



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Clinical Trial Information System (CTIS) Bitesize talk

How to submit a transitional trial in CTIS

Presented on 21 June 2023
European Medicines Agency

An agency of the European Union





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CTIS Bitesize talk: How to submit a transitional trial in CTIS

15:30 - 15:35 **Introduction**

15:35 – 16:55 **Presentation followed by Q&A Session**

16:55 – 17:00 **Closing remarks**

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Main Session: How to submit transitional trials in CTIS



Ann Marie Jason Lang

Expert, Clinical Assessor
Associate Professor,
MD, PhD



Monique Al

Coordinating
Special Advisor



Charalampos Drosos

CTIS Change
Management Officer



Noemie Manent

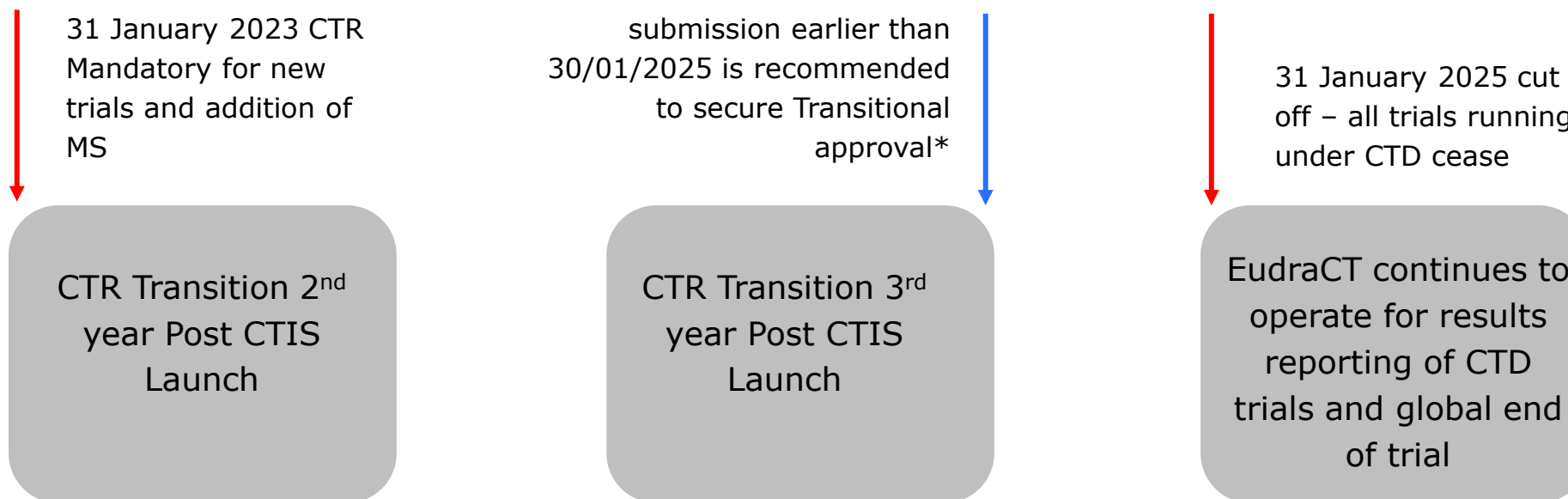
Principal Scientific
Administrator



Transition trials

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*** CTICG will publish updated guidance for sponsors on transition of multinational trials at the HMA website beginning of July (<https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html>, under key documents)**

- As of 31/01/2023, all new CTAs and additional MSC must be submitted under CTR using CTIS. They cannot be submitted under CTD in EudraCT.
- CTA authorised under the CTD can continue under the CTD till the end of the 3-year transition period (ends on 30/01/2025).
- If trials are expected to continue after the end of the transition period, sponsors need to transition them to CTR before the end of the transition period. To transition ongoing trials to CTR, sponsors will need to be submit them in time and before the end of the transition period, **considering the time needed for assessment** and the two-week winter clock stop.
- Sponsors are recommended to use the CTCTG expedited procedure to transition minimum dossiers restricted to documents already approved under the CTD.
- Only Member States with active sites (last-visit-last-subject did not yet occur) should be transitioned.

