

Clinical Trials HIGHLIGHTS



Welcome to Clinical Trials Highlights

A weekly **CTIS Newsflash** is now circulated to all CTIS users & Newsletter subscribers

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Welcome to the December 2022 issue of Clinical Trials Highlights.

We are now 40 days away from the end of the first year of the transition from the Clinical Trials Directive (CTD) to the Clinical Trials Regulation (CTR), with sponsors and regulatory authorities focussed on getting ready for the mandatory use of CTR and of the Clinical Trials Information System (CTIS).

Since the launch of CTIS on 31 January 2022, almost 200 clinical trial applications have been authorised and over 200 are under evaluation. During this time, EMA has collaborated with Sponsor and Member State users to identify and successfully resolve technical issues, providing proactive hands-on support to the CTIS user community and strengthening the system ahead of its compulsory use.

As of 31 January 2023, sponsors must submit all initial clinical trial applications under the CTR using CTIS and can no longer submit via the processes outlined in the Clinical Trials Directive. As we approach this key date, we encourage sponsors 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.

Some users have experienced problems with the system. EMA is working closely with Member States, the European Commission, and stakeholders to improve the CTIS user experience for core CTIS processes by the time the use of the system becomes mandatory for all new applications. The Agency has invested additional resources to achieve this goal.

On 15 December 2022 the EMA Management Board heard an update on the implementation of the CTR and the operation of CTIS and will be receiving weekly updates on the progress towards further system stabilisation. The [full MB highlights](#) are published on the EMA website.



- EMA CTIS Team

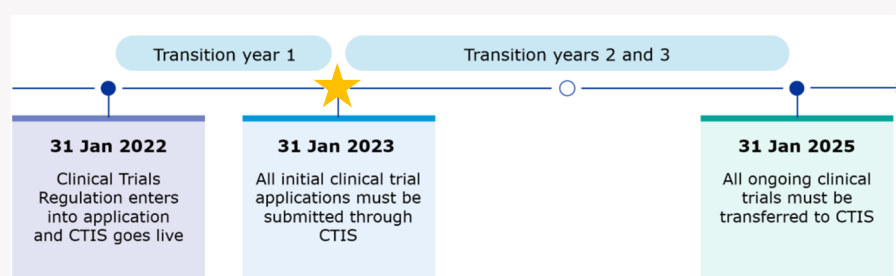


Image 1.
The Clinical Trials Regulation (CTR) foresees a 3 year transition period for sponsors.

New ACT EU webpage

A new [webpage](#), solely dedicated to the Accelerating Clinical Trials in the European Union (ACT EU) initiative, has been created with a layout mirroring the programme structure.

This will facilitate more direct access to ACT EU information for our stakeholders and contribute to strengthening the identity of the ACT EU programme. A definitive HMA¹/EC²/EMA standalone webpage is planned for 2023 and will be announced through a future issue of this Newsletter.

¹ HMA: Heads of Medicines Agencies

² EC: European Commission

Clinical Trials Training Strategy

ACT EU Priority action 10 aims to deliver a clinical trials curriculum, with a particular focus on building capacity in all aspects of drug development and regulatory science. In developing this curriculum, links to universities and Small & Medium-sized Enterprises (SMEs) will be established, building an educational 'ecosystem' where bidirectional exchanges will take place to enable training on clinical trials. A training strategy paper setting out high-level objectives, organisational aspects and timelines is currently being developed and will be published in Q1 2023.

Recommendation paper on implementation and conduct of decentralised elements in clinical trials

On 4 October 2022 EMA hosted a multi-stakeholder workshop on decentralised clinical trials (DCT) 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.

Regulators and sponsors, including patients, were engaged in discussions which covered topics such as clinical trial oversight, the informed consent process, and delivery of investigational medicinal product at home. The recording of the plenary session and presentations of the event have been made available on [the event page](#).

The EU DCT project has considered the feedback provided during the workshop and published a [recommendation paper](#). Further discussion on decentralised elements in clinical trials will continue with key players on the topic under the auspices of the ACT EU Multistakeholder platform which is currently being set up.

ACT EU concept paper on Multistakeholder Platform for public consultation

There is a need to establish a forum for regular dialogue between all stakeholders at EU level on clinical trials. Such dialogue will 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. It is envisaged that the platform will have several phases of development before reaching its final design.

The ACT EU Priority action 3 plans to consult stakeholders in early 2023 to gauge interest in the platform and get feedback on priority topics for discussion. The multi-stakeholder platform will have its kick-off meeting in 2023.

More information on this [open consultation](#) will be included in future issues of this Newsletter.



