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CTIS HIGHLIGHTS

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

Fergus Sweeney, Accountable executive for delivery of the Clinical Trials Information System (CTIS), European Medicines Agency

"Welcome to the first edition of CTIS Highlights, the newsletter for the Clinical Trials Information System (CTIS) Programme. It is an exciting time for the system as we progress to the audit and then to Go-Live. Future editions will give insight into the functionality that is being made available and information on the rollout of training and user support."

INSIDE THIS ISSUE

CTIS Overview

The implementation of the Clinical Trial Regulation (Regulation (EU) No 536/2014) (CTR) will bring a major change in the authorisation, conduct, supervision and reporting of clinical trials in the European Union (EU). The Regulation harmonises the submission, assessment and supervision processes for clinical trials throughout the EU via CTIS. Articles 80 and 81 assign the European Medicines Agency (EMA) to set up and maintain the information system, in collaboration with the Member States and the European Commission. CTIS will enable the implementation of the Regulation.

CTIS will be the single-entry point for submitting, assessing, authorising, supervising and reporting a clinical trial in all Member States of the EU. The system is currently under development and will have collaboration and communication tools, workflow and document management capabilities. It will include a user management tool to enable access for sponsors, Member States and the European Commission via dedicated workspaces. It will also provide general public with access to clinical trials information. CTIS will centralise the submission process for clinical trial applications and the assessment and authorisation by Member States in a single unique platform.

It will facilitate day-to-day business processes of Member States and sponsors of clinical trials throughout the lifecycle of a clinical trial harmonising submission and maintenance of trial applications, assessment and supervision of trials and promoting patient safety and transparency.

More information....

The CTIS user community will consist of clinical trials sponsors including academia, commercial and non-commercial organisations, marketing authorisation applicants, Member States' national competent authorities and ethics committees, the EMA, the European Commission and the general public. Except for the general public, all users will access the CTIS functionalities via the two restricted dedicated workspaces: the sponsor workspace and the authority workspace. The general public will be using the public website to access CTIS. Image 1 depicts the different workspaces and user groups.

