GCP| ENHEDERNE
God klinisk forskning

The Danish GCP Units guide

to transition of trials from EudraCT to CTIS

Content

1 What is a Transitional trial

Clinical Trials authorised under the Clinical Trials Directive (CTD) 2001/20/EC with at least one active site in the EU on 30 January 2025 need to be transitioned to CTIS as transitional trials. The transition needs to take place before 30 January 2025. When the trial is transitioned to the CTIS database, it is authorised under the EU Clinical Trials Regulation (CTR) No 536/2014 and all the Regulation requirements will apply.

'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, will take place after 30 January 2025. Hence, clinical trials with no active sites on and after 31 January 2025 do not need to be transitioned.

Further readings on transitional trials:

EMA training module 23:
EMA Quick Guides for sponsors – please refer to module 23

Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation

Info box:
If a clinical trial does not fully comply with the CTR, the sponsor shall request a substantial amendment under the CTD before switching to the CTR, specifying its intention to align the trial with the CTR. When the substantial amendment is accepted, sponsor can transition the trial to CTIS and thereafter follow the CTR.

Trials for which a request for a substantial amendment is under assessment cannot be transitioned until the procedure is completed

EMA recommends transition of ongoing trials not later than September 2024:

Figure 5.1.2. Schematic representation of the Clinical Trial Regulation transition period from 31 January 2023.

Info box:
Please notify the local Ethics Committee (e.g. Danish VEK) if the trial is transferred to CTIS before 31 January 2025.

2 Create and submit a Transitional Trial

2.1 How to get the role as "CT Admin" in CTIS

If you have previously registered a new CTA in CTIS you already have the "CT admin" role.

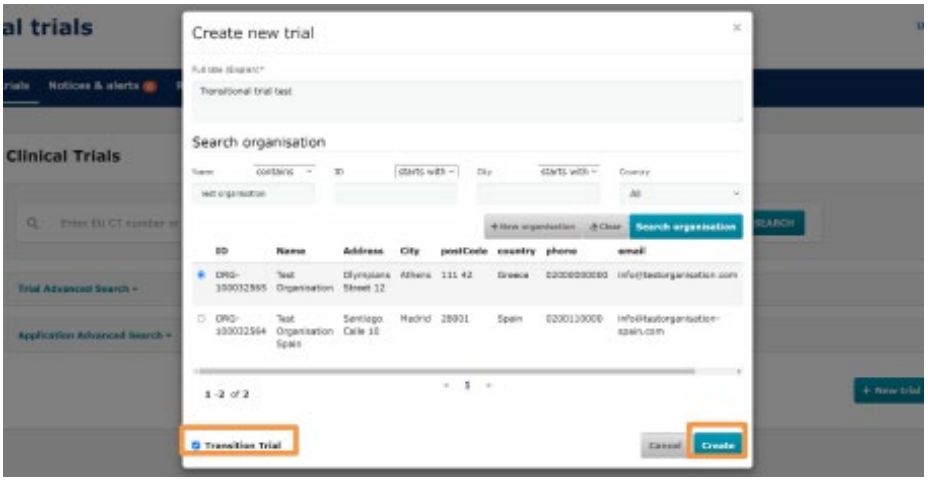
When sponsors create a CT application for a transitional trial, due to the current system configuration, the 'Transitional trial' checkbox is not visible. In such cases, sponsors are advised to first create a "dummy" non-transitional clinical trial application. Once the CT Admin role for that specific clinical trial is granted to the creator of the application, the user should log out and log back in.

The system will then enable the 'Transitional trial' checkbox for this user which will enable the creation of a CT application for a transitional trial. The "dummy" non-transitional clinical trial application can be cancelled afterwards.

2.2 How to create a Transitional trial

Go to the CTIS 'Clinical trials' tab and create a trial by selecting the '**New trial**' button at the bottom-right corner.

A pop-up window opens, and users can populate all the required fields:



- 'Full title',
- Organisation details (search for the sponsor organisation address)
- When fields are populated, select the checkbox '**Transitional trial**'. *If users do not select the checkbox, they need to cancel the CTA (clinical trial application) and create a new one.*

Click on the '**Create**' button to create a draft Transitional trial.

Info box:
It must be indicated that it is a Transitional application at the moment of creating the draft Initial application in CTIS; if users do not select the checkbox, they need to cancel and start over.

2.3 Documents required under the CTR

Sponsor needs to submit an initial application relying on the existing CTD dossier, already assessed and authorized. The following minimum set of data/documentation is required:

Structured fields and forms

- All mandatory application structured data fields in CTIS need to be completed
- Statement on GDPR compliance (*new, required for CTIS users*)
- Cover letter (se section 2.4 for content)

Part I

- Protocol (latest approved version)
- ”Synopsis of the protocol” – previous written protocol resume can be used (language Danish or English)
- Investigators Brochure or SmPC
- IMPD (if applicable)

- Documents related to non-investigational medicinal products (i.e. auxiliary medicinal products under the CTR, if applicable)

Part II

- Subject information sheet
- Informed consent form (ICF)

Some of the documents listed in Annex I of the CTR are new as they were not required under the CTD.

