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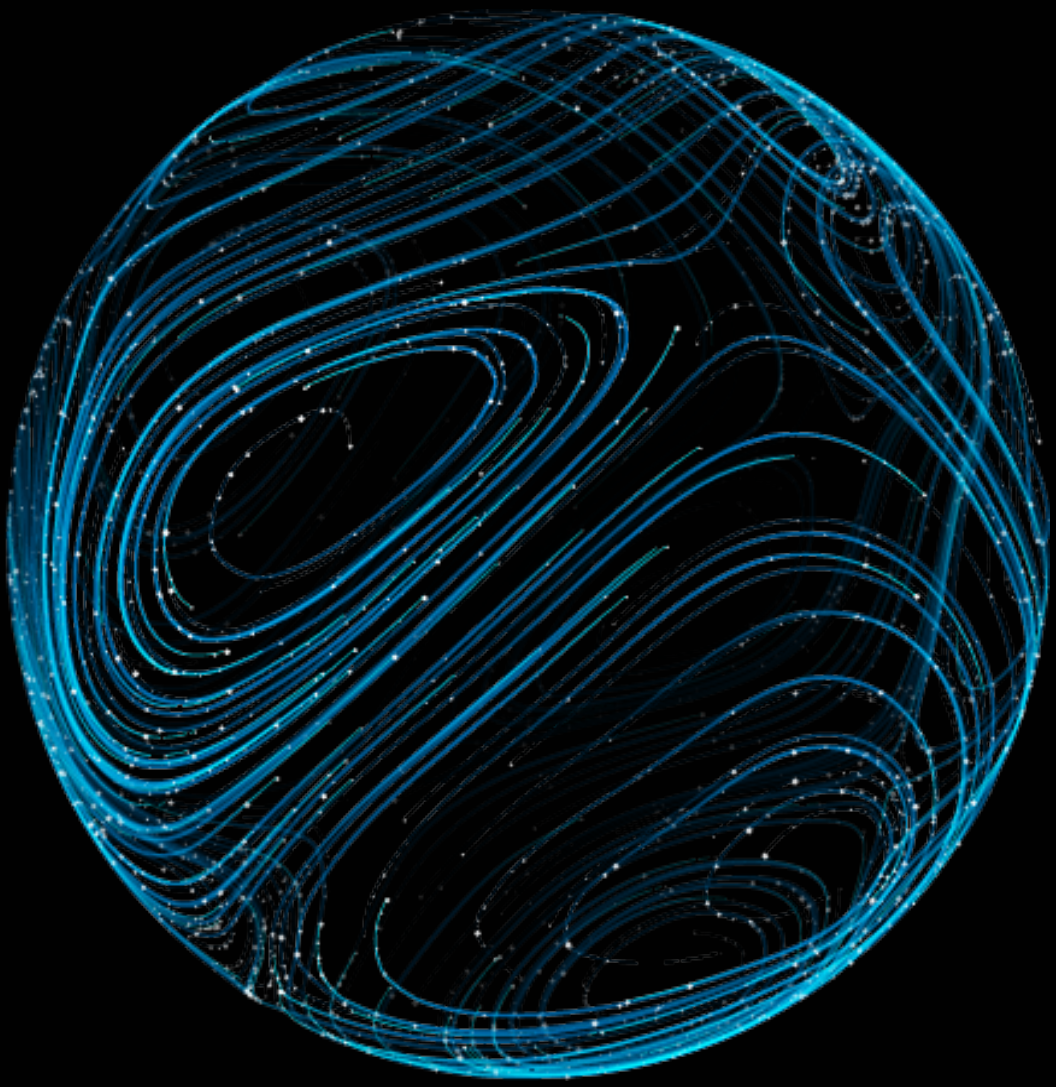


EU Clinical Trial Regulation & Clinical Trial Information System

Optimisation of EU CTR readiness

MAKING AN IMPACT THAT MATTERS since 1845

January, 2023

Abbreviation	Description
ACT	Accelerating Clinical Trials
API	Application Programming Interface
CCI	Commercially Confidential Information
CeSHarP	Clinical electronic Structured Harmonised Protocol
CRO	Contract Research Organisation
CTA	Clinical Trial Application
CTCG	Clinical Trial Coordination Group
CTD	Clinical Trial Directive
CTIS	Clinical Trial Information System
DARWIN	Data Analysis and Real World Interrogation Network
EC	Ethics Committee
EHDS	European Health Data Space
EMA	European Medicines Agency
EU CTR	European Clinical Trial Regulation
ICH	International Conference on Harmonization
ISO IDMP	International Organization for Standardization - Identification of Medicinal Products
KPI	Key Performance Indicators
MS	Member States
MSC	Member State Concerned
MVP	Minimum Viable Product
NCA	National Competent Authority
OMS	Organisation Management Service
PPD	Personal Protected Data
RFI	Requests for Information
xEVMPD	Extended EudraVigilance Medicinal Product Dictionary

