

Clinical Trials HIGHLIGHTS

News, views and interviews for European Clinical Trials

An agency of the European Union



Welcome to Clinical Trials Highlights



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Welcome to the July 2022 issue of Clinical Trials Highlights. We are now six months away from the end of the first year of the [transition period](#) from the Clinical Trials Directive to the Clinical Trials Regulation.

As of 31 January 2023, all initial clinical trial applications in the EU must be submitted via CTIS and can no longer be submitted via national systems. As we approach this key date, sponsors are encouraged to familiarise themselves with the new submission processes in CTIS. Sponsors can make use of the extensive [CTIS training and support materials](#) to get their organisations ready for the transition. Member States remain on hand to support sponsors with queries regarding national assessment processes.

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ACT EU multi-stakeholder events

ACT EU seeks to engage all clinical trials stakeholders to support inclusive patient-oriented medicines development and delivery. The ACT EU programme will host multi-stakeholder events on a variety of clinical trials topics throughout 2022 and 2023.

On 4 October 2022, the ACT EU programme will host a [multi-stakeholder workshop on decentralised clinical trials \(DCT\)](#) on behalf of the EU DCT project. The DCT project group consists of a core team of clinical trial experts from the Clinical Trials Coordination Group (CTCG), ethical experts from the Commission Expert Group on Clinical Trials (CTEG) and Good Clinical Practice (GCP) inspectors from the GCP Inspectors Working Group (GCP IWG). The workshop will provide an opportunity for participants to discuss and provide input to the content of the upcoming recommendation paper on the use of decentralised elements in clinical trials, planned for publication in Q4 2022. The event will include a live broadcast virtual plenary session, open to all interested parties, where the work of the European Medicines Regulatory Network (EMRN) on the DCT recommendation paper will be presented, and in-person breakout sessions for invited attendees to discuss topics of relevance to decentralised clinical trials.

ACT EU multi-stakeholder events (cont'd)

In Q4 2022, the ACT EU programme will hold a multi-stakeholder workshop on complex clinical trials. During the workshop, representatives of ACT EU will present the recommendations published in the [complex clinical trials Q&A](#), and will gather input from stakeholders which will help to feed future versions of the Q&A. Further details regarding this workshop will be provided in due course.

The ACT EU programme will organise a series of workshops on the third revision of the ICH guideline on Good Clinical Practice (GCP), known as ICH E6 (R3). The ICH E6 (R3) guideline describes the responsibilities and expectations of all stakeholders in the conduct of clinical trials, and covers monitoring, reporting, and archiving of trials. The revision to the guideline aims to provide GCP guidelines that are responsive to current clinical trial practices, acknowledging the diversity of trial designs, data sources, and



*Image 1.
The ACT EU programme will host multi-stakeholder events on a variety of clinical trials topics throughout 2022 and 2023*

and the different contexts in which clinical trials can be conducted and highlighting that GCP principles can be satisfied in a variety of ways. The ACT EU programme seeks to gather the perspectives of the EU clinical trials community in a first workshop in Q4 2022 prior to the opening of the public consultation on the revised guideline. Following this initial workshop, further stakeholder engagement will be organised by the ACT EU programme. Further details regarding these workshops will be provided in future issues of this newsletter.

Survey on the implementation of the Clinical Trials Regulation

A survey has been created to gather the views of clinical trial sponsors on the implementation of the Clinical Trials Regulation (CTR), with a focus on critical hurdles that sponsors perceive or experience when submitting a clinical trial application under the CTR. Sponsor associations and sponsors that have submitted a clinical trial application under the CTR which has been authorised, not authorised, withdrawn by the sponsor or lapsed have been invited to respond to the short survey. The results will be analysed and addressed as part of the ACT EU initiative.