Updates on scientific advice on clinical trials

ACT EU Priority action 7 brings together key actors involved in scientific advice in the EU, with the aim of critically analysing the existing landscape in line with stakeholder needs. The action aims to develop consolidated processes to efficiently manage scientific advice and enhance coordination across relevant stakeholders, in particular in relation to advice on Clinical Trial Applications and advice for Marketing Authorisation Applications. This will further foster collaboration between the HMA's [Clinical Trial Coordination Group](#) (CTCG) and EMA's [Scientific Advice Working Party](#) (SAWP) and [Emergency Task Force](#) (ETF). The project will include a number of pilot phases planned until the end of 2025.

With a view to clarify the scope of current scientific advice activities, ACT EU Priority action 7 has mapped information on existing voluntary procedures available from EU regulators (see [questions and answers](#)). This mapping provides information on how developers can get informal advice, voluntary regulatory advice or formal Scientific Advice, and where to discuss a new technology or methodology.

The mapping includes information on the simultaneous national scientific advice (SNSA) phase 2 pilot which the EU Innovation Network (EU IN), in consultation with ACT EU, has recently launched. SNSA is intended to be used in situations where an applicant wishes to obtain national scientific advice from more than one national competent authority (NCA) at the same time. This phase of the SNSA pilot will have a specific focus on scientific advice to facilitate clinical trials within the EU.

The optimised SNSA process will continue to complement and provide a bridge between purely national scientific advice and centralised European scientific advice procedures from the EMA. The experience gained during the pilot will be used to inform the development of the final consolidated process for the provision of clinical trial-related advice, a key deliverable in the ACT EU multi-annual work plan ([Heads of Medicines Agencies: EU-Innovation Network - hma.eu](#)).



Image 2.
ACT EU Priority Action 7 aims to develop processes to efficiently manage scientific advice and enhance coordination.

Open consultation on ICH M11 Guideline

The purpose of this new harmonised Guideline on Clinical electronic Structured Harmonised Protocol (CeSHaP) is to introduce the clinical protocol template and the technical specification to ensure that protocols are prepared in a consistent fashion and provided in a harmonised data exchange format acceptable to the regulatory authorities.

The ICH M11 Clinical Electronic Structured Harmonised Protocol Template provides comprehensive clinical protocol organization with standardized content with both required and optional components. The Technical Specification presents the conformance, cardinality, and other technical attributes that enable the interoperable electronic exchange of protocol content with a view to develop an open, non-proprietary standard to enable electronic exchange of clinical protocol information.



Further information can be found on the [ICH M11 page](#). The public consultation is open until 26 February 2023.

Publication of ICH E19 Guideline

Article 41 of the Clinical Trials Regulation (EU) No 536/2014 provides for the possibility for the sponsor to designate in the protocol some adverse events for which the systematic collection by the investigator may not be necessary. The [new ICH E19 guideline](#) provides internationally harmonised guidance across all ICH regions on the use and implementation of selective safety data collection that may be applied in specific late-stage clinical trials in the pre-approval or post-approval setting. ACT EU Priority action 9 will support the implementation of the guideline at EU level.



The European Commission also published [recommendations in 2017](#) to provide some guidance on how selective safety data collection can be implemented in clinical trials in a risk proportionate approach.

Guideline on sponsor responsibilities on handling & shipping of IMPs for human use in accordance with GCP & GMP

The [Guideline](#) on the responsibilities of the sponsor with regard to handling and shipping of investigational medicinal products (IMPs) for human use in accordance with Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP) has been published on [EudraLex - Volume 4](#) and on [EudraLex - Volume 10](#). This Guideline supplements the [Detailed Commission guidelines on GMP for IMPs for human use](#), pursuant to Article 63(1) of the CTR (EU No 536/2014), laying down the principles for management of investigational medicinal products for use in a clinical trial in accordance with GCP and GMP. In addition to describing the interface between the Qualified Person (QP) and the sponsor in relation to release and transportation to the clinical trial site, other concepts concerning the cooperation between the QP and sponsor are encompassed, namely contractual arrangements and technical agreements, transportation, unblinding and recalls. This new guideline is effective from 1 January 2023.

Pilot on using Clinical Trials Raw Data in medicine evaluation

EMA, on behalf of the EU regulatory network and in partnership with the Committee for Medicinal Products for Human Use (CHMP), is conducting a proof-of-concept pilot to investigate the benefits and practicalities of access to individual patient data from clinical studies (raw data) in the assessment of medicines. Following consultation with the EU Regulatory Network and industry, the pilot started in September 2022 and is expected to include 10 regulatory procedures submitted to EMA over the next two years.



