

CTIS HIGHLIGHTS

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

An agency of the European Union



Welcome to CTIS Highlights

The Clinical Trials Regulation will ensure harmonisation of the submission, assessment and supervision of clinical trials throughout the EU. CTIS is the business tool of the Clinical Trials Regulation. With CTIS, clinical trial sponsors can apply for a clinical trial in up to 30 EU/EEA countries with a single application which covers submissions to national competent authorities, ethics committees, and public registration of the clinical trial.

Member States will work in CTIS from go-live, as soon as clinical trials applications are submitted to them through the system. Until 31st January 2023, sponsors can choose to submit initial clinical trial applications under the Clinical Trials Regulation and through CTIS, or under the Clinical Trials Directive. By 31 January 2025, all ongoing clinical trials must be transferred under the Regulation to CTIS.

As we look forward to the launch of CTIS and beyond, sponsors are reminded to make use of the [available training and support materials](#) to prepare for using CTIS.

EMA has engaged with future users of CTIS in preparation for go-live and will continue to support and collaborate with the user community by focussing on ensuring a smooth go-live, assisting sponsors and Member States with CTIS processes through communication, training and operational support, and strengthening and further developing CTIS.

- **The CTIS team**

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Clinical Trials website

On 31 January 2022 at 9:00 CET, EMA will launch a new Clinical Trials website to support the launch of CTIS. The public website will provide information on CTIS and will also allow anyone to publicly search information on clinical trials authorised through CTIS. In addition, the Clinical Trials website will provide tailored information for sponsors and authorities including the login link for the secure domains, links to

training and support materials and the link to the CTIS User Support Service. The URL for the Clinical Trials website will be made available on the EMA website and social media channels on 31 January 2022.



*Image 1.
A new Clinical Trials website will be launched on 31 January 2022 to support CTIS go-live.*

Transition to the Clinical Trials Regulation and CTIS

The Clinical Trials Regulation foresees a 3-year transition period for sponsors to use CTIS.

From 31 January 2022 to 31 January 2023 sponsors will be able to choose whether to apply for an initial clinical trial application under the regime of the Clinical Trials Directive, or to submit an application under the Clinical Trials Regulation, using CTIS.

From 31 January 2023, submission of initial clinical trial applications under the Clinical Trials Directive will no longer be possible. Such applications must be submitted under the Clinical Trials Regulation using CTIS.

All clinical trials that were authorised under the Directive can continue to run and complete under that Directive until 31 January 2025. By 31 January 2025, these clinical trials must either have ended in the EU/EEA or have been transitioned to CTIS.

To prepare for the transition to CTIS, sponsors are advised to consult the [CTIS Sponsor Handbook](#) and ensure they have all registrations for EMA systems in place by consulting the [Getting started with CTIS quick guide](#). Sponsors will also be able to consult a dedicated training module on the transition (Module 23), to be published by end of January 2022 on the [CTIS online modular training programme](#).



Image 2.
3-year transition period for sponsors to use CTIS.

Sponsor end user training programme

As mentioned in the previous issue of CTIS Highlights, EMA offers sponsor end user training courses, organised by DIA, in 2022. The programme focuses on explaining and demonstrating CTIS functionalities related to the use of CTIS by sponsors.

More details about the next sponsor end user training courses, including how to register, can be found in the links below:

Upcoming Courses

February course 15/02/2022 to 18/02/2022
March course 01/03/2022 to 04/03/2022
April course 05/04/2022 to 08/04/2022
May course 10/05/2022 to 13/05/2022
June course 20/06/2022 to 23/06/2022

Updates to the safety assessment of clinical trials

The European Commission Implementing Regulation on the cooperation of the Member States in safety assessment of clinical trials ([Regulation \(EU\) 2022/20](#)) has been published and will become applicable on 31st January 2022, the same day as the entry into application of the Clinical Trials Regulation and the go-live of CTIS. The overall aim of the implementing regulation is the harmonization of the safety standards for clinical trial participants and future patients, improving the data generated in terms of reliability and robustness.

