31 July 2023

EMA/172843/2021

Marketing Authorisation Application (MAA) Pre-submission interactions form

This pre-submission interactions 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 with the EMA product team. For each topic, a reference is included to the corresponding ‘question and answer’ in the EMA Pre-authorisation Procedural Advice for Users of the Centralised Procedure, which is available on the [EMA website](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196). It should be noted that suchpre-submission interactions are not intended to be used to provide a pre-assessment of any of the (draft) documents submitted.

The EMA’s pre-authorisation 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 interactions form.

There should not be a need to check or confirm answers provided in the pre-authorisation guidance document as part of pre-submission interactions. EMA commits to keeping the pre-authorisation guidance document updated. A topic should only be proposed, when the applicant’s questions are not fully answered by the pre-authorisation 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.

The EMA would furthermore like to highlight that the United Kingdom (UK) formally left the European Union (EU) on 31 January 2020 and became a [third country](https://www.ema.europa.eu/en/glossary/third-country). From 1 January 2021, EU pharmaceutical law applies to the UK in respect of Northern Ireland only. This is based on the **Protocol on Ireland / Northern Ireland**. The Protocol forms part of the [withdrawal agreement](http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ%3AC%3A2019%3A384I%3AFULL&from=EN) concluded by the EU and the UK that established the terms of the UK's withdrawal from the EU. For details on the impact of the Protocol, see [Brexit-related guidance for companies](https://www.ema.europa.eu/en/about-us/brexit-uk-withdrawal-eu/brexit-related-guidance-companies).

For any questions that you may have further to the Q&As publication, you are advised to liaise with your EMA contact point.

SUBMISSION OF THE APPLICATION

* Intended submission date of application:

BACKGROUND INFORMATION

* Annex 1: Briefing document including an overview of the product and its development programme covering quality, non-clinical and clinical aspects:
  + With regard to quality aspects: Please clearly highlight key pharmaceutical aspects in relation to the product such as for example: active substance (AS) synthetic scheme with starting materials labelled, synthetic peptide developed with reference to an innovator recombinant product, cell line development and cell banking strategy, novel/non-standard processes (e.g. 3D printing), novel expression system, novel/non-standard testing methodology/purification methods, viral removal steps, bioassay, novel/innovative formulation, QbD elements/Design Space, Real Time Release Testing, digital technology, continuous manufacturing (CM), drug-device combinations, submissions with elements from ICH Q12 (e.g. ECs, PACMPs), nanotechnology, modelling (CM, *in-silico* models (e.g. PBBM), clinically relevant specifications, biowaivers- Regulatory freedom), incomplete CMC data package, bridging data (different manufacturing sites, formulations, etc.), comparability data, deviation from guidelines, rationale for New Active substance (NAS) claim, etc;
  + With regard to non-clinical aspects: Please briefly summarise the non-clinical development strategy and any critical toxicological findings, with focus on human relevance or how these have been or are to be followed-up in patients. The applicant can also present the strategy for the environmental risk assessment (ERA); In case of medicinal products containing or consisting of GMO, the applicant can specify whether a specific ERA applies, the need for risk management and the most appropriate risk minimisation measures (including specific SmPC recommendations e.g. for the handling, disposal, accidental exposure, shedding, blood/organ donation) can be presented;
  + With regard to clinical aspects: Please present a general overview of the clinical development programme (PK/PD and pivotal studies and/or literature data supporting the application). If there are any deviations from a guideline or previous scientific advice this should be mentioned. The applicant should also present the proposed indication versus the study population (based on inclusion and exclusion criteria and primary endpoint) and any planned justification for extrapolations. The applicant can highlight challenges during the clinical development programme, statistical analysis and its appropriateness with relevant clinical guidelines. The applicant can explain which data are planned to be provided or collected post-authorisation in view of the proposed type of marketing authorisation (e.g. specific obligations for conditional marketing authorisation or marketing authorisation under exceptional circumstances and/or post-authorisation safety study (PASS), post-authorisation efficacy study (PAES)).
* Annex 2: Draft risk management plan (RMP): with a particular focus on safety specification, pharmacovigilance plan and risk minimisation measures, if available. Please specify the data sources that are expected to be used to support post-authorisation monitoring [e.g. randomised clinical trial/s, ‘real world’ data, patient/ disease registries, health / pharmacy claims, electronic medical records, prescription event monitoring, other (specify)].
* 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: Draft SmPC, annex II, labelling text and package leaflet (1 relevant example)
* Annex 5: Draft Application Form
* Annex 6: Draft justification for new active substance request (when applicable);
* Annex 7: 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), as applicable;
* Annex 8: Draft information related to orphan market exclusivity (when applicable);
* 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. (when applicable)
* Annex 11: Draft justification of accelerated assessment (when applicable)
* Any additional background information needed related to the questions.

