CHMP <Protocol Assistance> <Scientific Advice>

Document type: Choose an item

Active substance name – Applicant name

Proposed indication

Procedure number

The use of this template for the **briefing document** is mandatory and standard headings in the template should be used; It is important to follow the template as the document will be subsequently used for assessment whereby sections marked as <draft CHMP answers> will be completed by SAWP coordinators.

This annotated template should be read in conjunction with the relevant guidelines that can be found on the website of the European Medicines Agency: ‘[EMA Guidance for applicants seeking requesting Scientific Advice and Protocol Assistance](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-guidance-applicants-seeking-scientific-advice-protocol-assistance_en-0.pdf).

The briefing document should contain all necessary information and function as a ‘stand-alone’ argument. Cross-references to annexes can be included only when additional detail is needed to support the argument.

Bracketing convention:

{text}: required text

<text>: optional text

Formatting convention: Body Text Agency (Verdana 9 pt, Line spacing: At least 14 pt, After: 7 pt).

References convention: For citation of literature references, footnotes are preferred, alternatively the format (first author <et al.>, publication year) is recommended. For footnotes, a smaller font size can be used.

**Text in light blue** is for regulators’ use only (i.e., at the time of First and Joint Report) and should not be amended or deleted by the applicant.

***Regulator’s use only ~~-~~***

*This section can be deleted at the time of the Joint report.*

Coordinator’s Executive Summary <Member State>

**Coordinator:**

**Experts:**

**EMA scientific officer:**

**EMA procedure assistant:**

[**Expected plenary discussion:**](#plendis)Choose an item.

**Discussion Meeting proposed:** Choose an item.

1. Advice profile

**Product and target indication**

*- a brief description of the product(s) and mechanism(s) of action*

*- the proposed wording for the intended indication*

*- very short essential information on main features of the targeted disease and current standard therapy ONLY focused on the specific setting of the target indication*

*- a very short statement on the placing in therapy and the rationale supporting the use of the product in the intended indication*

[**Regulatory status (existing licensure, prev. SAs, etc)**](#RegStatus)

*- specify if already authorised in EU and/or in other Countries*

*- describe type of existing MA in EU, if relevant (e.g., full/mixed dossier; advanced therapy, biosimilar, generic/hybrid MA legal basis; conditional or exceptional circumstances MA)*

*- describe ongoing/planned MAA and/or variation(s), if relevant*

*- Orphan Designation in EU, if relevant*

*- PIP, if relevant*

*- PRIME status (if applicable)*

*- Previous CHMP SA, national SA or advice instances from other regulators: include here details only if relevant to the present procedure*

*Any further regulatory information only if deemed relevant*

**Rationale for seeking scientific advice and scope of questions: Quality, Non-Clinical, Clinical, Significant Benefit**

*Describe the scope of the questions and the rationale for the advice request (Quality, Clinical, Non-Clinical, etc.).*

*Specify if this is a parallel advice with HTA, FDA or if there are other parallel procedures submitted by the same applicant that are relevant and should be dealt together.*

1. Advice content

**[High Level Overview of the Advice Setting](#Overview" \o "A short summary of the advice, may include a figure of the study design.)**

*This section should provide a more detailed description of the scope of the request, with essential information on the product development that are relevant to the scope of the advice. A schematic of clinical trial(s) with details on study design, if relevant, should be included.*

**[Key Messages of Answers to All Questions](#KeyMess" \o "Please indicate what is asked and if it is acceptable or not with your motivation, and with a reference to the number of question)**

*In this section list all Questions/sub-questions (e.g., Q1a, Q1b, etc.) divided by the main scope (Quality, Multidisciplinary Quality/Non-Clinical/Clinical, Non-Clinical, Multidisciplinary Non-clinical/Clinical, Clinical and Significant Benefit).*

*For each Question, please indicate the specific topic and provide a short summary of the response.*

*The summary could be the same as the conclusion of the Draft answer stating* *clearly if the Applicant’s position is fully supported or partially supported, or not optimal but acceptable with caveats (to be specified). If the applicant’s position is not agreed, specify what is rejected (with a rationale and potential alternatives to be considered based on scientific evidence and guidelines). If a question cannot be fully answered because further information/clarification is needed, the coordinator, depending on the expected complexity and likely availability/unavailability of the additional information, should clearly indicate whether these should be provided in the context of the present procedure (via written response or in a discussion meeting) or whether this should be the subject of a follow-up advice.*