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- EudraCT remains active beyond the end of the transition for sponsors:
 - to notify global end of the trial and submission of summary results of trials completed under the Directive.
 - to keep registering in EudraCT trials conducted exclusively outside of the EU/EEA that are part of a Paediatric Investigation Plan (PIP) and/or in scope of Article 46 of the Paediatric Regulation (EC) 1901/2006, until a relevant functionality is delivered in CTIS.

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- Trials that should not be transitioned:
 - Trials that have already ended or will end before the end of the transition period (by 30/01/2025) in the EU/EEA.
 - If an end of trial notification has been submitted in all EU/EEA member states, but the global end of the trial has not been notified, the trial should not need to be transitioned. Global end of the trial and trial summary results should be posted via EudraCT under the Directive.
 - Trials that are old and started prior to the Directive 2001/20/EC coming into application. If they are interventional and need to continue to run after the end of the CTR transition period, then a new CTA under the CTR needs to be submitted.
 - EudraCT trials conducted exclusively outside of the EU/EEA that are part of a Paediatric Investigation Plan (PIP) and/or in scope of Article 46 of the Paediatric Regulation (EC) 1901/2006

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- Trials that can be transitioned: Only trials authorised under the CTD and likely to be ongoing beyond 30 January 2025 need to be transitioned if they meet these criteria:
 - are interventional clinical trials in humans;
 - involve at least one site in the EU/EEA where the trial is still ongoing;
 - there are no substantial amendments ongoing in any Member State Concerned (MSC) under CTD.
- General considerations:
 - Retrospective documents do not need to be submitted to CTIS. Only the latest approved versions should be included in the transition application.
 - CTCG will publish updated guidance for sponsors on transition of multinational trials at the HMA website beginning of July (<https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html>), key documents.
 - Where a mandatory document is expected to be uploaded to CTIS that does not exist for the transitioning trial, then a blank document is expected to be uploaded with a comment that the document does not apply, and it has been provided to allow transition from the CTD to the CTR.

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- General considerations (2):
 - When completing the CTA, consideration should be given to the transparency requirements of the CTR, including the need to remove personal data from submitted documentation and to apply for a deferral of publication, if applicable.
 - Multi-national clinical trials should be transitioned as a single multi-country CTA under the CTR, utilising a harmonised or at least consolidated protocol. Sponsors may need to consider harmonising the protocol by substantial amendments under the CTD before they transition them as one trial under CTR with one EU Clinical Trial number.
 - The CTCG expedited approval procedure for minimum dossiers restricted to documents already approved under the CTD also allows a consolidated protocol without prior authorisation under the CTD. The cover letter should provide detailed information on the approved version per Member State that is the basis for the consolidated protocol version.

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- General considerations (3):

- After the submission of the transition trial in CTIS, the CTR workflow is triggered. The RMS selection (multinational CT), validation, assessment Part I, Part II and decision milestones are released in CTIS. The CTCG expedited assessment procedure for Part I minimum dossiers restricted to documents approved under the CTD shortens the assessment phase to about 7 days, unless critical mistakes in the trial category and deferral selected by the sponsor are communicated as an assessment RFI.
- It is unlikely that a validation RFI is raised for transitional trials unless the documentation submitted does not correspond with the documents approved under the CTD. In such a case, the timelines would be extended by 15 days during the validation phase.
- Once Transition trial is authorised in CTIS, the sponsor will be able to submit the start/recruitment date of the trial in each MSC.
- The sponsor will continue to address their obligations under the CT Regulation and use the CTIS functionalities to prepare updates to the clinical trial. The trial is marked as 'trial now transitioned' in EudraCT by the MS. The sponsor and the MS will not input information in EudraCT for this trial.