Executive summary

The European Clinical Trials Regulation (EU CTR) entered into application on 31 January 2022.

Under the Regulation, clinical trial sponsors and regulators use the Clinical Trials Information System (CTIS) as single-entry point for submission and assessment of clinical trial data. The introduction of the CTIS changes the way how clinical trials in Europe are submitted, authorised and supervised. The CTIS was launched on 31 January 2022, kick-starting the transition period.

On 31 January 2023, the use of the CTIS became mandatory for initial applications of clinical trials with at least one site in the EU/EEA.

Many clinical trial sponsors have already put in significant effort to adjust their processes in order to be compliant with the EU CTR. However, the end of the first year of transition provides an opportune moment to refine EU CTR processes within organisations due to gained CTIS user experience and system updates. In this Point of View we provide an overview of the current state of progress following the first year of transition from the Clinical Trial Directive (CTD) to EU CTR, as well as some of the key challenges industry have faced in preparing for the EU CTR and the transition. In addition, we provide key considerations for transitioning trials and what industry must do to further optimise their EU CTR readiness.

The prompt initiation of action is crucial to the success of the transition. Delaying decisions and actions while awaiting additional information can impede progress and compound the pressure on the organization. An evaluation and optimization of existing EU CTR process solutions already in place within the organization, in conjunction with the incorporation of automation, can enhance efficiency, streamline the transition process and alleviate any strain on resources in the future. Regularly monitoring and refining the transition strategy to maintain its realism and timeliness is critical to ensuring a successful outcome.

The realisation of these steps will enable the EU CTR implementation to unfold its intended benefits of harmonising clinical trials across the EU. By ensuring CTIS readiness is implemented in a comprehensive manner within an organisation, a strong foundation is set for greater standardisation and guidance compliance promoted by ACT EU (Accelerating Clinical Trials in the EU), CeSHarP (ICH M11 Clinical electronic Structured Harmonised Protocol), DARWIN EU (Data Analysis and Real World Interrogation Network), EHDS (European Health Data Space) or ISO IDMP (Identification of Medicinal Products).

One year into transition – What have we learnt?

Since the launch of the CTIS on 31 January 2022, several organisations have obtained hands-on experience with initial submissions in the system. Many organisations have taken steps to ensure compliance with EU CTR such as writing new procedure instructions, setting up dedicated workgroups and performing risk analyses. EMA has been working closely with Member States, the European Commission, clinical trial sponsors and stakeholders to facilitate the change by publishing extensive training materials and guidelines. Despite these preparations, organisations remained hesitant to submit new clinical trial data in the CTIS during the first months of 2022 as indicated in the CTIS Key Performance Indicators (KPI)[1] published by EMA. The numbers also indicated that there are still more Clinical Trial Applications (CTA) uploaded in EudraCT under the CTD compared to initial CTAs submitted in the CTIS under the EU CTR.

