**The following information should be provided in the cover letter of applications for transitioning a Clinical Trial authorised under the Directive 2001/20/EC (CTD) to the Clinical Trial Regulation (CTR)[[1]](#footnote-1)**

Description of changes in vs.3 compared to earlier version: Listing of authorised Auxiliairy Medicinal Products used within marketing authorisation in the cover letter.

Description of changes in vs.4 compared to earlier version: Adding guidance on IMPD-Q only submissions in the cover letter.

Each of the Part I documents **Protocol**, **Investigator’s brochure (IB)** and/or **Investigational Medicinal Product Dossier (IMPD)** for transition is either \_\_\_\_fully harmonised or \_\_\_ consolidated (describe/tick as appropriate for each document) across all Member States Concerned.

I hereby declare that the contents of the submitted version of the respective documents (protocol, IB, IMPD) in relation to the trial [insert EudraCT number] (version x, dated x) have been approved in the following Member States, and do not contain any substantial changes.

# Harmonised Protocol (version x, date x)

|  |  |  |  |
| --- | --- | --- | --- |
| Member State | Date of approval | | |
|  | National Competent Authority | Ethics Committee | Name of Ethics Committee |
|  |  |  |  |

(add rows as appropriate)

# Consolidated Protocol (version x, date x)

In case of a consolidated protocol, complete the table below describing Member State-specific aspects (e.g. restricted trial population, particular local requirements etc.) and where they are specified (i.e. annex number or protocol section number)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Member State | Version and Date of the protocol approved per Member State on which the consolidated protocol is based | Date of approval | | | National specific aspect | |
| National Competent Authority | Ethics Committee | Name of Ethics Committee | Content | Page reference/location |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |

(add rows if required). As applicable, **similar tabular information** with details on **each document, Member State, approval dates** and **particular national aspects** should be provided for the **harmonised/consolidated IB** and/or **IMPD**.

# Non-substantial changes of Part I documents

The following **non-substantial changes** in line with Annex IV of CLINICAL TRIALS REGULATION (EU) No 536/2014 QUESTIONS & ANSWERS document have been included as compared to approved Part I documents.

Specify non-substantial changes in different documents in separate lists, e.g. protocol, and briefly describe the non-substantial changes in each of them

Document type, e.g. protocol (version x, date y)

|  |
| --- |
| Non-substantial changes |
|  |

(add rows as appropriate)

Add tables, each with the name of the document in the header (e.g. IB, IMPD) as appropriate if needed for non-substantial changes in line with Annex IV of the European Commission Q&A for other Part I documents.

# Other documents than the minimum Part I and Part II transition dossier approved in some but not all MSCs under the CTD

If the Part I Dossier contains documents in addition to the minimum dossier approved by some, but not all MSCs (e.g. DSMB Charter, see CTCG Best Practice Guide for sponsors of multinational clinical trials under Directive 2001/20/EC that will transition to Regulation (EU) No 536/2014), these should be clearly described in the cover letter with information in which Member State the document was approved under CTD.

For clarity, Part II documents approved under the CTD are recommended to be listed in a similar way per MSC.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Member State | Type of document | Version and Date of the document approved per Member State | Date of approval | | Comment |
| National Competent Authority  (if applicable) | Ethics Committee  (if applicable) |
|  |  |  |  |  |  |

(add rows as appropriate)

# Auxiliary Medicinal Product

If the Auxiliary Medicinal Product (AxMP) is authorised or modified, where such modification does not affect the product quality and/or GMP requirements and is covered by the marketing authorisation, it only requires to be listed in the cover letter. All other AxMPs need to be registered in CTIS.

# IMPD-Q only submission

If the sponsor is not the product owner of an IMP used in the trial and the IMPD-Q is already submitted in another trial application in CTIS, a reference to this trial number should be provided in the cover letter. If the IMPD has only been submitted under the CTD, a reference to this trial should be made[[2]](#footnote-2).

# Declaration

I hereby declare that the application transitioning the trial from the Clinical Trials Directive to the Clinical Trials Regulation is in line with the Guidance published at [EudraLex volume 10](https://health.ec.europa.eu/document/download/10c83e6b-2587-420d-9204-d49c2f75f476_en?filename=transition_ct_dir-reg_guidance_en.pdf) and the [CTCG Best Practice Guide for sponsors of multinational clinical trials](https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2024_03_CTCG_Best_Practice_Guide_for_sponsors.pdf) published at the HMA website. All documents common to all Member States Concerned (i.e. documents within the Part I dossier) are the same and have been approved by all Member States under CTD or are described in detail above. I also declare that all Part II submitted documents have been approved by the respective Member State under CTD.

1. *The content of this document (with the table(s) completed) should be included in the cover letter of the clinical trial dossier for multinational clinical trials that transition from the Directive 2001/20/EC to the Regulation (EU) No 536/2014. The cover letter without signature to be submitted in CTIS should be an exact copy of the version signed by the sponsor or legal representative of the sponsor kept in the Trial Master File.* [↑](#footnote-ref-1)
2. <https://health.ec.europa.eu/document/download/bd165522-8acf-433a-9ab1-d7dceae58112_en?filename=regulation5362014_qa_en_0.pdf> [↑](#footnote-ref-2)