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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Clinical Trials HIGHLIGHTS

An agency of the European Union

Welcome to Clinical Trials Highlights

Welcome to the October 2022 issue of Clinical Trials Highlights.

Since the launch of CTIS, sponsors can apply for clinical trial approval either through the Clinical Trial Regulation (CTR) via CTIS, or via the Clinical Trials Directive (CTD). We are pleased to report that over 100 clinical trials have now been authorised through CTIS.

Key objectives of this transition year are for all sponsors and Member States to learn and adapt to the CTR and to detect issues in CTIS so that they can be fixed prior to the compulsory use of the CTR in early 2023. While the vast majority of clinical trials submitted in CTIS have been approved without blocking issues, some users have experienced technical difficulties that have been challenging and needed collaboration between the affected sponsors, the concerned Member States and the EMA. We are grateful for this collaboration, for the excellent reporting of issues and for their successful resolution. In this way we can strengthen CTIS and ensure we are ready for its compulsory use for all new clinical trial applications (CTAs) starting from 31 January 2023.

The ACT EU Steering Group is mandated to ensure that CTIS is optimised by overseeing the CTIS implementation delivery plan for Q4 2022. This plan will ensure that the system is further strengthened and that fixes are introduced for blocking issues before the CTR is made mandatory for new clinical trial applications in early 2023. Technical challenges encountered with the CTIS workflow for some very large multi-Member State CTAs are being managed through workarounds to minimise the impact on applications. This is in place while further testing of the system continues to develop definitive fixes. EMA is also improving the deferral functionality on the public portal and as a temporary measure, clinical trials with any type of deferrals with a decision issued after mid-August 2022 will not be published until the functionality of the deferral mechanism is reinforced.

A big 'thank you' to all CTIS users for the collaborative approach to working, which enables us to be ready for the compulsory use of the CTR in early 2023.

- EMA CTIS Team

INSIDE THIS ISSUE

Publication of the ACT EU 4-year workplan for 2022-2026

The European Commission (EC), the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) have published the 2022-2026 workplan of the Accelerate Clinical Trials in the EU (ACT EU) initiative. The ACT EU initiative launched in January 2022, just before the CTR became applicable, seeks to further develop the EU as a focal point for clinical research, promoting the development of high-quality, safe and effective medicines by strengthening the European clinical trials environment.

The 4-year workplan is structured in line with the ten priority actions of ACT EU and highlights key focus areas, such as innovation in clinical trials, robust methodologies, and supporting academic sponsors to conduct large, multinational clinical trials. It intends to deeply engage with all stakeholders of clinical research, including sponsors, service providers, regulatory authorities, patients and healthcare professionals.

ACT EU will hold several multistakeholder events in 2022 and 2023, and will launch a multistakeholder platform in 2023 to bring together all stakeholders to support a more holistic discussion across the clinical research landscape and facilitate the evolution of the clinical trials environment by helping to identify key advances in clinical trial methods, technology and science, and by finding practical solutions to enable and drive change. For more information, please visit the ACT EU initiative webpage.

Image 1.
The 4-year workplan is structured in line with the ten priority actions of ACT EU.

ACT EU multi-stakeholder events update

The ACT EU programme has refined the schedule for the upcoming multi-stakeholder events that are planned throughout 2022 and 2023 to engage all clinical trials stakeholders into supporting inclusive patient-oriented medicines development and delivery. More specifically:

Multi-stakeholder meeting on decentralised clinical trials (DCTs)

On 4 October 2022 EMA hosted a multi-stakeholder workshop on decentralised clinical trials on behalf of the EU DCT project, bringing together participants from all areas of the research community to share perspectives on these types of clinical trials.

The EU DCT project seeks to optimise the EU environment for clinical research in Europe, whilst maintaining high-level participant protection, data robustness and transparency. It also aims to provide a harmonised and transparent approach for the use of DCT elements in clinical trials by the European Medicines Regulatory Network. The key focus points are implementation of DCT elements with a risk-based mindset and a focus on trial participant perspective ensuring trial participant's safety, rights and dignity.