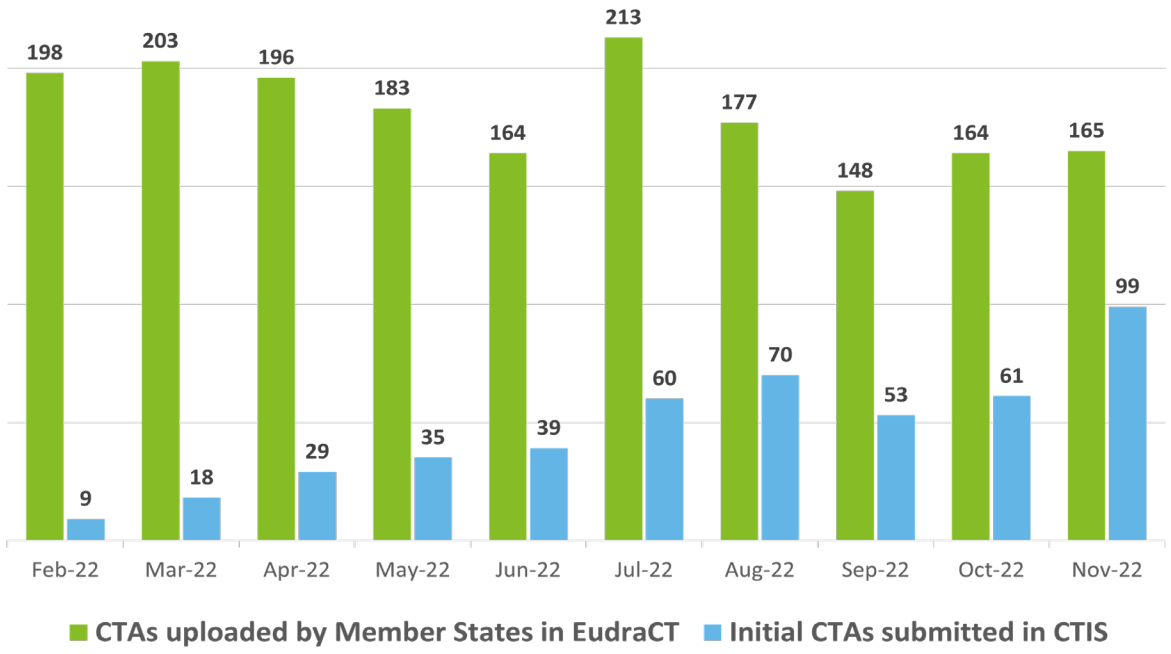


Figure 1: Number of CTAs under the CTD uploaded by Member States in EudraCT vs CTAs under the EU CTR submitted in CTIS.

Moreover, the CTIS KPIs indicated that by 30 November 2022 a total of 473 initial CTAs were submitted in CTIS wherefrom 174 trials received a decision. Despite the recent increase in CTIS submissions, it must be noted that still about 20% of the submitted trials in CTIS are withdrawn, lapsed or not valid.

[1] Key performance indicators to monitor the European clinical trials environment (edition 8), https://www.ema.europa.eu/en/documents/report/key-performance-indicators-kpis-monitor-european-clinical-trials-environment-1-30-november-2022_en.pdf

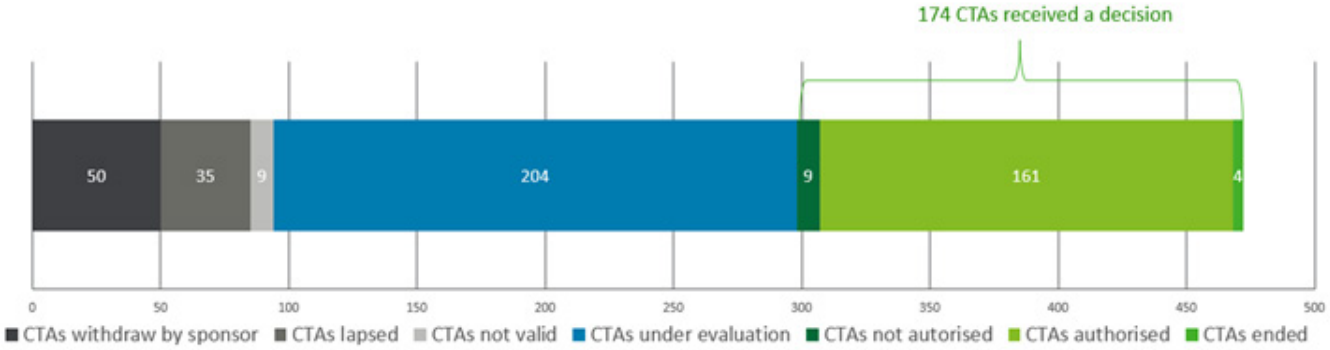


Figure 2: Status level of submitted CTAs in the CTIS.

Companies continue to have questions on how best to prepare their organisations, processes and data to work within the CTIS. With multiple users having experienced problems with the system, organisations have started working together by sharing experiences and lessons learnt. Multiple sponsors, but also Ethics Committees (EC) raised concerns that the CTIS portal suffers from serious deficiencies and have even requested a postponement of the mandatory transition date (31 January 2023).[2]

During the first year of transition, EMA remained in close contact with clinical trial sponsors and Member States to improve the CTIS and user experience. Training materials continue to be regularly updated, training & discussion webinars were planned. EMA has invested in additional resources with the goal to improve the CTIS processes by the time the use of the system becames mandatory for new clinical trial applications on 31 January 2023.