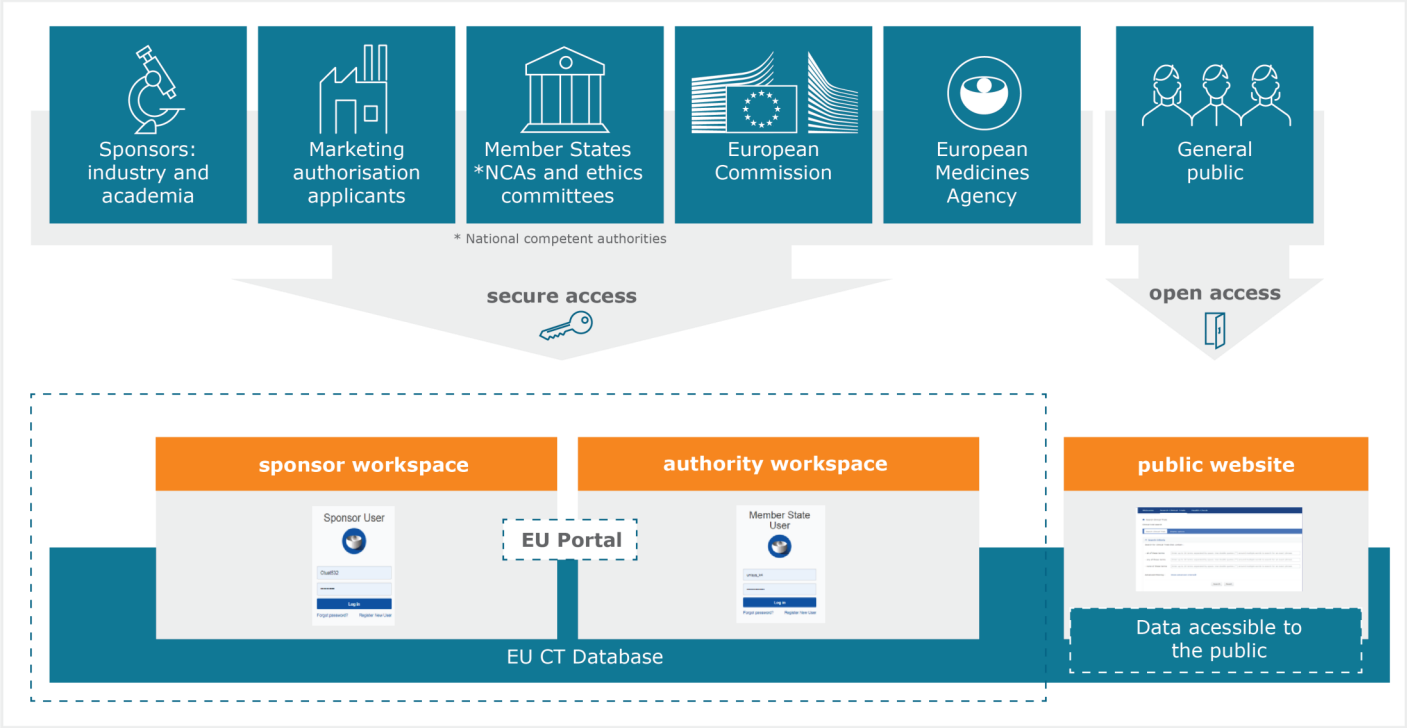

Image 1

Technical Environment

CTIS is connected to various databases that are managed by EMA, as depicted in Image 2.

EMA Individual Account Management is a user registration system that provides individuals with EMA accounts. Via those accounts the users access the applications that are managed by EMA, CTIS included. The CTIS users will use Individual Account Management to obtain appropriate profiles with roles needed for their work in CTIS.

Organisations need to be registered through the Organisations Management Service (OMS). OMS will maintain the master data (name, location address, communication details) of organisations of the medicines regulatory network and the pharmaceutical industry.

EudraVigilance Human (EV Human) has various components such as extended EudraVigilance Medicinal Product Dictionary (XEVMPD) which provides CTIS with information on authorised and non-authorised medicinal products and their active substances. EV Human manages and analyses information on suspected adverse reactions (ADR) to medicines which have been authorised or being studied in clinical trials in the European Economic Area.

The data warehouse system maintains the structured data of the clinical trial applications. The Business Intelligence component is connected to the data warehouse to provide users with reports.

A system supports users to upload, view and manage documents that are associated to the submitted clinical trial application.

Image 2 below shows a high-level overview of the technical environment of CTIS.

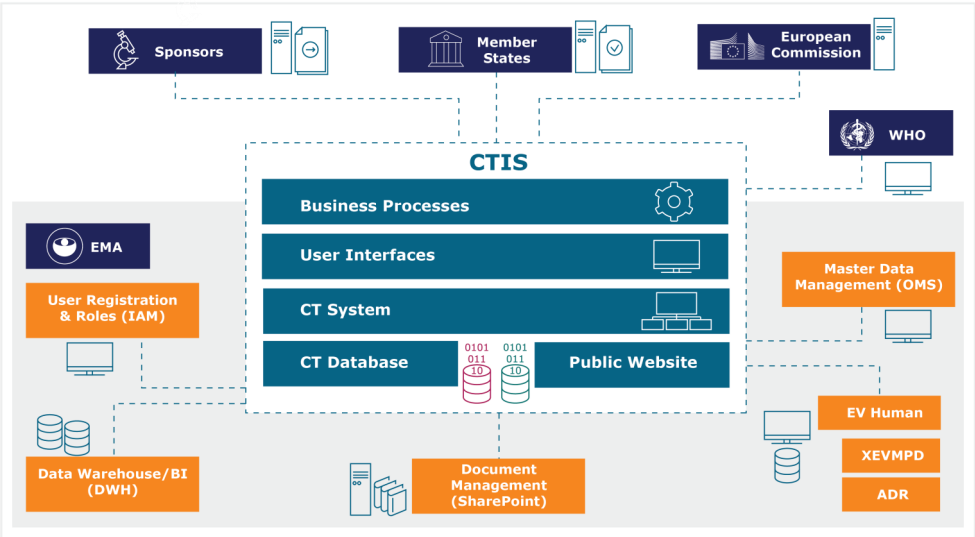

Image 2

Common Functionalities

While each of the two restricted workspaces (Sponsor workspace and Authority workspace) has its specific functionalities, both share a common set of functionalities (Image 3). Clinical trials overview and search functionalities, Notices and alerts, Annual safety report (ASR) and User administration are functionalities that can be used by users of both restricted workspaces. Depending on their roles, the users might have visibility on different levels of information.