At the same time, the reliability of the generated and reported data has to be maintained.

The DCT approach seeks to take advantage of the technological and scientific progress to introduce new methodologies to the conduct of clinical trials with the aim to make clinical trials more easily accessible and participation more convenient for trial participants.

During the workshop, the EU DCT project group presented the work of the European medicines regulatory network on decentralised clinical trials collaboration, including the planned publication of a **recommendation** paper on the use of decentralised elements in clinical trials in the fourth quarter of 2022. A **video recording** of the plenary session will be made available on the EMA event page.

Update on ICH E6 multistakeholder workshops

A single multistakeholder workshop to discuss the third revision of the ICH guideline on Good Clinical Practice (GCP) will be organised during the public consultation of ICH E6. Details of the workshop, which is scheduled to take place in Q1 2023, will be published in due course on the EMA events page.

Publication of the 3rd Big Data Steering Group workplan for 2022-25

The joint EMA/HMA Big Data Steering Group has published its third workplan that sets key big data deliverables to be completed between 2022-25. The workplan follows the priority recommendations for regulators on the best approaches to use and generate data, set by the former Big Data Task Force in 2020. The revised workplan allows further enhancement of efficient integration of data analysis into the evaluation of medicinal products by regulators. Importantly the plan includes a pilot of receiving and analysing raw data (patient-level data) from clinical trials submitted as part of marketing authorisation applications. The use of novel technologies and evidence generated from big data will benefit public health by accelerating medicine development, improving treatment outcomes, and facilitating earlier patient access to new treatments. The work carried out by the Big Data Steering Group builds on the Regulatory Science Strategy to 2025 and supports the European Medicines Agencies Network Strategy to 2025. For more information, you may contact bigdata@ema.europa.eu

Update on the draft guidance on personal data & CCI protection in CTIS

On 14 July 2022, EMA hosted a dedicated workshop on the draft guidance on the protection of personal data and commercially confidential information (CCI) in CTIS. Many sponsors and Member States' representatives were very positively engaged in sharing experiences on the use of CTIS and initiating a discussion towards a common understanding and expectations on the protection of personal data and CCI while using the new system. Workshop documents, including presentations and summary, have been made available on the event page.

EMA will consider the feedback provided during the workshop as part of the revision of the guidance document, as well as the feedback provided during the 5-month public consultation period for the draft guidance that concluded on 8 September 2022. The discussion will continue on major points in dedicated fora engaging with key players on the topic. The publication of the updated guidance will be announced through future issues of this newsletter.

CTIS Forum

The inaugural meeting of the Clinical Trials Information System Forum took place on 12 October 2022. The Forum includes CTIS users and experts from Member States, from EU sponsors (Academia, Industry), from Clinical Research Organisations (CROs), from patients (representatives from Patients/Consumers Working Party, PCWP) and from healthcare professionals (representatives from Healthcare Professionals Working Party, HCPWP). Participants are nominated by the official contact points of EU level Stakeholder associations.

The CTIS Forum will meet on a quarterly basis to allow direct exchanges of information and discussion of user experience. It aims to promote dialogue between Member States, external stakeholders, the European Medicines Agency and the European Commission on CTIS functionalities, system use and development, as well as user support and knowledge acquisition. The Forum may also escalate general business operational aspects of CTIS to the CTIS Member State Product Owners Experts Group (MS POEG) and, if needed, to the ACT EU Steering Group.

CTIS events update

EMA and the EMRN continue to provide training events and information sessions to support CTIS users. All EMA-run events are live broadcast in Amsterdam time and a video recording is made available after each session on the respective event pages found under CTIS Training and information events webpage.