Organisations are advised to keep sharing their hands-on CTIS/EU CTR experiences, stay up-to-date with recent guidance and training and refine their EU CTR processes to increase the percentage of authorised trials and avoid unexpected delays.

[2] Press release from the Working Group of Medical Ethics Committees in the Federal Republic of Germany (28 November 2022), https://www.akek.de/wp-content/uploads/Pressemitteilung-AKEK_28.-November-2022_engl.-Version.pdf

Key challenges – How to tackle them?

Although industry have been preparing for the implementation of the EU CTR, several key challenges remain around transparency, timelines, CTIS developments, national requirements, and submission planning.

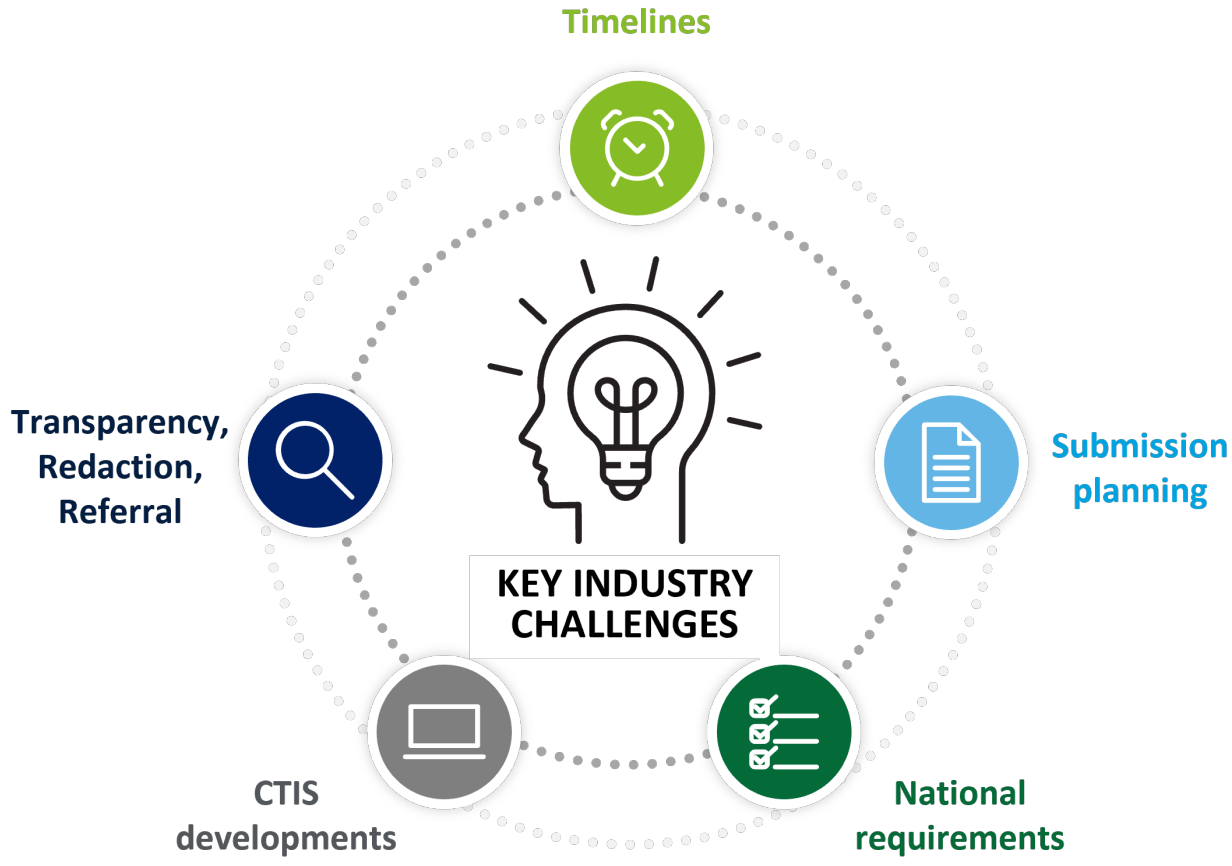


Figure 3. Overview of key challenges after the first year of transitioning to the EU CTR.