Image 3

Sponsor Workspace

In the Sponsor workspace, users will be able to submit an initial clinical trial application, as well as to submit substantial and non-substantial modifications or add a new Member State to an existing clinical trial application. Users may submit documents to update the clinical trial dossier, that is part of their application, and reply to requests for information coming from the Member States during the assessment of a trial application. Sponsor users can also submit notifications such as start of trial, start of recruitment, end of trial, serious breaches and summary of results. Search functionalities will help users to find clinical trials by using various criteria.

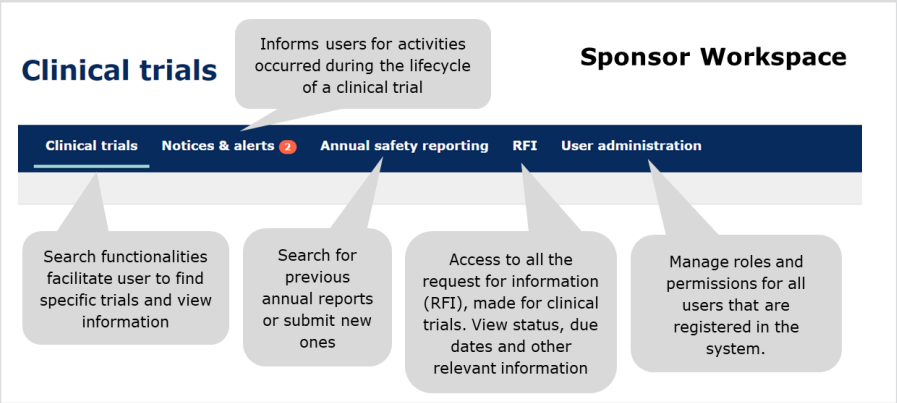

Image 4

In Image 4, the various functionalities might be accessed by the respective tabs, found on the menu, on the top of the landing page.

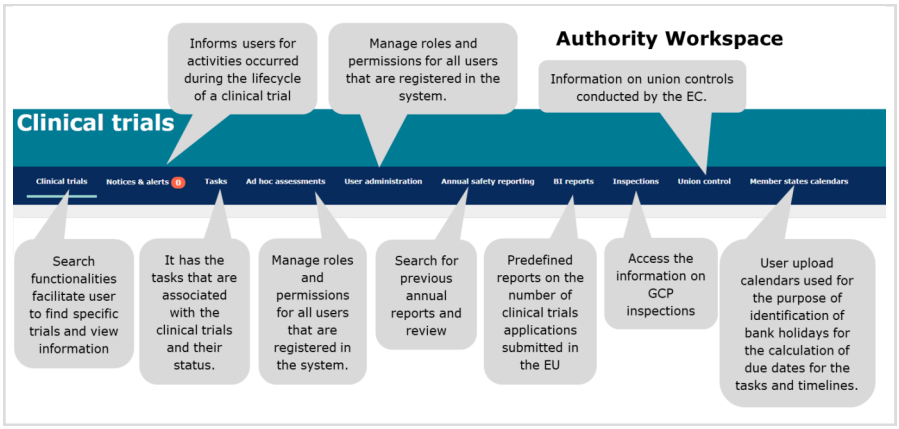

Image 5

Authority Workspace

In the Authority workspace, users will be able to validate, assess, request additional information from sponsors, issue a decision on a clinical trial application and supervise the conduct of the clinical trials. Performance of daily activities on the assessment of a clinical trial application will be supported by the use of a workflow.

Collaboration tools have been developed to facilitate communication among the participating Member States evaluating a clinical trial application as well as with the sponsor representatives submitting the application. In Image 5, the various functionalities can be accessed by the respective tabs, found on the menu, on the top of the landing page.