***<Quality>***

***<Multidisciplinary Quality/Non-Clinical/Clinical>***

***<Nonclinical>***

***<Multidisciplinary Non-Clinical/Clinical>***

***<Clinical>***

***< Significant Benefit>***

1. [Coordinator's critical topics for SAWP plenary discussion](#CritTop" \o "List only keywords for main topics for plenary discussion. E.g.:Starting material, Population, Inclusion criteria)

*Please, clearly indicate and list the specific topics proposed for discussion.*

1. [Draft questions for discussion meeting list of issues](#DMQs" \o "Please outline the questions)

1. [Need for consultation and/or information from previous advice/ authorisations](#PrevAd" \o "Indicate if you need information from relevant SAs/MAs; if you have questions to a WP, Committee or patient. Comment on the expected real life vs enrolled population (geriatrics, exclusion criteria, formulation?))

1. [Additional comments for SAWP plenary presentation](#AddComments" \o "Please indicate any comment you may have regarding the presentation, if needed.)

***~~-------------------------------------~~***

Table of Contents

[List of Figures 7](#_Toc116299065)

[List of Tables 7](#_Toc116299066)

[List of Abbreviations 7](#_Toc116299067)

[1. Introduction 8](#_Toc116299068)

[1.1. Background information on the disease to be treated 8](#_Toc116299069)

[1.2. Background information on the product 8](#_Toc116299070)

[1.3. Regulatory status 8](#_Toc116299071)

[1.4. Rationale for seeking advice 9](#_Toc116299072)

[2. Overview of product development 9](#_Toc116299073)

[2.1. Quality background information 9](#_Toc116299074)

[2.1.1. <Active substance> 10](#_Toc116299075)

[2.1.2. <Finished product> 10](#_Toc116299076)

[2.2. Non-clinical background information 10](#_Toc116299077)

[2.2.1. <Pharmacology> 10](#_Toc116299078)

[2.2.2. <Pharmacokinetics> 10](#_Toc116299079)

[2.2.3. <Pharmacodynamics> 10](#_Toc116299080)

[2.2.4. <Toxicology> 10](#_Toc116299081)

[2.3. Clinical background information 10](#_Toc116299082)

[2.3.1. <Clinical pharmacology> 10](#_Toc116299083)

[2.3.2. <Pharmacokinetics> 10](#_Toc116299084)

[2.3.3. <Pharmacodynamics> 10](#_Toc116299085)

[2.3.4. <Clinical efficacy> 10](#_Toc116299086)

[2.3.5. <Clinical safety> 11](#_Toc116299087)

[3. Questions and Applicant’s positions 12](#_Toc116299088)

[3.1. < Questions on Quality development> 12](#_Toc116299089)

[3.2. <Multidisciplinary Question<s> on Quality and Non-clinical development> 13](#_Toc116299090)

[3.3. <Questions on Non-clinical development> 14](#_Toc116299091)

[3.4. <Multidisciplinary Question<s> on Non-clinical and Clinical development> 14](#_Toc116299092)

[3.5. <Questions on Clinical development> 14](#_Toc116299093)

[3.6. <Questions on Significant Benefit> 15](#_Toc116299094)

[3.7. <Other CHMP comments not directly related to the questions> 15](#_Toc116299095)

[List of References 16](#_Toc116299096)

[List of Annexes 17](#_Toc116299097)

List of Figures

List of Tables

List of Abbreviations

Any acronyms or abbreviations used should also be defined the first time they appear in the text.

1. Introduction

The objective of this section is to briefly introduce the disease setting, the product, its regulatory status and the rationale for seeking advice.

* 1. Background information on the disease to be treated

Outline main features of the disease and current standard therapy, referring to relevant publications.

* 1. Background information on the product

Include mode of action, chemical structure and pharmacological classification.

Please specify the proposed wording for the intended indication, posology, and any special precautions or recommendations for use of the product (including a possible risk management strategy).

* 1. Regulatory status

Describe the worldwide regulatory status of the product (e.g., any existing MA, or planned MAA timelines), indicating planned type and timelines of marketing authorisation application (MAA) (e.g., full/mixed dossier; advanced therapy, biosimilar, generic/hybrid MA legal basis; conditional or exceptional circumstances MA, if relevant) or variation.