Transparency, redaction & referral

An important consideration for organisations is the increased transparency of clinical trial information under the Regulation.

CTIS is a publicly accessible system that contains the data submitted in accordance with the EU CTR which may result in the publication of sensitive information. In order to protect personal protected data (PPD) and commercially confidential information (CCI), organisations must have redaction and deferral strategies (e.g. Standard Operating Procedures) in place to ensure that all documents and data submitted to CTIS are reviewed, redacted and/or deferred according to the EU CTR transparency principles. It should be noted that once deferral periods lapse, the version of the documents "for publication" uploaded in the CTIS will still be automatically published.

Industry have taken various approaches to transparency with some taking a more risk-based approach by applying thorough redaction of documentation and others applying maximum deferral timelines. Determining which approach to take is considered a challenge, deciding whether a more conservative or less conservative approach is best considering the transparency goals of the Regulation.

Various learnings have been collected over the first year of transition. Generally, industry have shared that Member States have not given pushback on requests for deferrals. Some Member States have also indicated that they primarily evaluate the categorisation of the trial itself instead of justification for deferrals. However, some pushback by Member States has been noted on the level of redaction in documents as sponsors tended to redact too much information. It may be prudent for organisations to have justifications for why certain information is redacted from documents as part of the internal redaction processes.

In addition to internal processes, there have also been challenges within the CTIS itself with functionality issues reported for the deferral mechanism; some information of clinical trials was prematurely published on the public website. Temporary mitigations have been put in place until the functionality of the deferral mechanism is restored. These measures include that clinical trials with a decision issued mid-August 2022 onwards, that have any type of deferrals, are not available in the public domain. Sponsors still have the possibility to apply for deferrals of clinical trial data, which will be published in due course once the issue is resolved.

Overall, industry has taken various approaches to addressing transparency. Some have used the opportunity to bring more efficiency into their processes by making documents more redaction friendly, limiting PPD and CCI and using consistent formatting and terminology to facilitate redaction processes. Those that have not would do well to incorporate such efficiencies in their processes and to re-evaluate the current processes to ensure there are no issues around redaction and deferrals in the future.

Timelines

The EU CTR has stricter and shorter timelines which are challenging for both sponsors as well as for Member States. Some Member States have been updating their internal procedures based on recent CTIS experiences in order to complete their evaluation tasks on time.

Sponsors with hands-on experience with clinical trial submissions cite timely responses to Requests for Information (RFI) as a major challenge. The Regulation requires a 12-day turnaround for RFI responses.

Organisations have taken various approaches to addressing this timeline, by for example setting up rapid response teams to ensure timely responses to RFIs and to update translations. Moreover, CTIS does not send notifications outside of the system meaning that sponsors need to have dedicated resources in place to monitor and follow-up on CTA statuses daily. An additional challenge may be the involvement of third parties such as Contract Research Organizations (CROs) in clinical trial processes, requiring clear agreements between parties to ensure that RFIs are responded to in a timely manner. Organisations are therefore advised to have clear procedures in place to tackle the challenging RFI timelines.

CTIS development

One of the key challenges for both industry and Member States has been the technical issues with the CTIS. Over the past year, several challenges with the system have come to light, including site registration and technical problems across various fields in CTIS. A list of known issues and proposed workarounds has been released by EMA including an overview of improvements in functionality[3].

The CTIS continues to be updated and issues are being addressed. Examples of some of the issues that have been raised and resolved are:

1. File size: There were issues around the document size limit, the limit has now been increased to 50 MB.
2. Site registration: Difficulties were observed when entering site information in EMA's Organisation Management Service (OMS) for facilities that are not part of national business registries, such as private clinicals and hospitals. New CTIS features enables the creation of those organisations direct in CTIS, without the need to register them in OMS.

Meanwhile, the CTCG (Clinical Trial Coordination Group) has released a "Best Practice Guide for Sponsors of document naming in CTIS"[4]. For the document's codes and titles, it is recommended to adhere to the structure of EU CTR Annex 1.[5] Version number and date should not be in the document title, instead indicate the correct version number and date in the corresponding fields in the upload window.

[3] Website outages and system releases, https://euclinicaltrials.eu/website-outages-and-system-releases

Industry have also made suggestions for further improvement of the CTIS. For example, a request has been made to add the option to produce an overview of all submitted and approved documents for filing purposes. Both sponsor and Member State representatives issued calls for development of an Application Programming Interface (API) that would improve efficiency of the application process.

