July 2015
EMA/571057/2010

Marketing Authorisation Application (MAA) Pre-submission meeting request form

This pre-submission meeting request form provides an overview of the most relevant topics that an applicant is advised to consider when preparing their upcoming application for initial marketing authorisation, and which can be discussed at a MAA pre-submission meeting. For each topic, a reference is included to the corresponding 'question and answer' in the EMA Pre-Submission Guidance for Users of the Centralised Procedure, which is available on the EMA Website. It should be noted that the pre-submission meeting are not intended to be used to provide pre-assessment of any of the (draft) documents submitted.

The EMA's pre-submission guidance addresses a number of questions together with hyperlinks to relevant legislative documents and procedural guidelines which complement the advice given. Applicants are asked to refer to this guidance first before completing this pre-submission meeting request form.

There should not be a need to check or confirm answers provided in the pre-submission guidance document at a pre-submission meeting. EMA commits to keeping the pre-submission guidance document updated. A topic should only be proposed for discussion, when applicant's questions are not fully answered by the pre-submission or other available guidance documents, due to certain particularities of the upcoming application and/or nature of the product. In that case, applicants are advised to clearly describe the issues in the 'comments' box under the topic concerned, and to provide relevant background information. Other topics not listed in the form may be added.

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PRE-SUBMISSION MEETING AT EMA

- Date of request:
- Proposed date(s):
- Names of participants* and function:

SUBMISSION OF THE APPLICATION

- Proposed submission date of application:

BACKGROUND INFORMATION

- Annex 1: Overview of the product and its development programme covering quality, non-clinical and clinical aspects (i.e. Draft Quality overview (Module 2, section 2.3) + non-clinical (Module 2, section 2.4) + clinical (Module 2, section 2.5) overviews, if available)
  - With regards to quality aspects: Please highlight key pharmaceutical aspects in relation to the product such as for example: API synthetic scheme with starting materials labelled, cell line development and cell banking strategy, novel/non-standard processes/ novel expression system/ testing methodology, purification methods, viral removal steps, bioassay, novel/innovative formulation, QbD elements/Design Space, Real Time Release Testing, bridging data (different manufacturing sites, formulations, etc.), comparability data, deviation from guidelines, rationale for New Active substance (NAS) claim, etc.
- Annex 2: Draft RMP elements: safety specification, pharmacovigilance plan and risk minimisation measures, if available
- Annex 3: Copy of any scientific advice given by the CHMP and National Competent Authorities (NCAs) related to the application (if applicable), copy of any ATMP classification, ATMP certification (when applicable)
- Annex 4: Protocol and Statistical Analysis Plan for the pivotal studies (if module 2.5 is not available)
- Annex 5: Overview of paediatric studies and overview of indications in relation to the conditions in the PIP
- Annex 6: Draft SmPC, labelling text and package leaflet (1 relevant example)
- Annex 7: Draft Application Form (CTD Module 1.2 – with annex 5.23 (justification for new active substance only)
- Annex 8: Module 1 indents, as applicable;
  - 1.5 Draft justification related to any specific requirements for different types of application (e.g. bibliographical, abridged, generic, hybrid or biosimilar applications, exceptional circumstances, conditional marketing authorisation)
  - 1.6 Draft ERA (GMO/non-GMO)
  - 1.7 Draft information related to orphan market exclusivity
- Annex 9: Draft Table of Content of the Application, listing studies performed for each CTD heading

- Annex 10: Copy of any other early EMA contacts such as SME RA advices, ITF minutes, Orphan and/or paediatric advices etc. (if applicable)
- Annex 11: Draft justification of accelerated assessment (if applicable)
- Any other information in relation to the issues to be discussed with the EMA (see form)
- Applicant's presentation (in Power Point format) in accordance with question 37.5 of the "Presubmission guidance: questions and answers"
- Any additional background information needed related to the questions.

EMA CONTACT

Please send the completed form at least 6 weeks in advance of the proposed meeting date, to:

Product and Application Business Support (B-BD-BUS)
European Medicines Agency
30 Churchill Place
Canary Wharf
London E14 5EU
UK Phone: +44 (0)20 3660 6000
E-mail: pa-bus@ema.europa.eu

Subsequently, all of the above-mentioned meeting background information including the presentation should be provided to the EMA **at the latest 2 weeks** before the agreed meeting date. Late receipt of the complete background information and the presentation may require re-scheduling of the meeting.