Public Portal

Via an open access portal, members of the public will be able to search and access detailed information, made public in compliance with the disclosure rules, on all clinical trials conducted in the EU registered in CTIS. The user interface of the public portal will be available in all official EU languages.

Stakeholder Engagement

The involvement of stakeholders (EU Member States; sponsors – industry; sponsors – academia; EU Institutions and groups; Non EU governance bodies; EU national governance bodies; international healthcare and standardization bodies; EMA committees and management; public, patients and healthcare professionals) in the elaboration of CTIS was ensured at very early stage. It was done via the stakeholders consultations EMA held on the draft functional specifications in 2014 and on implementing the transparency rules in 2015.The feedback received was thoroughly analysed and used when appropriate as an input for further system advancement. A training was organised in 2014 and a series of workshops aiming to seek users input in the course of 2017 and 2018. The collaboration with stakeholders continues through the regular meetings held with the CTIS Members States' Group, CTIS Expert Group and CTIS Stakeholders' Group in order to inform attendees about the progress in the delivery of CTIS , the future actions planned, as well as to provide feedback from the past governance groups meetings. Currently the stakeholders as well as general public are kept informed about the CTIS state of play via the respective sections on the corporate website and User community Confluence website.

Product Owners nominated from the Member States and the sponsor associations are directly involved in all phases of the CTIS delivery. They provide direct input to the IT developer, regarding the existing and expected system functionality and are the main source of business requirements. The Product Owners are involved in multiple activities like assessing the Audit and Go-live readiness of the system, establishing the delivery priorities to prepare the system for audit, describing to the IT developer how the system should behave to comply with the Regulation and with the user needs, and verifying that the system is being delivered in alignment with their expectations and in compliance with the Regulation.

The governance structure of CTIS consists of EMA's Management Board (EMA MB), EU CTR Coordination Group, CTIS Expert Group, CTIS Members States' Group and CTIS Stakeholders' Group. The EMA MB is the EMA's integral governance body and has a decision-making role. It has the oversight of the CTIS governance. The EU CTR Coordination Group, supported by the Monitoring Subgroup, has also a decision-making role at strategic level, monitoring the implementation activities in relation to the Regulation and coordinating the activities of the various working parties. The CTIS Expert Group participates in the decision-making from a tactical level, contributing with expertise to the definition and development of the system. The CTIS Members States' Group and the CTIS Stakeholders' Group do not possess decision-making roles.

Delivery Model of CTIS

The current delivery model of CTIS was implemented in 2019 and is based on agile design and development principles that entail an iterative methodology with short cycles (sprints – lasting 4 weeks and releases – consisting of 3 sprints and lasting 12 weeks) to promote better planning of design, development, end user testing and validation, as well as better engagement with the stakeholders. It consists of different phases: release planning, analysis and design, sprint planning and development and testing. (Image 6).

The requirements established for the system by the legislation are set out in the Functional Specifications. These are detailed in the design and supplemented with issues arising from user assessments and testing. Items and areas for development are prioritised from this collective set of requirements to feed in the analyses and design process in accordance with the development Milestones and the Release and Sprint planning. The Release plan describes the specific goals of each release, the functionalities to be addressed and the Key Performance Indicators (KPIs). The Sprint plan gathers the relevant requirements and items from the backlog and organises them in different sprints (regularly).

With the current delivery model, a small number of nominated Product Owners (POs) representing Member States and Sponsors take ownership of the CTIS delivery and are continuously in direct contact with the IT developer. The close collaboration between Product Owners and IT developer and the adoption of a plan of shorter and thus more predictable development cycles, releases consisting of sprints, results in regular collection of feedback and alignment with users' expectations.