Despite recent CTIS improvements, many of the issues have led to delays in CTA submissions, RFI response submissions and have impacted overall planning at both the sponsor and Member State side, resulting in timelines for recruitment being pushed back. Organisations should be aware of this impact and take this into account in the planning of submissions (new and transitioning) to ensure they can submit clinical trial applications in 2023 and beyond. Besides having procedures in place with regards to the use of CTIS, it is also recommended for organisations to have clear procedures related to the use of other systems that are linked to CTIS for example EudraVigilance system, Extended EudraVigilance Medicinal Product Dictionary (xEVMPD) registrations and OMS organisation registrations.

National requirements

The EU CTR aims to harmonise clinical trial processes and information across Europe. However, such harmonisation has not been seen across Member States. Member States continue to apply national requirements on the submission documentation. Mixed messages have been shared by Member States with some reflecting EMA and the Commissions guidance that there is no legal basis to request additional documentation beyond the EU CTR, whereas the reality is that others are continuing to request such information. Industry have expressed frustration regarding the differences in national requirements and specifically the lack of transparency around this.

Currently, there is no single overview of the national requirements per Member State for part II documentation. As support, a set of part II document templates was developed6 and a list has been created that indicates where sponsors can find the national requirements per Member State[7].

[4] Best Practice Guide for Sponsors of document naming in CTIS, https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2022_09_CTCG_Instruction_naming_documents_CTIS_EU_v1.4.pdf

[5] Regulation (EU) No 536/2014, https://health.ec.europa.eu/system/files/2016-11/reg_2014_536_en_0.pdf

[6] Part II application document templates, https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014

[7] Regulation (EU) No 536/2014: Questions & Answers (version 6.3, December 2022), https://health.ec.europa.eu/system/files/2022-12/regulation5362014_qa_en.pdf

Submission strategy

Besides having clear CTIS processes and resources in place, organisations are also advised to revise their submission strategies based on recent experiences with the EU CTR/CTIS.

The selection of the submission procedure and (Reporting) Member State are influencing the approval timelines and therefore also downstream planning and recruitment targets.

There are various approaches to CTIS submissions, including the following:

Submission strategy		Pros	Cons
Full	Submit part I and part II at the same time to multiple countries	Trial can start in all MSC on the same time after being approved	Preparation time may be longer to collect documents for all MSC
Staggered	Submit first part I followed later by part II	More time available to create country specific documents like Informed Consent Form	Part II documents can only be submitted once conclusion of part I is available
Mixed	Submit a whole application (part I and II) to some Member States Concerned (MSC) and at the same time an application limited to part I only to other MSCs	Some countries will receive full approval and can start recruitment after decision while more time can be used to develop part II documents for MSC whereby document collection/ preparation takes more time	More time needed to start the clinical trial in all countries, Part II documents for some MSC can only be submitted once conclusion of part I is available

Table 1. Overview of pros and cons per type of submission strategy.

Each procedure has its pros and cons which sponsors should evaluate for each trial separately, as each trial has its own specific milestones and objectives (see Table 1).

The selection of the (Reporting) Member State also influences the timelines. For example, in a multi-country trial, the last Member State notifying its decision determines when a subsequent addition of a Member State can be submitted (the "slowest" MS drives the process).

Member States have been setting-up different internal procedures to process CTIS applications resulting in different experiences, review timelines but also different levels of support towards the sponsors with regards to national requirements. Across the EU, the average time from submission to reporting date is currently 85 days. Member States such as France, Germany, Spain and Italy have built relevant experience with the CTIS as they received the most clinical trial applications as Member State according to the CTIS KPIs [8]. However, it is Denmark and Spain who provided the most decisions as Reporting Member State while this number is significantly lower for Italy.

[8] Key performance indicators to monitor the European clinical trials environment (edition 8), https://www.ema.europa.eu/en/documents/report/key-performance-indicators-kpis-monitor-european-clinical-trials-environment-1-30-november-2022_en.pdf

Transition your trials – Where to begin?

Transitioning to the EU Clinical Trials Regulation is only required for trials authorised under the Clinical Trial Directive, which will have at least one site active in the EU/EEA countries on 31 January 2025. Only active clinical trials without any pending/ongoing assessment in any of the EU/EEA countries are eligible for a switch of the regulatory regime.

