<date>

Doc. Ref.:

Applicants are free to add proprietary header and/or footer should they wish

Responses to <D90><D120><D180> <list of questions><list of outstanding issues> - <quality<-ASMF>> <nonclinical> <clinical>

\* more granular documents e.g. Efficacy, Safety, Product Information can be submitted, but at minimum, 1 response document for each module (i.e. quality, nonclinical and clinical). Please make sure the title of the document is very clear as regards the contents.

<Product name>

International non-proprietary name: <INN> or <Common name>

\*\*eg for vaccines and some ATMPs

<Pharmaceutical form and strength>

Procedure No. EMEA/H/C/<XXX>

Applicant:

Tick boxes:

Confirmation that all questions have been transferred into this document without any amendments

Confirmation that word document and pdf document are identical

**Instructions to Applicants**

The applicant is expected to respond to all the questions directly in this document and submit both PDF and MS Word versions with their official responses in eCTD.

The questions should be copied/pasted verbatim, and must not be combined or amended. After each question, copy/paste the title for the Applicant’s response as well as the box for (Co)-Rapporteur’s assessment. The questions should follow the same order and numbering as included in the list adopted by the committee.

All sections (i.e., question, applicant’s response and assessment of the applicant’s response) should be replicated as many times as needed and questions placed under each relevant topic (i.e., drug product, drug substance; pharmacology, PK, toxicology; pharmacokinetics, pharmacodynamics, clinical efficacy, clinical safety, pharmacovigilance, orphan similarity and derogations, NAS status, additional data exclusivity/marketing protection, etc.). Questions on the closed part of the ASMF are to be answered separately by the ASMF holder.

If any sections are not applicable (e.g., if there are no major objections for a particular topic), please state “not applicable”. The headings <Orphan similarity and derogations>, <New active substance status>, <Additional data exclusivity/Marketing protection> can be deleted if not relevant.

The Applicant is expected to prepare - at minimum - separate response documents for quality, nonclinical and clinical aspects as well as a separate document on aspects on product information. In addition, the Applicant may choose to further separate the responses into more granular response documents, e.g., clinical pharmacology, clinical safety, clinical efficacy. In the case of multiple response documents, an informative title should be added on the front page.

The Applicant adds their complete responses concerning each question. It is not acceptable to just refer to appendices. However, appendices may be used and referred to if large data packages, new data, space-consuming tables or pictures need to be included to support the responses. Cross links are encouraged to ease the assessment. Study reports or similar should not be included as appendices but placed in the correct section of the eCTD and cross-referenced. Appendices referred to should be easily identified in the response. There should not be unnecessary repetition between the response body and the appendices.

Prior to the submission of the responses, the Applicant should delete all the blue guidance text in this document[[1]](#footnote-2).

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1. Abbreviations

Please add any abbreviations used in the document.

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1. Quality aspects

NB: This document should only address responses to questions pertaining to the open part of the ASMF.

* 1. Major Objections
     1. Drug substance

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Drug product

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* 1. Other concerns
     1. Drug substance

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Drug product

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

1. Non-clinical aspects
   1. Major Objections
      1. Pharmacology

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Pharmacokinetics

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP/Overview AR has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Toxicology

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* 1. Other concerns
     1. Pharmacology

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Pharmacokinetics

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Toxicology

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

1. Clinical aspects
   1. Major Objections
      1. Pharmacokinetics

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Pharmacodynamics

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Clinical Efficacy

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Clinical Safety

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Risk management plan

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Pharmacovigilance

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* 1. Other Concerns
     1. Pharmacokinetics

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Pharmacodynamics

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Clinical Efficacy

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Clinical Safety

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Risk management plan

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* + 1. Pharmacovigilance

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

1. Multidisciplinary questions
   1. Major Objections

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

* 1. Other Concerns

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

1. Other

For Rapporteurs: separate assessment reports are used for similarity, derogation to similarity, NAS and additional Data exclusivity/Marketing protection, therefore, please, copy/paste the entire section (including each question, the applicant’s position and the box with the Assessment of applicant’s response) from the sections below as needed to the relevant stand-alone assessment report.

