CTIS Webinar: Last Year of Transition

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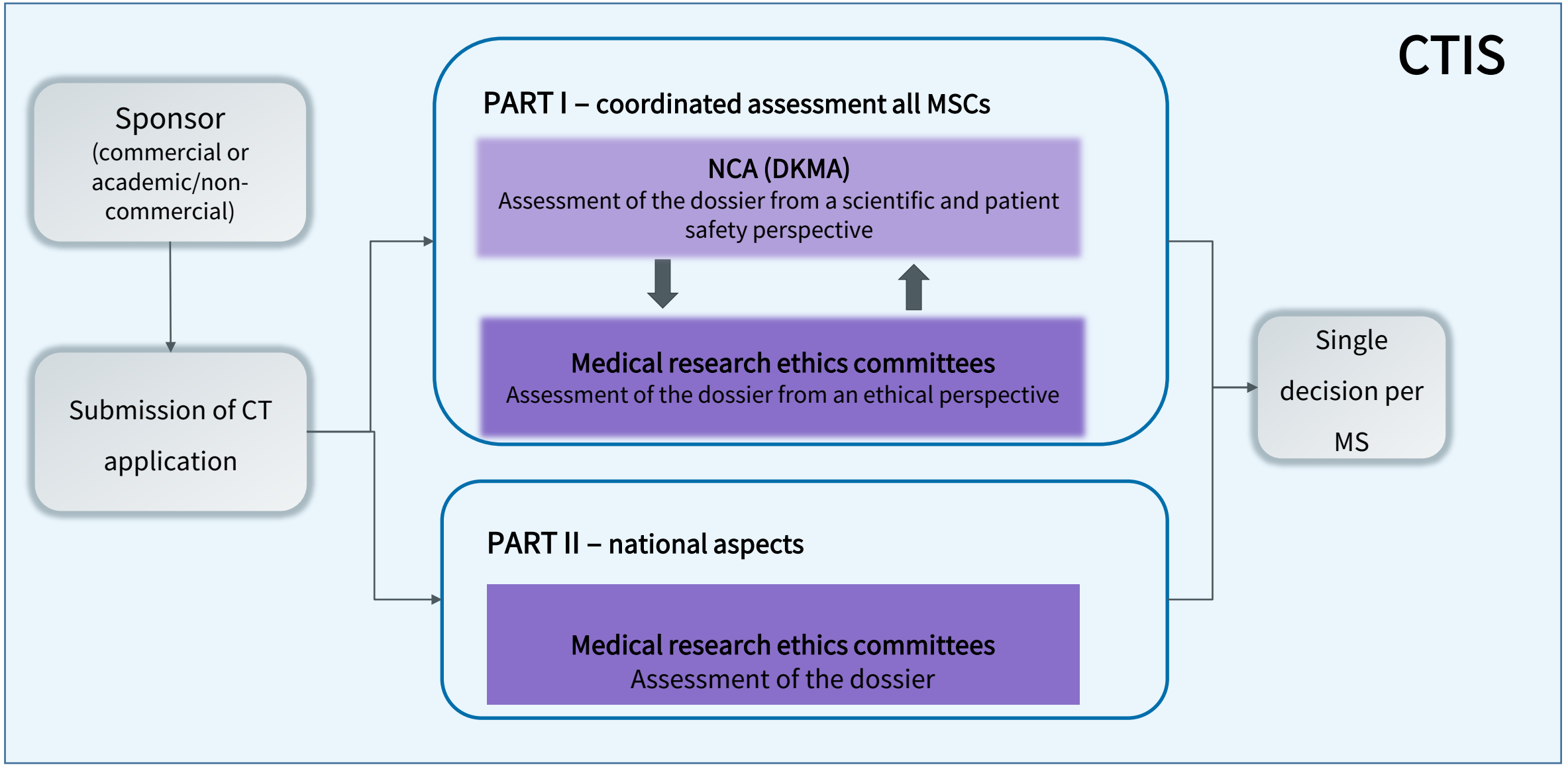
CT application and assessment procedure in CTIS – national perspective



Requirement for part II – Guidance for transition Volume 10

Annex I. Overview of requirements dossier part II for a transitioning CT application in the first administrative transition step

The table has to be considered as a living document as work is still ongoing to complete the rows for the missing countries.

AT	Yes	No	Yes
BE	Yes	No	Yes
BG			
CY	Yes	No	Yes
CZ			
DE	Yes	No	Yes
DK	Yes	No	Yes

- Subjects' information sheet(s)
- Informed consent form(s).

- Documentation on the damage compensation trial participants (insurance reference/certificate/other arrangements)

For all other part II documents, sponsors can upload on CTIS placeholder documents with a statement clarifying that this aspect was already assessed and approved under CTD.

