PART I

File/Document	CTR Annex I	References
B. Cover letter	B	• According to CTR annex I B. 6 to 12 of CTR • COMBO trials: important to mention in the cover letter if trial is a combined CTR/MDR-IVDR study
D. Protocol	D 24	• According to annex I of CTR • See also ICH E6 GCP • The protocol shall be accompanied by a synopsis of the protocol, provided as a separate document in Dutch, French and German (national law of 7 May 2017 on clinical trials). • DSMB charter (if applicable) • Patient facing documents* (same language requirements as for ICF. See annex II of the CTR Q&A on Eudralex volume 10)
E. Investigator's brochure	E	• According to annex I of CTR • See also ICH E6 GCP
F. Documentation relating to GMP for the IMP • Copy of the manufacturing authorisation • Certification by the Qualified Person	F	• EU template strongly recommended for QP declaration (if applicable)
G. IMPD dossier	G	• See also Eudralex volume 10 chapter III for content and Common Technical Document (CTD) format • GLP statement has to be part of the IMPD (see: point 44 of annex I of the CTR and http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/QAs_document_on_GLP_-_2017.pdf
G. Simplified IMPD	G	See CTR (annex I points 50 to 53) to see cases when a simplified IMPD is accepted
G. SMPC	G	If applicable.
H. AXMP dossier	H	AXMPD or SMPC if applicable
I. Copy of the summary of scientific advice	I 56	If applicable. The outcome of the scientific advice should be reflected : the summary of the scientific advice should include both the questions and the answers provided by the European Agency, or any Member State or third country otherwise the "advice" would be missing. A text limited to the questions does not summarise the scientific advice.
I. Copy on the agreement on the PIP	I 57	If applicable : please provide the full unredacted opinion of the Paediatric Committee on the agreed PIP (and waivers) including the EMA/PDCO summary report in the "Not for publication slot". This will be in the benefit of the application to do so if sponsor is compliant to the PIP, since that way also ECs will have access to the full information.
J. Content of the labelling	J	Example of the planned label in accordance with law of 7 May 2017: - 3 national languages - but specific label for the trial not mandatory if registered products - and allowed in 1 language (English included) if administered at site and patients do not deal with the product (please provide a justification in cover letter if labels provided in only one language)

*See question 1.24 of the CTR Q&A in Eudralex volume 10 for a description of what are patient facing documents.

PART II

File/Document	CTR Annex I	References
K. Recruitment arrangements, unless described in the protocol	K 59	Stand-alone document or reference to the applicable section of the protocol has to be provided A template developed by the EU Commission is available in Eudralex volume 10
K. Advertising material	K 60	If applicable
L. Subject (and legally designated representative) information and informed consent ICF and recruitment material	L 61&63	• Use of the existing template is strongly recommended. • **A template for interventional trials in adults is available** here. • ICF(s) to be submitted at least in the official national language(s) of the region(s) where the trial is conducted • Sponsor is responsible for appropriate translations. The EC only reviews the ICFs in one language • Recruitment material* (to be submitted at least in the official national language(s) of the region(s) where the trial is conducted) * See question 1.24 of CTR Q&A in Eudralex volume 10 for an explanation on the difference between recruitment material and patient facing documents
L. Informed consent Procedure	L 62	A stand-alone document or a reference to the applicable section of the protocol has to be provided A template developed by the EU Commission is available in Eudralex volume 10
M. List of the planned sites, name and position of PI and planned number of subjects at the sites	M 64	Not needed anymore as the planned number of subjects at the site is to be provided in the site suitability statement
M. CV and declaration of interest of the principal investigator of each site	M 65&66	• BE specific CV template strongly recommended. Any other template (e.g. TransCelerate) can be accepted but should at least contain the same information • GCP training should be documented (in the CV or by a GCP certificate), mentioning the name of the certifying organisation **and should not be older than three years** • Declaration of interest: template developed by the EU Commission available on Eudralex volume 10
N. Statement on the suitability of the sites	N	The EU template is slightly adapted to facilitate the dossier management in Belgium. The adapted version is available here and is now the only accepted version. Only one signature is requested: the signature of the CEO of the hospital or of her/his representative. The document should be prepared by the sponsor to allow the site signatory to make a correct evaluation of the requirements in terms of equipment, facilities and (human) resources to properly conduct the trial. **Please take into account the following guidance when completing this template.** Name of site, city and, if applicable, unique identification number of the site: 1) When it concerns a healthcare institution, use the name, city and recognition number of the hospital site(s) as given in the list of the FPS Public Health (belgium.be) and which are registered in CTIS. If the CEO of different hospital sites is the same, the sites can be listed in one statement.

<table>
<tr><td></td><td></td><td>2) With the recognition number is meant the "Erkenningsnummer van het ziekenhuis" / "Numéro d'agrément de l'hôpital".
3) If it does not concern a healthcare institution, mention the name of the Private organisation.

