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Committee for medicinal products for human use (CHMP)

Concept paper on the revision of the COVID-19 vaccines guidance documents

Agreed by the Emergency Task Force (ETF)	19 April 2024
Adopted by CHMP for release for consultation	17 June 2024
Start of public consultation	01 July 2024
End of public consultation	30 September 2024

The proposed guideline will replace the European Medicines Agency (EMA) considerations on COVID-19 vaccine approval (EMA/592928/2020) and the Reflection paper on the regulatory requirements for vaccines intended to provide protection against variant strain(s) of SARS-CoV-2 (EMA/117973/2021).

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

Keywords	Vaccine platforms, mRNA, immunobridging, effectiveness, SARS-COV-2, regulatory requirements, sarbecovirus, broad coverage

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1. Introduction

During the CoronaVirus Disease 2019 (COVID-19) pandemic, the EMA Emergency Task Force (ETF) and the CHMP adopted two guidance documents. The first document covered regulatory clinical requirements for COVID-19 vaccines approval and was published in November 2020 (EMA/592928/2020). The second covered quality, non-clinical and clinical regulatory requirements for vaccines intended to provide protection against variant strain(s) of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was published in February 2021 (EMA/117973/2021). Since these documents were published there have been several developments in the field of COVID-19 vaccines. In parallel, the predominant circulating variants of SARS-CoV-2 continue to evolve over time and the immunity of the European Union (EU) population to prior and current variants has increased due to natural exposures and vaccination campaigns.

Experience with applications for scientific advice and for marketing authorisation since 2021 have pointed to the need for revision of the guidance documents. It is proposed to consolidate the two guidance documents into a single guideline that covers the non-clinical and clinical aspects of the development of vaccines against COVID-19. It is intended that quality aspects of COVID-19 vaccines will be covered in a separate guideline (not in the scope of this concept paper).

2. Problem statement

The current guidance documents were developed at a time when the circulating virus variants were still closely related to the ancestral (Wuhan) strain and when the clinical efficacy of the COVID-19 vaccines in use had been assessed in large clinical trials conducted pre-licensure. The regulatory approach to developing vaccines against further variants was considered in the second document of February 2021. With widespread availability of vaccines, updating of vaccine content in line with epidemiological data and variable immunity of the EU population to the most recent variants that reflects prior natural exposures and vaccinations, the vaccine development landscape is now very different to that applicable when the prior guidance was published. These factors all have major implications for the design of feasible clinical trials. For example, placebo-controlled efficacy trials are no longer possible in subpopulations for which vaccination is recommended, leading to reliance on immunobridging to infer vaccine efficacy, for which guidance on primary immune parameters and acceptance criteria is needed. Considerable evidence is available on the use of neutralising antibodies as primary immune parameter for immunobridging. Moreover, there are some situations recognised in which it may not be necessary to conduct clinical trials prior to approval (e.g. when changing the composition of an approved vaccine solely to amend the [encoded] antigen[s]).

In addition, there have been new vaccine constructs proposed since 2021, including the possible development of mucosal (nasally administered) vaccines and vaccines based on other platforms. Furthermore, some early proposals have been made for vaccines intended to prevent not only COVID-19 but also diseases caused by related sarbecoviruses. Current guidance does not address the development of such products.

The current guidance does not address the conduct and reporting of vaccine effectiveness studies and the many difficulties there may be in obtaining reliable data, especially brand-specific data. There is a need to consider the feasibility and possible design of such studies.

Finally, current guidance (EMA/592928/2020 and EMA/117973/2021) includes only high level recommendations on non-clinical requirements for the approval of variant vaccines and this information should be updated in the context of any future COVID-19 vaccine approval.

3. Discussion (on the problem statement)

The following elements of the current guidance documents need to be revised or added:

- Novel platforms under development for SARS-CoV-2 vaccines, including new routes of administration;
- Requirements for changing the antigen composition of / antigens expressed by approved vaccines;
- Inferring efficacy via immunobridging;
- Vaccines intended to protect against several sarbecoviruses, including SARS-CoV-2;
- Vaccine effectiveness studies;
- Non-clinical studies and, where ethically feasible, human challenge studies to support the likelihood of vaccine efficacy;
- Requirements for paediatric development of SARS-CoV-2 vaccines;
- Editorial and structural changes to streamline and improve readability.

4. Recommendation

The ETF recommends revising the existing guidance documents on COVID-19 vaccines, taking into account the issues identified above.

5. Proposed timetable

The timetable for the concept paper is the following:
Discussion at ETF: 19 April 2024
Adoption by CHMP: 17 June 2024
Released for public consultation: 01 July 2024 – 30 September 2024
Adoption and publication of the final version: November 2024

The timetable for the revision of the guideline is the following:
Discussion at ETF on: Q4 2024
Expected date for adoption on: Q1/Q2 2025 followed by 6 months public consultation
Expected finalisation: 2025

Resource requirements for preparation
An estimate of 2-4 ETF members will be required to draft the updated GL.

6. Impact assessment (anticipated)

The revised guideline will address aspects of the non-clinical and clinical development of new SARS-CoV-2 or related sarbecovirus vaccines, including issues that are not covered by the current guidance

documents. This will guide applicants of new vaccines through product development to licensure. The revised guideline will also address post-approval issues including changes in antigenic composition/expression and the collection of vaccine effectiveness data.

All amendments foreseen will contribute to addressing primarily the need for safe and effective coronavirus vaccines including against COVID-19, taking new scientific knowledge and lessons learned from the COVID-19 pandemic into account.

7. Interested parties

EMA: VWP, BWP, PRAC, PDCO, CHMP, NcWP, CTCG

External parties: pharmaceutical industry and vaccine development consortia, academic networks and learned societies within the EU, patients and health care professional representatives.

8. References to literature, guidelines, etc.

- Guideline on clinical evaluation of vaccines (EMEA/CHMP/VWP/164653/05 Rev. 1)
- Guideline on good pharmacovigilance practices (GVP) - Product- or Population-Specific Considerations I: Vaccines for prophylaxis against infectious diseases (EMA/488220/2012 Corr)
- EMA, 2020; International regulators align positions on phase 3 COVID-19 vaccine trials International regulators align positions on phase 3 COVID-19 vaccine trials | European Medicines Agency (europa.eu)
- EMA considerations on COVID-19 vaccine approval - Scientific guideline | European Medicines Agency (europa.eu)
- Regulatory requirements for vaccines intended to provide protection against variant strain(s) of SARS-CoV-2 - Scientific guideline | European Medicines Agency (europa.eu)