The first two video recordings of the recently launched series of monthly **Organisation Management Service (OMS) troubleshooting sessions for CTIS users** have been published for June and July. After the latest session in October, EMA continues with one more for 2022 and invites CTIS users to submit their questions in advance via the Slido links announced on the event page:

24 November 2022 14:00-15:00 CET

On 16 November 2022 13:30–17:30 CET, EMA with support from DIA will host the **Clinical Trials Information System Webinar - 9 months on and going forward** targeted to all CTIS users. The focus of this virtual information day is to share practical advice regarding transitioning clinical trials from the Clinical Trials Directive (2001/20/EC) to the Clinical Trial Regulation (536/2014) as well as best practices on user management. Questions can be submitted by participants until 17 October 2022. For more information on key topics and registration process, please visit the event page.

Further dates have been announced for the **CTIS walk-in clinics**, which provide sponsor users the opportunity to raise questions about any CTIS functionality and receive advice from CTIS experts. CTIS users can submit and upvote questions *in advance* as well as during the live sessions via Slido as described on the event pages:

15 Nov 2022 16:00-16:45 CET 12 Dec 2022 15:00-15:45 CET

The video recordings for the first six walk-in clinics are now available on their respective event pages: 28 March, 22 April, 5 May, 19 May, 2 June, and 15 June and 31 August.

EMA continues with the monthly **CTIS bitesize talks** where sponsor users can learn from CTIS experts about a specific system functionality and have their questions answered live.

CTIS users can now submit and upvote questions not only live during the events but also *in advance* via Slido; two more sessions are scheduled for 2022:

23 Nov 2022 (14:30-16:00 CET) Notifications–Part 2

15 Dec 2022 (14:30-16:00 CET) Annual Safety Report

All 2022 video recordings are already published in the respective event pages for February, March, April, May, June, July and September.

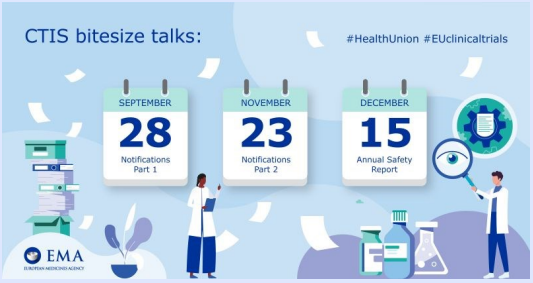


Image 2.
CTIS bitesize talks continue for 2022
View and share in Linkedin

The last session of the **Sponsor end user training** programme for this year will be held on 7-10 November 2022 14:00-18:30 CET. The programme will continue in 2023 with dates announced in future Newsletter issues.

CTIS training environment (CTIS Sandbox) update

The CTIS Training Environment allows sponsor users to explore the system configuration functionalities of CTIS and the processes related to submitting a clinical trial application in a test environment.

Survey 3.0 to collect expressions of interest from clinical trial sponsors for access to CTIS training environment was closed on 25 September 2022. EMA is currently reviewing all the responses and intends to provide eligible participants with access to CTIS Training Environment by the end of October 2022.

The web address to CTIS Training Environment has changed and users have been provided with the new web address through the e-mail account they have previously registered with at EMA.

CTIS training material update

A new document that provides CTIS users, sponsor and authorities, with an overview of the timelines and deadlines across the Clinical Trial Application process has been published in the CTIS Training and support webpage. In addition, it explains the dynamic character of the workflow.

Earlier completion of a task (before its deadline) might cause recalculation of the deadline of subsequent or relevant tasks, changing their initially projected deadlines.

Update on the MAH admin role

Following consultation with experts, the MAH Administrator assignment will be done directly in CTIS. The EMA administrator will perform the assignment of the role per trial. In order to authorise this assignment, the Marketing Authorisation Applicant/Holder will need to append to their request sent to CTIS User Support Service, the relevant documents required to perform the assignment. The information will be made publicly available in Module 13 (Clinical study reports submissions) on the CTIS online modular training programme.

