

# CTIS HIGHLIGHTS

News, views and interviews for the Clinical Trials Information System (CTIS)

An agency of the European Union



## Welcome to CTIS



### Kristof Bonnarens, Policy Officer at the European Commission

The European Commission had a hands-on role in the development of the different functionalities of CTIS. The Commission will interact with the system in different ways to ensure a greater level of harmonisation of the rules for clinical trials throughout the EU, by translating the Clinical Trials Regulation (CTR) into an IT system that is logical and workable. CTIS is unique in its objective covering the whole life cycle of clinical trials that take place in the EU. That makes CTIS an harmonised system, allowing a multitude of different submission pathways for applications in the different Member States.

We will be working in CTIS at the time of go-live for the planning and reporting of the Union Controls, set by art. 79 of the CTR. Those controls are set up by the CTR in order to verify the compliance with its principles both inside and outside the EU. We will be using the data in CTIS to measure key performance indicators, which generate a basis for the further policy making on clinical trials. The Commission will also further investigate on this basis which future role CTIS might have (e.g. on the assessment of safety reporting in clinical trials).

## Key organisation models in CTIS

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In the previous newsletter ([issue 2](#)) we presented the interaction between Member States and sponsors by defining, at high level, what these two parties can do in CTIS. Now it is time to touch upon the organisation-centric and trial-centric approach, which is the starting point in understanding the process of assigning roles in CTIS.

The organisation-centric and trial-centric approaches are two user management approaches in CTIS.

#### The organisation-centric approach:

- this approach is used by authority users (EU Member States and EEA countries) and by sponsors,
- a high-level administrator, namely the Member State administrator or sponsor administrator, must be registered in [EMA Account Management platform](#) via IAM ([Identity and Access Management](#)), and
- the management of users is done at organisation level with a top-down model.

In the organisation-centric approach, users become affiliated to the organisation of the high-level administrator in CTIS when they are

assigned with a role by this administrator.

The high-level administrators are validated by EMA outside CTIS following a submission of specific documentation.

For sponsors, the organisation-centric approach is particularly useful for large organisations because it allows for the management of many users who are administering several clinical trials. The advantages of this approach are that it allows the management of access and roles across trials within one organisation; thus, supporting data quality and integrity through a top-down validation process.

#### The trial-centric approach:

- this approach is only available for sponsor users;
- the registration of a high-level administrator in EMA IAM is not required;
- the management of users is at trial level.

In the trial-centric approach users become the clinical trial administrator of a clinical trial in CTIS by creating an application for this clinical trial. Therefore, further allocation of business roles to users is done at trial level.

This approach is intended to serve the needs of small organisations and specifically academic sponsors, as it allows to manage a smaller

## Key organisation models in CTIS

sponsors, as it allows for the management of a smaller number of users and for one clinical trial application. This allows a faster process (no need for registration of a high-level administrator) when submitting a first initial application, however it could become less convenient if more trials are managed by one clinical trial administrator.

In the trial-centric approach, users follow a bottom-up model that supports an easy way of submitting a small number of clinical trial applications and a straightforward management of a small number of users.

The image below describes the registration for sponsor high-level administrator

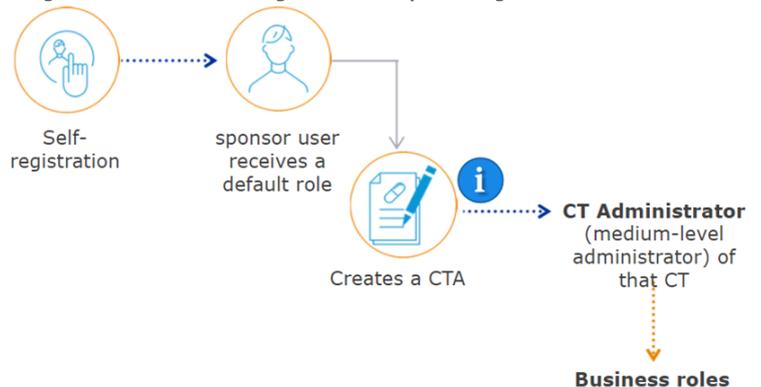


Image 1

## The high-level administrator role

The **registration of the high-level administrator** - sponsor administrator - **is planned to open in September 2021** via the [EMA Account Management platform](#) using IAM (Identity and Access Management). Member States and European Commission high-level administrators will follow a different process organised by EMA.