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- Transition a mono-national trial: Sponsor needs to submit an initial application relying on the existing CTD dossier, already assessed and authorised. The following minimum set of documentation is required:
 - All mandatory application structured data fields need to be completed.
 - A new Cover Letter. The cover letter should follow the CTCG guidance (update expected beginning of July, see under key documents <https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html>)
 - Protocol (part I). If not harmonized under CTD, a consolidated protocol describing all Member-State Specific items should be described in the protocol or in an appendix
 - Investigator's Brochure (part I)
 - GMP relevant documents (part I)
 - IMPD (part I)
 - Documents related to non-investigational MPs (part I)
 - Subjects' Information Sheet (Part II)
 - Informed Consent form (Part II)

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- Transition a mono-national trial (2):
 - For all other Annex I documents (not listed in the previous slide), if sponsor cannot provide them, it should replace them with a document clarifying that this aspect was assessed by National Competent Authority (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.
 - After authorisation of the transitioned trial, sponsor will need to submit all the documents that have been replaced by a document, as referred to the point above.

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- Transition a multi-national trial (1): A multinational clinical trial approved under CTD is a trial conducted in different Member States under the same EudraCT number.
 - Before transitioning the multiple CTD trials to one multi-national CTR trial, they need to be harmonised sufficiently via CTD SMs.
 - If one harmonised protocol cannot be provided, a consolidated protocol that reflects the common core provisions and capturing the minor differences as regards the nationally authorised trials, can be submitted.
 - A **consolidated protocol** can be provided **without prior CTD submission** if there are differences in procedures in different Member States, but in other ways the protocol text is identical (i.e. MS-specific issues are described within the protocol or in an appendix to the protocol). The differences between the Member States and the approved version per Member State that the protocol is based on should be listed in the cover letter as described in the CTCG guidance for sponsors on transition of multinational trials - to be updated at the [HMA website](#) beginning of July, under key documents.

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- Transition a multi-national trial (2):

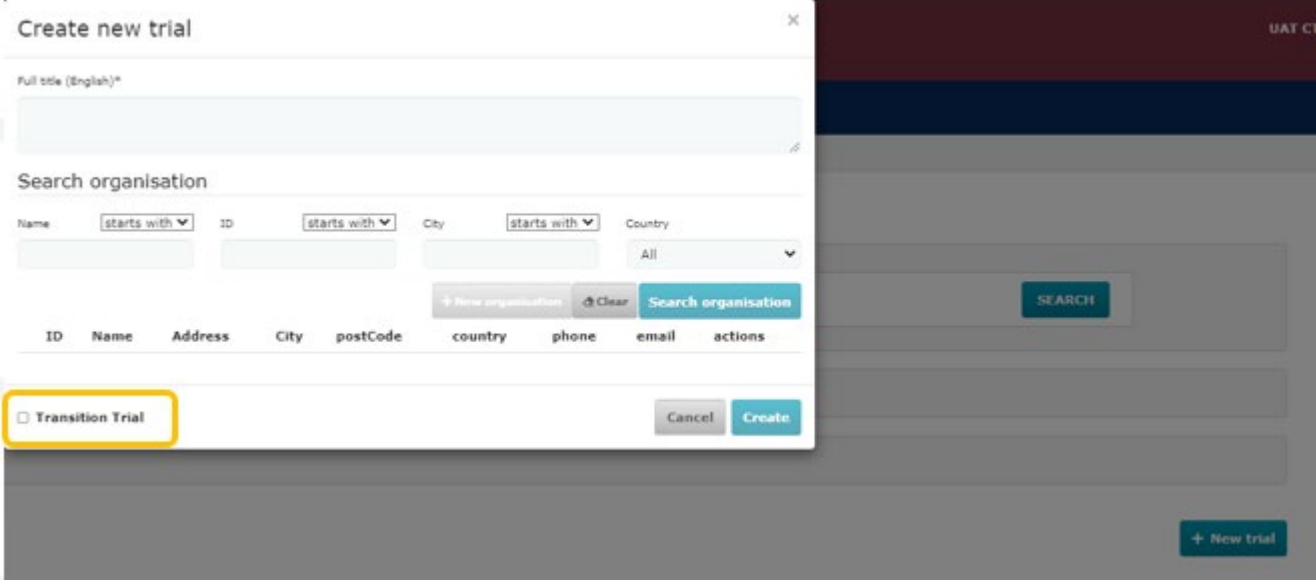
- Sponsor needs to submit the same data and documents (harmonised versions) that are required for mono-national trials. The process remain the same. Documents that cannot be provided with the initial application (and not indicated as minimum requirement for submission of an initial application for transition trial), need to be submitted after the authorisation of the trial, with the first substantial modification.
- The trial needs to be transitioned to CTR only for those MSCs (and sites) for which the trial is ongoing and it is not expected to end by 30/01/2025. A trial Member State without active sites is understood as a Member State where the last visit last subject has taken place at ALL trial sites. If the CTD trial has ended in some MSCs, it should not be transitioned to CTR for those MSCs.