Update on new process of requesting roles in EMA Account Management

All EMA account users can request access on behalf of their organisation for EMA applications such as CTIS, EudraVigilance etc. In July, a new access request workflow in the EMA Account Management platform was announced. This change came into practice on the 16th of August with the aim of ensuring that the registration and access management process is delivered in a simple, secure, consistent and user-friendly way. A transition period was foreseen until the end of September, where both new and the old functionalities were available.

Since the beginning of October, the 'Manage my access' tab, marked in red in the visual below, became obsolete, with all procedures now being managed through the 'Request Access for organisations' tab, marked in green. More information on the new process can be found in July's issue of this newsletter.

Further information on access-management aspects and procedures for requesting and managing access to EMA applications can be found in the recording of the "EMA Account Management training webinar". If you would have further questions or would like to share any feedback, please contact the EMA Service Now portal.

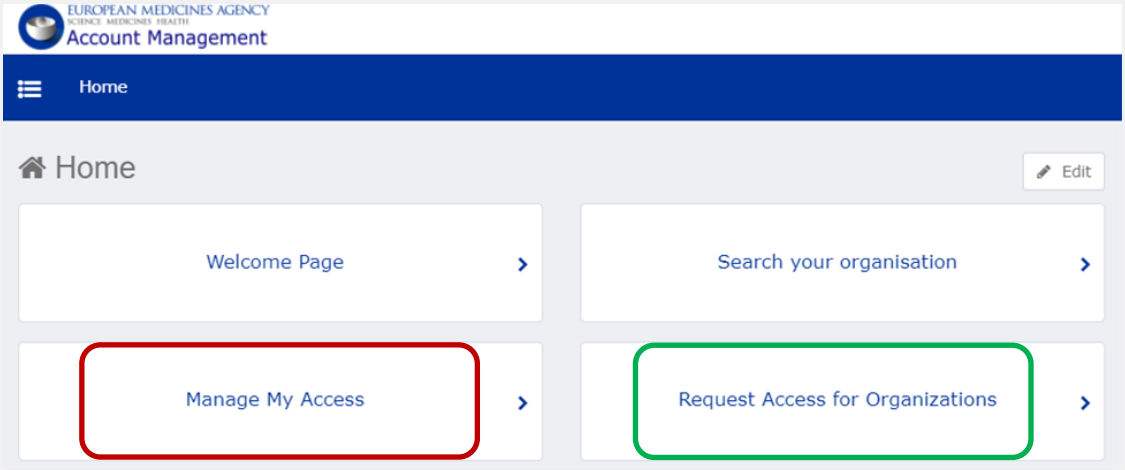


Image 3.
The obsolete (red) and new (green) tab for access request workflow by EMA Account users.

CTIS user email validation to assign roles

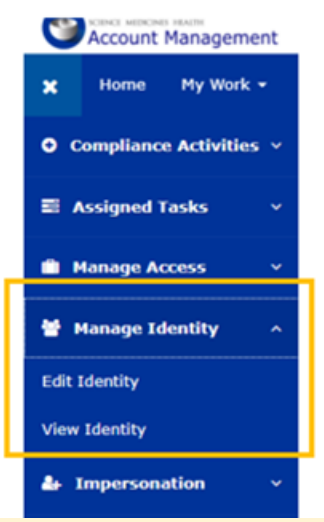
Currently, CTIS Member State or Sponsor Administrators can assign roles to users in their organisations by indicating the user ID. A change is occurring in CTIS whereby the Administrators will have to indicate both the user ID and the email address of the user. This change is being implemented to reduce the risk of assigning a role to unintended users due to similar user IDs.

If an Administrator attempts to assign a role to a user who does not have an email address registered in EMA Account Management, it will result in an error message in CTIS and the role cannot be assigned.

In preparation for the introduction of this change, each user who does not yet have an email address registered in EMA Account Management should open a ticket with EMA Service Now portal requesting to add the email address to their EMA Account Management profile.

Existing roles are not affected by this change in CTIS, which was implemented on 18 October 2022.