Article published: 'Estimators for handling COVID-19 related Intercurrent Events with a hypothetical strategy'

The ACT EU priority action on developing methodologies guidance includes implementation of the ICH addendum to the guideline on statistical principles for clinical trials on estimands and sensitivity analysis E9(R1). As part of this work, a new article from the EMRN has been published in [Pharmaceutical Statistics](#). The article explores statistical approaches for handling disturbances to ongoing clinical trials caused by the COVID-19 pandemic which affect the interpretability of the measured endpoints (for example, in cases where the outcome assessment was changed from in-person to remote assessment). It compares the performance of different statistical methods which can measure the effect of the disturbance of the investigated treatment and identifies a best performing method.

Introduction to the SAFE CT Joint Action

The Clinical Trials Regulation and the [safety implementing regulation \(IR\)](#) introduced the concept of safety cooperation and work-sharing among Member States (MSs)

Joint Action (JA) 12 of the [EU4Health Safety Assessment Cooperation and Facilitated Conduct of Clinical Trials](#) or SAFE CT supports these new concepts through provision of additional resources and expertise necessary to implement the new regulation.

The goal of this JA is to establish and maintain cooperation in safety data assessment in clinical trials via building capacities and performing training activities in the participating MSs. The experience gained during the JA will be used to update and improve the procedures on cooperation and training in safety surveillance in clinical trials.

The project is currently in the grant agreement preparation phase and will run for 36 months (with a retrospective start date from 01/05/2022 – 01/04/2025). The project will receive 80% funding from the Commission with the remaining 20% of costs contributed by all beneficiaries. With Croatia as the project coordinator there are 22 MSs participating (AT, BE, HR, CZ, DK, EE, FI, FR, DE, GR, HU, IE, IT, LV, LT, MA, NL, NO, PT, SI, ES and SE). EMA is providing in-kind contribution.

Update on the consultation on draft guidance on the protection of personal data and commercially confidential information (CCI) in CTIS

In May 2022, EMA published a [draft guidance on the protection of personal data and CCI in CTIS](#) for public consultation. The deadline for the submission of feedback is **8 September 2022**.

On 14 July 2022, EMA organised a stakeholder workshop to collect further feedback and to address questions related to the draft guidance. Event documents, including presentations from the workshop, will be [made available on the event page](#) in due course.

An academic sponsor's first experiences with CTIS

Can you tell us about the EU-SolidAct trial which was submitted via CTIS?

EU-SolidAct is part of EU-RESPONSE, a pan-European research project involved with rapid and coordinated investigation of new and repurposed medication to treat Covid-19. EU-SolidAct is an [Adaptive Platform Trial](#). The master protocol is developed for evaluating treatments in hospitalised patients with COVID-19. The protocol is designed such that it functions as the basis of a joint European response to combat infectious agents both now and in the future.

Oslo University Hospital is the sponsor of the EU-

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SolidAct platform trial. We are a small team of three operational and two clinical personnel, but we have delegated much of the operational tasks to Inserm (pharmacovigilance, data management and statistics), and to the European Clinical Research Infrastructure Network (ECRIN, monitoring and regulatory support).

An academic sponsor's first experiences with CTIS (cont'd)

Why did EU-SolidAct decide to submit a clinical trial application via CTIS?

From the outset in January 2021, we knew that we wanted to run the trial in as many European countries as possible. After discussions with our regulatory contacts, EMA and the Norwegian Medicines Agency, we decided to apply through the voluntary harmonisation procedure (VHP) as we were told this would save time and efforts in the long run, especially since it would pave the way nicely towards the Clinical Trials Regulation (CTR) that we knew was being implemented a year later. Once the Regulation came into effect on 31 January 2022 it was natural to transfer the VHP approval according to the CTR through the CTIS following the instructions set forth by the Expert Group on Clinical Trials of the European Commission.

What challenges did EU-SolidAct face with using CTIS and how did you overcome them?

Once we were ready for submission, only part I of the submission came through to the regulators. Due to this we had to resubmit the whole application again before we were finally successful in submitting the full dossier. The challenge then was that we had three different EU CT numbers which had been used interchangeably in different documents (protocols, informed consent forms etc). We have used and are still using quite a lot of effort to sort this out.