EMA CONTACT

Please send the completed form by raising a ticket via [EMA Service Desk](https://support.ema.europa.eu/esc?id=emp_taxonomy_topic&topic_id=ed0cc4d81b4fe1508ad7edf2b24bcbd4), selecting the tab “Business Services”, category “Human Regulatory”. The subcategory to be selected is “Pre-Submission Phase - Human”, followed by the sub-option: “Pre-Submission Interaction Request”. All above mentioned background documents should be provided at the same time.

If you do not have an EMA Account, please create it via the [EMA Account Management portal](https://register.ema.europa.eu/identityiq/login.jsf). For further information or guidance about how to create an EMA Account reference the guidance "[Create an EMA Account](https://register.ema.europa.eu/identityiq/help/selfregister.html)".

All documents should be provided in an electronic format only via [EMA Service Desk](https://support.ema.europa.eu/esc?id=emp_taxonomy_topic&topic_id=ed0cc4d81b4fe1508ad7edf2b24bcbd4).

EMA will provide responses in writing to the questions raised, within 3 weeks from the date of receipt of the pre-submission interactions form including the above background documents.

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| 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: |

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| 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: |

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| 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) |

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| 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 |

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| **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): |

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| ATC Classification:  Therapeutic indication: |

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| Has the product been granted eligibility to PRIME?  Yes  No  Other relevant information on the product: |

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| **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: |

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| **Is there an Orphan designation for this product?**   Yes  No  *If* ***‘Yes’,*** *complete this section. lf more than one, provide all community register numbers.*  Number in the community register of Orphan Medicinal Products: |

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

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| **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 REQUIRING EMA ADVICE**

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

***Therefore, please delete each section (e.g. 1.1, 1.2) that is not applicable.***

***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. 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: ASMF, AS synthetic scheme with starting materials labelled, synthetic peptide developed with reference to an innovator recombinant product, cell line development and cell banking strategy, novel/non-standard processes (e.g. 3D printing), novel expression system,* novel/non-standard *testing methodology / purification methods, viral removal steps, bioassay, novel/innovative formulation or technology (e.g. digital/devices), QbD elements/Design Space, Real Time Release Testing, digital technology, continuous manufacturing (CM), drug-device combinations, submissions with elements from ICH Q12 (e.g. ECs, PACMPs), nanotechnology, modelling (CM, in-silico models (e.g. PBBM), clinically relevant specifications, biowaivers- Regulatory freedom), incomplete CMC data package, bridging data (different manufacturing sites, formulations etc.), comparability data, statistical methods for the comparison of quality attributes, PMF aspects, 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 addressed:**

EMA’s response:

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* 1. GMP Inspections + Batch release in the EEA

See Q&A ‘[When can I expect a pre-authorisation GMP inspection and how are they conducted?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

Regarding Mutual Recognition Agreements (MRA) with the EU, please see related information published on the [EMA website](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001843.jsp&mid=WC0b01ac058005f8ac).

*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 addressed:**

EMA’s response:

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

See Q&As ‘[How should I submit an active substance master file (ASMF)?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ and ‘[What is the Community Vaccine Antigen Master File (VAMF) certification system?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Plasma Master File (PMF)

See Q&A ‘[What is the Community Plasma Master File certification system?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issuesto be addressed:**

EMA’s response:

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* 1. Genetically Modified Organisms (GMO)

See Q&A ‘[What should I submit if my medicinal product contains or consists of genetically modified organisms (GMOs)?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

*Please confirm understanding of consultation process with environmental competent authorities.*

**Summary/listing of issues to be addressed:**

EMA’s response:

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

See Q&A ‘[What information should I provide if my medicinal product contains materials of animal and/or human origin or uses them in the manufacturing process?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

*Please provide the relevant completed TSE table.*

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Medical Devices

See Q&A ‘[Medical devices](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issuesto be addressed:**

EMA’s response:

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* 1. Process Analytical Technology (PAT) + Design Space

See Q&A ‘[Can I apply for design space or process analytical technology (PAT) in my application?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

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

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. ATMPs

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

**Summary/listing of issues to be addressed:**

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EMA’s response:

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1. NON-CLINICAL + CLINICAL + GLP + GCP
   1. Non-Clinical Development

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

Highlight specific non-clinical aspects relevant for human risk assessment/SmPC (e.g. conclusions from reproductive toxicity studies, genotoxicity, carcinogenicity).

**Summary/listing of issues to be addressed:**

EMA’s response:

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* + 1. Environmental risk assessment

See Q&A ‘[When do I have to submit an environmental risk assessment (ERA)?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

Specify if the submitted ERA will include studies or a justification for not performing these, and related scientific basis.