The implementing regulation carries substantial changes for the Member States, such as enhanced coordination of Member States in the assessment of clinical trials with respect to safety, cooperation in the recommendations for corrective measures and/or mitigating actions and introducing the concept of the "safety assessing Member State" (saMS). The saMS will perform the coordinated assessment of Suspected Unexpected Adverse Reactions (SUSARs) and Annual Safety Reports (ASRs) for trials in the EU using the same active substance as the "investigational medicinal product".

EudraVigilance training for clinical trial sponsors

New live, virtual, hands-on training courses on EudraVigilance for clinical trial sponsors will be available from March 2022. The courses, organised in liaison with DIA, are designed for clinical trial sponsors who will directly report suspected unexpected serious adverse reactions (SUSARs) to EudraVigilance via EVWEB. More detailed information is available in the [EudraVigilance training and support webpage](#).

The EudraVigilance training and support webpage on the EMA website also contains information on the free EudraVigilance online training and competency assessment for non-commercial sponsors. This e-learning will be updated to reflect that from 31 January 2022, SUSARs will be sent to EudraVigilance only and are no longer required to be sent to Member states. Reporting obligations to ethics committees for trials approved under the Clinical Trials Directive are not changed by this update. More detailed information will be available in due course through the [EudraVigilance training and support webpage](#).

In addition, EMA is updating the EudraVigilance registration process to provide additional registration and user management assistance to non-commercial organisations. An updated EV registration manual has been published on the [EudraVigilance: How to register webpage](#).

Training material update

EMA provides an [extensive online training programme](#) to assist users in preparing for CTIS. Twenty two out of twenty four modules from the CTIS training catalogue are now available on the CTIS online modular training programme page. In December 2021, modules related to the CTIS public search and Union Controls were published. The module on transition of ongoing trials from Directive/EudraCT to CTR/CTIS (module 23) is expected to be published by end of January 2022.

Further updates will follow after CTIS go-live, such as the publication of a module on Business Intelligence (BI) tools, as well as revisions of the published modules to reflect updated CTIS system functionalities.



Image 3.
EMA provides extensive online trainings on CTIS.

CTIS Training environment (“CTIS Sandbox”)

Following the closure of the survey on 31 October 2021 (Survey 1.0) for clinical trials sponsors to express interest in access to the CTIS training environment (CTIS Sandbox), expressions have been evaluated and initial replies were provided by EMA to respondents in December 2021. On this basis, access will next be provided to those organisations with an intention to submit clinical trial applications in the first quarter of 2022 and concerned respondents can expect additional correspondence by the end of January 2022.

The survey to express interest and including a self-assessment of need and urgency for access to the CTIS training environment has been reopened ([Survey 2.0](#)) for those sponsor organisations who did not respond in October 2021. 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.

EU CTR/CTIS Query management

EMA, the European Commission and Member States have developed a query management process to ensure queries received primarily from associations at EU level that represent clinical trial sponsors about the Clinical Trials Regulation and CTIS are answered in a harmonised way. Associations have agreed to prepare consolidated lists of clear questions to avoid duplication.

Sponsors who have questions regarding CTIS functionalities arising from the use of CTIS are encouraged to first consult the [available training materials and FAQs](#) and [CTIS Sponsor Handbook](#) for answers. If an answer cannot be found in the existing materials, users of CTIS can make use of the [EMA Service Desk](#) as of 31 January 2022.

Sponsors who have queries of a more general nature regarding implementation of the Clinical Trials Regulation should make use of the Commission's guidance documents in [Eudralex volume 10](#), and available best practice documentation from Member States.

If answers cannot be found from these materials, sponsors should contact their national or EU-level associations with their queries. These associations can work with their members to prioritise a list of questions for sharing with EMA, the European Commission and Member States. The creation and submission of such prioritised and consolidated lists of questions will ensure that the most pertinent questions receive prompt responses, without overlapping efforts or duplication.

