**Date**

**Subject: Application EU Clinical Trial number – initial submission / resubmission**

**Sponsor: Sponsor Name**

**EU Clinical Trial number: Trial Number**

**Protocol Number: Protocol Number/Acronym**

**Protocol Title: Protocol Title**

**Instructions for applicant**

* Yellow text contains instructions and information, please remove this from the final version. Grey text should be filled in by the applicant.
* The cover letter should not describe the clinical trial in detail, and should focus on providing an overview of the submitted documents and on highlighting any relevant details.
* In case of resubmission: describe the reason for resubmission, and mention the EU trial number of the previous clinical trial application. Describe any changes compared to the previous submission, upload a track-changes version of changed documents, and specify how any unresolved issues from the first submission have now been addressed.
* If this trial is related to another clinical trial (e.g. part of a platform trial/complex design), then describe the relation and mention the trial number of the related trial(s).
* Adhere to the CTR coding and naming of documents based on CTR Annex I, as described in the CTCG ‘Best Practice guide naming of documents in CTIS’, which can be found on the [CTCG website](https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html) under ‘Key documents list’. Make sure that the document titles in CTIS do not contain a version number or date.
* Please consult Annex II of the [CTR Q&A of the European Commission](https://health.ec.europa.eu/document/download/bd165522-8acf-433a-9ab1-d7dceae58112_en?filename=regulation5362014_qa_en%2Epdf) for the language requirements per Member State for Part I documents, and for structured data (‘Fields of the application form’).
* When submitting, make sure to include Part II by ticking the Part II checkbox for each MSC .

Dear Madam, Dear Sir,

Please find enclosed the dossier for the application concerning the trial referenced above for your review. All documents needed for your review have been uploaded to the CTIS portal.

BRIEFLY describe the scope of the trial application, including any country-specific details. If the application contains multiple identical documents, e.g. GMP documentation applicable to multiple products, please specify.

Please tick items below which are applicable. Where necessary, complete the specific sections or delete the sections not applicable to your clinical trial

This is a complex clinical trial (CCT). See [CTCG website](https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html) for more information.

This clinical trial contains one or more decentralised elements that are identified as a critical-to-quality factor.

This clinical trial is linked to the IMPD-Q-only application with trial number [xxxx]. Please refer to [CTR Q&A of the European Commission](https://health.ec.europa.eu/document/download/bd165522-8acf-433a-9ab1-d7dceae58112_en?filename=regulation5362014_qa_en%2Epdf) (question 2.15 point 125) for information and requirements.

This is a partial application (without Part II, CTR article 11) for the following Member States: [mention Member States].

This clinical trial is identical to the CTA with EU CT number [insert trial number]. There are [no/the following] overlapping MS in both trials: [names of the overlapping MS]. If there are overlapping Member States, please choose one of these MS as the proposed RMS for both trials. Please also provide any additional information about these two identical studies in the cover letter if considered relevant for the RMS and MSCs. If possible, please submit both applications on the same day.

This clinical trial is related to a public health emergency. [provide description]

The study population consists of [subjects not able to give informed consent] / [emergency situation subjects (CTR Article 35)] / [minors] / [pregnant women] / [breastfeeding women].

The clinical trial involves the first administration of a new active substance to humans (first-in-human trial). If the IMP is a bioequivalent, indicate this here.

The clinical trial involves the administration of a biosimilar product  with/  without available previous clinical data in humans

Scientific advice relating to the clinical trial or the investigational medicinal product has been given by EMA, a Member State or a third country. This can be found in [insert name of document].

The clinical trial [is part] / [is intended to be part] of a Pediatric Investigation Plan (PIP) as referred to in Title II, Chapter 3, of Regulation (EC) No 1901/2006. The Agency [has issued] / [has not yet issued] a decision on the PIP: [enter here the link to the decision of the Agency on its website].

The investigational medicinal product (IMP) or auxiliary medicinal product (AxMP) is a [narcotic] / [psychotropic] / [radiopharmaceutical].

The investigational medicinal product consists of or contains a genetically modified organism.

The investigational medicinal product is considered a prophylactic vaccine.

An orphan designation for the IMP for an orphan condition has been obtained.

This trial investigates a new indication for an authorised medicinal product.

The trial is a low-intervention clinical trial (as defined in CTR article 2). [Please provide a justification here why this is considered to be a low-intervention clinical trial, and explain if the (proposed) RMS is one of the MS where the use of IMP is evidence-based].

Reduced safety reporting applies for the clinical trial (ICH E19, CTR article 41. Justification should be provided in the protocol).

