Summary of CEPI Scientific Advisory Committee (SAC) meeting

Teleconference, 10.01.2020

Committee members

Present

- Charlie Weller (CW)
- Paula Bryant (PB)
- Jim Robinson (JR)
- John Edmunds (JE)
- Phil Krause (PK)
- Mike Levine (ML)
- Stanley Plotkin (SP)
- Connie Schmaljohn (CS)
- Kenji Shibuya (KS)
- Peter Smith (PS)
- Michel de Wilde (MdW)
- Ali Alloueche (AA)
- Helen Rees (HR)
- Yves Levy (YL)
- Daniel Brasseur (sent in his written response to questions posed by CEPI)

Non-voting members

- Vaseeharan Sathiyamoorthy, WHO
- Ana-Maria Henao Restrepo (AR)
- Josie Golding (JG)
- Johan Van Hoof (JVH

CEPI Secretariat

- Richard Hatchett
- Melanie Saville
- Nick Jackson
- Mike Whelan
- Nicole Lurie
- Raimonda Viburiene
- Stig Tollefsen
- Valentina Bernasconi (VB)

Meeting minutes

Richard Hatchett opens the urgent ad hoc SAC meeting to evaluate the outbreak of the respiratory disease in Wuhan China, which has been reported in the media as a novel coronavirus. The SAC is sought for advice on if and potentially when CEPI should take specific action.

Please note, information provided within this meeting summary is correct as of 10 January 2020. Epidemiological information provided may change as the COVID-19 outbreak progresses.

Update from WHO[1]

Ana-Maria Henao Restrepo (AR) updated meeting attendees on the situation following the Global Coordinating Mechanism (GCM) just prior to the SAC.

As of **10 January 2020**, information reported to the World Health Organization reported 59 cases (later scaled back to 41 see below)[2], all in Wuhan, China, and all in contact with the animal market. No human to human transmission has been reported and no data shows easily passage from person to person; all cases identified have been transmitted from contact with animal potentially from the fish and live animal market in Wuhan. The animal source has not been identified yet. Risk of spread is unknown, but it is noted that this is a respiratory virus. Although seven severe cases have been reported, so far there have not been any fatalities and no spread form Wuhan. As per present information, there is 60-70% sequence homology with SARS (Update below). Patients have been screened for Legionnaires' disease, SARS and flu. WHO is activating Incident Response. We need to work with the Chinese authorities to ensure the genomic sequence is made publicly available.

SAGE advice for R&D Blueprint

1. Standardisation and sharing of data; how to collect it in systematic way
2. Need reliable diagnostics
3. Therapeutics for corona and MERS could be used
4. Will update vaccine response for MERS and adapt for this outbreak.
5. Look into trial designs
6. All partners need to share data widely

There was a brief discussion after the sharing of WHO status information, regarding the availability of the genomic sequence of the virus and what possible measures could be done to make the sequence public. All communication in China is through the government and the Ministry of Health.

It was underlined that the Chinese authorities have reported the virus as novel with a 50-70% genetic homology to other known coronaviruses. There are hundreds of contacts reported to be followed up. The last case was reported on 5 January. There is little knowledge of incubation period and based on newly reported cases it could be that the epidemiological peak of the outbreak is over. WHO hope that more information will be made available soon.

Vaccine pipeline overview

The CEPI pipeline analysis for MERs and SARs was presented by Melanie. This was last updated in November 2019.

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[1] Information correct as of 10 January 2020
[2] See 10 January 2020 WHO Western Pacific Regional Office Twitter thread,

CEPI is funding and facilitating the development of 4 MERS vaccine candidates. Three of these are in Phase I. In addition, CEPI has one platform developer that works on MERS (University of Queensland molecular clamp). CEPI has informally spoken to 4 developers in regard their willingness to work on a novel strain and received a positive feedback if help will be needed. As a part of the contract with the developers for rapid response platforms, there is the option for alive fire exercise which could be implemented here if needed. The current portfolio is at early stage and thus may have limitations for this exercise at this stage. However, the University of Queensland molecular clamp technology is rapidly approaching the stage for such testing.

