CTIS cover letter templates

Clinical Trials Coordination Group

CTIS Info Day
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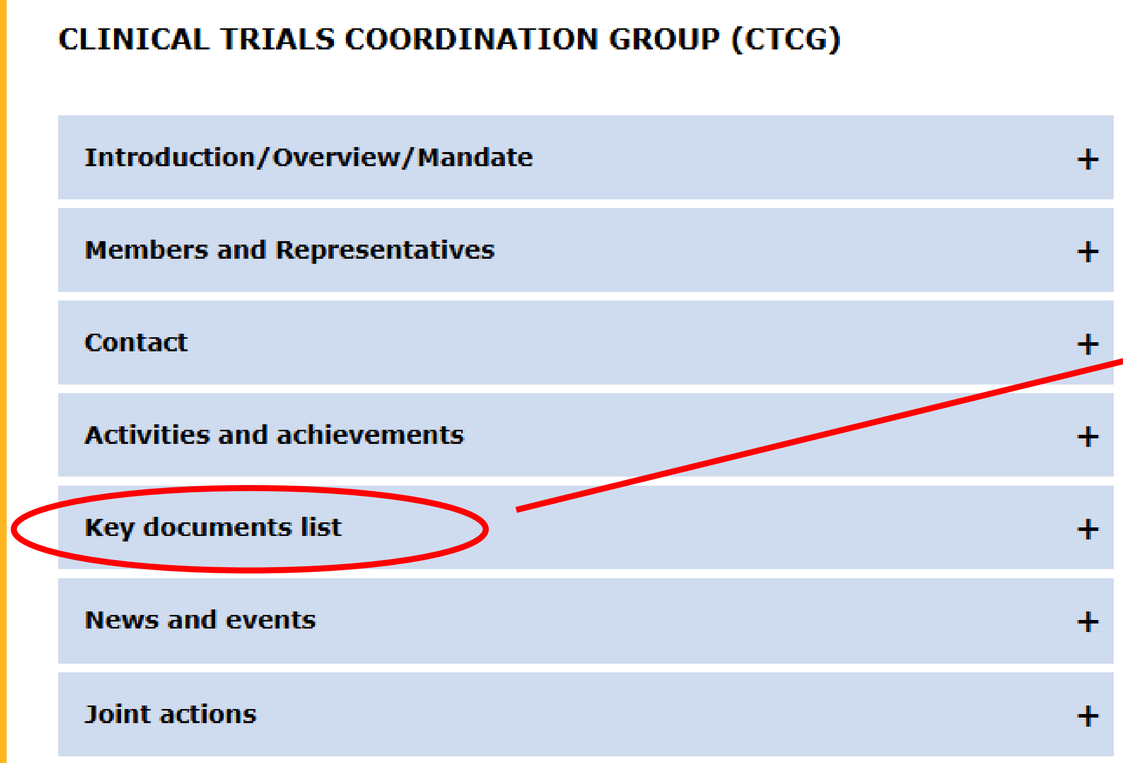
Jan Willem Kleinovink
CCMO, NL

Cover letter template package

CTCG website:
https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html



CTCG KEY DOCUMENTS LIST

TEMPLATE COVER LETTERS and RFI RESPONSE

- Initial application
- SM cover letter
- SM modification description
- RFI Response - List of Changes

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Initial application cover letter

- Provide trial context (medical/scientific/procedural/..), highlight relevant details
- Indicate related trials/applications (e.g. MDR/IVDR, platform trial, IMPD-Q-only, resubmission, duplicate trials)
- Instructions (in yellow) on EU/national requirements and CTIS
- Concise overview of relevant information spread across the application

→ facilitate validation and assessment
→ prevent considerations/RFI

IN – general instructions/information

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.
- For transition trials, please use the cover letter template for transition trials, available on the CTCG website (under Key Documents List).
- 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 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 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.

IN – tickboxes

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 for more information.

☐ This clinical trial contains one or more decentralized 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].

☐ 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

IN – product information

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

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

- RSI: 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.
- Only AxMPs that are not authorised in the EU, or are modified outside the scope of the marketing authorization, 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 art 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.

