • César Muñoz-Fontela, BNITM • Alina Ximena, WHO • Pierre Gsell, WHO

Meeting minutes

Welcome and brief introduction of today's item

Helen Rees and Richard Hatchett, CEO of CEPI, opened the SAC teleconference by welcoming everyone and thanking the Team for the efforts to prepare for this meeting.

#1 The ACT Accelerator

Richard Hatchett briefly introduced the Access to COVID-19 Tools (ACT) Accelerator, a landmark collaboration to accelerate the development, production and equitable distribution of vaccines, diagnostics and therapeutics for COVID-19.

A draft version of the governance structure of the Vaccine pillar - COVAX, was introduced, one of the three pillars under the ACT Accelerator. CEPI and Gavi have been named as co-convenors and representatives from both organisations and the World Health Organization (WHO) are working on further structure of COVAX. Three workstreams are being proposed:

1) Research, Development, and Manufacturing; CEPI
2) Procurement and delivery; Gavi
3) Policy and Allocation; WHO.

Further details were given for the envisioned structure of R&D&M Investment Committee. Briefly, SWAT Teams, comprised of industry partners, regulators and scientists and supported by CEPI staff, would look at key topics to accelerate vaccine development (regulatory, manufacturing, clinical, enabling) through multilateral discussions. Outcomes would feed into vaccine candidate Project teams R&D&M Investment Committee will be composed of non-conflicted individuals. The CEOs of CEPI, Gavi and the Bill and Melinda Gates Foundation (BMGF) will be part of this Committee and ex-industry expertise and will make decisions on resource allocation.

- There are now several national funding efforts underway to support part of the vaccine development process (i.e., R&D, clinical trials), allowing CEPI to position much of its investments into building manufacturing capacity to produce vaccine doses for the global allocation mechanism.
- The US has recently announced 'Operation Warp Speed' and it is reaching out both to US-based as well as international vaccine manufacturers.
- There may be opportunities to externalise/globalise manufacturing with the partners that recognise equitable access responsibilities.
- WHO is continuing to have productive technical interactions with multiple US bodies, including the US National Institutes of Health (NIH).
- There are opportunities to coordinate CEPI's investments with Biomedical Advanced Research and Development Authority
- The role of the CEPI SAC in the ACT Accelerator is still to be defined.

#2 Advances in scientific knowledge SARS CoV2- Immunology and preclinical testing.

William Dowling (Non-Clinical Development Lead at CEPI)who is a co-chair of two WHO COVID-19 workings groups under the R&D Blueprint Team, presented the recent advances in scientific knowledge regarding SARS-CoV-2 immunology and preclinical testing.

High-level summary on preclinical testing:

- SARS-CoV-2 causes a mild to moderate disease in relevant preclinical models.
- Not all preclinical models seem to reflect the severe aspects of the disease. Different models are needed to reflect the various aspects.
- The preclinical testing gives better understanding of the disease, with indications for immunity after one round of disease.

High-level summary on assays and immunology:

- Antibody responses were present in multiple cohorts of acute and convalescent patients.
- Neutralising antibodies were detected in patient sera by live virus and pseudovirion.
- Some cross reactivity with SARS-CoV-1 and MERS-CoV convalescent sera and certain SARS-CoV-1 mAbs has been observed.

https://www.who.int/teams/blueprint/covid-19.
https://bpspubs.onlinelibrary.wiley.com/doi/abs/10.1111/bph.15143

#3 Review of current portfolio

Nick Jackson, Head of Programs and Technology at CEPI, presented the current situation of CEPI's COVID-19 candidate selection and advancement process. He briefly described each of the nine current CEPI programmes in COVID-19 portfolio (Inovio Pharmaceuticals Inc., the University of Queensland, CureVac, Moderna Inc., Clover Biopharmaceuticals, a consortium led by Institut Pasteur and including Themis Bioscience and University of Pittsburgh, Novavax Inc., the University of Hong Kong, and the University of Oxford). Finally, Nick Jackson presented the portfolio's (known or potential) gaps, regarding platform technology, experience, geography, CMC and choice of immunogen, and addressed that the new Call for Proposals aims to close those gaps.