The WHO Blueprint team is in activation mode and will publish the development and on their web pages regarding:
1. Products in pipeline
2. Developing product selection criteria
3. Outline of trial design

Discussion

Helen Rees asked attendees three questions:
Q1: What actions if any should CEPI take now?
Q2: What would be epi trigger for taking actions?
Q3: What should CEPI be prepared to move quickly on, if anything?

In discussion:

- *Epidemiological triggers:*
    - WHO indicated the current epidemiology is insufficient to reach a clear conclusion. Nevertheless, WHO are in full alert mode – and are preparing for spill-over to other countries and to have clear pipeline, systems, and protocols in place.
    - Key triggers to act include evidence of human to human transmission, and a spread of infection outside of those in the market. Another consideration is the mortality rate.
- *CEPI actions*
    - The current vaccines in development within and outside the CEPI pipeline aim at other corona virus as MERS and the efficacy of these vaccines against the novel coronavirus from Wuhan is uncertain.
    - So far, CEPI has had an alert posture. There are a graded set of actions CEPI could take. While the threshold for clinical development is high, CEPI should consider what would necessitate action or what low-regret actions would be prudent.
    - Actions discussed:
        - Looking to start RNA sequencing and making DNA through rapid response platforms
        - View as a potential Disease X rehearsal: look at what needs to be put in place,
        - CEPI will support WHO's vaccine landscape mapping. At the Global Coordinating Mechanism CEPI expressed willingness to support
        - CEPI reaching out to current developers
        - At the moment CEPI and others are not in a position to make a threat assessment. However, low cost initial investigations are attractive and there is not a high threshold for this. There are other companies outside CEPI including Chinese ones. CEPI should discuss with developers it both funds, and those it does not, to see whether they are likely, to initiate work with this new strain in terms of:
            - 1) capacities (lab, manpower, etc.,)
            - 2) availability (prioritization amongst other running programmes to drop or postpone),

        - 3) starting material (ability to access the strain, its specific? Protein S or gene sequence considering the technology of the platform),
        - 4) delays versus production delays (how much after how many weeks),
        - 5) safety: how would/should this new strain be regarded in terms of safety (rather than efficacy) if behaving similarly with their pilot and considering the available information today of the pilot?
    - Consider if the CFP2R for immunoprophylactic technology platforms could be used to support the production of specific immune-globulins either artificially or based on recovered patients.

  - With the limited information available on the genetics and disease characteristics there is difficult to push any "go buttons" to get development of initial material for an efficient vaccine going. The isolated virus will also be needed for further development of a vaccine for testing in animal and challenge models. This could be a rehearsal for disease X, pointing back to the CEPI contract with platform developers.,

- *Other points raised in discussion*
  - Rapid access to the genetic sequence of the virus is the first step towards a 16-week development target.
  - Priming regulatory agencies would be sensible to do in this exercise to seek advice on development of the platform technologies.
  - Sequence comparisons will be important for developing a targeted vaccine. Other organisations may want to take a part in this too – e.g. BARDA, CDC and GloPID R.

Conclusions

- WHO is working at highest diplomatic levels to promote sharing of sequence and virus
- WHO convening a review process for all vaccine candidates and study designs. CEPI has agreed to provide as much information as possible from CEPI's landscape analysis
- More epidemiology data is really needed about human to human transmission, animal source etc.,
- This is a good rehearsal for a Disease X situation, and on this basis the SAC supported proceeding with exploring DNA and RNA
- Depending on how the epidemiology develops, CEPI may need to and should be prepared to work with developers beyond those it currently partners with
- The SAC should reconvene urgently if things change.