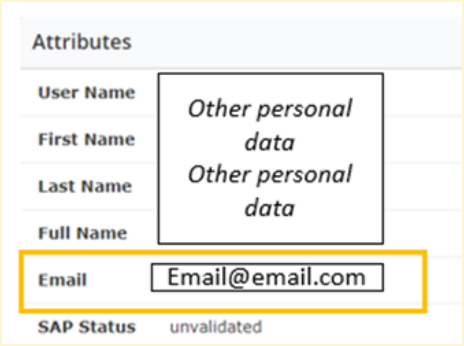
CTIS users can find out whether their email address is missing from their EMA accounts or not, by logging in their EMA account profile and following the instructions below:



1. Click on the three-line icon, found on the upper left corner of the landing dashboard.

2. In the revealed drop-down menu, click on the "Manage identity" tile, and from the drop-down list, click the "View identity" button.

3. In the landing form, one of the fields is dedicated to your email. If this field is empty, you will need to open a ticket with Service Now Portal, requesting to add you email address to your EMA Account profile.



More information on how to manage your EMA account profile, can be found in the EMA Account Management homepage.

Update on Multi-factor authentication (MFA) rollout timeline

EMA is rolling out a multi-factor (MFA) authentication strategy for user logins to EMA-managed systems. This strategy will effectively reinforce the security of user accounts. With MFA, users are asked to enter a second factor (besides username and password) when logging into an IT system to verify their identity. This second factor is:

- A token received in Microsoft Authenticator mobile app, or
- An automated phone call or a text to mobile phone, or
- A call to office phone.

Each user can choose and use their preferred second factor method. This choice can be amended at any time. In preparation for the introduction of MFA, it is recommended that each user is equipped with a mobile phone, or an office phone that can be used for any of the three methods of second factor authentication. The date of activation of MFA in CTIS is not yet confirmed and all CTIS users will be notified in advance.

Update on EMA's service desk

EMA's CTIS User Support Service continues to be available for users to raise Incidents, Requests and Questions regarding CTIS and users are advised to report any issues *directly* to this service desk in order to get a response in a short time.

For any other queries, EMA account users can make use of the new IT service management solution called ServiceNow. EMA Service Now portal, in alignment with the Agency's cloud strategy and the information security strategy, has replaced EMA's current tool (Jira), with a go-live date of 12 September 2022.

CTIS release notes and known issues

New CTIS release notes and known issues documents are available on the Website outages and system releases page of euclinicaltrials.eu.

These release notes reflect the updates made in the most recent technical release of CTIS, while the known issues documents outline the issues that sponsor and authority users may encounter when using the CTIS secure workspaces. Where possible, workarounds to apply are proposed. Note that the issue related to the cancel application pop-up warning has been fixed and the draft application is no longer cancelled when the user clicks on 'X' in the upper corner of the pop-up.

CTIS users are reminded of the 2 weekly and monthly **maintenance windows**, during which they are advised to avoid using CTIS or the website search:

Each Tuesday and Thursday: 18:00 – 21:00 Amsterdam time

Each first Saturday of the month, from 10:00 – 14:00 Amsterdam time

Best Practice Guide for Sponsors of document naming in CTIS by CTCG

The Clinical Trials Coordination Group (CTCG) have published a Best Practice Guide for Sponsors of document naming in CTIS with recommendations on how to name the documents uploaded by sponsors in CTIS. Although not mandatory, this name convention document and accompanying recommendations can be used as a set of instructions meant to facilitate both sponsors and member states by increasing effectiveness of submission and assessment procedures of clinical trial applications via CTIS.

Updated CTR Q&As by European Commission

An updated version of the "Questions & Answers" document on the Clinical Trials Regulation 536/2014 has been published by the European Commission in September 2022. This document is a helpful tool as many frequently asked questions posed by sponsors are answered with the aim to provide general guidance on the implementation of the CTR. CTIS users are recommended to consult the "Q&As" while preparing their clinical trial application dossiers to ensure the best possible alignment with CTR requirements.

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