If the product has received Orphan Designation (OD) related to the intended indication, state the orphan indication, the criteria on which the ODD was based and, if applicable, the development plan to support similarity or clinical superiority.]

Indicate if scientific advice has been previously requested from the CHMP, national or non-EU (e.g., FDA) regulatory authorities.

Indicate if relevant CHMP guidance/CHMP advice has been followed or if any deviations have been made or proposed.

Indicate applicability and status of the Paediatric Investigation Plan (with or without deferral or waiver).

Indicate availability and need for development in other special populations such as the elderly, male/female and ethnic minorities.

In case of follow-up advice, summarise the previous recommendations by the CHMP, indicate changes made to the development plans further to that advice and highlight points where follow-up is requested. A tabular presentation of this information can be considered.

* 1. Rationale for seeking advice

Describe the scope of the questions and the rationale for the advice request (e.g., clinical/non-clinical/quality/significant benefit/similarity/conditional approval/exceptional circumstances).

1. Overview of product development

This section should give a comprehensive scientific overview of the product development program, providing relevant systematic information in sufficient detail, together with a critical discussion. However, it should be kept in mind that any information essential for the justification of a given question should also be sufficiently discussed in the corresponding Applicant’s position. The proposed list of subsections is not meant to be exhaustive nor mandatory, since the relevance or applicability of each subsection may vary depending on the scope of the advice request. In this respect, the potential direct or indirect relevance of the information covered in relation to the questions posed should be considered. It is strongly recommended to address all elements outlined below related to the area (quality, nonclinical, clinical) of the scientific advice. For areas not within the scope of the advice, it is acceptable to include only high-level information. The briefing document should contain all necessary information and function as a ‘stand-alone’ argument. Cross-references to annexes can be included only when additional detail is needed to support the argument. The use of tabulated overviews and graphs is encouraged.

* 1. Quality background information

This section should provide an overview of the following aspects in addition to the Applicant’s position to quality/GMP questions: Active substance (AS) definition and structure, manufacture sites and process flow chart, AS and finished product (FP) specifications, stability, FP composition and primary packaging.

If a medical device is proposed, it should be described and the status of compliance with the Medical Devices Regulation (EU) 2017/745 mentioned.

Novel manufacturing approaches (e.g., decentralised manufacturing approaches, enhanced manufacturing approaches, digitalisation in manufacturing), where used as part of the manufacturing process, and innovative technologies such as nanomaterials or genome editing should be described.

* + 1. <Active substance>
    2. <Finished product>
  1. Non-clinical background information

It is recommended to include a tabulated overview of all non-clinical studies (completed, ongoing and planned), including study number, main design features and GLP status. Main findings and safety margins may be described in the narrative.

* + 1. <Pharmacology>
    2. <Pharmacokinetics>
    3. <Pharmacodynamics>
    4. <Toxicology>
  1. Clinical background information

A tabular overview of all clinical studies including study number, main design features, patient number and characteristics, and current study status (completed, ongoing, planned) etc. could be informative, if not provided elsewhere.

**A schematic of the clinical trial(s) for which advice is requested should be included. If this(ese) trial(s) is(are) ongoing, detailed information on the current status of the trial(s) should be provided, including number of patients currently enrolled, date of first patient enrolment, anticipated date of last patient enrolment, number of investigator sites currently participating by geographical region, date of the most recent protocol amendment, date of the most recent version of the statistical analysis plan (if any). Moreover, the impact on the integrity of the ongoing trial(s) from any potential changes to the study design related to the scientific advice questions should be considered and described.**

Whilst the focus should be kept on the intended indication, the development in other indications could be briefly summarised, where relevant.

* + 1. <Clinical pharmacology>
    2. <Pharmacokinetics>
    3. <Pharmacodynamics>
    4. <Clinical efficacy>

A general overview of the clinical development program should be based on a comprehensive discussion of e.g., the main clinical results so far, dose-response, exploratory trials, special populations, supportive and pivotal clinical studies, and any analyses performed across trials (pooled and meta-analysis). The discussion should identify the most important findings and challenges in the clinical development program, and its compliance with legal requirements, relevant clinical guidelines, previous scientific advice (sufficiently justifying any deviations), etc. Information on the geographical distribution of centres participating in the pivotal clinical studies can be reflected in this section.

* + 1. <Clinical safety>

A general overview of the safety profile of the product should be based on a comprehensive discussion of e.g., patient exposure (safety database), adverse events observed so far, serious adverse events and deaths, laboratory findings, safety-related discontinuations, specific safety findings, immunological events, safety in special populations, etc.

