EMA
EUROPEAN MEDICINES AGENCY

EMA HBV guideline update

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HBV Forum 15 Meeting

06 November 2025

Reasons for the guideline revision

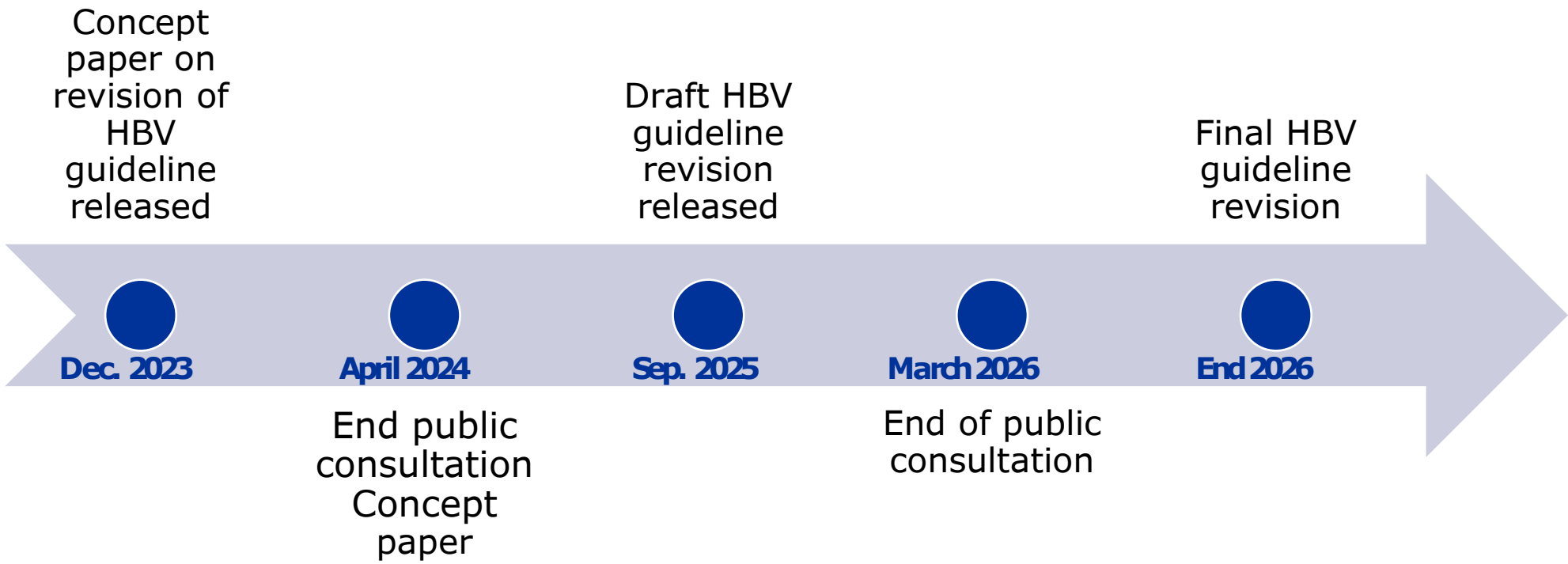
- First revision of the guideline on the clinical evaluation of medicinal products intended for the treatment of hepatitis B (CHMP/EWP/6172/03).
- Current Hepatitis B guideline (CHMP/EWP/6172/03) was **published in September 2006**
  - Addresses clinical study designs and endpoints applying to **Nucleoside analogues** and **interferons**
  - The treatment goal of **functional cure** has evolved → **changed** the **development landscape** of agents

    → Current guidance **did not address** agents with **other mechanisms of action** and **combination regimens** aiming at achieving **functional cure** of CHB infection.
- **International expert meetings** on treatment goals, treatment durations, endpoints, study populations and the definition of functional cure, **updated EASL treatment guidelines** and **methodological guidance documents** were published

  → **Considered** and **reflected** in the guideline
- **Combined endpoint** of sustained suppression of HBV DNA and sustained HBsAg loss → **accepted** as **surrogate markers** for efficacy