Before a user can register as a high-level administrator for a sponsor organisation, this organisation needs to be registered with the Organisation Management System (OMS), which provides a single source of validated organisation data (e.g. an organisations' name, location, address), keeping the details safe and reusable in case the organisation needs to register with other EMA systems (e.g. EudraVigilance etc.). Once assigned, sponsor administrators can then delegate user management permissions to clinical trial sponsor administrators. Sponsor administrators can then assign CTIS business roles to users in order to perform business activities in CTIS. Each user role comes with a set of permissions (user administration permissions or business permissions) linked to it.

More detailed information can be found in [module 03](#).

## The clinical trial administrator role

An important role for sponsors is the **clinical trial administrator** role. The clinical trial administrator can manage users not only for the trials of his/her concern but also to perform all sponsor business activities in CTIS related to a particular trial.

A clinical trial administrator can:

- \* Manage sponsor users i.e. assign/amend or revoke other colleagues' roles;
- \* Create, submit and withdraw an initial clinical trial application and subsequent applications (additional Member State Concerned, substantial modification and non-substantial modifications);
- \* Create, submit, update and withdraw notifications (e.g. start of trial/start of recruitment/end of trial, serious breaches/unexpected events etc.);
- \* Manage request for information (RFI) response i.e. incoming requests from Member States Concerned to sponsors during the evaluation process or in the context of ad hoc assessment;
- \* Create and submit sponsor's opinion in the context of corrective measures;
- \* Submit, update or withdraw the summary of results, including the lay person summary;
- \* View all clinical trial related information related to the above activities (e.g. clinical trials applications, assessment report, trial decision, notifications, requests for information, sponsor opinion in relation to corrective measures and summary of results).

Additional information is published on the EMA Corporate website under the Training Programme - User access management ([Module 3](#)).

The image below shows the assignment of roles in the organisation centric model.



Image 2

### New!

- Online training materials of the webinar held on 3 & 4 February 2021 using EMA's [Organisation Management Service \(OMS\)](#) and [Referentials Management Service \(RMS\)](#), relevant for **industry users** of CTIS, are now available on the [EMA Corporate website](#).

- Registration for sponsor high-level administrators is scheduled to open in September 2021.

## CTIS system functionalities

CTIS allows sponsor users to manage a clinical trial during its life cycle through different system functionalities:

1. **Submission of an initial application dossier** and subsequent applications which require an evaluation by the Member State Concerned (MSC) such as: substantial modification for part I, part II, part I and II, addition of a new MSC and submission of non-substantial modifications which do not require evaluation by the MSC;
2. **Reply to a request for information** raised by the Member State Concerned during the evaluation of an initial application and subsequent modifications;
3. **Submission of notifications**, that allow the sponsors to notify the relevant Member State Concerned (MSC) of events during the conduct of clinical trial (e.g. start trial, start of the recruitment, end of trial, etc.);
4. **Reply to a request for information raised as part of ad hoc assessment that** enable Member State Concerned to assess information about notifications, or any information relevant to the supervision of a clinical trial;
5. **Provide an opinion as part of corrective measures, that** can be applied by MSC by revoking an authorisation, suspending a clinical trial, or requesting the sponsor to modify any aspect of the clinical trial. In this specific process, the MSC can request a sponsor's opinion and/or can consult the other Member State Concerned;
6. **Submit trial results:** this is a functionality that allows sponsors to submit the summary of the results (also in a layperson language) and the marketing authorisation applicants to submit the clinical study report.

### New!

On 22 February & 4 March 2021 EMA organised a **CTIS training for SMEs & Academia**.

A recording of the webinars are available [here](#) under the section "Virtual training sessions".