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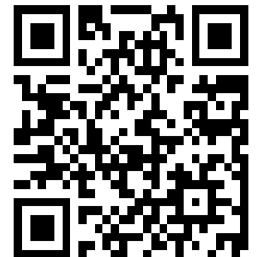
- To facilitate the transition, CTIS has functionalities that enable the sponsor to:
 - Create an initial application for a new trial in CTIS (own CT EU number);
 - Associate this new initial application to an existing EudraCT number.

Step 1



The screenshot shows the 'Create new trial' form. The 'Transition Trial' checkbox is highlighted with a yellow box. The form includes a 'Full title (English)*' field, a 'Search organisation' section with filters for Name, ID, City, and Country, and a 'Transition Trial' checkbox. The 'Transition Trial' checkbox is highlighted with a yellow box.

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CTIS functionalities for Transition trials (2)



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Step 1

Form details

Initial Application details

Cover letter

Transition Trial

☒ Transition Trial
EUDRA CT number *

+ Add EudraCT Trial

Step 2

EudraCT Trial Search

EUDRA CT number

CLEAR SEARCH

Search result

Cancel Add EudraCT Trial

Step 3

EUDRA CT number

2019-00000-00

CLEAR SEARCH

Search result

Sponsor
Test Organisation Spain
Full title
Test Trial for BiteSize event 21 June 2023

Cancel Add EudraCT Trial

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- Reference documents to Transition trials have been published in Commission website, EMA website and CTCG website:
 - EC: [Questions and Answers Document – Regulation 536/2014](#) (link to webpage EudraLex – Vol.10).
 - EMA: [BiteSize event June 2022 dedicated to Transitional trials](#) (demo of functionality included).
 - EMA: [BiteSize event June 2023 dedicated to Transition trials](#) (CTCG participation).
 - EMA: [Sponsor Handbook / Chapter 05](#).
 - EMA: [Training Module M23](#).
 - CTCG: [Best Practice Guide for sponsors of transition multinational clinical trials](#) (at the HMA webpage <https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html>), under key documents. CTCG is working on an updated version that is expected to be published soon.

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- If trials are not expected to end in EU/EEA by 30/01/2025, transition them as soon as possible.
- There will be no legal grounds for CTD trials (EU/EEA) to continue from 31/01/2025.

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Q&A session

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CTIS training environment Survey 4.0

Survey 4.0 remains open where new potential users of CTIS can express interest to access the CTIS training environment (CTIS Sandbox).

CTIS Sandbox Survey 4.0

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CTIS upcoming events

- [Clinical Trials Information System Webinar: Second Year of Transition - 4 Jul 2023 - 13:00 - 17:30 CEST](#)
- [CTIS Walk-in Clinic – 19 Jul 2023 – 16:00 – 17:00 CEST](#)

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Further information

For the [Clinical Trials Highlights](https://ec.europa.eu/newsroom/ema/user-subscriptions/3201/create) sign up at <https://ec.europa.eu/newsroom/ema/user-subscriptions/3201/create>

Latest CTIS Newsflash can be consulted [here](#)

For upcoming CTIS events, visit the [EMA event page](#).

Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands

Telephone +31 (0)88 781 6000

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