EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Emergency Task Force (ETF)

Concept paper on the development of a guideline on the non-clinical and clinical evaluation of antiviral medicinal products and monoclonal antibodies for the prevention and treatment of COVID-19

Agreed by ETF	December 2023
Adopted by CHMP for release for consultation	February 2024
Start of public consultation	22 February 2024
End of consultation (deadline for comments)	30 April 2024

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

Keywords	COVID-19, SARS-CoV-2, clinical study design, monoclonal antibodies, antiviral drugs

1. Introduction

Disease due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to be an important public health problem. This concept paper addresses the need to develop a guideline on the non-clinical and clinical evaluation of antiviral medicinal products and monoclonal antibodies intended for the treatment and/or prevention of coronavirus disease 2019 (COVID-19) for which there is currently no regulatory guideline in the European Union.

The scope of the guideline will be limited to antiviral medicinal products and monoclonal antibodies (mAbs) that are directed specifically against the viral target SARS-CoV-2. Medicinal products that target the host's immune system (for example those blocking the angiotensin-converting enzyme 2 (ACE2) receptor or cytokines) will be out of scope of the document, as these require different

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considerations for evaluating their safety and efficacy. The development of vaccines to prevent COVID-19 will not be covered in this guideline.

2. Problem statement

This concept paper concerns the development of a scientific guideline on the non-clinical and clinical evaluation of antiviral medicinal products and monoclonal antibodies for the treatment and prevention of COVID-19.

During the declared public health emergency of SARS-CoV-2 and thereafter, the EMA Emergency Task Force (ETF) has responded and continues to respond to many requests for scientific advice concerning the development of antiviral medicinal products and monoclonal antibodies intended for the treatment and/or prevention of COVID-19. While the public health emergency has passed, the virus continues to evolve and to cause significant morbidity and variable mortality. There is a need for guidance built on experience so far that addresses appropriate and feasible clinical study designs, including study populations, endpoints and, where appropriate, choice of active comparators. Also, at a joint EMA/FDA Workshop in December 2022, immunobridging approaches for novel monoclonal antibodies that are manufactured on the same platform technology as approved monoclonal antibodies were agreed. Therefore, immunobridging strategies for monoclonal antibodies to expedite the development and access to mAbs for the prevention of COVID-19 will be discussed in the guideline.

Overall, considering all the abovementioned critical new aspects in the field of antiviral medicinal products and monoclonal antibodies directed against the viral target SARS-CoV-2 there is a need for the development of a guideline.

3. Discussion (on the problem statement)

The following elements will be addressed in the proposed guideline:

- Guidance on the non-clinical investigation of antiviral medicinal products and monoclonal antibodies, including the *in-vitro* and *in-vivo* investigation of antiviral activity and any considerations for evaluation that are specific to antiviral medicinal products and monoclonal antibodies;
- Clinical study designs for treatment and prevention strategies using antiviral medicinal products and monoclonal antibodies, with considerations of any differences that may be appropriate for clinical development programmes;
- Guidance specific to patient populations, primary efficacy endpoints and statistical analysis for therapeutic and prevention options with a reference to the ICHE9(R1) addendum on estimands and sensitivity analysis;
- Guidance on the evaluation of any specific safety considerations that may apply;
- Guidance on when it may be acceptable to apply an immunobridging approach to expedite the development of novel monoclonal antibodies for the prevention of COVID-19 and on considerations for the immunobridging exercise;
- Guidance on paediatric requirements.

4. Recommendation

The ETF recommends drafting a guideline on the non-clinical and clinical evaluation of antiviral medicinal products and monoclonal antibodies indicated for the treatment and prevention of COVID-19 taking into account the issues identified above.

5. Proposed timetable

Timetable for the concept paper is the following:

Discussion at ETF:	December 2023
Adoption by CHMP:	February 2024
Released for public consultation:	March 2024
Adoption and publication of the final version:	April 2024

6. Resource requirements for preparation

The drafting of the guideline will be carried out by the ETF, in co-operation with Infectious diseases working party (IDWP). A drafting group of 4-5 members will be constituted. The ETF will appoint a rapporteur among its members who will lead the drafting group and the discussion at ETF during the development of the guideline. The guideline will be discussed at ETF and other meetings as necessary and at IDWP/Interested Parties meetings.

CHMP will discuss and adopt the concept paper, the draft guideline before external consultation and the finalised guideline before publication. Member States will provide input via their ETF members.

7. Impact assessment (anticipated)

The guideline will clarify requirements for regulators and industry with respect to the development of antiviral medicinal products and monoclonal antibodies directed against the viral target SARS-CoV-2.

Overall, it is anticipated that the revised guidelines will have a positive impact on the development of new treatment and prevention options for COVID-19.

8. Interested parties

EMA: IDWP, NCWP, CHMP and CTCG. Consultation with other parties and committees will be initiated as appropriate.

External parties: European learned societies and scientific organisations, EU/EEA regulatory authorities, patient representatives and pharmaceutical industry.

9. References to literature, guidelines, etc.

1. ETF warns that monoclonal antibodies may not be effective against emerging strains of SARS-CoV-2| European Medicines Agency (europa.eu) etf-statement-loss-activity-anti-spike-protein-monoclonal-antibodies-due-emerging-sars-cov-2_en.pdf (europa.eu)

2. European Medicines Agency. Summary report of the joint EMA-FDA workshop on the efficacy of monoclonal antibodies in the context of rapidly evolving SARS-CoV-2 variants. Published 08 February

2023. https://www.ema.europa.eu/en/documents/report/summary-report-joint-ema-fda-workshop-efficacy-monoclonal-antibodies-context-rapidly-evolving-sars_en.pdf. Accessed 19 September 2023.