



SUMMARY REPORT

Global regulatory workshop on COVID-19 vaccine development

A virtual meeting, held under the umbrella of the International Coalition of Medicines Regulatory Authorities (ICMRA), convening experts from medicines regulatory authorities, the World Health Organisation (WHO) and the European Commission

18 March 2020

The SARS-CoV-2 pandemic that has infected to date more than 200,000 people worldwide presents an extraordinary challenge to global health. Commercial vaccine manufacturers and other entities are developing SARS-CoV-2 vaccine candidates using different technologies and platforms including RNA, DNA, protein and viral vectored vaccines. The rapid spread of SARS-CoV-2 requires accelerated development timelines for SARS-CoV-2 vaccine candidates to enter expeditiously into Phase 1 clinical trials. Hence, the type and extent of preclinical and preliminary clinical data needed to inform the clinical development program for SARS-CoV-2 vaccines must be weighed against the overall risk-benefit assessment of the unmet medical need for vaccines to confront this challenge.

During the first global regulatory workshop on 18 March 2020, delegates from 17 countries, representing more than 20 medicines regulatory authorities globally, and experts from the WHO and the European Commission discussed regulatory considerations related to the development of SARS-CoV-2 vaccine candidates and preclinical data required to support proceeding to first-in-human (FIH) clinical trials. The discussion was co-chaired by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA).

Meeting highlights

The meeting was structured around two presentations and a roundtable discussion between representatives of global medicines regulators.

Key topics:

- Preclinical data required to support proceeding to First in human clinical trials
- The need to address the theoretical risk for SARS-CoV-2 vaccine-induced disease enhancement prior to proceeding to FIH clinical trials

The following represents generally agreed positions among global regulators in attendance.

Preclinical data required to support proceeding to FIH clinical trials

- The extent of preclinical data to support proceeding to FIH clinical trials depends on the vaccine construct, the supportive data available for the construct and data from closely related products.
- Opportunities to leverage knowledge accumulated with platform technology should be considered to accelerate the development of a SARS-CoV-2 vaccine manufactured using the same platform.
- If a platform technology utilized to manufacture a licensed vaccine or other investigational vaccines is well characterized, it is possible to use toxicology data (e.g., data from repeat dose toxicity studies, biodistribution studies) and clinical data accrued with other products using the same platform to support FIH clinical trials for a SARS-CoV-2 vaccine candidate.
- The vaccine manufacturer should provide a rationale supported by data to justify why certain preclinical studies such as toxicity studies would not need to be conducted prior to proceeding to FIH clinical trials.
- CMC characterization should be adequate to support the safety of the SARS-CoV-2 vaccine construct prior to proceeding to FIH clinical trials.
- For all SARS-CoV-2 vaccine candidates it is necessary to obtain data in animals and to characterize the immune response induced by a SARS-CoV-2 vaccine candidate.
- It is not required to demonstrate the efficacy of the SARS-CoV-2 vaccine candidate in animal challenge models prior to proceeding to FIH clinical trials.

Addressing the theoretical risk for SARS-CoV-2 vaccine-induced disease enhancement prior to proceeding to FIH clinical trials

- Participants acknowledged the urgency of proceeding to FIH trials with SARS-CoV-2 vaccine candidate in light of the current pandemic but stressed the importance of risk mitigation strategies so that human subjects enrolled in clinical trials would not need to be exposed to unreasonable risk.
- The potential for vaccine induced disease enhancement is a special circumstance that needs to be evaluated according to available science, which may include the use of relevant animal models currently in development.
- Even though there are limitations in the current knowledge and understanding of risk of enhancement of disease and the value of these models in predicting likelihood of occurrence in humans, studies in animal

models are considered important to understand the potential for vaccine induced disease enhancement with SARS-CoV-2 vaccine candidates.

- It needs to be recognized that there is limited availability of non-human primates and requiring such studies with every SARS-CoV-2 vaccine candidate prior to FIH trials is not possible and would significantly delay clinical vaccine development.
- The need to address the potential for vaccine-induced enhanced disease to enable FIH clinical trials with SARS-CoV-2 vaccines should be based on the totality of available data relevant to the particular SARS-CoV-2 vaccine candidate including the vaccine construct, the immune response induced by it, e.g., Th1-type skewed immune responses and titers of neutralizing antibodies, and the design of the FIH clinical trial.
- Although not unanimous, participants generally agreed that:
 - Some vaccine constructs for which there is adequate support from the knowledge around the immune response elicited, may be allowed to proceed to FIH trials without first completing animal studies to assess the potential for enhanced disease provided adequate risk mitigation strategies are put in place in these FIH trials.
 - For some vaccines, preclinical data (e.g. postvaccination challenge data from animal models, immunopathology studies in animal models, etc.) may be required prior to advancing to FIH clinical trials.
 - In the event that FIH clinical trials are allowed to proceed in the absence of studies in animals that would address the potential for enhanced disease, such studies are, in general, expected to be conducted in parallel with FIH trials so that these data are available prior to enrolling large numbers of human subjects into Phase 2 and 3 clinical trials.
- Risk mitigation strategies to be considered for FIH clinical trials include enrollment of healthy younger adults, proper informed consent to ensure that subjects are aware of the theoretical risks and careful safety follow up and frequent monitoring.
- Regulators expressed the need for developing mechanisms that would allow sharing of data from animal models and clinical trials to alert the global regulatory community regarding the outcomes of trials in an ongoing and timely manner.