The following Ethics Committees are proposed to assess the application, if applicable:

|  |  |
| --- | --- |
| **Member State** | **Proposed Ethics Committee** |
|  |  |
|  |  |
|  |  |

The following IMPs and AxMPs are used in the clinical trial:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Name product** | **Role**  **(IMP / AxMP)** | **EU Regulatory status**  **(authorised / unauthorised)** | **Documents submitted**  **(e.g. IB/IMPD/ SmPC)** | **RSI location** |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

* RSI (only for IMPs, unauthorised AxMPs, modified authorised AxMPs): specify for each product whether the reference safety information (RSI) can be found in the IB or the SmPC, and in which section. More information is provided in section 7.8 of the CTR Q&A.
* For authorised modified IMPs where the modification of the product affects the quality dossier: please indicate this status, ‘authorised and modified’, in the table
* Diluents and/or placebo are used: if authorised, submit SmPC. If not authorised, include information in IMPD or as separate document.
* Only AxMPs that are not authorised in the EU, or are modified outside the scope of the marketing authorisation, need to be entered in CTIS. Unmodified AxMPs authorised in the EU should be listed in the table above, but not entered in CTIS.
* An unauthorised AxMP may only be used if no authorised alternative is available (CTR Article 59). This must be justified in the protocol.
* If clinical batches of an authorised IMP are used, provide a justification why authorised batches are not used instead, and submit a simplified IMPD (sIMPD) or Summary of Changes (SoC) that clearly indicates the differences between the clinical and authorized batches in tabular format.

**Product labelling**:

No additional labeling is required in accordance with CTR Article 67, because the medicinal product is authorised and commercially available in the countries of use, locally sourced through local pharmacies or country vendors as an open label product in its original unmodified commercial packaging intended for use in authorised indication, similar to the use per SmPC.

Additional labelling is proposed for authorised IMPs/AxMPs.

The address and telephone number of the main contact are not included on the labels (CTR Annex VI), but the sponsor confirms that these details have been provided on a leaflet or card to the trial participants, who have been instructed to keep this in their possession at all times.

**Combined studies** (interplay CTR with MDR and/or IVDR)

The following **medical devices** in this clinical trial are also part of a clinical investigation application submitted under the Medical Device Regulation (EU MDR 2017/745): Only mention devices that are investigated or in development in this trial, not devices that are used but not investigated. Please provide a list of the national MDR applications, with (expected) submission dates and national dossier numbers, if applicable and available.

|  |  |  |  |
| --- | --- | --- | --- |
| **Name of device** | **Not CE-marked** | **CE-marked but used outside intended use** | **In-house device** |
|  |  |  |  |
|  |  |  |  |

The following **in vitro diagnostics** (IVD) in this clinical trial are also part of a performance study submitted under the In Vitro Diagnostics Regulation (EU IVDR 2017/746): Only mention IVD that are investigated or in development in this trial, not IVD that are used but not investigated. Please provide a list of the national IVDR applications, with (expected) submission dates and national dossier numbers, if applicable and available.

|  |  |  |  |
| --- | --- | --- | --- |
| **Name of IVD** | **Not CE-marked** | **CE-marked but used outside intended use** | **In-house assay** |
|  |  |  |  |
|  |  |  |  |

**Optional additional information/documentation:** in Annex I to this template cover letter, recommendations are given to provide additional information and/or documentation to facilitate the assessment of the clinical trial. Please describe the additional information or submitted documentation.

Should you have any questions, please do not hesitate to contact [insert contact name].

Yours sincerely,

Applicant Name and Function:

Organisation / Department:

**Annex I – additional information (remove if not applicable)**

**IMPD-Q and IB history:**

For unauthorised IMPs where the sponsor is the Product Owner: mention the most recently authorised version of the IMPD-Q and IB. Either attach a Summary of Changes (SoC) as an appendix to the cover letter or submit the IMPD-Q/IB with tracked changes in CTIS.

Most recently authorised version of the IMPD-Q and/or IB

|  |  |  |
| --- | --- | --- |
| **Name of IMP** | **EU CT number** | **Document, version, date** |
|  |  |  |
|  |  |  |

**Batch release site(s)**:

An overview of batch release sites responsible for certification of IMPs is provided in IMPD-Q section [XXXX]. If the IMPD does not specify the EU batch release sites, then provide a list here in this appendix.

**Clinical trial is part of an agreed (stepwise or full) Paediatric Investigation Plan (PIP):**

All applications for marketing authorisation for new medicines have to include the results of studies as described in an agreed PIP, unless the medicine is exempt because of a deferral or waiver. In the review of a submitted paediatric clinical trial which is part of the PIP, it will facilitate the assessment if assessors (NCA and Ethics) have direct access to the PIP to be informed about the key binding elements as described in the PIP.

The agreed Paediatric Investigation Plan (PIP) is submitted in the slot Paediatric Investigation Plan in CTIS.

**Pre-CTA advice**:

If the clinical trial has been part of a CTCG pre-CTA advice, please indicate the number of the pre-CTA advice and the date of the advice.

The clinical trial has been part of a CTCG pre-CTA advice procedure with number [insert number pre-CTA advice] and date [insert date of the advice].