All documents should be provided in an electronic format only.

It is advisable to send the above documents *via* a Secure Message Transfer Application (Eudralink). In order to set up an account, please complete this form and send it to the above email address (PA-BUS).

INFORMATION ON THE APPLICANT

Please fill in all of the requested data.

Applicant:

Company Name:

Address

Line 1:

Line 2:

Line 3:

City:

Post Code:

Country:

SME Status: ☐ Yes ☐ No

Expiry Date of SME Status:

SME Number:

CONTACT PERSON

Please fill in all of the requested data.

Title:

Last Name:

First Name:

Company Name:

Address

Line 1:

Line 2:

Line 3:

City:

Post Code:

Country:

Telephone:

Fax:

Email:

ELIGIBILITY (For Eligibility to the Centralised Procedure Request (according to Regulation (EC) No 726/2004))

Eligibility basis*:

Date of CHMP confirmation:

*For example: Mandatory Scope (Article 3(1) of Regulation (EC) No 726/2004, Optional Scope (Article 3 (2) of Regulation (EC) No 726/2004), Automatic access-For substances already authorised via the Centralised Procedures)

INFORMATION ON THE PRODUCT

Product Name:

Product Number (assigned at Eligibility): H00

Additional Information on strength(s) with units, Pharmaceutical form(s) and route of administration(s):

Non-prescription product (OTC): ☐ Yes ☐ No

Application for ancillary medicinal substance in medical devices: ☐ Yes ☐ No

ACTIVE SUBSTANCES

Active Substance name:

INN, if available:

Or Common Name:

Chemical Name:

Company Code:

Substance Type:

Method of manufacture:

Biological Source:

Orphan: ☐ Yes ☐ No

Radiopharmaceutical: ☐ Yes ☐ No

Nanotechnology: ☐ Yes ☐ No

ATMP classification (provide ATMP classification in Annex 3, if applicable):

Contains GMO: ☐ Yes ☐ No

Description of ATMP finished product (precise):

ATC Classification:

Therapeutic indication:

Other relevant information on the product:

Medical Device(s) (integral or as delivery device or ("companion") diagnostic device):
☐ Yes ☐ No

If 'Yes, complete all sections. If more than one medical device, repeat the whole section per medical device

Name of Medical Device:

Description device:

The device has CE Mark: ☐ Yes ☐ No

The device has been assessed by a Notified Body (NB):

☐ Yes ☐ No

If device has a CE Mark, complete this section:

Notified Body (NB) name:

Address (Line 1):

Line 2:

Line 3:

Line 4:

City:

Post Code:

Country:

NB Contact Person:

Title:

Last Name:

First Name:

Address (Line 1):

Line 2:

Line 3:

Line 4:

City:

Post Code:

Country:

Telephone:

Fax:

Email:

Is there an Orphan designation for this product? ☐ Yes ☐ No

*If **'Yes',** complete this section .If more than one, provide all community register numbers.*

Number in the community register of Orphan Medicinal Products :

Scientific Advice provided (please provide copy in Annex 3): ☐ Yes ☐ No

Information on the Paediatric Investigation Plan

PIP Submitted:

If 'Yes', PIP procedure number (please also provide Annex 5 as mentioned above):
If 'No', Date of planned PIP submission:

Waiver:

TOPICS FOR POSSIBLE DISCUSSION AT THE PRE-SUBMISSION MEETING

You only need to complete sections below if you have specific questions to ask.

Therefore please delete each section (e.g. 1.1, 1.2) that you do not wish to discuss during the meeting.

When submitting your questions, please also provide the related information requested in italics or make reference to the background information (see pages 2-3 of this document).

1. QUALITY + GMP

1.1. Quality Development

Please provide details as part of Annex 1 to this form.

Please highlight key pharmaceutical aspects in relation to the product such as for example: API synthetic scheme with starting materials labelled, cell line development and cell banking strategy, novel/non-standard processes/ novel expression system/ testing methodology, purification methods, viral removal steps, bioassay, novel/innovative formulation, QbD elements/Design Space, Real Time Release Testing, bridging data (different manufacturing sites, formulations etc.), comparability data, deviation from guidelines, rationale for the New Active Substance claim if applicable, etc. (see also background information on pages 2-3).

