ACT EU Training on transition trials for non-Commercial sponsors

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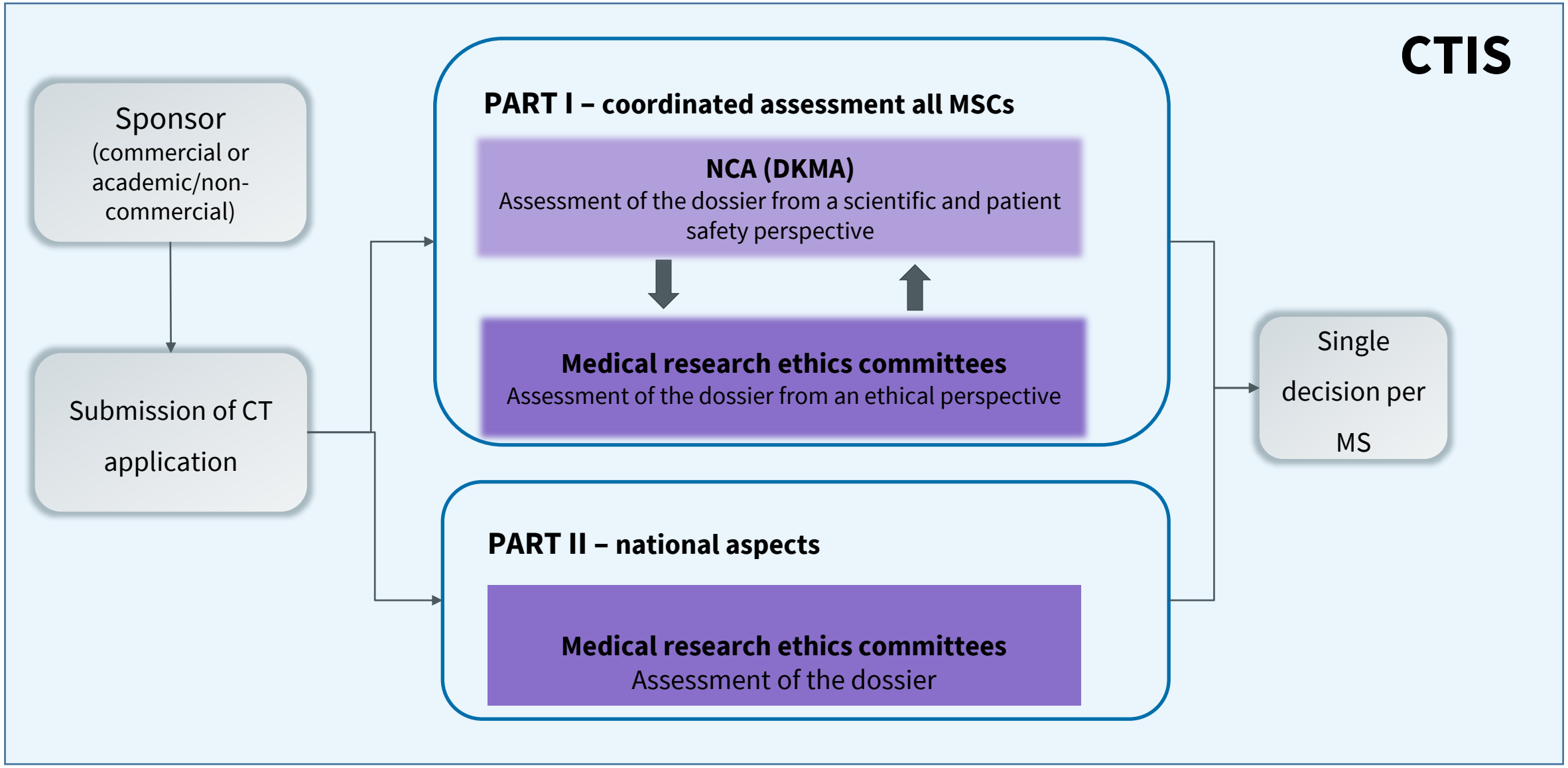
CT application and assessment procedure in CTIS – national perspective



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Criterions for transition from CTD to CTR

- Only interventional trials
- transitioning to the Clincial Trial Regulation (CTR) is only required for Clinical Trial Directive (CTD) trials which will have **at least one site active in the EU on 30/01/2025**.
- An application to transition a CTD trial only needs to be submitted to those MSC where the trial is **ongoing (active site** in the context of transition trials means that the last visit of the last subject, or other trial-specific interventions with the subject specified in the protocol)

- OBS; Sponsors should however take into account the time necessary for completion of the authorisation procedure

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Trials not transitioned

– For CTD trials that do not transition to the CTR, the obligations for result reporting in EudraCT remain in place and accordingly, EudraCT will remain open for the submission of trial result summaries even after 31/01/2025.