→ Concise overview of product information and documentation
→ CTAG recommendations on AxMPs (Mar 2024): not required to enter unmodified authorised AxMPs in CTIS.

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.

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.

→ Optional: recommended additional information in Annex
→ Other optional information in Annex: PIP and CTCG pre-CTA advice

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IN – Combination trials (MDR/IVDR)

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
	☐	☐	☐
	☐	☐	☐

→ Valuable information as Difficult situation to recognize

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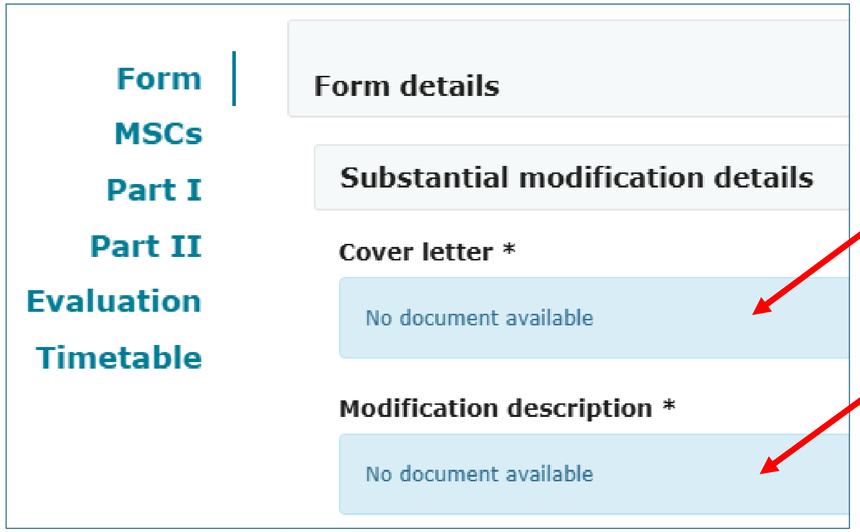
Substantial Modifications

→ Cover letter
→ Modification description

- Substantial Modification (SM)
  - Cover letter | docx
    Provides background information on the SM application
    Version 2 - July 2024
  - Modification description | docx
    Provides an overview of all changes and submitted documents
    Version 2 - July 2024
- RFI Response List of Changes to the Application | docx
  To be uploaded within each RFI – mandatory upload if Changes to the Application were made.
  Version 1 - July 2024

- Overview of submitted changes → CTIS currently does not facilitate recognizing new information/documentation
- CTIS instructions (in yellow) on uploading/changing/submitting



→ Description of changes

→ Overview/list of changes

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SM cover letter

→ Description of changes

BRIEFLY describe the reason and scope of the SM, including any country-specific details.

Instructions for applicant

- Yellow and blue text contains instructions and information, please remove this from the final version. Grey text should be filled in by the applicant. The section between the blue header and footer should be included only for the first substantial modification (SM) after transition.
- When uploading documents for this SM in CTIS, please enter the SM-number as a Comment in the upload 'pop-up' window (e.g. enter "SM-6").
- For each modified document:
  - The new version should be uploaded using the Update button in CTIS (3rd symbol) behind the title of the existing document.
  - A track-changes (TC) version should always be submitted. If this is not possible (e.g. insurance certificates, QP declarations, MIA, GMP certificates), then the changes should be described in the cover letter.
  - In addition to the track-changes version, a Summary of Changes (SoC) should be provided for the protocol, IB and IMPD (either as a separate document, or as part of the main document itself).
- Please adhere to the CTR document coding and naming 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 under 'Key documents list'.

Instructions on uploading:

update button (new version)

Only if this is the first SM for a transition trial, add the following information to clarify whether the SM application contains new, updated or already authorised documents

- This application contains: (delete those that are not applicable)
  - Documents that were already authorised under the CTD and not included in the transition initial application
  - Updates to CTD documents/placeholders that were included in the transition application
  - New documents in line with CTR requirements

Complicated application – distinguish types of changes

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SM modification description

→ Overview/list of changes

Changes to documents under Form section in CTIS (examples)

Section	Document name Version and date	Details
Substantial modification details	B1_Cover letter 2024-xxxxxx-xx-00 SM-6 V1.0 22Jan2024	New
Substantial modification details	B1_Modification Description 2024-xxxxxx-xx-00 SM-6 V1.0 22Jan2024	New
Proof of Payment	Proof of Payment MSC	New
…	…	…..

