EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 August 2026
EMA/189190/2026

The EU Submission, Timelines and Review Talk (EUSTART)

Aim

This document aims to support the participants in preparation for the EUSTART joint pre-submission meeting (PSM) to identify issues for discussion between the applicant, the Rapporteur(s), NCAs' assessment teams, and the EMA. Ultimately, it is expected to help:

- Facilitate a smooth assessment procedure and prevent the need for clock-stop extensions,
- Avoid applications supplemented with substantial new data during the review period, which should have been presented at the time of the initial application submission ("premature dossiers"),
- Support agreement of the Rapporteurs and the applicant on the submission date.

The applicant should

- Inform the EMA Product Lead (PL) about their request for an EUSTART with the Rapporteur(s)' and NCAs' assessment teams.
- Cover all points below and provide additional information, as applicable, in the briefing package and send this to the NCA(s)/EMA PL at least 3 weeks prior to the EUSTART.
- Be prepared to discuss any dossier-related issues during the EUSTART.
- Provide the meeting minutes within 2 weeks, including the conclusion on dossier maturity and the anticipated submission date.
- Raise regulatory, administrative, and procedural aspects in writing with the EMA team (during Pre-submission Interactions), prior to the EUSTART with the Rapporteurs and NCA(s).

Reminder

As stated in the CHMP guideline EMEA/75401/2006 Rev. 2: *"Applicants are reminded that, in general, no substantial data derived from new studies should be introduced as part of the responses to the List of Questions (LoQs) or List of Outstanding issues (LoOIs) that were not specifically requested by the CHMP. However, new analysis might be included, such as follow-up data from previously submitted studies. This is particularly important at day 180 where assessment time is limited*." Hence, clock-stops granted by the CHMP have a fixed standard duration. No substantial data derived from new or ongoing studies are to be introduced unless explicitly requested *https://www.ema.europa.eu/en/time-allowed-*

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applicants-respond-questions-issues-raised-during-assessment-new-marketing-authorisation-applications-centralised-procedure.

Disclaimer

Pre-submission interactions are not intended to provide pre-assessment of any of the documents provided. The views expressed during the meeting by the Rapporteur(s)/assessor(s) and EMA are based on the information provided and are not binding to CHMP.

General topics

- Choice of legal basis for the marketing authorisation application (MAA)
- Applications falling under the Art 10 of EU Directive 2001/83:
  - reference product and medicinal product used as comparator used in bridging studies
  - literature and proposed dataset for bridging strategy
  - scope and range of any new clinical efficacy/safety data
  - details of the bridging exercise and specific SAWP consultation on this topic
- NCA or CHMP scientific advice/protocol assistance:
  - topics covered
  - deviations from SA/PA
- Applicable (CHMP, ICH, other) scientific guidelines and deviations from these during development
- Claimed indication
  - proposed wording
  - orphan designation, orphan condition
  - other products authorised in this condition/indication
- PDCO opinion/PIP
  - compliance of the current development with PIP
  - specific paediatric formulation
- Accelerated assessment
- Conditional Marketing Authorisation (MA) or MA under exceptional circumstances (EC)
  - fulfilment of relevant criteria for conditional MA or MA under EC
- New active substance status
- Details of request for +1year market protection
- Comprehensiveness of data at the time of MAA filing
  - proposed data package for conditional MA or MA under EC, if intended
  - proposed post-authorisation commitments or obligations

Quality and GMP topics

- Starting materials[1]
- Use commercial batches of the proposed medicinal product in the confirmatory clinical trials and comparability exercise[1]
- Quality specifications[1]
- Compliance of risk of nitrosamines' presence investigations with the valid guidance and short overview of results[1]
- Description of a medical device (either co-packaged or integrated)
    - notified body opinion/fulfilment of the requirements of the MDR, as applicable
- Flow chart with identification of steps and sites for manufacturing and testing, including details of sites performing testing for the purpose of batch release and batch release sites.
- Availability of:
    - key product specific aspects, e.g. dissolution method development, manufacturing process validation, comparison of quality attributes, biosimilarity, etc[1]
    - validation data of manufacturing process at time of submission[1]
    - validation data of key analytical procedures in the drug substance and drug product specification at time of submission[1]
    - final stability data at submission
    - manufacturing authorisations for all finished product manufacturing sites
    - valid GMP certificates issued by an EU authority (or if located in a Mutual Recognition Agreement territory, GMP compliance confirmation from the concerned partner authority) for all third country sites for the proposed activity
- Need for inspection of third country sites to confirm GMP compliance during the MAA evaluation

Non-clinical topics

- Description of the non-clinical development[2]
- Compliance with the ICH S9 guidance
- Description of any literature data for (geno-, carcino-, etc.) toxicity, their reliability and comprehensiveness
- Environmental Risk Assessment (ERA) development
- Major concerns from preclinical studies (SmPC, RMP wording)
- Planned non-clinical post-authorisation measures

[1] If applicable, please address SAWP consultation on the topic
[2] If applicable, please address SAWP consultation on the topic

Clinical and GCP topics

- Pharmacokinetics development/characterisation and it's completeness (special patient populations, drug-drug interactions, patients' age, gender, etc.)
- Description of PK/PD modelling
- Model-Informed Drug Development (MIDD)
- Details and content of pivotal clinical data package
- Proposed target population in the indication and its consistency with tested pivotal study patient population
- Proposed posology and its consistency with that in the pivotal study
- Definition of population biomarkers[2]
    - validation for the current use
    - exploration in the clinical trials
    - companion diagnostic use
- Availability of final CSRs at the time of submission
    - potential proposed timelines for data availability during evaluation
- Conducted GCP inspections/audits
    - description of findings/concerns including information on actions taken
- List of GCP inspections planned by any regulatory authority in the future
- Definition of estimands for the pivotal study[2]
- Description of any non-inferiority or equivalence studies
    - pre-specification of analyses and margins [2]
- Description of pre-specified margin for clinical relevance of the outcome(s)
- Any major safety concerns and planned additional risk minimisation measures
- Proposed post-authorisation monitoring or development commitments/plans
- Availability of mature PI at the submission

Submission date

- Planned submission date
- Foreseen issues leading to risks with respect to the accuracy of the currently proposed submission date
- Up-to-date details of any ongoing or planned developments (incl. quality) and when any data/results might be available.