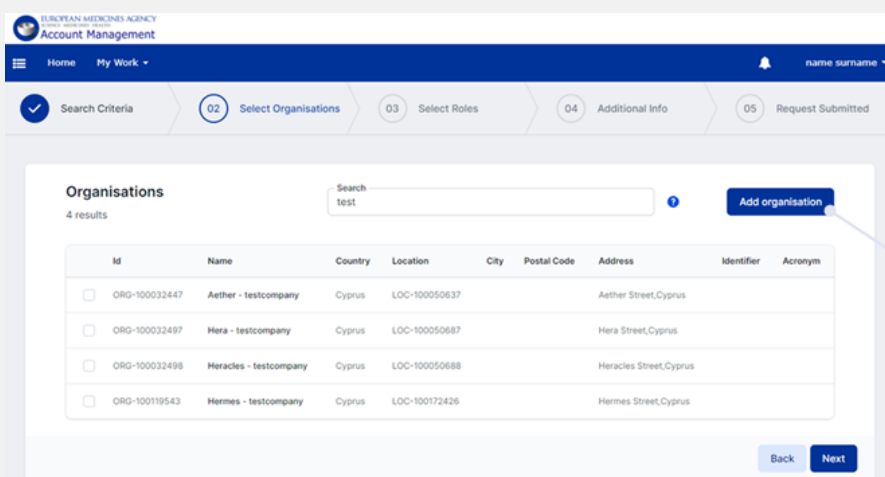
Image 3.
Raw data for the first pilot procedure has already been received by EMA.

Raw data for the first confirmed pilot procedure have been successfully received by EMA for a neurology initial marketing authorisation application. The pilot stems from the 10 priority recommendations issued by the Big Data Task Force in 2020. Information on the pilot's scope, data protection related documents as well as guidance for Applicants and Marketing Authorisation Holders (MAHs) is now available on [EMA's Big Data website](#).

Update on recent changes to EMA Account Management Platform

Collaboration with stakeholders is at the core of EMA’s activities. This interaction is facilitated by the systems and applications maintained by EMA, such as IRIS, and the first interface with EMA’s systems and applications is the [EMA Account Management](#) platform. Given the importance of this gateway to EMA’s applications, the Agency embarked on a project aimed at ensuring that the registration and access management process is simple, secure, consistent and user-friendly.

If the organisation you are looking for is not yet registered in the EMA Organisation Management System (OMS) the [new access request form](#) now provides the possibility to [request a new organisation directly from EMA Account Management](#); once an organisation has been approved users will receive a [link](#) to **progress the access request**.

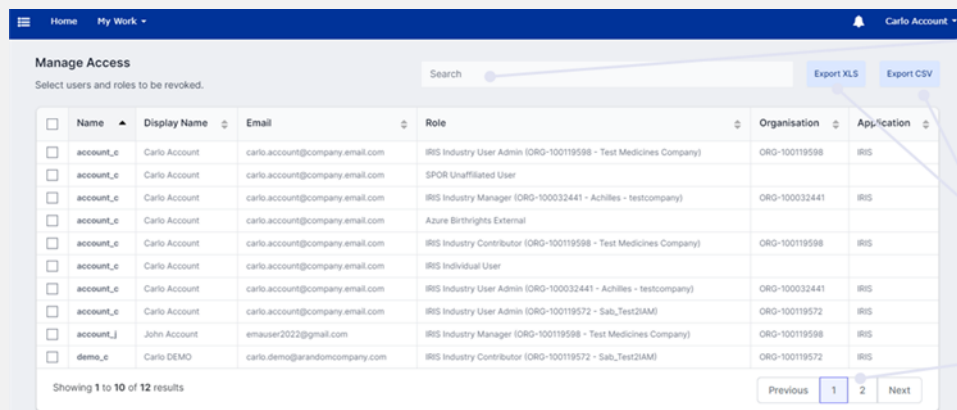


To request creation of an organization, click the **“Add Organisation”** button

Image 4.
Request a new organisation directly from EMA Account Management.

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.

Furthermore a new **“Manage Access”** tab allows [users](#) and [user administrators](#) to list and revoke access for themselves and for the users of the organisation they manage.



The **Search** bar can be used to filter results on organisations, users or roles.

Use the **export** buttons to export data and perform more complex filters

10 results are displayed, further results can be navigated using the paging buttons

Image 5.
Users and user administrators can manage their access in EMA Account Management.

Update on recent changes to EMA Account Management Platform (cont'd)

As previously announced 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 and the 'Manage Access' tab, marked in green.



Image 6.
'Manage my access' tab has been replaced by the new tabs 'Request Access for organisations' and 'Manage Access'.

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 have further questions or would like to share any feedback, please contact us via the [EMA ServiceNow portal](#).