Changes to Part I Documents (examples)

Section	Document type	Document (including clean and track changes versions, if applicable) Version and Date	Details
Protocol information	Protocol	D1_Protocol 2023-xxxxxx-xx-00 v3.0 31Jan2024 CLEAN	Updated
Protocol information	Protocol	D1_ Protocol-2023-xxxxxx-xx-00 v3 31Jan2024_TC	New
Products	IMPD-Quality	G1_IMPD Q CLEAN v2.0 15Dec2023	Updated
Products	IMDP-Quality	G1_IMPD Q_TC v2.0 15Dec2023	New
Products	IMPD-Quality	G1_SoC IMPD Q v2.0 15Dec2023	
Products	Compliance with GMP	QP declaration vNA 25Dec2023	New
…	…	…	…

Changes to Part II Documents per Member State Concerned (examples)

Member state: MSC name (copy for each MSC)

Section	Document name (including clean and track changes version, if applicable) Version and Date	Details
Recruitment Arrangements	K1_Recruitment Procedure	Updated

Changes to structured data fields (examples)

Section	Description of changes	Justification for changes
MSCs	Subject number updated for MSC	Addition of study arm in MSC
Part I	Inclusion criterion #x added	Refer to updated protocol v4 01Jan2024
Part II Member State	Trial site X added	…..
Part II Member State	PI change at site X	…..

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RFI – List of Changes

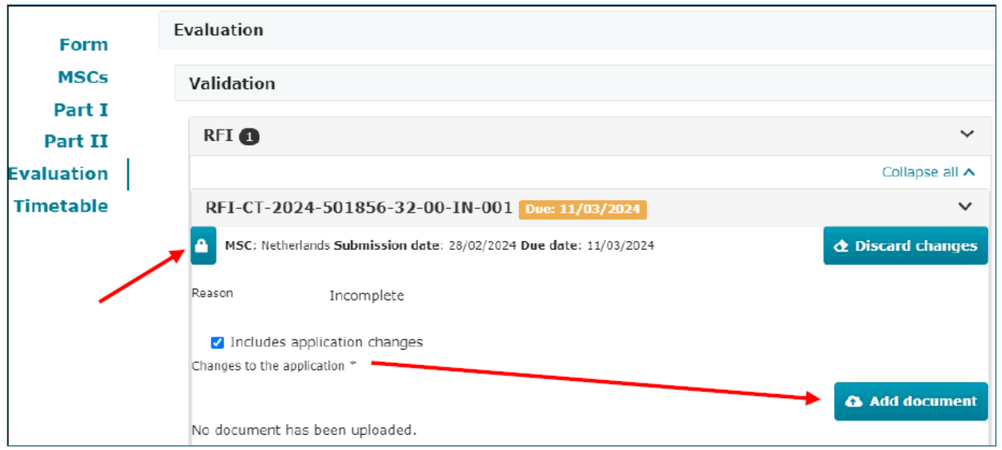
→ Overview of submitted changes

→ Technical instructions on uploading, and submitting RFI Response

The following changes have been made to the application:
Applicants are free to use their own table/list format, if this provides the same level of overview and detail, so that it is immediately clear for assessors which changes were made.

Consideration Number	Section	Document name (including clean and track changes version, if applicable) Version and Date	Details
…-01	Part II DK - Suitability of the investigator	M1_CV Investigator [name & site] V2.0 12Jan2024	Updated version submitted
…-02	Part I	D1_Protocol 2024-…. V3.0 18Feb2024	[Textual response to question]
…-03	Part I	N/A	Updated inclusion criterion 5 (Part I Structured data)

The RFI Response can only be submitted if a written response has been entered for each consideration, the individual locks of all considerations are opened, and the master lock in the top-left corner of the RFI is closed.



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Thank you for your attention!