It is not a requirement to submit the form," Suitability of the clinical trial sites facilities" (one per site) with the transition application. This is only required if new sites are added as substantial modification AFTER transition is complete).

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.

Users can upload a placeholder document to continue the creation of the transitional trial application if a document was not a requirement under the CTD, but mandatory to be submitted for the CTA in CTIS.

The placeholder document must clarify that e.g. "*this aspect was assessed by National Competent Authority (NCA) and/or Research Ethics Committee (REC) and therefore is covered by the conclusion of the assessment under the CTD*".

Documents that have been replaced by a placeholder document will need to be submitted as part of the first substantial modification application after the transition authorisation.

2.4 Content of new cover letter

A new cover letter must be uploaded for the transitional trial (the old cover letter from the original application is not valid).

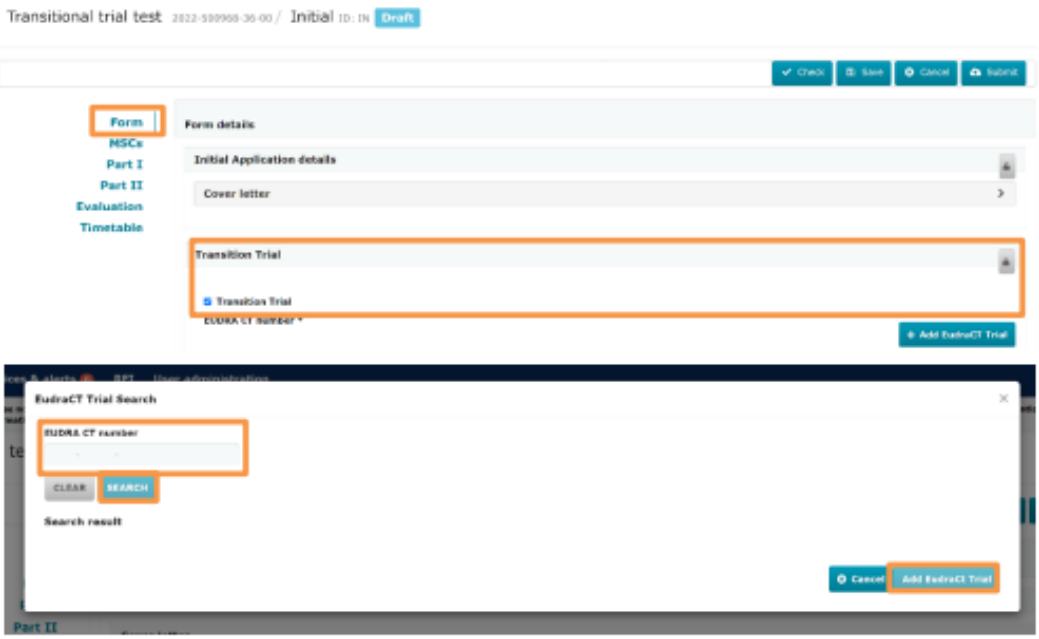
The following text must be included in the cover letter:

- Declaration, that the clinical trial is in line with the requirements for transitioning from the CTD to the CTR, and with the authorisation given under the CTD
- Declaration that all documents which need approval and are transitioned have been approved by the Member State concerned (MSC) prior to transition
- The name of the Ethics Committee who has given a positive opinion on the clinical trial under CTD
- The EudraCT number
- Change in the archiving period to 25 years
- For multinational trials only, the cover letter template must be used

2.5 How to populate a Transitional trial

Once the draft Transitional trial application has been created, users can start populating CTIS with the required fields of the sections: **Form', 'MSCs', 'Part I' and 'Part II'.**

In the Form section, in the Transition trial sub-section, users can **include the relevant EudraCT number** for that respective Transitional trial. This sub-section is only available when a user has marked the 'Transitional trial' checkbox when creating the CTA. Click on the '+ Add EudraCT Trial' button, then search the respective trial via the search bar.



Thereafter users must populate the rest of the CTA sections.

In the section 'MSCs', only those sites (and MSC) where the clinical trial is still ongoing need to be mentioned.

For filling in Part I and II information and documents, please see our overall guideline - The Danish GCP Units guide to the Clinical Trials Information System (CTIS).

The GCP units must be added as third party.

2.6 How to submit a Transitional trial

Check that all information has been populated correctly by clicking on the 'Check' button. The system will highlight the sections where mandatory data or documents are missing.

The draft Transitional trial cannot be submitted if any mandatory fields or documents are not filled in or uploaded.

2.7 Transition of multinational trials

It is required to harmonise all documents common to all Member States concerned (i.e. documents from Part I). Sponsors are only allowed to upload **one version of the protocol for each trial**.