31 January 2023 marked the start of the second year of transition post CTIS launch. Previously, sponsors could choose to either apply for a new CTA under the CTD using EudraCT, or under the EU CTR using CTIS. With the start of the second year of transition only the second option is possible for new CTAs. Furthermore, the addition of new Member States is no longer possible under the CTD since 31 January 2023. Trials authorised under the CTD must first be transitioned to the EU CTR before an additional MSC can be added by submitting a substantial modification using CTIS.

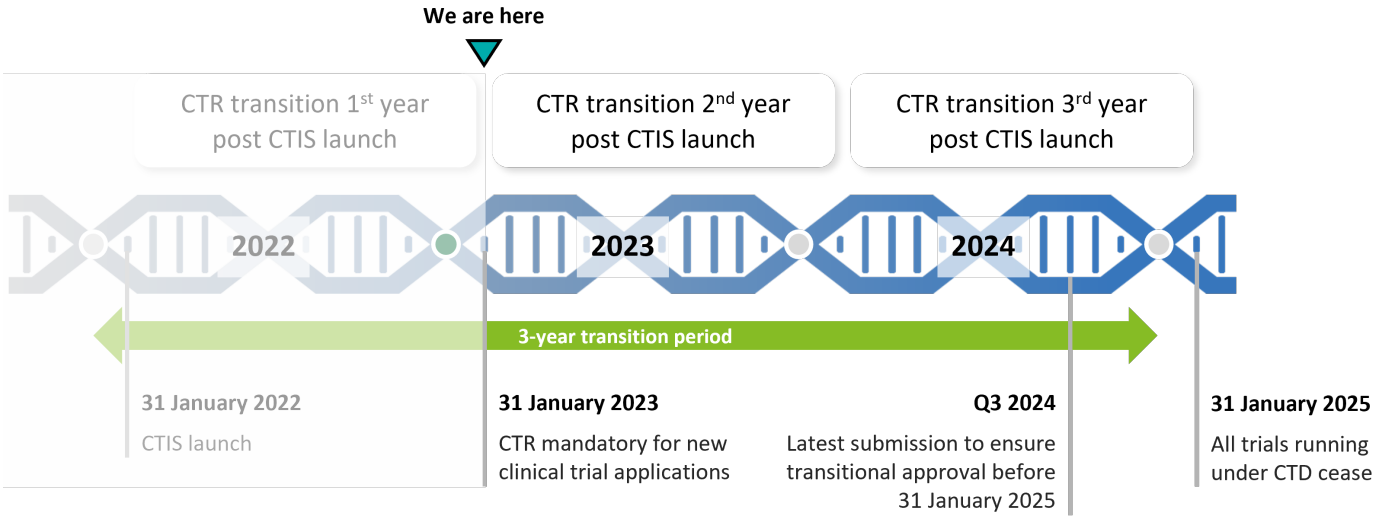


Figure 4. Schematic representation of the three-year EU CTR transition period.

At any time during the three-year transition period (31 January 2022 to 31 January 2025), clinical trials can be transitioned to the EU CTR via the CTIS without the need to discontinue the trial or to put the trial on hold.

Important to understand is that ongoing clinical trials can continue to run under the CTD only until 31 January 2025. Before this date all ongoing trials needs to be transitioned to the EU CTR. If the end of trial is notified in all EU Member States before 31 January 2025, transitioning of the trial is not necessary even in the case where the global end of trial has not yet been reached. Paediatric trials that are being conducted entirely outside the EU/EEA but for which a EudraCT number has been issued should not be transitioned.

Generally, the submission of a clinical trial transition to the EU CTR is only required for those Member States where the trial is ongoing. From the moment the transition application is authorised in each MSC, the EU CTR applies in its entirety.

Principles and considerations for transitioning trials

Clinical trials authorised under the CTD and that will run beyond 31 January 2025 can be transitioned if they:

- are interventional clinical trials in humans;
- involve at least one site in the EU/EEA where the trial is ongoing;
- are not on hold; and
- have no substantial modifications ongoing in any Member State Concerned.