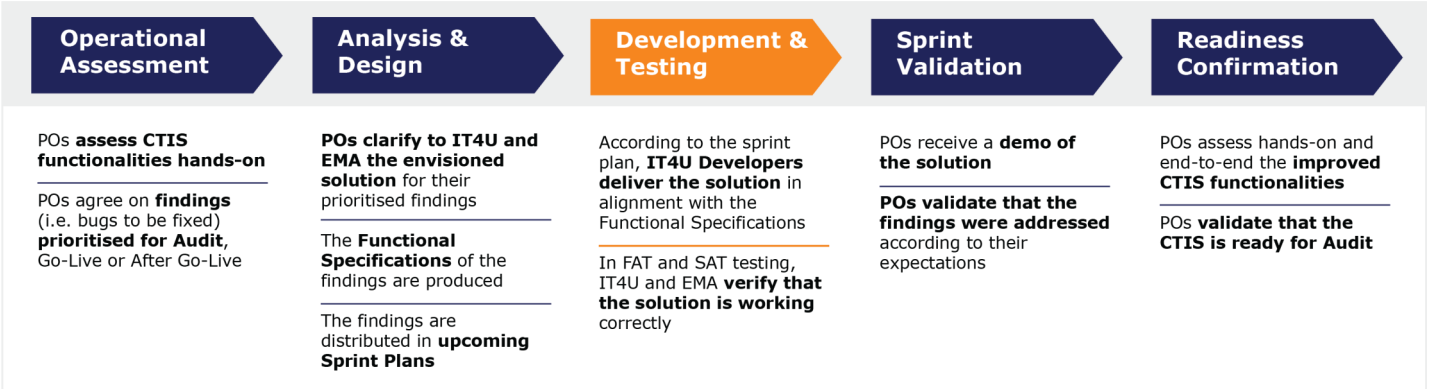

Image 6

CTIS Status

The IT developer, in close cooperation with the Product Owners and the EMA, has been developing the various functionalities for CTIS, achieving notable progress in the areas of authorisation and supervision of clinical trials applications, communication between sponsor and Member States and preparation of documents and data. In the last releases, the CTIS team has been working on improvements related to the access management, the evaluation of clinical trial applications including the corresponding workflow. In the following months, the CTIS team will be focusing on further improvements on functionalities related to the evaluation of a clinical trial application, data submission and the public portal.

Training

Training is important to facilitate user and organisation preparedness for implementation of CTIS. A training strategy including underlying principles and concepts has been developed with the aim to provide the CTIS users with the skills, capabilities and knowledge they need to successfully adopt the changes required to drive successful transformation and adoption of CTIS.

A strong multi-modal and gradual online presence of training modules is foreseen for all user groups. The production of the first batch is expected to start in summer 2020. Presentations, quick guides, FAQ sheets, e-learnings, webinars and short videos will be available on-line. The CTIS users will be able to follow the on-line training at their convenience and own pace.

In addition, a train-the-trainer approach will be followed. Representatives of user groups will be trained and will act as Master Trainers of their respective groups, disseminating this knowledge and accomplishing the training objectives in shorter time.

Audit and CTIS Go-Live

The application of Regulation (EU) No. 536/2014 ("Clinical Trial Regulation") is conditional on the conduct of an independent audit to verify that the EU portal and EU database, that form the major parts of CTIS, have achieved full functionality and meet the functional specifications, as required by Article 82, paragraph 2 of the Clinical Trial Regulation. On the basis of the audit report EMA MB and then the European Commission need to agree that these conditions have been met. After that, a notice by the Commission must be published in the Official Journal and the Clinical Trial Regulation enters into application six months thereafter. The CTIS Go-Live date is the end of the six month period following the publication of this notice.

The EMA MB at its meeting held in March 2020 endorsed the audit methodology for CTIS enabling the process for the selection of supplier for the audit of the system to commence, targeting start of the audit in December 2020.

At its meeting held in June 2020 the EMA MB endorsed the methodology and next steps to further develop the CTIS 'Go -Live' plan. As mentioned in the press release from this meeting (https://www.ema.europa.eu/en/news/highlights-management-board-june-2020-meeting), as a working assumption, it is proposed to fix the Go-Live date of CTIS to December 2021, which means the Clinical Trial Regulation would also enter in application at that time (i.e. that is the end of the six months after the European Commission publishes its notice in the Official Journal).

In the next issue

- **CTIS Update**
- **Recent and Future Developments**
- **Focus on CTIS Features**
- **Training opportunities**

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