Other points raised under discussion:

- To mitigate known or potential portfolio gaps, CEPI has a robust selection process where internal CEPI experts, as well as experienced consultants and SAC members, will have as impartial view as possible to make the right selections.
- CEPI will be pro-actively approaching potential applicants in order to fill portfolio gaps.
- Not clinically relevant mutations of S protein have just been identified. Mutations observed are away from the RBD domain. Further development is being followed closely to assess any impact of mutations on the potential effectiveness of the portfolio.
- CEPI has begun conversation with several developers regarding clinical trials in Africa at competent sites that can move very quickly and aid the vaccine development.
- CEPI is in discussion with the African Vaccine Regulatory Forum (AVAREF) that has put together a rapid review process, which will further enable vaccine developers to conduct clinical trials in Africa.
- SAC chair Helen Rees and others are working with the African Union to increase awareness of the vaccine development pipeline. In addition, they are engaging the African Union and other African stakeholders to counteract anti-vaccine sentiment/language.
- The importance of engaging stakeholders to understand local manufacturing capacity in African countries, and to manage expectations from local manufacturers, was noted.
- WHO has a Call for sites around the world to evaluate vaccines /clinical trials, receiving interest to participate from many groups worldwide.

The full protocol is now posted on WHO website for comments. Spike protein references:
https://pubmed.ncbi.nlm.nih.gov/32225175/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7225408/

#4 Review of Landscape

Nick Jackson gave an overview of our current knowledge of the COVID-19 vaccine landscape:

- The US currently has the largest number of vaccine candidates in development
- China advances candidates in earnest with their front runners based on inactivated or Ad5 platforms.
- Vaccine developers may be lacking the development expertise or manufacturing infrastructure to succeed in short order.
- The field benefits from a wide range of platforms being tested.
- The S protein is the favored antigen, as expected.
- CEPI is proactively engaging with developers to learn more.
- CEPI will calculate Probability of Technical and Regulatory Success (PTRS) / Probability of Success (POS) as more data becomes available – important to have open-access to data to support such calculations.
- CEPI is encouraged to see MNCs come forward.

- With the newly launched CEPI Call for Proposals "Achieving an unprecedented acceleration of vaccine development and global manufacturing capacity to prevent COVID-19" the eligibility and review criteria will guide the judgement going forward. CEPI is proactively reaching out to MNCs, DVCMNs & other developers to communicate key features of the new Call.
- The new Call for Proposals will support the rapid development of vaccines striving for licensure/emergency authorisation in 12-18 months or less and, to ensure the availability of sufficient doses for wide-spread global deployment as soon as possible in 2021.

Other points raised under discussion:

- To be able to assess and compare the different technologies already invested in, a better understanding of correlates of protection is needed.
- Spike protein with adjuvant can induce neutralising antibodies as shown in preclinical models. Neutralising antibodies seem to be important.
- Passive protection using antibody technology, will give needed information and data will be available soon, to inform about efficacy of neutralising antibodies. The available data will provide information on the threshold level for protection.
- Antibodies will potentially offer protection and stop spread of viremia. Longer-lasting protection offered through vaccines is needed.
- The pandemic will slow down and there will be a need for different strategies for vaccination of people. Vaccines offering one shot protection will be of importance.
- Investments focused on variants of the S protein could be a concern. RBD domain should also be important.
- There are veterinary vaccines against coronavirus, but these are mainly based on old technology and not for use in the current outbreak to offer lasting immunity.
- With the current portfolio there is a general lack of experienced manufacturers. Could CEPI take on a stronger role in matchmaking? CEPI should bring groups together.
- Parallel development of vaccines must be coordinated on a national and worldwide level.
- For development and production of adjuvants, manufacturing capacity on a global level is critically important.

#5 Solidarity 3 protocol

Ana Maria Henao Restrepo (WHO) updated the meeting on the Solidarity protocol regarding global clinical trials for COVID-19 vaccine candidates.

- Trials will include all the necessary measurements that the regulators and the developers will have in mind.
- Reduce timeline to 3 months (for 1 dose vaccine candidates) and 6 months (to two dose vaccine candidates).
- Common core protocol that will allows to test several vaccines with common placebo control group and the randomization 1:1:1.
- Vaccines that will come in later will not be negatively affected.
- Will be flexible in a way to add on measurement to inform regulators/developers/countries.
- Close to 50 sites have already expressed interest in participating in this global trial and WHO is currently looking at the number of subjects and transmission rates at those sites https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

Final remarks

Helen Rees and Melanie Saville closed the meeting, reminding the SAC about the important non-COVID programmes that will need attention and follow up.