Q&As developed by the COVAX Regulatory Advisory Group (RAG): Jan2021

SARS CoV-2 Variant WHO Webinar Overview + RAG Discussion

Emerging SARS-CoV-2 variants is currently a high-on-the-agenda topic in the COVID-19 vaccine community and CEPI/WHO brought this item to the RAG for a high-level early discussion.

WHO had recently hosted a webinar under the R&D Blueprint Agenda. It focused on COVID-19 vaccines: knowledge gaps and research priorities. The potential impact of the variants was considered in the discussion, together with other issues related to the methodology and translation of basic knowledge to the development of vaccines as well as safety and pharmacovigilance considerations.

It was mentioned that variants had been extensively monitored by WHO and by others and that there was no impact being identified at that moment for the vaccines being deployed, except for the societal impact arising from the increasing number of infection cases. On return, this was increasing the pressure to deploy existing vaccines faster as well as to develop further candidates available in the pipeline and to evaluate them regulatory-wise.

The key messages arising from two WHO webinars, the one described above (held 15 January) and another one devoted to variants (held 12 January). Both meetings were organized by the R&D Blueprint Group in the context of the 2021 R&D Agenda:

- Mike Levine (University of Maryland) commented that the SARS-CoV-2 landscape may be moving from a “measles-like situation” (i.e. single vaccine protecting all different measles virus strains) to an “influenza scenario” with a need to changes in the vaccines’ composition.
- An early thinking is needed to prepare for the worst-case scenario, which would imply regular changes to the COVID-19 vaccine composition.
- It was felt that no global picture is available yet with regards to the variants of concern; sequencing data are biased to few geographies in contrast to the influenza situation.
- A need was identified to already think about regulatory pathways in case changes to the vaccines’ composition would be necessary and the potential urgency to do so.
- Influenza vaccine processes were considered a good starting point to model since they represent well established mechanisms proven over many years (assessing circulating influenza viruses, antigenic, genetic, epidemiological and efficacy elements, reference reagents, etc.).
- SARS-CoV-2 specific considerations should be taken along.

It was further informed about a WHO internally held meeting bringing together relevant groups. It was also announced a SARS-CoV-2 virus evolution group being established to develop a risk framework, to evaluate variants of concern and to assess the impact these may have on vaccines, diagnostics as well as on therapeutics.

RAG members were invited to share early thoughts and perspectives in case changes to vaccine composition should be adopted for SARS-CoV-2.

The discussion opened with a summary from the European region and the legislation in place to adopt changes to seasonal vaccine via variation process, though currently limited to Influenza indication. EMA is working with the European Commission to explore mechanisms that could be utilized for SARS-CoV-2 vaccines, acknowledging that a monovalent vaccine could no longer be applicable but rather a multivalent composition would be needed. Discussions being held from a Quality perspective and considering the available technologies (mRNA and adenoviral platforms) indicate that those lend themselves well for adaptations to new strains (possibly by transgene replacements). This situation could be different for other types of vaccines. From the clinical perspective discussions are equally ongoing with no outcome yet.

It was clarified that WHO/CEPI's objective was to gather first preliminary thoughts that would allow to put together a more elaborated plan that could be presented to the RAG at a later time point.

Health Canada confirmed there was a focused interest on the variants' topic at that moment in time. The willingness for flexibility in this jurisdiction was highlighted to potentially adopt a similar mechanism as with flu or multi-antigenic vaccine preparations. The importance to broaden diagnostics was mentioned as well as the need for obtaining sera through immunisation programs that would help to deepen the knowledge of the variants' origin. This point had been taken by the animal working group and more efforts were needed. According to news at the time of the meeting, vaccines had not been impacted by the variants yet but a loss of one particular diagnostic and potentially a loss of one therapeutic had been identified. It was mentioned that vaccine manufacturers were already working on new variants and updating Health Agencies as they advance.

It as commented that as long as the pandemic remained active there needed to be preparatory work and developments to have vaccines from multiple platforms available, both from a regulatory and from a manufacturing perspective.

It was expressed that a preparation phase was first foreseen in which vaccine manufacturers could generate data in advance to allow for a rapid move. In this context RAG members were invited to share any preliminary indications with respect to the kind of data Regulators would think necessary to make these platform technologies more robust. Also, it was inquired which other actions companies could take today for a position that would enable a rapid change when needed.

It was acknowledged that this topic served to open a rolling discussion that would need to be taken along in further meetings to continue exploring the regulatory framework accordingly.

A comment was made with regards to the unknowns about the impact of variants for vaccines being deployed. It was stressed the fact that those vaccines are still rolling out and there is a need to monitor breakthrough cases and identify virus strains genetically for those breakthrough cases.

It was acknowledged the existence of a huge knowledge gap and that probably so far there did not seem to be an impact on vaccines for the UK variant only. It was also commented on the importance of the vaccine's mode of action for the different technologies, to assess whether neutralizing antibodies are decreasing. Further variants need to be closely characterized.

It was noted that data generated so far were collected with pseudo-type viruses and not with wild-type virus strains.

It was stated that authentic viruses for each of the variants needed to be tested with vaccinees' sera. A first challenge was noted with regards to the preparation of sufficient virus stocks that were representative of the circulating virus strains. Culturing viruses in the lab has a risk of introducing additional modifications that should be avoided. A second challenge was noted for the transfer of these stocks across international boundaries, to be shared with multiple research groups. Last, it was reinforced the importance of research work related to breakthrough cases in people being immunized, with the aim to collect data from these individuals in a coordinated and harmonized approach.

In closing, it was stated that this the topic would likely be included on the agenda of upcoming meetings in a routine basis. Should there be any developments in this area between meetings, RAG members were invited to reach out (to CEPI/WHO).