Clinical Trials Information System for clinical trial applications in Europe

The Clinical Trials Information System (CTIS) is a portal, the single entry point for clinical trials information in the European Union (EU) and the European Economic Area (EEA), created by the European Medicines Agency (EMA). CTIS is used for submissions of clinical trial applications (CTA) in Europe and it is the public registry of clinical trials in Europe.

The Clinical Trials Regulation (CTR), Regulation (EU) No 536/2014 harmonizes the assessment and supervision of processes. Similar as in the clinical trials directive, the CTR has a major focus on that:

- the rights, safety, dignity and well-being of subjects protected;
- the data generated should be reliable and robust; and
- the interests of the subjects should always take priority over all other interests.

New elements of the CTR are that the Member States should cooperate, the timelines for evaluation are pre-set and in addition transparency is of major importance.

The CTR entered into application on 31 January 2022, simultaneously with the go-live date of CTIS. A transition period has been determined:

- 31 January 2022 – 30 January 2023: sponsors were allowed to choose: either submit the CTA under CTR using CTIS or submit under the clinical trials directive (using EudraCT) as before.
- 31 January 2023: As of this date all CTAs are to be done under the CTR using CTIS. It is no longer allowed to submit a CTA under the clinical trials directive.
- 31 January 2025: all trials running under the clinical trials directive will need to comply to CTR and be recorded in CTIS.

CTIS has two restricted and secure workspaces (for sponsors and for authorities) that are only accessible to registered users, and a website open to the general public. In order to perform an action in CTIS, such as preparing, submitting or viewing a CTA, notifications, summary of results or clinical study reports, a user must be assigned with a CTIS user role to obtain appropriate permissions.

CTIS public website

CTIS offers searchable clinical trial information to the patient, the healthcare professional and the general public, without having an EMA account. Clinical trial results are available both as a technical summary and in lay language. Information can be retrieved by searching for a particular trial or across trials for treatment-related details.

In view of transparency, the CTR states that the database shall be publicly accessible, except for the confidential data. Data can be confidential for protecting personal data in accordance with Regulation (EC) No 45/2001, for protecting commercially confidential information or for protecting confidential communication between Member States in relation to the evaluation of a clinical trial. CTIS allows for three different categories in relation to publication of information, and, depending on the category, deferral for a maximum of 5 or 7 years can be requested at the time of the submission.

Authority workspace
The authority workspace is accessible to national competent authorities, ethics committees, the European Commission, and the EMA. It supports the activities of Member States and the European Commission in assessing and overseeing clinical trials.

Sponsor workspace
The sponsor workspace provides clinical trial sponsors (commercial and non-commercial) with the functionalities for submission of CTAs to Member States, and management of information throughout the lifecycle of clinical trials. The sponsor functionalities include:

- Assignment and management of users
- Compilation of clinical trial dossiers
- Receiving of alerts and notices for ongoing trials
- Compilation of responses to requests for information
- View deadlines, search, and access clinical trials
- Compilation of notifications related to the life cycle of the trial including submission of a summary of clinical study results.

Content of the submission
CTR Annex I provides details for the content of the submission in CTIS. Content is divided in Part I and Part II. Part I focuses on the assessment of the scientific documentation of the clinical trial intended to be performed, whereas Part II focuses on the assessment of country-specific aspects relating to the recruitment of subjects, data protection requirements, format, and content of the informed consent, and other aspects of a regulatory nature.
Note that several details will come from other EMA systems. The sponsor and the sites must be registered in the Organisation Management Service (OMS). Details of the medicinal products used in the clinical trial must already be registered in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD).

Evaluation of a CTA
The evaluation process of an initial application includes three main phases: validation, assessment, and decision and it aims at determining if a clinical trial is fit to be performed in a Member State of the EU. A Reporting Member State (RMS) is selected and the sponsor can propose an RMS. Evaluation of Part I consists in a joint assessment by the Member States Concerned (MSC) led by the RMS, who submits the Part I conclusion. Part II consists in a separate assessment performed by each MSC, each of which results in the submission of an individual conclusion. Note that the MSCs include the national competent authorities and the ethics committees.

Timelines

The CTR establishes an overall timeline of 60 days for the Member States to evaluate an initial application: 10 days for validation, 45 days for Part I and II in parallel, and 5 days for decision. Timelines can be extended up to 15 days for Requests for Information (RFI) raised in the validation phase (10 days for the sponsor to respond and 5 days for MSC to review the response), and up to 31 days for RFIs raised in the assessment phases (12 days for the sponsor to respond and 19 days for MSC to review the response).

Help

A lot of training for CTIS has been made available by EMA. A sponsor handbook has been written and there is an online modular training program.

At Zwiers, a member of the ProductLife Group of companies, we have experience with clinical trial strategy, CRO selection, and management, preparing clinical trial documents like Protocols, Investigator's Brochure and CTA. We can of course support you with your CTA submission to health authorities or with the transition from Eudra CT (Clinical trial directive) to the new CTIS (Clinical Trial Regulation).