CTIS Sponsor handbook updated version

EMA is pleased to announce that a new version of the '[CTIS Handbook for clinical trial sponsors](#)' is available on our website. This document is aimed at pharmaceutical companies, contract research organisations (CROs), SMEs, academic sponsors and other organisations working on clinical trials. The Handbook provides guidance to clinical trial sponsors to prepare for using CTIS, covering priority topics with reference and links to further supporting materials.



New 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. All EMA-run events are live broadcast and a video recording is made available after each session on the respective event pages found [here](#).

On 16 November 2022, EMA with support from DIA hosted the **Clinical Trials Information System (CTIS) Webinar - 9 months on and going forward** targeted to CTIS users. The focus of this virtual information day was 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.

EMA continues with the regular **CTIS bitesize talks** where sponsor users can learn from CTIS experts about a specific CTIS functionality and have their questions answered live. Since this September, CTIS users can submit and upvote questions in advance as well as live during the events via Slido. Video recordings are published on the respective event pages found [here](#). In 2023 EMA will organize these events on a bi-monthly basis and dates will be announced in upcoming issues of this newsletter.

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. CTIS users can submit and upvote questions in advance as well as during the live sessions via Slido as described on the [event pages](#), where the event recordings are also available.

The **OMS troubleshooting sessions for CTIS users** have been concluded for 2022 with the recordings published in the respective [event pages](#).

In 2023, the **Sponsor end user training programme** will continue, and the first dates are:

- [7-10 February 2023](#)
- [2-5 May 2023](#)
- [27-30 June 2023](#)

CTIS training material update

The [Quick Guide](#) and the [FAQ sheet](#) of Module 13 of the [CTIS Training Material catalogue](#) have been recently updated to include the process that CTIS users need to follow, to request the role of MAH Administrator (applicable from October 2022). Once assigned the MAH Administrator role for a specific clinical trial, users can submit the CTIS clinical study report (CSR) associated to that trial. Users will need to attach an affiliation letter ([a template is provided by EMA](#)) to their requests to [CTIS User Service Desk](#).

CTIS training environment update

The survey ([Survey 4.0](#)) for the CTIS training environment (CTIS Sandbox) has now been reopened. This survey collects expressions of interest in accessing the CTIS training environment, information and contact details of representative individuals, the organisations that they represent and their planning for use of CTIS. These details serve to identify the needs and intention for use of CTIS and support decisions on granting CTIS Sandbox access.

New processes: Registration in OMS & CTIS

Sponsor registration in OMS

A new process is in place since 3 November 2022, enabling any Sponsor not registered in a National Business registry to request their registration in the Organisation Management Service (OMS). In their request to OMS, Sponsors should attach a CT registration Headed letter available in the [OMS portal](#).

Site registration in CTIS

Additionally, a new CTIS release on 12 December 2022 enabled the creation of organisations locally in CTIS, without the need to register them in OMS, in the following five areas of the system:

- Part I: Sponsor section- "Third-party organisations"
- Part II: "Trial sites"
- Serious Breach Notification: "Details of the site where the serious breach occurred"
- Third Country inspectorate Notification: "Third country inspection site"
- MS Inspections: "Inspected site"

Organisations created locally in CTIS behave and function in the same way as the ones sourced from OMS and can be searched and selected once they have been registered in CTIS.

This new feature replaces the temporary process which has been in place since 3 November 2022, enabling users to record organisations in OMS which were not registered in any public national business registry by attaching a CT registration headed letter to their OMS request. Now that the new functionality is in place to allow direct recording of organisations in CTIS, the temporary process is discontinued.

Step-by-step instructions on how to register sites in CTIS have been circulated to all users. The CTIS training material will be revised accordingly and updates will be provided in future issues of this Newsletter.

Update on Multi-factor authentication (MFA) rollout timeline

As previously announced, EMA is rolling out a multi-factor (MFA) authentication strategy for user logins to EMA-managed systems. This strategy will reinforce the security of user accounts. 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 second factor authentication.

Users can already log into the [EMA ServiceNow](#) portal to set up their MFA for EMA systems, which will work also for CTIS once deployed and activated. The date of activation will be communicated to all CTIS users in advance.

Reminder for SMEs & Academia CTIS users

SMEs and Academia conducting clinical research can face challenges with regards to use of CTIS. In previous newsletter issues, EMA has announced the publication of dedicated training and guidance materials adapted to these users' needs. We would like to remind the community of the [online training module 19 for SME/Academia](#), the [recordings of CTIS webinars targeted to SME & Academia](#) and the infographic [Sponsor Quick Guide to CTIS](#). Finally, EMA also regularly publishes a [newsletter for SMEs](#) with key updates on the European regulatory environment.

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