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Guidance volume 10

– EU-Commission Eudralex Volume 10: transition_ct_dir-reg_guidance_en.pdf (europa.eu)

Guidance for the

Transition of clinical trials

from the Clinical Trials Directive

to the Clinical Trials Regulation

21 December 2023

This Guidance reflects the agreement reached by CTAG Contact Points and supersedes the chapter 11 of the Q&A on the application of the CTR (version 6.4).

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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 3 – November 2023

- 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 3 – November 2023

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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.

Consolidated protocol, IB, IMPD

- 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

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]

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

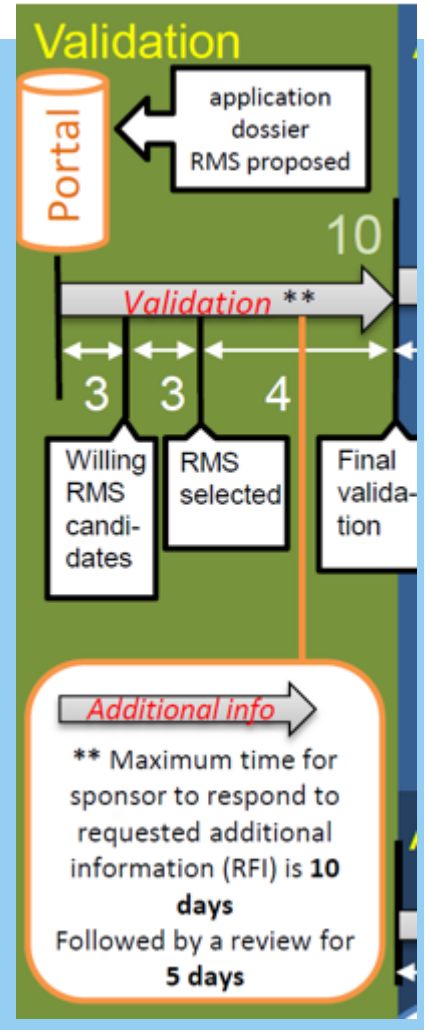
In case of a consolidated protocol, complete the table below describing Member State-specific aspects (e.g. restricted trial population, particular local requirements etc.) and where they are specified (i.e. annex number or protocol section number)

Member State	Version and Date of the protocol	Date of approval			National specific aspect	
		National Competent	Ethics Committee	Name of Ethics	Content	Page reference/location

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



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No assessment – only validation

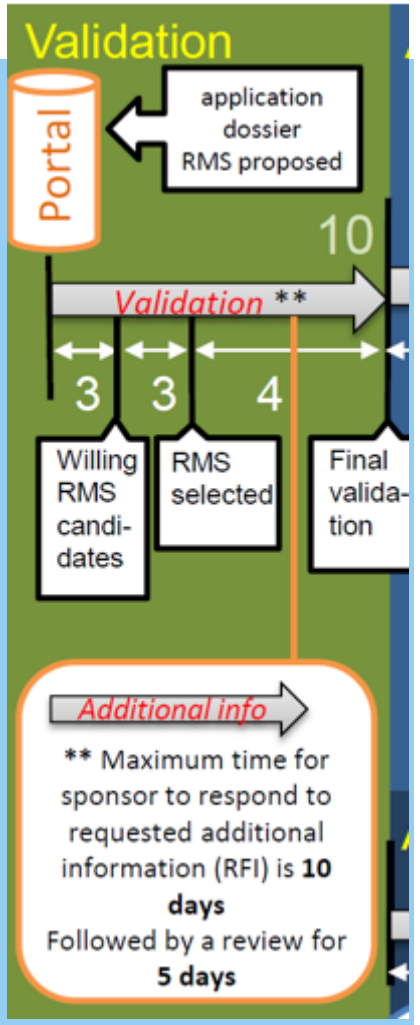
The validation process:

- ✓ 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 9this 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

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!



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Obligations for the sponsor after transition

Clinical trials that were started under the CTD and subject to transition to the CTR will have to comply with the obligations of the Regulation even if these are not included in the protocol, such as:

- obligations of notification via CTIS;
- safety reporting rules;
- archiving requirement;
- transparency requirements;
- rules for requesting substantial modification and addition of a MS, see Question 9); and
- rules for submitting the summary of results and the clinical study report (CSR).

When is a Sponsor Expected to update Trial documents and labels?

- The sponsor should bring documents related to the clinical trial in line with the CTR requirements at the first Substantial Modification (part I and/or part II).
- The upload of new template documents for procedures in the trial already completed is not required.
- For the labelling of IMP and AxMP, it is expected that the sponsor updates the label for those batches that are (re)labelled after the authorisation under the CTR. There is no need to pro-actively relabel released IMPs. Old label can still be used after transition for IMP batches manufactured after transition if the new label is not yet approved in an SM Part I application.

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.

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