Info box:
For multinational trials only, the **cover letter template** must be used

Adopted by the Clinical Trial Coordination Group (CTCG) under the Heads of Medicines Agency (HMA)

Sponsors will be required to have a harmonised or consolidated protocol approved under Directive 2001/20/EC, prior to transitioning. Differences in a consolidated version of the protocol are limited to the Member State-specific requirements.

- **A harmonised protocol**, IB and/or IMPD means that the respective document(s) is (are) identical and includes the same trial procedures in all countries approved across all EU Member States under the CTD.
- **A consolidated protocol,** IB and/or IMPD means that there are substantial differences in the respective document(s) in different Member States, but the document itself is identical, i.e. Member State-specific issues are outlined within the document text or in an appendix to the respective document. The consolidated protocol, IB and/or IMPD do not need prior approval under CTD before the transition.

A declaration of the harmonized/consolidated protocol must be included in the cover letter for multinational trials (please see cover letter template in info box).

For more information for transition of multinational trials:

CTCG Best Practice Guide for sponsors of multinational clinical trials with

3 Respond to Request for Information (RFI) for a Transitional trial

3.1 How to respond to RFI

Sponsors can access the 'Evaluation' section about information that needs to be clarified, called RFI. For more information on how to respond to RFIs, sponsor users can refer to the materials of Module 11.

EMA training module 11 for responding to RFI:

EMA Quick Guides for sponsors – please refer to module 11

There will be no re-assessment of the submitted dossier during the transitioning application. The documentation of which the ongoing trial was authorised is already available within the Member State(s).

4 Timelines

Member States Concerned (MSCs) may choose to authorise the trials within or in **less than 60 days**. In case of Requests for Information (RFIs) the trial will be authorised within a **maximum period of 106 days**.

Info box:
Please be aware to check "Notices & alerts" in CTIS regularly, if a RFI is received.

The authorities have committed to an expedited timeline for trials transitioned before September 2024.

The maximum timeline for the expedited transition procedure of minimum dossiers for multinational trials restricted to documents already approved under the CTD is estimated to be maximum 22 days provided that no Requests For Information have to be sent: 10 days (validation phase without Request For Information) + 7 days (assessment phase provided no Request For Information is needed) + 5 days (decision).

When the trial is authorised under the CTR in CTIS, all requirements of the Regulation will apply (e.g. obligations of notification via CTIS, safety reporting rules, archiving requirements, transparency requirements, procedures for submission of substantial modifications and summary of results).

5 What are the consequences of the transition for a clinical trial?

- In CTR the requirement for archiving is 25 years for all documents in TMF and CRF. Source data from the medical records should be archived according to national law.
- Notifications must be updated in CTIS – e.g. update recruitment start date
- Safety reporting rules (annual safety report in CTIS)
- Transparency requirements
- New rules for requesting addition of a member state
- New rules for reporting summary of results and final report in CTIS
- New rules for requesting substantial modifications (see Annex IV in CLINICAL TRIALS REGULATION (EU) NO 536/2014, QUESTIONS & ANSWERS, VERSION 6.8)

6 How to submit notifications for a Transitional trial

Notifications can be submitted when the trial has been authorised. The sponsor must submit a 'Start trial' notification with a trial start date in the past and prior to the authorisation date documented in CTIS, as the application was already authorised under the CTD.

EMA training module 5 for submission of notifications:

EMA Quick Guides for sponsors – please refer to module 5

In connection with transition to CTIS, the system will automatically send a mail saying that the trial is "on hold", hence right after authorisation in CTIS the trial start dates (start of recruitment and start of inclusion) needs to be mentioned for all MSCs where the trial is ongoing.

7 Transparancy requirements under CTR

Documents submitted by the sponsor in the transition application fall under the transparency requirements of the CTR and have to be made publicly available.

When transitioning a minimum dossier (see section 2.3), the sponsor must prepare redacted versions for publication of:

- the protocol,
- subject information sheet(s)
- informed consent form(s).

Name the document "(for publication)" in the file name.

The other documents in the dossier can be submitted as the non-redacted documents already approved by the Member State(s). Instead of redacted versions for other parts of the application dossier, a document referring to the previous approvals under the Directive from health authority and/or ethics committee, can be uploaded in CTIS.

Users can click on the 'Add' button (+) that appears in the document section after uploading the first version of the document intended for publication (only available in CTIS sections where the documents to be uploaded are published).

At the time of the next substantial modification application, redacted versions must also be submitted for publication for the rest of the dossier.

Any new notification after the trial has been transitioned, will fully fall under the transparency rules of the CTR (including deferrals) for making certain documents publicly available.

8 Changes log

Version 1.0

Version 1.1: Updated with recommendation of transition not later than Sep. 2024 and that sponsor must notify local EC when trial is transitioned to CTIS.

Version 1.2: Added requirement for updating the protocol with the archiving period 25 years when submitting the transition.

Version 1.3: Updated according to European Commission guidance for transition of clinical trials

Version 1.4: Updated with new knowledge and experience and information from other guidelines.