Summary / listing of issues to be discussed:

1.2. GMP Inspections + Batch release in the EEA

See Q&A 34 of the pre-submission guidance document

Please provide a flow-chart indicating the sequence and activities of the different manufacturing sites involved in the manufacture of the drug product and drug substance, including batch release testing sites, and specify whether the production steps are synthetic, semi-synthetic or using biotechnology.

Summary / listing of issues to be discussed:

1.3. Active Substance Master File (ASMF) + Vaccine Antigen Master File (VAMF)

See Q&A 24 + 57 of the pre-submission guidance document

Summary / listing of issues to be discussed:

1.4. Plasma Master File (PMF)

See Q&A 56 of the pre-submission guidance document

Summary / listing of issues to be discussed:

1.5. Genetically Modified Organisms (GMO)

See Q&A 25 of the pre-submission guidance document

Please confirm understanding of consultation process with environmental competent authorities.

Summary / listing of issues to be discussed:

1.6. Materials of animal and / or human origin (TSE)

See Q&A 26 of the pre-submission guidance document

Please provide the relevant completed TSE table.

Summary / listing of issues to be discussed:

1.7. Medical Devices

Summary / listing of issues to be discussed:

1.8. Process Analytical Technology (PAT) + Design Space

See Q&A 49 of the pre-submission guidance document

Please provide a brief description of the proposed PAT or Design Space.

Summary / listing of issues to be discussed:

1.9. ATMPs

When applicable, please provide copy of the ATMP classification and ATMP certification (Annex 3).

Summary / listing of issues to be discussed:

2. NON-CLINICAL + CLINICAL + GLP + GCP

2.1. Non-Clinical Development

Please provide details as part of Annex 1 to this form.

Summary / listing of issues to be discussed:

2.1.1. Environmental risk assessment

See Q&A 47 of the pre-submission guidance document

Please provide details as part of Annex 1 to this form.

Summary / listing of issues to be discussed:

2.2. Clinical Development

Please provide details as part of Annex 1 to this form.

Summary / listing of issues to be discussed:

2.3. GLP + GCP Inspections

See Q&A 29 and Q&A 35 of the pre-submission guidance document

Please provide details:

- *GCP: a listing of the pivotal clinical trials + countries involved and most important clinical trial sites, which GCP standard used, details of inspections by regulatory authorities (who, where, when, outcome)*
- *GLP: A listing of the pivotal non-clinical study sites, details of inspections by regulatory authorities (who, where, when, outcome).*

Summary / listing of issues to be discussed:

2.4. Paediatric Development

See Q&A 54 and 55 of the pre-submission guidance document

Please provide the draft PIP compliance document and Annex 5 (see pages 2-3 of this document).

Summary / listing of issues to be discussed:

2.5. Orphan medicinal product(s) information

See Q&A 10-14 of the pre-submission guidance document

2.5.1. Orphan designated substances

Please specify if orphan designation has been applied for this medicinal product and if it is based on 'significant benefit' criteria.

Summary / listing of issues to be discussed:

2.5.2. Information relating to orphan market exclusivity

Please specify if any medicinal product has been designated and authorised as an orphan medicinal product for a condition relating to the proposed therapeutic indication.

Summary / listing of issues to be discussed:

3. PHARMACOVIGILANCE

3.1. Pharmacovigilance System

See Q&A 43 of the pre-submission guidance document

Summary / listing of issues to be discussed:

3.2. Pharmacovigilance Inspections

Summary / listing of issues to be discussed:

3.3. EudraVigilance

See Q&A 58 of the pre-submission guidance document

Summary / listing of issues to be discussed:

3.4. Risk Management Plan

See Q&A 42 of the pre-submission guidance document

Please provide the draft RMP elements: safety specification, pharmacovigilance plan and risk minimisation measures.).

Summary / listing of issues to be discussed:

4. REGULATORY + PROCEDURAL

4.1. Eligibility for the Centralised Procedure

See Q&A 1+2 of the pre-submission guidance document

Please provide a draft eligibility request. [For generic/hybrid applications of a national/MRP authorised product, the draft eligibility request should relate to Article 3(2) of the Regulation.]