* 1. <Orphan similarity and derogations>
     1. Major Objections

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

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| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The similarity/derogation report and the CHMP AR/Overview have been updated accordingly><No update to the similarity/derogation report and the CHMP AR/Overview required>. |

* + 1. Other Concerns

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The similarity/derogation report and the CHMP AR/Overview have been updated accordingly><No update to the similarity/derogation report and the CHMP AR/Overview required>. |

* 1. <New active substance status>
     1. Major Objections

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The New Active Substance report and the CHMP AR/Overview have been updated accordingly><No update to the New Active Substance report and the CHMP AR/Overview required>. |

* + 1. Other Concerns

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The New Active Substance report and the CHMP AR/Overview have been updated accordingly><No update to the New Active Substance report and the CHMP AR/Overview required>. |

* 1. <Additional data exclusivity /Marketing protection>
     1. Major Objections

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The additional data exclusivity /marketing protection report and the CHMP AR/Overview have been updated accordingly><No update to the additional data exclusivity /marketing protection report and the CHMP AR/Overview required>. |

* + 1. Other Concerns

Question <number>

<Not applicable><Question text>

* + - 1. Applicant’s response:

<Not applicable><Response text>

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The additional data exclusivity /marketing protection report and the CHMP AR/Overview have been updated accordingly><No update to the additional data exclusivity /marketing protection report and the CHMP AR/Overview required>. |

1. Product information

There are a number of different ways to address questions on the product information. Any questions, even if related to product information, included in the quality, non-clinical or clinical lists of questions by the Rapporteurs should be addressed in that context and not copied here.

If the Rapporteurs have provided comments and questions on the product information directly on the annexes with comments and/or track changes, the applicant may choose to respond to those also directly in the annexes.

The following sections, unlike the previous, are not structured in Major Objections or Other concerns, rather they illustrate a variety of options for responding to comments on the annexes.

Clean and track-changes versions of the annexes must be provided in eCTD module 1.3.1. in any case.

Question <number>

<Question text>

* + - 1. Applicant’s response:

<Response text>

Example of tabular response (a landscape layout is preferrable)

|  |  |  |  |
| --- | --- | --- | --- |
| **Original Text** | **Rapporteur edits/comments** | **Applicant’s response** | **Proposed revision** |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

|  |
| --- |
| <Co->Rapporteur’s assessment of applicant’s response:  <Text>  Conclusion:  <Issue considered resolved><Issue not considered resolved><Follow-up question(s):>  <The CHMP AR/Overview has been updated accordingly><No update to the CHMP AR/Overview required>. |

1. <Additional remarks from the applicant>

Any additional changes proposed by the Applicant should be listed here, e.g. change of applicant, change of invented name, change of contact persons, etc. If none are applicable, please delete the header.

The addition of information in this response does not preclude the requirement to submit changes formally. Please consult the relevant guidelines and processes related to each type of change.

<Text>

1. References

Include here any references used in the responses above.

<Text>

1. Appendices

Include here any additional information referenced in the responses above. Appendices can be organised by number or letter and should be included in the bookmarks in the document. In the eCTD version of this document, please ensure cross-linking.

Wherever possible, additional data, reports, etc should be placed in the correct locations in the eCTD and cross-referenced in the response body, not appended to this response document.

<Text>

1. To quickly delete all the blue guidance text, use the following instructions: Click on Ctrl-Alt-Shift-S to view the “styles” window. Select “guidance notes for applicant” and click on the drop-down menu icon on the right, chose “Select all XXX instances”, press the “Delete” key on the keyboard. [↑](#footnote-ref-2)
2. Applicants can also add a table of contents for tables and a table of figures if they want. [↑](#footnote-ref-3)