  → **Change of acceptable and recommended primary endpoints for clinical trials**

Timeline for the revision of the EMA guideline on the clinical evaluation of medicinal products intended for the treatment of chronic hepatitis B



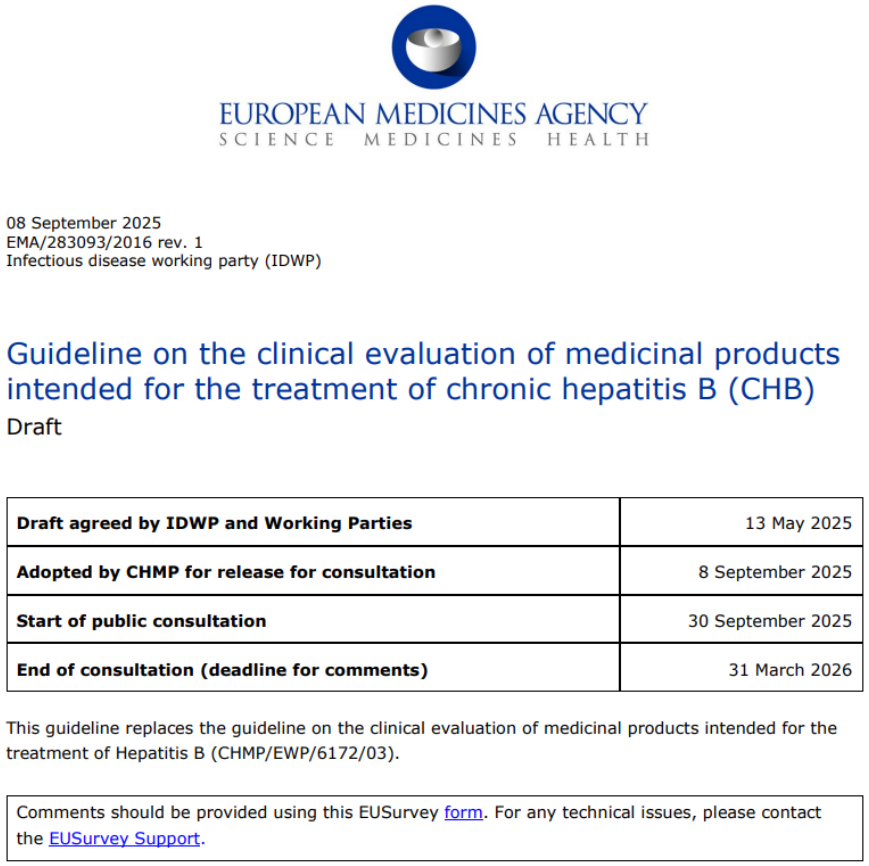
Topics revised/added

- **Clinical trial requirements** including trials that aim to demonstrate the efficacy of novel treatments or combination treatment regimens for viral suppression, including **chronic and finite treatment**, and/or **finite treatment for functional cure** of chronic hepatitis B (CHB)
- Update **recommendations for primary efficacy endpoints** to include endpoints relevant for achieving viral suppression or functional cure.
- **Efficacy and safety considerations** when **stopping suppressive NUC treatments** in clinical trials that evaluate finite regimens and regimens intended to achieve functional cure.
- **Specific considerations** for the development of agents with **novel mechanisms of action** and **patient characteristics**
- **Statistical analyses** in trials that evaluate **finite treatment regimens**.
- **Definitions** of **HBV cure** and **diagnostic criteria**.

Public consultation and EUSurvey form

- The draft guideline is currently out for **public consultation**
- Deadline for comments: **31 March 2025**
- **Comments** can be sent via the **EU survey form**

- **Link** to the **draft guideline**: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-clinical-evaluation-medicinal-products-intended-treatment-chronic-hepatitis-b-chb-revision-1_en.pdf
- **Link** to the **EU survey form** (can be also found in the guideline): https://ec.europa.eu/eusurvey/runner/6511ea34-88c2-d6f7-7666-65d671102974



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08 September 2025
EMA/283093/2016 rev. 1
Infectious disease working party (IDWP)

Guideline on the clinical evaluation of medicinal products intended for the treatment of chronic hepatitis B (CHB)
Draft

Draft agreed by IDWP and Working Parties	13 May 2025
Adopted by CHMP for release for consultation	8 September 2025
Start of public consultation	30 September 2025
End of consultation (deadline for comments)	31 March 2026

This guideline replaces the guideline on the clinical evaluation of medicinal products intended for the treatment of Hepatitis B (CHMP/EWP/6172/03).