1. Questions and Applicant’s positions

**Questions** should conform to the **scope** of the Scientific Advice/Protocol Assistance procedure as detailed in the [EMA guidance for Applicants seeking scientific advice and protocol assistance](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-guidance-applicants-seeking-scientific-advice-protocol-assistance_en-0.pdf). It is recommended that questions are phrased in a way to allow for an unambiguous understanding of the question. The scope should be carefully considered in order to avoid too broad or too narrow questions.

The wording of the question should be clear and concise, avoiding extended reference to the justifications (which should be discussed in the Applicant position) and starting with e.g. “Does the CHMP agree that/with …?”).

Questions should be ordered in the corresponding section according to the expertise (also multidisciplinary) required for the assessment and numbered sequentially.

**IMPORTANT INFORMATION**

**Each question should be followed by a corresponding, separate Applicant’s position including a comprehensive justification of the chosen approach.**

**All key information about the topic should be sufficiently discussed, so that the Applicant position can function as a ‘stand-alone’ argument. Issues to be covered could include the following: context and proposal, other options (potentially) considered together with a critical discussion on the relative merits and drawbacks of various approaches, possible consequences and eventual measures to ameliorate these. Statements regarding the properties (e.g., type I error control) of novel and/or complex statistical procedures should be justified with reference to the relevant scientific literature, or otherwise. In general, an extension of 1 to 3 pages for each Applicant position is recommended.**

**Cross-references to the relevant parts of the briefing document or annexes can be included if additional detail is needed to support the argument.**

* 1. < Questions on Quality development>

Question 1

**Does the CHMP agree that/with…?**

Applicant’s position

{}

Draft CHMP answer to Question 1

*Scientific discussion*

*Conclusion*

Question {X}

**Does the CHMP agree that/with…?**

Applicant’s position

{}

Draft CHMP answer to Question {X}

*Scientific discussion*

*Conclusion*

* 1. <Multidisciplinary Question<s> on Quality and <Non-clinical> and <Clinical>development>

Question {X}

**Does the CHMP agree that/with…?**

Applicant’s position

{}

Draft CHMP answer to Question {X}

*Scientific discussion*

*Conclusion*

* 1. <Questions on Non-clinical development>

Question {X}

**Does the CHMP agree that/with…?**

Applicant’s position

{}

Draft CHMP answer to Question {X}

*Scientific discussion*

*Conclusion*

* 1. <Multidisciplinary Question<s> on Non-clinical and Clinical development>

Question {X}

**Does the CHMP agree that/with…?**

Applicant’s position

{}

Draft CHMP answer to Question {X}

*Scientific discussion*

*Conclusion*

* 1. <Questions on Clinical development>

Question {X}

**Does the CHMP agree that/with…?**

Applicant’s position

{}

Draft CHMP answer to Question {X}

*Scientific discussion*

*Conclusion*

* 1. <Questions on Significant Benefit>

*For Protocol Assistance, the questions should be within the scope of the designated orphan indication (see* [*EMA guidance for Applicants seeking scientific advice and protocol assistance*](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-guidance-applicants-seeking-scientific-advice-protocol-assistance_en-0.pdf)*).*

Question {X}

**Does the COMP agree that/with…?**

Applicant’s position

{}

Draft COMP answer to Question {X}

*Scientific discussion*

*Conclusion*

* 1. <Other CHMP comments not directly related to the questions>

List of References

In general, any potentially relevant publications included in the list of references should be annexed. In case a relevant publication is not included at the time of validation, it should be ensured that it can be made available upon request.

List of Annexes

Annexes (to be submitted as separate files) should include any information potentially relevant to the questions, e.g.

Investigators’ brochure

Study protocols (final, draft or outline/synopsis, statistical analysis plan)

Study reports (final/draft/synopses)

Pharmacokinetic modelling and simulations reports

Previous scientific advice received relevant for the present request (e.g., CHMP Scientific advice/Protocol Assistance, any relevant official correspondence and meeting minutes with National Competent Authorities in EU-Member States, FDA and other non-EU Authorities)

Relevant guidelines (non-EMA)

Documents related to Orphan Designation (e.g., COMP summary report)

Documents related to Paediatric Investigation Plans (e.g., PDCO summary report, opinion)