Further challenges followed when we wanted to apply for a new arm in the EU-SolidAct platform.

Because the CTR was conceived before the introduction of platform trials we had to decide if we wanted to submit AXL-SolidAct as a separate trial or as an amendment to the EU-SolidAct trial/platform. After advice from the EMA and the EU Commission we decided with the separate-trial option, which is not the core premise of a platform trial.

Lastly, we have experienced many technical problems, which I guess is expected with such a new system. Many have been resolved by the EMA team, and on some we continue to collaborate for their resolution.

What benefits did EU-SolidAct see from the use of CTIS?

From our perspective there are three major benefits from the use of CTIS and the CTR: Firstly, it is a tremendous step forward on transparency. Most, if not all, submitted documents will be available for all who are interested. This will make a huge impact on scientific rigour and value of European clinical trials. Secondly, while the amount of documentation seemingly has increased, it is very nice that we now have a single-entry point of applications for all countries. This makes it very easy to know exactly what has been approved at any time. Thirdly, while the maximum timeframes are quite long both for the applicant and the authorities, it is good that there are firm timeframes and that surpassing the timeframe by the authorities will lead to a tacit approval.

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.

CTIS events update

EMA and the EMRN continue to provide training events and information sessions to support CTIS users.

In June 2022, a series of monthly **Organisation Management Service (OMS) support sessions for CTIS users** was launched. In the sessions, OMS experts address issues and questions from CTIS users related to registering the organisation or location data in OMS for use in clinical trial applications. CTIS users are invited to submit questions via Slido prior to each session. The sessions are live broadcast and a video recording is made available after each session. The dates of future sessions and other event details are available below:

[30 Jun 2022 – 14:00 – 15:00 Amsterdam time](#)

[21 Jul 2022 – 14:00 – 15:00 Amsterdam time](#)

[22 Sep 2022 – 14:00 – 15:00 Amsterdam time](#)

[19 Oct 2022 – 14:00 – 15:00 Amsterdam time](#)

[24 Nov 2022 – 14:00 – 15:00 Amsterdam time](#)

On 1 July 2022, EMA hosted a **CTIS information webinar** which outlined user experiences from the first six months of CTIS and provided a reminder that from 31 January 2023, sponsors must use CTIS to submit all initial clinical trial applications. A video recording of the webinar will be made available [on the event page](#) in due course.

Further dates have been announced for the **CTIS walk-in clinics**, which provide sponsor users with the opportunity to raise questions about any CTIS functionality and receive advice from CTIS experts.

[22 Aug 2022 – 16:00 – 16:45 Amsterdam time](#)

[20 Sep 2022 – 16:00 – 16:45 Amsterdam time](#)

[05 Oct 2022 – 15:00 – 15:45 Amsterdam time](#)

[15 Nov 2022 – 16:00 – 16:45 Amsterdam time](#)

[12 Dec 2022 – 15:00 – 15:45 Amsterdam time](#)

The video recordings for the first three walk-in clinics are now available on their respective event pages: [28 March](#), [22 April](#) and [5 May](#).

EMA continues to hold monthly **bitesize talks** where sponsors can learn from CTIS experts about a dedicated CTIS functionality and ask questions related to that functionality. The upcoming bitesize talks will focus on the Notifications functionality in CTIS.

[28 Sep 2022 - 14:30 - 16:00 Amsterdam time](#)

[20 Oct 2022 - 14:30 - 16:00 Amsterdam time](#)

In addition, further dates have been announced for the **sponsor end user training programme**, which prepares users to submit clinical trial applications and manage the life cycle of clinical trials in CTIS.

[20-23 Sep 2022 - 09:00-13:30 Amsterdam time](#)

[7-10 Nov 2022 - 14:00-18:30 Amsterdam time](#)

CTIS training material update

The CTIS training material catalogue is continuously updated, including the publication of new materials to meet user needs and update existing materials to match the current status of system functionalities.