Guidance from CTCG

– Clinical Trials Coordinations Group Heads of Medicines Agencies: Clinical Trials Coordination Group (hma.eu) **Transitional Trials**

In the light of the huge number of Clinical trials to be transitioned to the CTR, the CTCG Best Practice Guide for sponsors of multinational clinical trials with different protocol versions approved in different Member States under the Directive 2001/20/EC that will transition to the Regulation (EU) No. 536/2014 will be adapted to newly arising problems as needed. Please check the guidance document regularly.

- CTCG Best Practice Guide for sponsors of multinational clinical trials with different Part I document versions approved in different Member States under the Directive 2001/20/EC that will transition to the Regulation (EU) No. 536/2014 | pdf
  Version 4 – March 2024

- Cover letter template | pdf
  Annex to the Best Practice Guide for sponsors of multinational clinical trials with different protocol versions approved in different Member States under the Directive 2001/20/EC that will transition to the Regulation (EU) No. 536/2014
  Version 4 – March 2024

Transition: What should be submitted to part I

For Part I, the latest authorised versions of the following documents need to be provided as a minimum in the transitioning clinical trial application:

- ✓ Protocol; consolidated/harmonised.
- ✓ investigator's brochure (IB); consolidated IB is accepted
  - – SmPC for the IMP if marketed product is used
- ✓ good manufacturing practice (GMP) relevant documents;
- ✓ investigational medicinal product dossier (IMPD) consolidated IMPD is accepted; and
- ✓ documents related to non-investigational medicinal products (i.e. auxiliary medicinal product under CTR if applicable) if not authorised.

No assessment – only validation

The sponsor should commit in the cover letter that all documents are the latest submitted and approved in the MSC and attach the list (and versions) of documents, as of CTR Q&A and CTFG recommendations. RMS will check if statement and list of approved versions are submitted – but not check the list in detail

– Validation process follows the timelines in the Regulation for the validation

➢ Not possible to apply for low intervention in transition as this would require assessment

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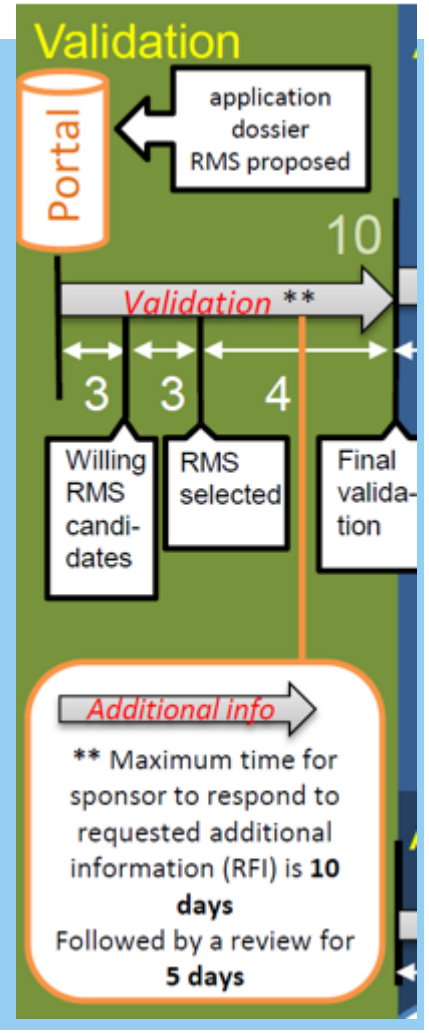

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Consolidated protocol, IB, IMPD

- Consolidated protocol, reflecting the common core provisions and capturing the differences as regards the nationally authorised trials

- Guidance: https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2023_11_CTCG_Annex_cover_letter_template_-_CTCG_Best_Practice_Guide_for_sponsors_on_transition_vs3.docx

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**.

No assessment – only validation

The validation process:

- ✓ check cover letter and compliance with submission rules. All required documents (harmonised/consolidated where necessary) already authorised under the Clinical Trials Directive (CTD) should be included.
- ✓ Accept document with EudraCT trial number (=approved under CTD).
- ✓ Check that the upload does not include any unauthorised documents that would require new assessment (note: GDPR compliance document acceptable, required for CTIS use).
- ✓ The approved IMPD could be uploaded in the slot for IMPD-Q, providing a reference to this document or to the IB/SmPC in the CTIS slot for IMPD S&E
- ✓ Non-substantial amendments compared to the version authorised under the CTD are acceptable if justified and addressed in the cover letter (only NSMs defined in CTR Q&A Annex IV), to enable a smooth transition process
- ✓ Invoice details for DK for an annual fee – no fee for transition in Denmark.

