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

29 February 2024

Event supported by Marianne Lunzer (AGES); Lene Grejs Petersen(Clinical Trials Unit, Danish Medicines Agency); Noémie Manent (Data Analytics and Methods Task Force, EMA);

A few housekeeping rules

Questions were collected in advance on **www.sli.do**
With event code **#bt29feb**

Tips for optimal screen viewing

- Make use of the instructions under the **Live broadcast** section on the event page and connect directly to the **EMA's Vimeo channel 1** *for the full-screen experience*
- Have a stable internet connection

Agenda

- How to submit transitional trial in CTIS
- Q&A session

The experts for this events are:

Moderator: Noémie Manent

Noémie Manent

Principal Scientific Administrator
CTIS Expert, EMA

Marianne Lunzer

CTCG, Austrian Agency for Health and Food Safety

Lene Grejs Petersen

Senior Adviser, Clinical Trials Unit, Danish Medicines Agency

How to submit transitional trial in CTIS

Transition period

31 January 2023 CTR Mandatory for new trials and addition of MS

CTR Transition 2nd year Post CTIS Launch

Submission **as per the CTCG guidance*** earlier than 30/01/2025**

CTR Transition 3rd year Post CTIS Launch

31 January 2025 cut off – Clinical trials can only run under CTR

EudraCT continues to operate for results reporting of CTD trials and global end of trial

Since 31/01/2023, all new CTAs and additional MSC must be submitted under CTR using CTIS.

***CTCG published updated guidance for sponsors on transition of multinational trials at the HMA website (https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html, under key documents)**

****Sponsors need to take into account the time for the finalisation of the application procedure**

Transition period: Principles (1)

- Trials to be transitioned: Only **trials authorised under the CTD** and likely to be ongoing beyond 30 January 2025 that meet these criteria:
  - are **interventional clinical trials** in humans;
  - involve at least **one active site** in the EU/EEA where the trial is still ongoing;
  - only **Member States with active sites** (last-visit-last-subject did not yet occur) should be transitioned;
  - Only **active sites** in those Member States
  - there are **no substantial amendments ongoing** in any Member State Concerned (MSC) under CTD.
- Sponsors are to follow the recommendation of the **CTCG expedited procedure** to transition minimum dossiers restricted to documents already approved under the CTD.

Transition period: Principles (2)

- Trials that should not be transitioned:
  - Trials that **have already ended** or have **no active sites** by 30 January 2025
  - 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 be transitioned. Global end of the trial and trial summary results should be posted via EudraCT under the Directive.
- EudraCT remains active beyond the end of the transition for sponsors:
  - to notify **EU/global end of the trial** and for 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.

Transition period: Principles (3)

- General considerations (1):
  - Retrospective documents do not need to be submitted to CTIS. Only the **latest approved versions** should be included in the transition application.
  - **CTCG updated guidance** for sponsors on transition of multinational trials at the HMA website (https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html), key documents.
  - For **mandatory documents beyond the minimum set of documents** it is expected to upload to CTIS a statement 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) and provides the document as part of the first substantial modification request at its best convenience after the authorisation of the transitioning application

Transition period: Principles (4)

- General considerations:
  - 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 triggered 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 there is disagreement on the trial category and deferral selected by the sponsor communicated as an assessment RFI.
  - It is **possible that a validation RFI is raised** for transitional trials. 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 (CTD dates should be entered).
  - 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. No more input information in EudraCT for this trial.

Transitioning a trial (1/3)

- Transition a multi-national trial : 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 harmonized/consolidated sufficiently.
  - 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.
- 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 (see under key documents **https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html**
  - GDPR statement

Transitioning a trial (2/3)

The following minimum set of documentation is required (Cont'ed):

- Protocol (part I). If not harmonized under CTD, a consolidated protocol describing all Member-State Specific items should be provided in the protocol (or in an appendix)
- Investigator's Brochure (part I) or Consolidated IB if not previously harmonised under CTD (acceptable when submitting a transition application)
- GMP relevant documents (part I)
- IMPD (part I) or Consolidated IMPD if not previously harmonised under CTD (acceptable when submitting a transition application)
- Documents related to non-investigational MPs (part I)
- Subjects' Information Sheet (Part II)
- Informed Consent form (Part II)

Transitioning a trial (3/3)

Consideration to be given to the transparency requirements:

- When completing the CTA, consideration should be given to the **transparency requirements of the CTR.** It is foreseen that the new rules will be technically implemented in Q2 2024. In the meantime, for initial clinical trials applications sponsors may already follow the principles of the **revised CTIS transparency rules**. A sponsor may therefore refrain from deferring publication of documents and provide a version 'for publication' and 'not for publication' only for those documents in scope of the revised rules (Annex I of the revised CTIS transparency rules).