EMRN has [published a new document](#) which outlines the latest updates to the CTIS training materials. The goal of this document is to assist users in identifying which training materials have been updated most recently, and which new materials have been added. It also includes a quick guide on how to search for updated documents on the EMA website.



CTIS training environment ('CTIS Sandbox') update

The CTIS training environment allows sponsors users to explore the system configuration functionalities of CTIS and the processes related to submitting a clinical trial application in a testing environment.

Following the closure of the Survey 2.0, provision for access to survey respondents will be completed in July 2022. A [new survey \(Survey 3.0\) has been published](#) where new potential users of CTIS can express interest to access the CTIS training environment. The deadline for participation in Survey 3.0 is **23 September 2022**. EMA will use the survey results to determine whether additional organisations will be granted access to the CTIS training environment. It should be noted that currently **no** decision has been taken on whether additional access to the CTIS Sandbox will be granted and the survey response will help inform that decision.

Upcoming changes to EMA Account Management

Collaboration with stakeholders is at the core of EMRN's activities. This interaction is facilitated by the systems and applications maintained by EMA, such as CTIS, and the first interface with EMA's systems and applications is the [EMA Account Management](#) platform. Given the importance of the Account Management platform as a gateway for stakeholders, the Agency will embark on a new project aimed at ensuring that the registration and access management process is delivered in a simple, secure, consistent and user-friendly way. The new look and feel of the EMA Account Management platform is presented below, together with some of the revised functionalities that will support users.

The new access request form will provide users with a guided process and an enhanced Organisation Search, making it easier for users to find their affiliated organisation based on different criteria (see image 2 below).

The screenshot displays a multi-step process for requesting access. The first step, '01 Search Criteria', is active. It includes a list of instructions: 'Provide the search criteria to look for the desired organisations:', 'Select one or more country by typing in the Country field, selected countries will appear under the field', 'Provide one of the other search criteria like the organisation name', and 'By default searches are performed in English (EN)'. A link to 'step by step documentation' is provided. The form fields include: 'Country' (with 'Italy' and 'Netherlands' selected), 'Organisation ID', 'Organisation Name' (with 'Eur' entered), 'Location ID', 'City', 'Postal code', 'Address', and 'Language' (with 'EN' selected). 'Reset' and 'Next' buttons are at the bottom right.

Image 2.
The new look of the EMA Account Management platform: Search Criteria

Moreover, EMA will introduce the possibility to select multiple organisations within the same request, making the process more efficient and saving time for users associated with more than one entity (see image 3 in next page).

Upcoming changes to EMA Account Management (cont'd)