CTIS press briefing

On 25 January 2022, EMA, the European Commission and the Heads of Medicines Agencies (HMA) held a press briefing on the Clinical Trials Regulation and CTIS. The press briefing described the Clinical Trials Regulation, CTIS and what is changing for clinical trials stakeholders to journalists and other interested parties. The event was livestreamed and open to all to attend. Details and a recording of the event are available [here](#).



Image 4.
EMA, EC and HMA's press briefing on CTR and CTIS.

Protection of personal data in CTIS

Many actors can enter, or have access to, personal data in CTIS while using the system or during the clinical trial lifecycle, including as part of clinical trial authorisation and supervision processes. These actors include the clinical trial sponsors, Marketing Authorisation Applications/ Holders, the European Commission, EMA and the EU/EEA Member States.

To guarantee the protection of personal data in accordance with the requirements of the Regulation (EU) 2016/679 General Data Protection Regulation ([GDPR](#)) and Regulation (EU) 2018/1725 on the protection of personal data by EU institutions and agencies ([EUDPR](#)), a Joint Controllership Arrangement has been established by the European Commission, EMA and Member States in consultation with representatives of industry associations, academia and learned societies.



Image 5.
The JCA guarantees personal data protection in CTIS.

The Joint Controllership Arrangement outlines the role and responsibilities that each party to the Arrangement must deal with regarding processing of personal data in CTIS. It also outlines how the parties must handle personal data breaches related to data processing in CTIS, and measures to ensure the security of processing of personal data in CTIS.

When accessing CTIS for the first time, sponsor, Member State and European Commission users will be made aware of the contents of the JCA before they can progress with the use of CTIS.

The Joint Controllership Arrangement can be found [here](#).

Member States organisation modelling

EMA has conducted Member State organisation modelling sessions with representatives of national competent authorities and ethics committees of each of the 30 EU/EEA Member States. The sessions focussed on user configuration and business processes for the use of CTIS for Member States. Positive feedback was received from Member States about these sessions, which allowed Member State users to experience CTIS hands-on, building competency and gaining insights into ways of working in the system in preparation for go-live.

Accelerating Clinical Trials in the EU (ACT EU): for better clinical trials that address patients' needs

The European Commission (EC), the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) have joined together to optimise the environment for clinical research in Europe by launching Accelerating Clinical Trials in the EU (ACT EU). This initiative will use the momentum of the incoming Clinical Trials Regulation on 31 January 2022 to further promote the development of high quality, safe and effective medicines.

The implementation of ACT EU will contribute to delivering the European medicines agencies network strategy to 2025 and the European Commission's Pharmaceutical Strategy. The ACT EU strategy lists ten priority actions for 2022/2023, including enabling innovative trial methods, establishing a multistakeholder platform, and supporting the modernisation of Good Clinical Practice. Together, they will contribute to achieving the ambitious goals for innovation in clinical trials in the EU. To find out more, please click [here](#) for the joint press release on ACT EU.



Image 6.
EC, HMA and EMA have launched the ACT EU initiative.

Quality requirements concerning IMPs in clinical trials

Following a targeted public consultation in 2021, CHMP has adopted revised versions of the guidelines on quality of chemical and biological Investigational Medicinal Products (IMPs) in clinical trials. The chapters which describe quality changes requiring submission of substantial or non-substantial modifications to the Investigational Medicinal Product Dossier (IMPD) have been updated in line with the provisions of the Clinical Trials Regulation (CTR). Both chemical and biological IMP guidelines now include a summary table of changes to IMPD indicating which type of modification should be submitted in each case.

The documents, to be published shortly, will apply as of the application of the Clinical Trials Regulation on 31 January 2022.

- [Requirements for quality documentation concerning biological investigational medicinal products in clinical trials](#)
- [Requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials](#)

Read [previous issues of CTIS Highlights](#)

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