Further information is available:

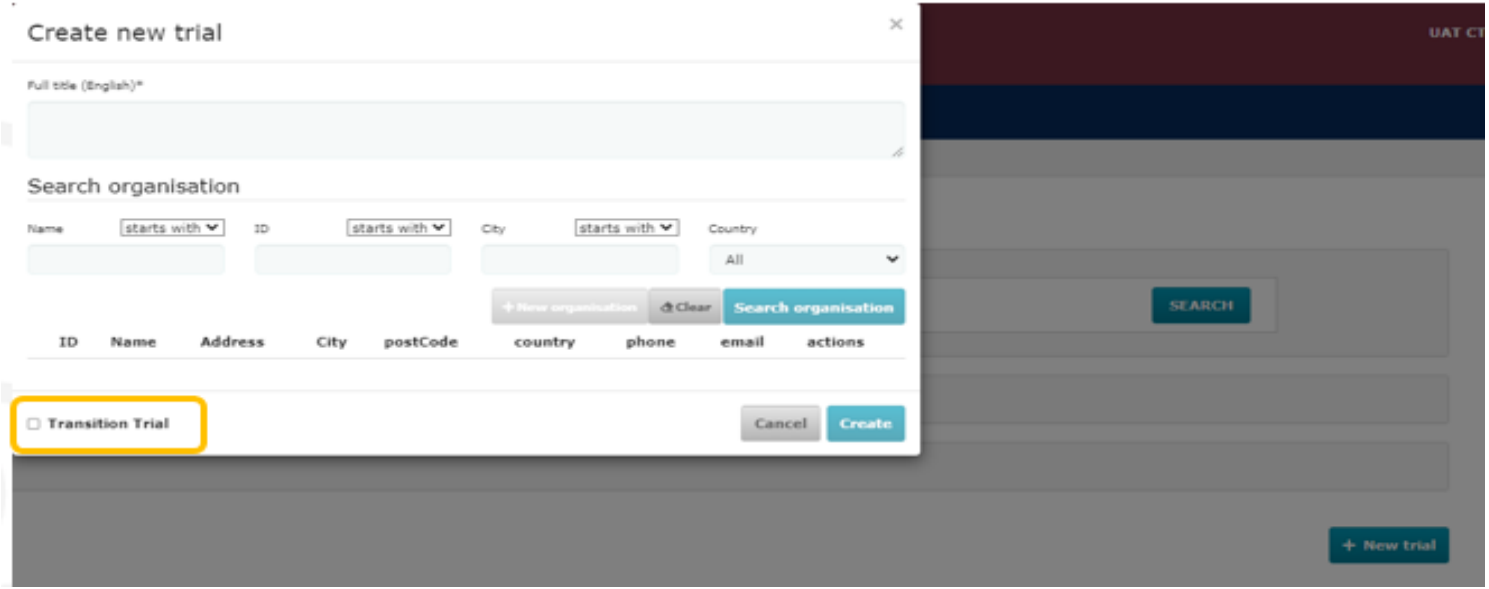
- In section 4 of the updated Q&A on protection of confidential information and personal data in CTIS which includes information on the interim period until the new rules are in effect and on historical trials (all trials submitted until this date);
- The quick guide for users published on the ACT EU website which provides a summary of what will be published under the revised rules and the relevant timings of publication.
- The video recording and presentation of the CTIS Bitesize talk on 29 November 2023, now available on the event page.