Suggested epidemiological triggers for taking action:

1) Evidence for human to human transmission
2) Evidence for infections outside the Wuhan market
3) Mortality (CFR)

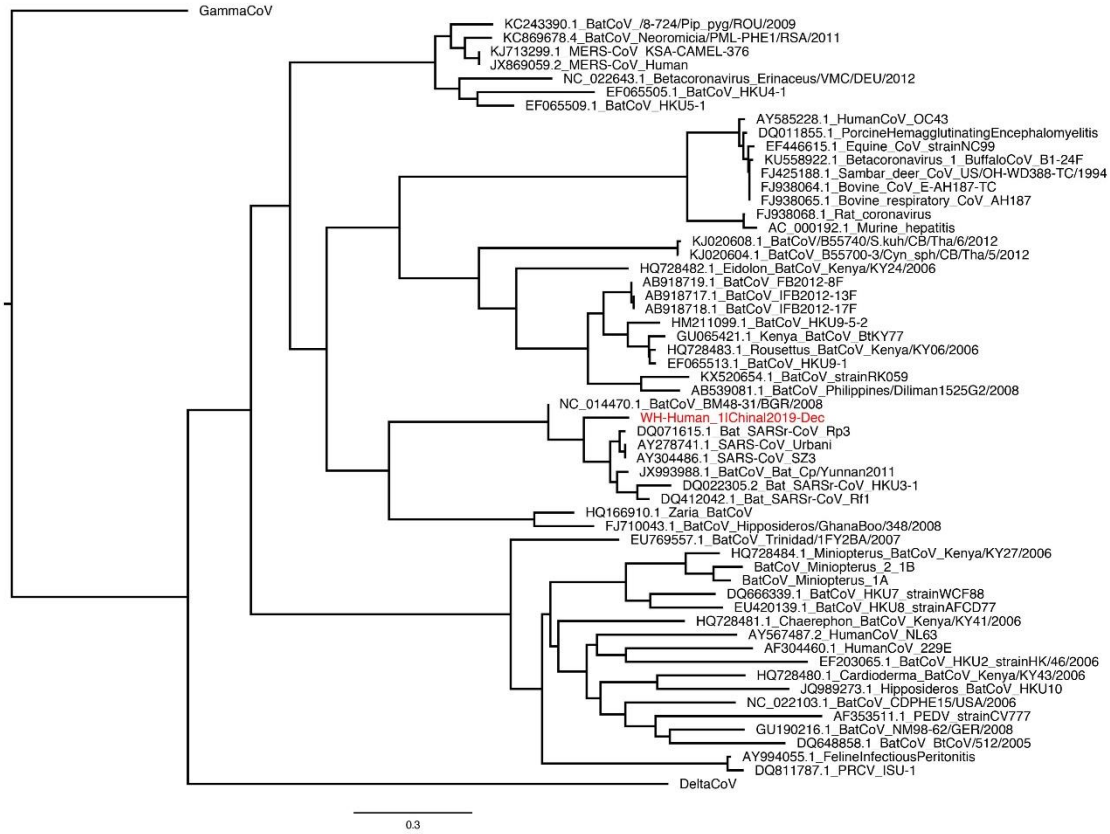
Next Steps

- Follow the epidemic development and evaluate the need for CEPI to take action.
- Follow up requests from WHO sharing information of relevant vaccine pipelines
- Discuss with developers for "live fire exercise" or other actions that can help in the situation.
- Share experience in vaccine trial design with WHO
- Reconsolidate with SAC before for potential action to take place.

Updated information January 12-13.

- Sequence of Corona virus has become public:
  - http://virological.org/t/initial-genome-release-of-novel-coronavirus/319
- The published nCoV is 89% similar to SARS-related bat coronavirus in the Sarbecovirus group of beta coronaviruses. See phylogenetic tree below.
- Number of cases which has been reported has been scaled back to 41 and the first noted the death has been reported: www.cidrap.umn.edu/news-perspective/2020/01/china-releases-genetic-data-new-coronavirus-now-deadly
- The patient who died is apparently a 61-year-old man who had chronic liver disease and was a frequent customer at the market at the center of the investigation
- Symptom onset of the 41 confirmed nCoV cases ranges from 8 December 2019 to 2 January 2020. No additional cases have been detected since 3 January 2020.

Phylogenetic tree of Corona virus with WH-Human CoV:



Preliminary maximum likelihood phylogenetic analysis of novel Wuhan, China human CoV GenBank (accession MN908947).
Tree based on partial RdRp gene sequence (410bp), aligned with representative human and animal CoV sequences from Genbank.
Rapid analysis by Kevin Olival, EcoHealth Alliance - 11 Jan 2020 (12:30pm EST)

EcoHealth Alliance