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

EMA guidelines on Gene-editing and Advanced therapy medicinal products

Guidelines:

- Structure and data **requirements** for a **clinical trial application** for **exploratory and confirmatory trials** with advanced therapy investigational medicinal products: Guideline on quality, non-clinical and clinical requirements for investigational advanced therapy medicinal products in clinical trials - Scientific guideline | European Medicines Agency (EMA)
- **Quality, Preclinical** and **Clinical aspects** of **gene transfer medicinal products** including aspects on development and evaluation: Quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells - Scientific guideline | European Medicines Agency (EMA)
- Aspects of the **active clinical follow-up of patients** to detect signals of early or delayed adverse reactions, to prevent clinical consequences of such reactions, to ensure timely treatment and to gain information on the long-term safety and efficacy of the intervention: Follow-up of patients administered with gene therapy medicinal products - Scientific guideline | European Medicines Agency (EMA)
- Aspects of **pharmacovigilance, risk management planning, safety** and **efficacy** and **clinical follow-up** of **authorised ATMPs**: Guideline on safety and efficacy follow-up and risk management of advanced therapy medicinal products - Scientific guideline | European Medicines Agency (EMA)
- Aspects on the **environmental risk assessment** of GMO-containing gene therapy medicinal products: Scientific requirements for the environmental risk assessment of gene-therapy medicinal products - Scientific guideline | European Medicines Agency (EMA)
- **Non-clinical studies required before** the **first use** of a GTMPs in human subjects: Non-clinical studies required before first clinical use of gene therapy medicinal products - Scientific guideline | European Medicines Agency (EMA)
- Application of the **risk-based approach** in the preparation of a marketing authorisation application: Risk-based approach according to Annex I, part IV of Directive 2001/83/EC applied to Advanced Therapy Medicinal Products - Scientific guideline | European Medicines Agency (EMA)
- **Non-clinical inadvertent germline transmission testing** needed to support clinical development Non-clinical testing for inadvertent germline transmission of gene transfer vectors - Scientific guideline | European Medicines Agency (EMA)
- **Quality aspects** that are relevant for lentiviral vectors Development and manufacture of lentiviral vectors - Scientific guideline | European Medicines Agency (EMA)

- For information on **clinical study designs** the **new guideline** on ATMPs is a **good starting point.**
- For **gene-editing,** experience is limited → **come for scientific advice**

General overview on all relevant guidelines and documents:

- Multidisciplinary: gene therapy | European Medicines Agency (EMA)

EMA documents on gene-editing and advanced therapy medicinal products

Reflection paper:

- Design modifications of gene therapy medicinal products during development - Scientific guideline | European Medicines Agency (EMA)
- Quality, non-clinical and clinical issues relating specifically to recombinant adeno-associated viral vectors - Scientific guideline | European Medicines Agency (EMA)
- Management of clinical risks deriving from insertional mutagenesis - Scientific guideline | European Medicines Agency (EMA)

Q&A documents:

- Questions and answers on comparability considerations for advanced therapy medicinal products (ATMP) - Scientific guideline | European Medicines Agency (EMA)
- Questions and answers on gene therapy - Scientific guideline | European Medicines Agency (EMA)

ICH guideline:

- ICH guideline S12 on nonclinical biodistribution considerations for gene therapy products - Step 2b - Scientific guideline | European Medicines Agency (EMA)
- ICH Considerations: general principles to address virus and vector shedding - Scientific guideline | European Medicines Agency (EMA)
- ICH Considerations: oncolytic viruses - Scientific guideline | European Medicines Agency (EMA)

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Thank you

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