## Sponsor views on CTIS and how to prepare for it

### Gaby di Matteo, Senior Clinical Submission Manager, Pfizer Global Regulatory Operations (EFPIA)

*"Pfizer is welcoming the implementation of CTIS with the benefits of a greater level of harmonisation of the rules for conducting clinical trials throughout Europe.*

*Although the Clinical Trial Regulation (CTR), and consequently CTIS, will require changes in the current practice for sponsors and Member States, the CTIS, as a single point of entry, will be adding value to the conduct of clinical trials in Europe, together with a speed-up process for the review and approvals of the clinical trial application & Central Ethics Committee (CEC).*

*Therefore, the authorisation procedure based on a single submission, via a single EU portal and an assessment procedure leading to a single decision, will allow for aligned execution of clinical trials and Member State/CEC review."*

### Andrea Seidel-Glätzer - Head of Project Management, Coordination Centre for Clinical Trials (KKS), Heidelberg University Hospital

*"Academia in Germany is looking forward to the new Clinical Trials Regulation (CTR) coming into force and to the use of CTIS as a centralized system. It will change significantly the way academia is working and have a huge impact on our daily work. The organization of the entire life cycle of a clinical trial in CTIS requires adaptation of working methods and workflows.*

*Cooperation and communication with authorities and especially ethics committees via the portal will also be completely new territory for all of us. CTIS is where all the threads will come together to help us organize the clinical trial and to increase transparency."*

### New: CTIS Sponsor Handbook

EMA, in a collaborative approach including sponsor representatives, will prepare a sponsor handbook to provide sponsors with an overview of materials available to help them prepare for and use CTIS. A first version is expected to be published in Q3 2021.

## Initial clinical trial application process in CTIS

The initial clinical trial application workflow consists of a series of steps to ensure that the application form is fit for purpose, and it contains all the relevant features and characteristics which will enable the concerned authority to validate, assess the application and issue a decision. The image below shows the steps and the timetable of the clinical trial application process:

1. Once an initial clinical trial application dossier is submitted by the sponsor in the CTIS, it goes into the 'validation' phase which will end with the final validation of the application by the Reporting Member State (RMS). This phase lasts 10 days from the date of the receipt of the application. It can be further extended of 15 days in case a request for information is raised.
2. The assessment of Part I starts with the initial assessment done by the Reporting Member State and the draft assessment report sent to all Member State Concerned (MSC). After the Member State Concerned submit their considerations, these are consolidated in a final report of the assessment of Part I of a clinical trial application. This phase will last 45 days, and it can be further extended of 31 days in case requests for information are raised.

3. The assessment of Part II fits into the individual assessment of each Member State Concerned on the clinical trial application. This assessment includes review of documents such as informed consent, subject recruitment, data protection, compensation of investigators/subjects, suitability of trial sites etc. This phase has the same timetable as Part I.
4. After Part I and Part II assessment, a notice of single decision by each Member State Concerned is sent to the sponsor through CTIS, and this phase is completed in 5 days.

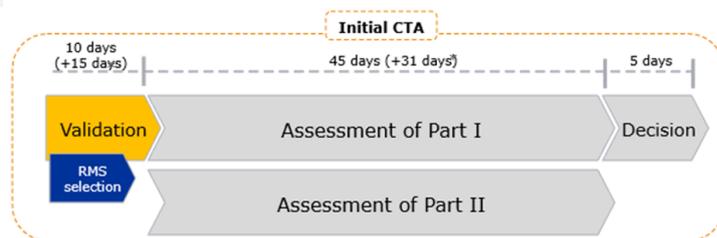


Image 3

### Highlights!

You can provide your feedback on the CTIS Newsletter [here](#)

## Training Programme update

EMA is proud to announce that the [CTIS Training Programme](#) is now available on the EMA Corporate website. This is a major step towards a training resource providing sponsors, staff of the EU Member States, European Commission and other organisations with documents and videoclips to support users in understanding and using CTIS.

The training materials feature e-Learning courses, quick guides, infographics, videos, frequently asked questions (FAQs) and instructor's guides. Some modules cover common functionalities for CTIS, other modules are tailored only at authorities or sponsors.