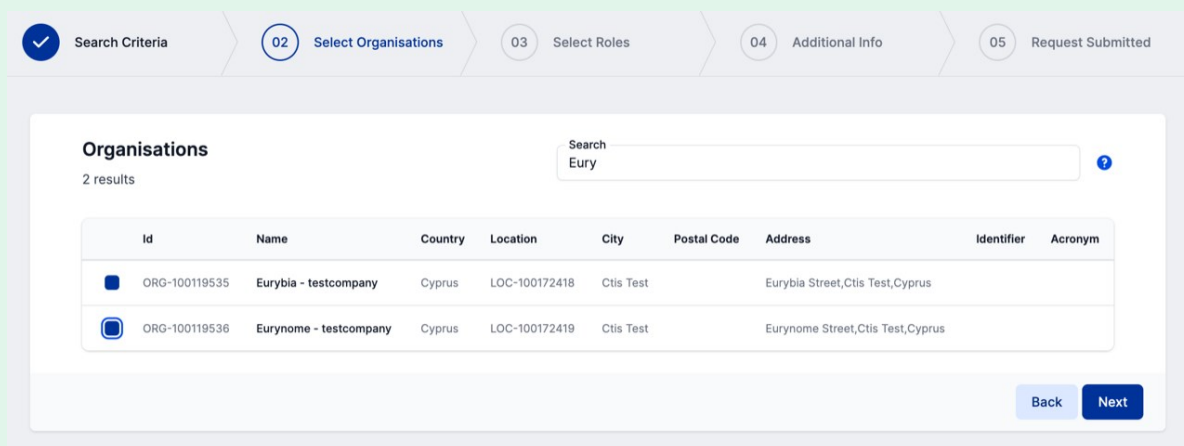


Image 3.
The new look of the EMA Account Management platform: Select Organisations

A clearer overview and description of potential roles based on the selected organisation will be added, providing users with clarity dependent on their user needs (see image 4 below).

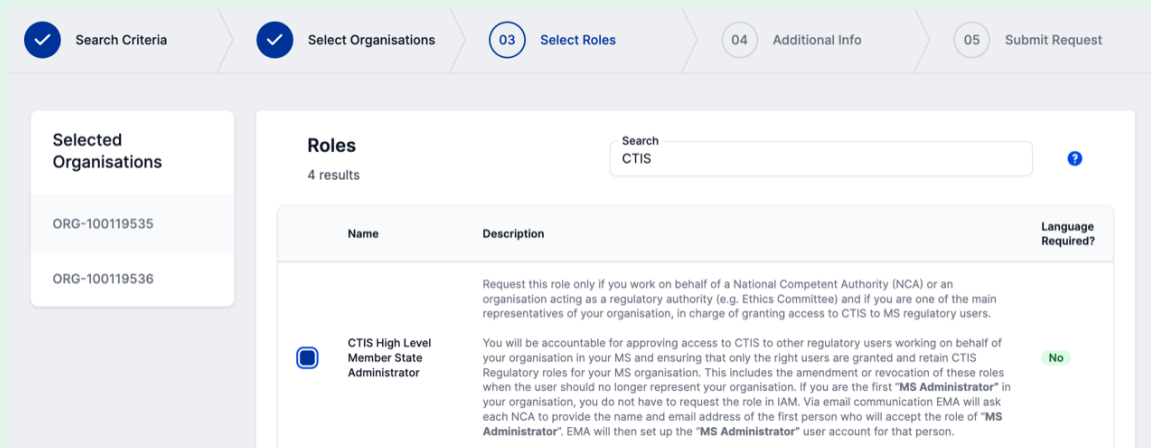


Image 4.
The new look of the EMA Account Management platform: Select Roles

Once a role has been selected, users will be prompted to attach the required documentation only if necessary and documentation requirements will be made explicit, ensuring our users have a clear overview of documentation requirements for approval, ensuring the fastest possible access to EMA's applications and systems.

The overall aim of the new access request workflow is to better guide our users through the entire process, minimise the number of rejections and to ensure that users can access EMA's applications and systems in a swift and efficient manner.

The new access request workflow will become available in July, and the [current access request workflow](#) will be available until end of September. During the transition period users will be able to use the new and the old functionality, meaning there should be no disruption for users.

Additional information on further upcoming changes to EMA Account Management will be provided in future Clinical Trials Highlights newsletters. If you would like further details on the EMA Account Management project, please contact InformationSecurity@ema.europa.eu.

New KPIs to track the European clinical trials environment published

The EMRN publishes KPIs to track the performance of the European clinical trials environment on a monthly basis. The latest KPI document, covering the period of 1 – 31 May 2022 is now available on the [Clinical Trials Regulation: progress on implementation page](#).

Multi-factor authentication strategy at EMA

EMA is rolling out a multi-factor authentication (MFA) strategy for user logins to EMA-managed systems. This strategy will reinforce the security of user accounts. With MFA, users must provide additional information on top of their username and password when logging into an IT system to verify their identity. Further details of the CTIS MFA rollout timeline will be provided in due course. CTIS users will be informed at least two months before any effective rollout occurs.

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