Summary / listing of issues to be discussed:

4.2. Legal Basis of the Application

See Q&A 3 of the pre-submission guidance document and the European Commission Notice to Applicants, Volume 2A, Chapter 1 (http://ec.europa.eu/health/files/eudralex/vol-2/a/vol2a_chap1_2013-06_en.pdf)

In addition to the general requirements for applications submitted under Article 8(3) of the Regulation, for the applications listed below please provide:

- For **generic, hybrid and similar biological** medicinal products ("bio-similar") applications:
  - *Full details on the reference product(s) should be provided under section 1.4.2/1.4.3/ 1.4.4 of the Module 1.2 Application Form.*
  - *Expiry date of the data exclusivity period of the reference medicinal product:<insert date>*
  - *Please attach a comparative table of the SmPC of the reference product and the proposed SmPC for the generic/hybrid/biosimilar product.*
  - *Please complete the Appendix to this form, addressing specific issues to be discussed for generic/hybrid/biosimilar applications.*
  - *Please complete the "overview of the chosen reference product for comparability" table (see the Appendix to this form) – for biosimilar applications only.*
- *For **informed consent** applications:*
  - *Full details on the authorised product should be provided under section 1.4.7 of the Module 1.2 Application Form.*
- *For **fixed combination** applications:*
  - *Full details on the authorisation status of the individual components should be provided.*
- *For **well-established use** applications:*
  - *Details on the first date of authorisation of the substance in EU should be provided.*
  - *Please attach a draft WEU justification.*

Summary / listing of issues to be discussed:

4.3. Legal Status

See Q&A 6 of the pre-submission guidance document

Summary / listing of issues to be discussed:

4.4. Accelerated review

See Q&A 8 of the pre-submission guidance document

Please provide a draft justification for the accelerated review request.

For applications for which accelerated assessment is to be proposed, please provide the following information required for early identification of a need for pre-authorisation inspections:

- *For all manufacturers to be included in the planned dossier:*
  - *name and address of the manufacturer*
  - *short description of activities performed by the manufacturer*
  - *compliance history of the manufacturing site*
  - *confirmation of inspections readiness of the manufacturer*
- *The list of all the pivotal clinical studies (protocol number and title) and for each pivotal study:*
  - *the study synopsis (or a mature draft with information at least on the design and conduct of the study)*
  - *a short discussion of the GCP compliance status (listing any GCP non-compliance identified, any breach of GCP, providing information on any site excluded including the reasons etc.)*
  - *list of investigators and their addresses*
  - *number of subjects enrolled at each site*
  - *list of GCP inspections conducted/planned by any regulatory authority (indicating the site inspected/to be inspected, the date of inspection and the regulatory authority involved). Alternatively, a confirmation that no inspections had been requested nor taken place and that no inspections are planned*

Summary / listing of issues to be discussed:

4.5. Multiple applications for the same medicinal product

See Q&A 9 of the pre-submission guidance document

Please provide a draft justification for the multiple applications.

Summary / listing of issues to be discussed:

4.6. Conditional MA + Exceptional Circumstances

See Q&A 50 + 38 of the pre-submission guidance document

Please provide a draft justification for the conditional approval or approval under exceptional circumstances.

Summary / listing of issues to be discussed:

4.7. Data Exclusivity / Market protection

See Q&A 6 of the pre-submission guidance document

Please provide a draft justification for requesting a '+1' for a new indication or for a legal status switch.

Summary / listing of issues to be discussed:

4.8. Small and Medium-Sized Enterprises

See Q&A 53 of the pre-submission guidance document

Summary / listing of issues to be discussed:

4.9. Co-Promotion

Summary / listing of issues to be discussed:

5. PRODUCT INFORMATION

5.1. SmPC guideline + QRD Templates

See SmPC guideline and annotated QRD template, and further detailed guidance provided on the Agency webpage on Product information requirements

Summary / listing of issues to be discussed:

5.2. Expression of strength

See QRD recommendations on the expression of strength

Summary / listing of issues to be discussed:

5.3. Labelling exemptions

See Exemptions to labelling and package-leaflet obligations

Summary / listing of issues to be discussed:

5.4. Mock-ups and Specimens

See Q&A 19 of the pre-submission guidance document

Please provide details and include a draft mock-up (if relevant for the discussion and if available).