Examples:
<table><tr><td>Name of site[1], city</td><td>Onze Lieve Vrouwziekenhuis, campus Asse (1730 Asse), campus Aalst (9300 Aalst), campus Ninove (9400 Ninove)</td></tr><tr><td>If applicable, unique identification number of the site[2]</td><td>126</td></tr></table>
<table><tr><td>Name of site[1], city</td><td>Kliniek Sint-Jan, campus Leopold I (1090 Jette), campus Kruidtuin (1000 Brussel), campus Middaglijn (1210 Sint-Joost-ten Node)</td></tr><tr><td>If applicable, unique identification number of the site[2]</td><td>110</td></tr></table>
<table><tr><td>Name of site[1], city</td><td>Centre Hospitalier Universitaire de Liège, site Ourthe-Amblève (4130 Esneux), site Notre-Dame des Bruyères (4032 Chênée), site Sart-Tilman (4000 Liège-1), site CNRF (4557 Fraiture-en-Condroz)</td></tr><tr><td>If applicable, unique identification number of the site[2]</td><td>707</td></tr></table>
<table><tr><td>Name of site[1], city</td><td>CTU of the Institute of Tropical Medicine (2000 Antwerpen)</td></tr><tr><td>If applicable, unique identification number of the site[2]</td><td>Not applicable</td></tr></table></td></tr>
<tr><td>O. Proof of insurance cover or indemnification</td><td>O</td><td>Certificate with specification of the amount insured and reference to the Belgian law of 7 May 2017 Art. 12. § 1er (no fault insurance)</td></tr>
<tr><td>P. Brief description of the financing of the CT</td><td>P 69</td><td>If applicable</td></tr>
<tr><td>P. Information on financial transactions and compensation paid to subjects and investigator/site</td><td>P 70</td><td>• Draft version of the contract with (draft) amounts is currently accepted
• It is advised to contact the CTCs of the concerned sites as soon as possible in order to gain time in the evaluation of the financial agreements
• A template has been developed by EU Clinical Trials Expert Group for "Compensation for trial participants" and is available on Eudralex volume 10</td></tr>
<tr><td>P. Description of any other agreement</td><td>P 71</td><td>Clinical trial agreements and others related to the trial if applicable</td></tr>
<tr><td>R. Statement that data will be collected and processed in accordance with the GDPR</td><td>R</td><td>We currently still accept that only a general document is provided in the FORM section of CTIS.
This document should at least contain:
"[name of sponsor] confirms that collection and processing during clinical trials is done in full compliance with the European Regulation 2016/679 of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (GDPR)"

No specific document for Belgium currently requested.</td></tr>
<tr><td>S. "Collection, storage and future use of human biological samples"</td><td></td><td>A template has been developed by EMA and is available on Eudralex volume 10. This template is currently not mandatory for Belgium if the information is properly available in the dossier.</td></tr>
</table>

Additional clarifications

CTR General e-mail address:

For any question on the content of the dossier to be submitted for Belgium in CTIS or on the clarification of a consideration in the RFI list on Part I (when Belgium is RMS) or on Part II, please contact : CT.RD@fagg-afmps.be

Fee for Belgium:

No payment will be requested at the moment of the submission of the dossier. Therefore no proof of payment must be provided for Belgium in the CTIS submission dossier.

However the fee related to the safety follow up of CTIS dossiers (as stated in the "Loi de financement" from February 2022) will be requested by the mean of an invoice to the sponsor. This invoice will be applicable for all CTA applications (initial dossiers and substantial modifications) submitted in CTIS for Belgium. A fee will also be requested (only once) by the mean of an invoice to the sponsor for GCP inspections (also stated in the "Loi de financement" from February 2022). For the details of these invoices, please follow the link here below.

For 2024 the amounts may be consulting by following this link (FR) and this link (NL).

Transitioning trials:

Please consult the CTCG Best practice guide on transition trials and template cover letter on the CTCG (Clinical Trials Coordination Group) website, in section CTCG Key documents list/Guidance. Please also consult the Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation as published by the European Commission. This Guidance supersedes the chapter 11 of the Q&A on the application of the CTR.

All information related to transition of trials from CTD to CTR has been gathered on the EMA CTIS website : here

Combined CTR/MDR-IVDR studies:

Please state clearly in the cover letter whether the trial is a COMBO CTR/MDR-IVDR study, providing the MDR-IVDR study number if available and indicating whether the MDR-IVDR study has been submitted in parallel via the CESP. This will allow the CT College to be informed as soon as possible so that the same ethics committee can be selected to assess both the CTR trial and the MDR-IVDR study.

Preliminary list of sites in case of staggered submission:

In case only Part I is submitted for Belgium, please provide the preliminary list of sites for Belgium if already available. Purpose is to avoid selection of a non-independent ethics committee by the College and need for selection of a new one when Part II is submitted. We are well aware that this preliminary list can be modified before submission of Part II.

Signatures in documents

Signed documents uploaded in CTIS should be uploaded in the "Not for publication" slot. Please note that the only documents mandatory to be signed are the site suitability statement in Part II (only to be signed by the CEO of the hospital or by her/his representative) and the QP declaration of the qualified person in Part I (if applicable).

Track changes versions of modified documents:

Track changes versions of modified documents should be provided with the answers to the Part I and Part II assessment RFIs and with the applications for substantial modifications. Tracked change documents should be uploaded in the slot "Not for Publication". See ACT EU Q&A on protection of Commercially Confidential Information and Personal Data while using CTIS (europa.eu), point 1.9.

Naming of the documents:

Following rules are not mandatory. In case these rules are not respected, validation of the CTA applications will not be blocked. However applying these rules is of great help for the review of the dossier by the ethics committees and by the national competent authorities.

Please precede the name of the document with CTR annex I corresponding letter. This will allow the member states to have a structured list of documents after download of each Part of the dossier from CTIS. Version number and dates should not be part of the name of the document and have to be directly entered as structured data in CTIS.

See also the new version of the Best Practice guide for Sponsors on document naming in CTIS on the website of the CLINICAL TRIALS COORDINATION GROUP (CTCG).

In order to simplify the re-submission process to CTIS, CTCG accepts that the CT numbers within the documents uploaded into the system are shortened concerning the last 2 digits which only show how often the sponsor created previous submissions and re-submitted the applications.

In case of a decision letter the full number including the last 2 digits will be reflected.

If the full number is reflected in the documents and a re-submission takes place, there is no expectation that these numbers are immediately corrected within the documents during the ongoing procedure. This can be done at a later stage when the documentation is updated during a SM procedure.