As a complement to the online training materials and considering the high volume of users, a cascading approach 'train-the-trainers' is being implemented involving nominated representatives of EU Member States (MS Master Trainers). Master Trainer programmes for sponsors and Members States are on-going, three training events took place between December 2020 and March 2021 to gather knowledge on CTIS and disseminate it to other colleagues within their own organisations. More trainings are foreseen in the coming months.

In addition, EMA organised training sessions tailored for SME/ Academia held on 22 February and 4 March resulting in high

demand for participation of users.

An important aspect of the training programme is the communication which helps all these activities to be advertised and be visible to a vast number of interested parties.

The Agency uses different communication channels (internal and external) such as the EMA Corporate website, where news and information are published on a regular basis, the newsletter with the mean to reach both the users of CTIS and the general public, direct email distribution, social media (Twitter and LinkedIn) and presence during conferences.

### Facts!

On 9 & 10 March 2021 EMA in collaboration with EU Commission, CTFG and HMA organised a [Joint Training on Clinical Trials Regulation \(EU\) 536/2014](#) for Member State assessors and responsible administrators, inspectors at the National Competent Agencies, Ethics Committees, and other associated regulatory bodies.

### Save the Date!

A CTIS **information event** on how sponsor organisations can prepare for CTIS will be held on **Thursday 29th July 2021**, with a further event focussing on Member State and sponsor user preparedness for CTIS in Q4 2021. Further information and registration links for these events will be published on the [EMA website news and events](#) page shortly.

Image 4

## CTIS User Personas

The CTIS Change Management team, in collaboration with CTIS user representatives, are currently developing CTIS user personas.

A user persona is a visual model developed to represent different end-user groups.

Personas describe a group of users whose basic tasks and needs are similar and can provide insights into the needs and preferences of different end user groups.

The CTIS user persona focus on describing the typical people who will use CTIS, their role in their organisation, and what user roles and training they may need to use CTIS successfully.

For CTIS, user personas will be used to help link end-users to CTIS user roles and to further enhance training and communications activities by tailoring them to the needs of different end-user groups. The personas will also be used to enhance storytelling techniques by bringing users to life in training and communication materials.

### Member State National Competent Authorities



### Member State Ethics Committees



Image 6

### Large Pharma/CROs



### SMEs/Academia



Image 5

## Audit update

The independent audit of the EU Portal and Database (EUPD), which was initiated in September 2020, concluded in April 2021.

In accordance with the agreed audit plan, the second audit field work took place from 14 to 19 March 2021 resulting in the final audit report, which was shared with the EMA Management Board on 14 April 2021. At an Extraordinary Meeting held on 21 April 2021, EMA's Management Board confirmed on the basis of the independent audit report, that the EU clinical trials Portal and Database is fully functional and meets the functional specifications as required by Article 82(2) of the Clinical Trial Regulation. A letter on behalf of the Board was sent to the European Commission informing them of this outcome. The European Commission will consider if the conditions set by the Regulation are met and, once confirmed, will publish a notice in the [Official Journal of the European Union](#).

Six months after this publication, the Clinical Trial Regulation will start to apply and CTIS will go live. It is the desire of the EMA Management Board, EMA and European Commission that the system goes live on 31 January 2022, which would require the notice in the Official Journal to be published on 31 July 2021.

- ⇒ If you want to give feedback on the **CTIS Highlights Newsletter** click [here](#)
- ⇒ If you want to give feedback on the **CTIS Training materials** click [here](#)
- ⇒ If you want to **subscribe/unsubscribe** to the CTIS Highlights Newsletter write to this email: [CT.Communication@ema.europa.eu](mailto:CT.Communication@ema.europa.eu)
- ⇒ If you want to **read the previous issue** click [here](#)

## In the next issue

Future issues of the CTIS Newsletter will have an updated format. The new format will focus on actions organisations and users can take to prepare for CTIS, including organisation and user registration in OMS and IAM, accessing training materials and attending CTIS informational events.

The first issue in the new format is expected to be published in summer 2021.

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