Summary / listing of issues to be discussed:

5.5. Consultation with target patient groups

See Q&A 39 of the pre-submission guidance document

Summary / listing of issues to be discussed:

5.6. Linguistic review

See Q&A 36 of the pre-submission guidance document

Summary / listing of issues to be discussed:

5.7. ATC + INN

See Q&A 48 of the pre-submission guidance document

Summary / listing of issues to be discussed:

5.8. Braille on outer packaging

See Q&A 40 of the pre-submission guidance document

Summary / listing of issues to be discussed:

5.9. (Invented) Name

See Q&A 4 of the pre-submission guidance document

Summary / listing of issues to be discussed:

6. TRANSPARENCY

6.1. Publication on applications and opinions

Summary / listing of issues to be discussed:

7. ADMINISTRATIVE

7.1. Application fees

See Q&A 15 + 16 + 18 of the pre-submission guidance document

Summary / listing of issues to be discussed:

7.2. Dossier submission requirements

See Q&A 28 + 30 of the pre-submission guidance document

Summary / listing of issues to be discussed:

7.3. Dossier format (incl. electronic submission)

See Q&A 28 + 29 of the pre-submission guidance document

Summary / listing of issues to be discussed:

7.4. Application assessment timetable

See Q&A 31 of the pre-submission guidance document

Summary / listing of issues to be discussed:

8. OTHER

In case you wish to obtain guidance on any other topic, please include your question(s) in the relevant sections 1-7 or below with relevant background information in the appropriate annex.

Summary/listing of issues to be discussed:

ADDITIONAL TOPICS TO BE ADDRESSED IN CASE OF GENERIC, HYBRID OR BIO-SIMILAR APPLICATIONS

9. Special issues for Generic applications under Article 10 (1) (if applicable)

- Is the **active substance** the **same in terms** of salt, esters, ethers, isomers, mixtures of isomers, complexes or derivatives than the reference medicinal product?

If not, please provide details:

- Does the product have the **same qualitative composition in excipients** as the reference medicinal product?

If not, please provide details:

- If the composition is different, are there any **excipients** included that require **special safety warnings** in the product information compared to the reference medicinal product?

If yes, please provide details:

- Are there any **impurities** above the qualification threshold?

If yes, please provide details:

- Please provide an **overview table**, listing all studies/trials (incl. BE studies) indicating the product name, strength, pharmaceutical form, MA number, country of manufacturing of the finished product, country of batch release site, batch number, expiry date of the product used.

Summary/listing of issues to be discussed:

10. Special issues for hybrid applications under Article 10(3) (if applicable)

- Difference(s) compared to the reference medicinal product:

☐ Changes in the active substance(s)

☐ Change in therapeutic indication(s)

☐ Change in strength (quantitative change to the active substance(s))

☐ Change in pharmaceutical form

☐ Change in route of administration

☐ Where BE cannot be demonstrated through BA studies

Please indicate which of the above applies and provide background information/details in the relevant Annexes.

Summary / listing of issues to be discussed:

11. Special issues for bio-similar applications under Article 10(4) (if applicable)

- Please provide an **overview table of the chosen reference medicinal product** used throughout the comparability programme for quality, safety and efficacy studies during the development of the similar biological medicinal product (using template below)

Summary / listing of issues to be discussed:

- Are there **any difference(s)** compared to the reference medicinal product?

If yes, please identify change

☐ change(s) in the raw material(s)

☐ change(s) in the manufacturing process(es)

☐ change in therapeutic indication(s)

☐ change in pharmaceutical form(s)

☐ change in strength (quantitative change to the active substance(s))

☐ change in route of administration(s)

☐ other

Summary / listing of issues to be discussed:

OVERVIEW OF THE CHOSEN REFERENCE PRODUCT FOR COMPARABILITY

Applicant's product details

Name of applicant:	
Product Name, Strength, Pharmaceutical Form:	

Overview of the chosen EU reference medicinal product used in the quality comparability exercise

Reference Product Name Strength, Pharmaceutical Form	Marketing Authorisation number in EU (Specify country)	Country of Manufacture of the finished medicinal product	Country of Batch Release Site in EEA	Comment

Overview of the chosen reference medicinal product used in the non-clinical comparability exercise

Reference Product Name Strength, Pharmaceutical Form	Marketing Authorisation number in EU (Specify country)	Country of Manufacture of the finished medicinal product	Country of Batch Release Site in EEA	Study No[†]	Comment

[†] Short mention of the nature of the study, e.g. PK, PD, toxicology

Overview of the chosen reference medicinal product used in the clinical comparability exercise

Reference Product Name Strength, Pharmaceutical Form	Marketing Authorisation number in EU (Specify country)	Country of Manufacture of the finished medicinal product	Country of Batch Release Site in EEA	Study No[‡]	Comment

[‡] Short mention of the nature of the study, e.g. PK, PD, toxicology