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

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Clinical Development

*Please provide details as part of Annexes 1to this form.*

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. GLP + GCP Inspections

See Q&As ‘[Which information do I need to provide in my marketing authorisation application regarding GCP inspections and GLP compliance?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ and ‘[When can I expect a pre-approval GCP inspection and how are they conducted?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation 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 addressed:**

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EMA’s response:

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1. PHARMACOVIGILANCE
   1. Pharmacovigilance System

See Q&A ‘[What are the requirements for my pharmacovigilance system?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-submission authorisation document

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Pharmacovigilance Inspections

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. EudraVigilance

See Q&A ‘[What is EudraVigilance? How will it apply to my marketing authorisation?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Risk Management Plan

See Q&As ‘[Risk management plan (RMP)](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

*Please provide the draft RMP: with a focus on safety specification, pharmacovigilance plan and risk minimisation measures.*

**Summary/listing of issues to be addressed:**

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EMA’s response:

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1. REGULATORY + PROCEDURAL
   1. Eligibility for the Centralised Procedure

See Q&As ‘[Is my medicinal product eligible for evaluation under the centralised procedure?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ and ‘[How and when should the eligibility request be sent to EMA?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation 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 addressed:**

EMA’s response:

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* 1. Legal Basis of the Application

See Q&A ‘[What will be the legal basis for my application?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document and the European Commission Notice to Applicants, Volume 2A, Chapter 1 (<https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-2/vol2a_chap1_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 addressed:**

EMA’s response:

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* 1. Paediatric Development

See Q&As ‘[What is an application for a paediatric use marketing authorisation (PUMA)?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ and ‘[Do I need to address any paediatric requirements in my application?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com) of the pre-authorisation guidance document

*Please provide information on the status of the PIP/product specific waiver or class waiver in case articles 7 or 8 of Regulation 1901/2006 apply to your initial MAA .*

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Orphan medicinal product(s) information

See Q&As ‘[What aspects should I consider if my medicinal product has been designated as an orphan medicinal product at the time of submission of my application?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’, ‘[What aspects should I consider if the designation for my orphan medicinal product is still pending at the time of submission of my application for marketing authorisation?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’, ‘[What aspects should I consider if there are other orphan medicinal products for a condition related to my proposed therapeutic indication?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’, ‘[What aspects should I consider if my medicinal product is considered similar to an orphan medicinal product?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document and the [Guideline on aspects of the application of Article 8(1) and (3) of Regulation (EC) No 141/2000](https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2008:242:0012:0016:EN:PDF).

* + 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 addressed:**

EMA’s response:

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* + 1. 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 addressed:**

EMA’s response:

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* 1. Legal Status

See Q&A ‘[What legal status can I obtain for my medicinal product?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Accelerated review

See Q&A ‘[Is my product eligible for an accelerated assessment?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation 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 addressed:**

EMA’s response:

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* 1. Multiple applications for the same medicinal product

See Q&A ‘[What should I do if I want to submit multiple applications for the same medicinal product?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

*Please provide a draft justification for the multiple applications.*

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Parallel application for an opinion under EU-M4all for a medicine to be used outside the EU and an EU [marketing authorisation](https://www.ema.europa.eu/en/glossary/marketing-authorisation) under the [centralised procedure](https://www.ema.europa.eu/en/glossary/centralised-procedure).

In addition to the EU-M4all procedure exclusively intended for third-country markets, the EMA is now offering the possibility to run the evaluation of centralised and EU-M4all applications in parallel, to obtain an EU-M4all Scientific Opinion and a Centralised Marketing Authorisation at about the same time. This initiative offers opportunities for work-saving and reduced duplication of efforts since most elements of the CHMP scientific advice and assessment for the centralised procedure and EU-M4all are the same.

For applications evaluated under this initiative, WHO experts and experts/observers nominated by WHO from target countries act as scientific expert reviewers to the rapporteurs’ assessment reports and provide specific expertise and input, as for a standalone EU-M4all procedure.

See [Parallel application for EU-M4all (Article 58) opinion and Centralised Marketing Authorisation procedure](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/public-guidance-parallel-application-eu-m4all-article-58-opinion-centralised-marketing-authorisation_en.pdf) and [EMA procedural advice for medicinal products intended exclusively for markets outside the European Union in the context of co-operation with the World Health Organisation (WHO)](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-procedural-advice-medicinal-products-intended-exclusively-markets-outside-european-union-context_en.pdf)

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Conditional MA + Exceptional Circumstances

See Q&As ‘[Could my application qualify for a conditional marketing authorisation?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ and ‘[Is my medicinal product eligible for approval under exceptional circumstances?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

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

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Data Exclusivity/Market protection

See Q&A ‘[What is the period of protection for my medicinal product?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation 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 addressed:**

EMA’s response:

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* 1. Small and Medium-Sized Enterprises

See Q&A ‘[What special support is available for micro, small and medium-sized enterprises (SMEs)?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