No assessment – only validation Part II

- For Part II, the latest authorised versions of the subjects' information sheet(s) and the informed consent form(s) are those documents that are required as a minimum.
- The sponsor may submit additional documentation in addition to what is required above for the transitioning application, if these documents were assessed and authorised under the CTD. No other documents should be submitted.
- For Part II, there is no need to retrospectively create a site suitability form.
- In the cover letter, the name of the ethics committee which has given a positive opinion on the clinical trial under the CTD and the EudraCT number shall be included.

Example of validation consideration from Denmark:

- *EC: Please state in the cover letter the name of the specific Danish Research Ethics Committee that assessed and approved the application under the Clinical Trial Directive. We recommend using the cover letter template developed by the CTCG: 15.2 Update proposal - Annex cover letter template - CTCG Best Practice Guide for sponsors of multinational clinical trials under CTD transitioned to CTR (hma.eu).*

Example of validation consideration from Denmark:

- *EC: The placeholder documents in the sections "Recruitment arrangements", "Financial and other arrangements" and "Proof of insurance cover or indemnification" must all be updated with a description/confirmation that this aspect was assessed and approved by the Research Ethics Committee that assessed the application under the Clinical Trials Directive. This is in line with Guidance for the Transition of clinical trials of Marts 24th 2024 (https://health.ec.europa.eu/system/files/2023-12/transition_ct_dir-reg_guidance_en.pdf)that states that "Except for the minimum set of required documents for Part I and for Part II, it is acceptable that the sponsor uploads a document in the corresponding document slots in CTIS clarifying that this aspect was assessed by NCA and/or ethics committee who has given a positive opinion on the clinical trial under the CTD (and therefore is covered by the conclusion of the assessment under the CTD)".*

Example of validation consideration from Denmark:

– *EC: The transition of clinical trials from the Clinical Trials Directive into CTIS is solely an administrative process and no re-assessment of documents is performed. It is therefore important that NO new documents are added to the application. Please remove xxxx…*

Tips:

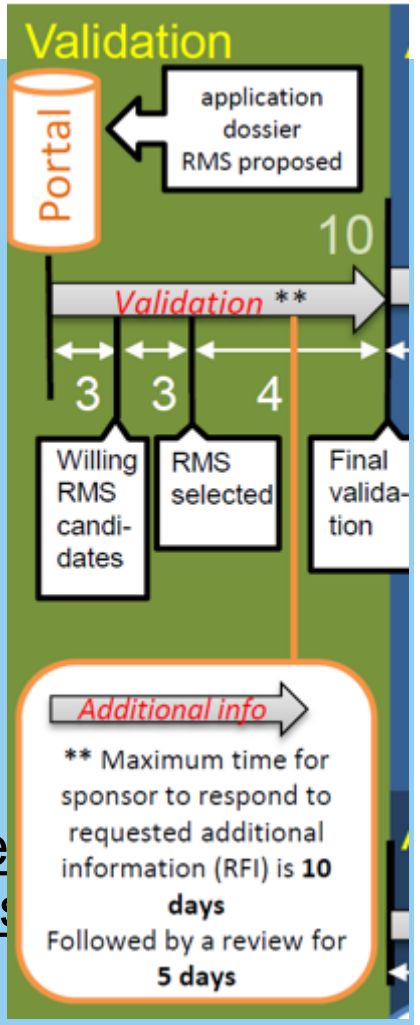
– Optional to upload ‘Danish amendment’ used for trials under the Directive

– The structured data in CTIS is advised to be in compliance with the information in EudraCT e.g. GCP-monitor

Request for Information via CTIS if not valid

For Incomplete submission considerations by MSCs are forwarded as concluded by RMS in a validation Request for Information (RFI) via CTIS

- **No notifications** is send to sponsor when a RFI is issued.
- Please keep an eye in CTIS in order for your application not to lapse!



More information from the Danish Ethics Committe: Overførsel af kliniske læge
fra Direktivet til EU-forordningen (CTR) | De Videnskabsetiske Komitéer (videns

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Assessment phase in CTIS for transition

- No assessment – no full assessment report is uploaded.
- CTCG have agreed on a proces for maximum 22 days, so only few days for consolidation (if question on catagory according to CTCG BP) between concerned Member States.
- Only creation of a short administrative Final Assessment Report for upload in CTIS to sponsor

Expedited Review

For multinational transition trial applications, CTCG has agreed on

- an **expedited, harmonised Member State evaluation procedure open until 16th of October 2024** focussing on the validation of minimum application dossiers restricted to documents already authorised under the CTD.
  - After this date, an expedited procedure might not be feasible depending on the workload. Unless an assessment RFI is raised with considerations questioning the trial category/deferral proposed by the sponsor, the assessment phase is shortened to one week for these minimum dossier transition applications.

Thank you

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