CTIS functionalities for Transition trials

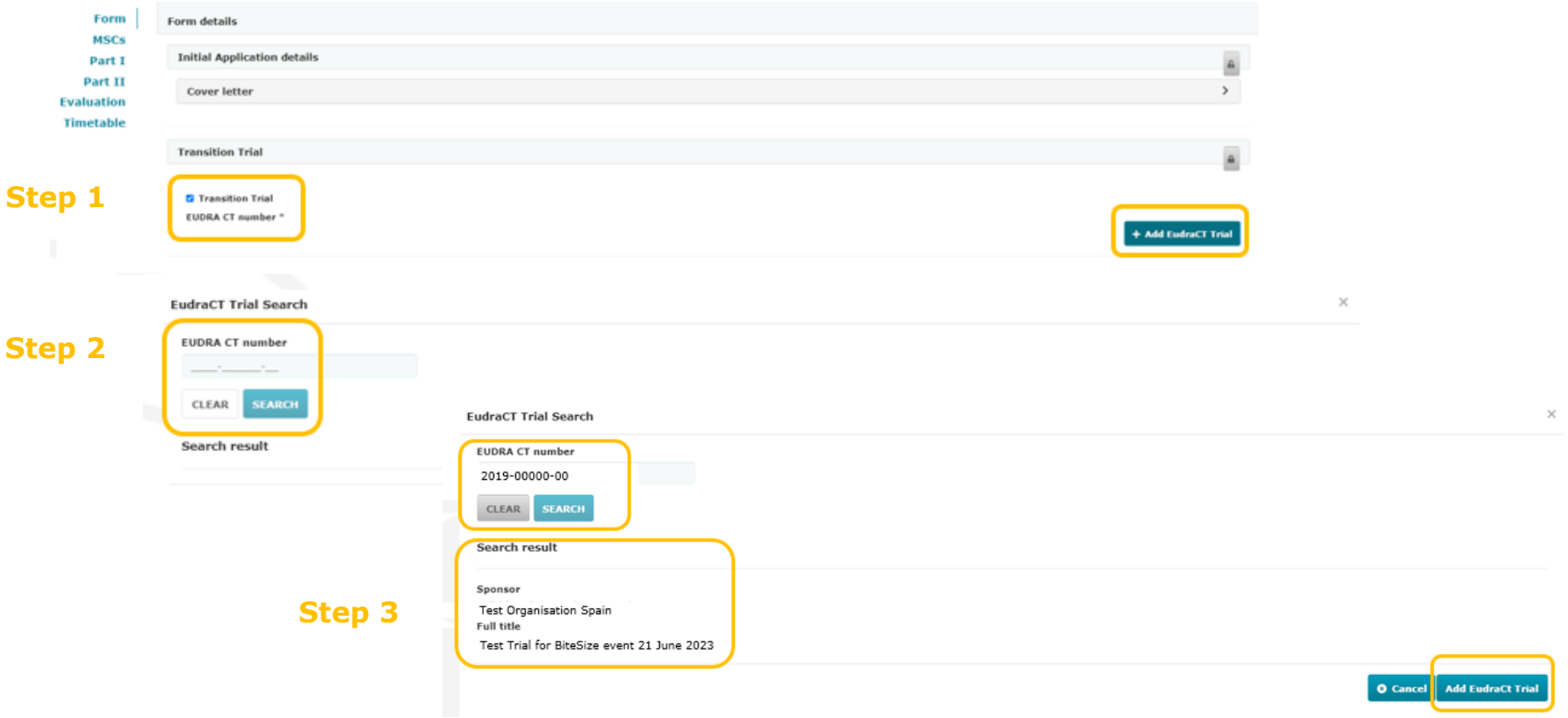
To facilitate the transition, CTIS has functionalities that enable the sponsor to:

- Create an initial application for a new trial in CTIS (own EU CT number);
- Associate this new initial application to an existing EudraCT number.

Step 1



CTIS functionalities for Transition trials (2)



Reference list to Transition trials

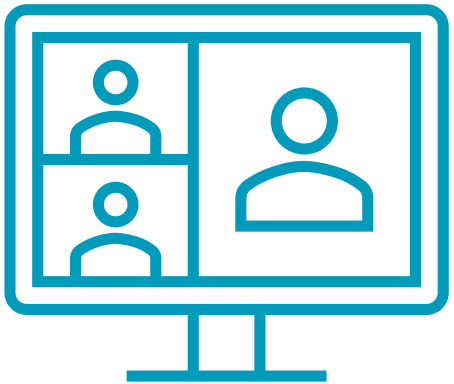
- Reference documents to Transition trials have been published in Commission website, EMA website and CTCG website:
  - EC: Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation
  - CTCG: CTCG Best Practice Guide for sponsors of multinational clinical trials (at the HMA webpage https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html), under key documents.
  - 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: Training for non commercial sponsors event February 2024
  - EMA: Sponsor Handbook / Chapter 05
  - EMA: Training Module M23

Conclusions

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

Q&A session

Upcoming CTIS events



- **12 March 2024**, 16:00 – 17:00 CET – CTIS Walk-in Clinic
- **25 March 2024**, 13:30 – 17:00 CET – Clinical Trials Information System Webinar: Last Year of Transition
- For 2024 CTIS events, please consult Clinical Trials Information System: training and support | European Medicines Agency (europa.eu) and EMA events pages

Thank you for attending today's event

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Further information

For the CTIS Newsletter sign up at https://ec.europa.eu/newsroom/ema/user-subscriptions/3201/create

For upcoming CTIS events visit the EMA event page.

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