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EMA’s response:

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1. PRODUCT INFORMATION
   1. SmPC guideline + QRD Templates

See [SmPC guideline](https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-2/c/smpc_guideline_rev2_en.pdf) and [annotated QRD template](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000134.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac0580022c59), and further detailed guidance provided on the[Agency webpage on Product information requirements](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000199.jsp&mid=WC0b01ac0580022bb3)

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Expression of strength

See [QRD recommendations on the expression of strength](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000254.jsp&mid=WC0b01ac058008c34c)

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Labelling exemptions

See [Exemptions to labelling and package-leaflet obligations](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000386.jsp&mid=WC0b01ac0580816ad1)

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Mock-ups and Specimens

See Q&A ‘[When should I submit mock-ups and/or specimens?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation 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 addressed:**

EMA’s response:

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* 1. Consultation with target patient groups

See Q&A ‘[When and how should I submit information on user consultation?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Linguistic review

See Q&A ‘[What is the QRD review of the product information?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document an ‘[The linguistic review process of product information in the centralised procedure - human](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/linguistic-review-process-product-information-centralised-procedure-human_en.pdf)’

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. ATC + INN

See Q&A ‘[How are ATC codes and international non-proprietary names (INN) applied within the centralised procedure?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Braille on outer packaging

See Q&A ‘[Do I need to include Braille on the packaging of my medicinal product?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. (Invented) Name

See Q&A ‘[How will I know if the proposed (invented) name of my medicinal product is acceptable from a public health point of view?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document and the ‘[Guideline on the acceptability of names for human medicinal products processed through the centralised procedure](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-acceptability-names-human-medicinal-products-processed-through-centralised-procedure_en.pdf)’.

**Summary/listing of issues to be addressed:**

EMA’s response:

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* 1. Digital technologies in the product information

See ‘[Mobile scanning and other technologies in the labelling and package leaflet of centrally authorised medicinal products](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/mobile-scanning-other-technologies-labelling-package-leaflet-centrally-authorised-medicinal-products_en.pdf)’.

**Summary/listing of issues to be addressed:**

EMA’s response:

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1. TRANSPARENCY

See related information on the [EMA website](http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000526.jsp&mid=WC0b01ac0580789730).

* 1. Publication of information on the application and procedure outcome

See [Guide to information on human medicines evaluated by EMA](http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500206484) available on the [EMA website](https://www.ema.europa.eu/en)

**Summary/listing of issues to be addressed:**

**EMA’s response:**

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* 1. Publication of Clinical Data – Policy 070

See related information on the [EMA website](http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000555.jsp&mid=WC0b01ac05809f363e) including [guidance to industry](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001743.jsp&mid=WC0b01ac0580ae88cc).

**Summary/listing of issues to be addressed:**

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**EMA’s response:**

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1. ADMINISTRATIVE
   1. Application fees

See Q&As ‘[What fee do I have to pay?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’, ‘[What definition of strength is used for the calculation of fees?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ and ‘[When could a fee waiver/fee reduction be granted?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

**EMA’s response:**

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* 1. Dossier submission requirements

See Q&As ‘[When should I submit my marketing authorisation application?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ and ‘[How and to whom should I submit my dossier?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

**EMA’s response:**

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* 1. Dossier format (incl. electronic submission)

See Q&As ‘[How and to whom should I submit my dossier?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ and ‘[How are initial marketing authorisation applications validated at EMA?’](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com) of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

**EMA’s response:**

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* 1. Application assessment timetable

See Q&A ‘[How long does it take for my application to be evaluated?](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196.com)’ of the pre-authorisation guidance document

**Summary/listing of issues to be addressed:**

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**EMA’s response:**

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1. 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 addressed:**

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**EMA’s response:**

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Additional topics to be addressed in case of generic, hybrid or bio-similar applications

1. 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:**

**EMA’s response:**

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* If **excipients** are different from the reference medicinal product, 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:**

**EMA’s response:**

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

**If yes, please provide details:**

**EMA’s response:**

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* 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:**

**EMA’s response:**

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1. 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 addressed:**

**EMA’s response:**

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1. 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 addressed:**

**EMA’s response:**

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* 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 addressed:**

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**EMA’s response:**

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

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| --- | --- | --- | --- | --- | --- |
| 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[[1]](#footnote-1) | Comment |
|  |  |  |  |  |  |
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### Overview of the chosen reference medicinal product used in the clinical comparability exercise

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| --- | --- | --- | --- | --- | --- |
| 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[[2]](#footnote-2) | Comment |
|  |  |  |  |  |  |
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1. Short mention of the nature of the study, e.g. PK, PD, toxicology [↑](#footnote-ref-1)
2. Short mention of the nature of the study, e.g. PK, PD, toxicology [↑](#footnote-ref-2)