Overall, the sponsor retains the responsibility to assess and declare compliance with all principles and documentary requirements (see Annex I of the EU CTR [9]) when transitioning from the CTD to the EU CTR. This includes the documentation of the transition application dossier. It is critical for a successful transition that the dossier of the transition application reflects the application that was already approved by an EC and authorised by a National Competent Authority (NCA) under the CTD. A re-assessment of the dossier by the MSC during transitioning will not be performed as documentation on the basis of which the ongoing trial was authorised is already available within the Member States. For multinational trials, a submission for transition should only be submitted to those MSCs where the trial is ongoing. It should be noted that applications according to Article 11 of the EU CTR (sequential application for part I and part II authorisation) are not allowed when transitioning ongoing clinical trials.

To transition, sponsors must ensure that the clinical trial has a harmonised or consolidated protocol (see Table 2) approved under the CTD in all MSCs prior to transitioning. Next to this, all other documents common to all MSCs are required to be harmonised across Member States (part I documents other than the protocol, e.g. the investigator brochure).

Member States will check compliance of the transition application documents with the EU CTR during the validation phase.

Harmonised protocol	**Consolidated protocol**
Identical protocol that includes identical trial procedures in all countries has been approved across all EU Member States	Preparation time may be longer to collect documents for all MSC

Table 2. Main difference between harmonised and consolidated protocol.

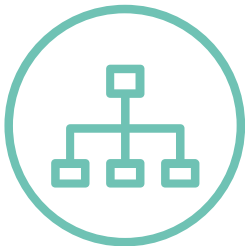
In case the documentation of a clinical trial does not comply with the principles and requirements of the EU CTR, sponsors need to request a substantial modification under the CTD, specifying its intention to align the trial with the CTR, before switching the regulatory regime. Only after acceptance of the substantial modification can the sponsor start the transition procedure. Such issues highlight the importance of timely planning. Industry should ensure that there is enough time to transition a study, leaving room for unforeseen issues such as non-compliance with the EU CTR.

[9] Regulation (EU) No 536/2014, https://health.ec.europa.eu/system/files/2016-11/reg_2014_536_en_0.pdf

Solely active clinical trials without any pending/ongoing assessment of the documents required in any of the EU/EEA countries are eligible for a switch of the regulatory regime. That means, that for example temporarily halted trials cannot be transitioned before restart of the trial. Trials for which a modification is pending must obtain the result of the assessment before applying for transition. Once a clinical trial is (tacitly) approved under the EU CTR, sponsors must comply with all requirements and obligations of the EU CTR, for example publication of summary, trial notifications, GMP requirements and GCP inspections.

Transitioning application must reflect previously approved application

Clinical trials authorised under the CTD can transit to the CTR upon submission and authorisation of a transitioning application. The application must reflect the application that was already approved by the Ethics Committee and authorised by a National Competent Authority under the CTD. A re-assessment will not be performed.



Transition of multinational trials

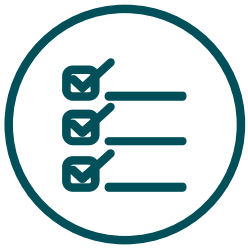
A submission for transition of a multinational trial should only be submitted to those MSCs where the trial is still ongoing. In order to transition, all documents common to all MSCs other than the protocol are required to be harmonised across Member States.

Harmonised or consolidated protocol required

With regards to the protocol, sponsors are required to have a harmonised or consolidated protocol approved under the CTD prior to transitioning.

Substantial amendment may be required prior to transition

If a clinical trial would not comply with the CTR, a sponsor shall request a substantial amendment under the CTD before switching to the regulatory regime of the CTR. Once accepted, the transition procedure can start.



Submission of results under CTD

EurdaCT will remain operational for the submission of trial results and global end of trial even after 31 January 2025.

Figure 5. Key principles and considerations for transitioning clinical trials from the CTD to the EU CTR.

There are many considerations for transitioning clinical trials, some of which industry can foresee (e.g. creating harmonised documents for multinational studies) and other organisations may come across as they go through a transition (e.g. non-compliance with documentation, incomplete documentation in initial submission). For this reason, it is highly advisably to plan and to take such foreseen and potentially unforeseen issues into account to ensure there are no delays in transition or that studies must be terminated due to not being transitioned in time.

Defining an optimal transition strategy

With the start of the second year of transition, the definition of an optimal strategy for transitioning ongoing clinical trials by sponsors is increasingly important. The analysis and overview of ongoing, submitted and planned clinical trials sets the basis for a successful strategy for transitioning applications/trials to the EU CTR.

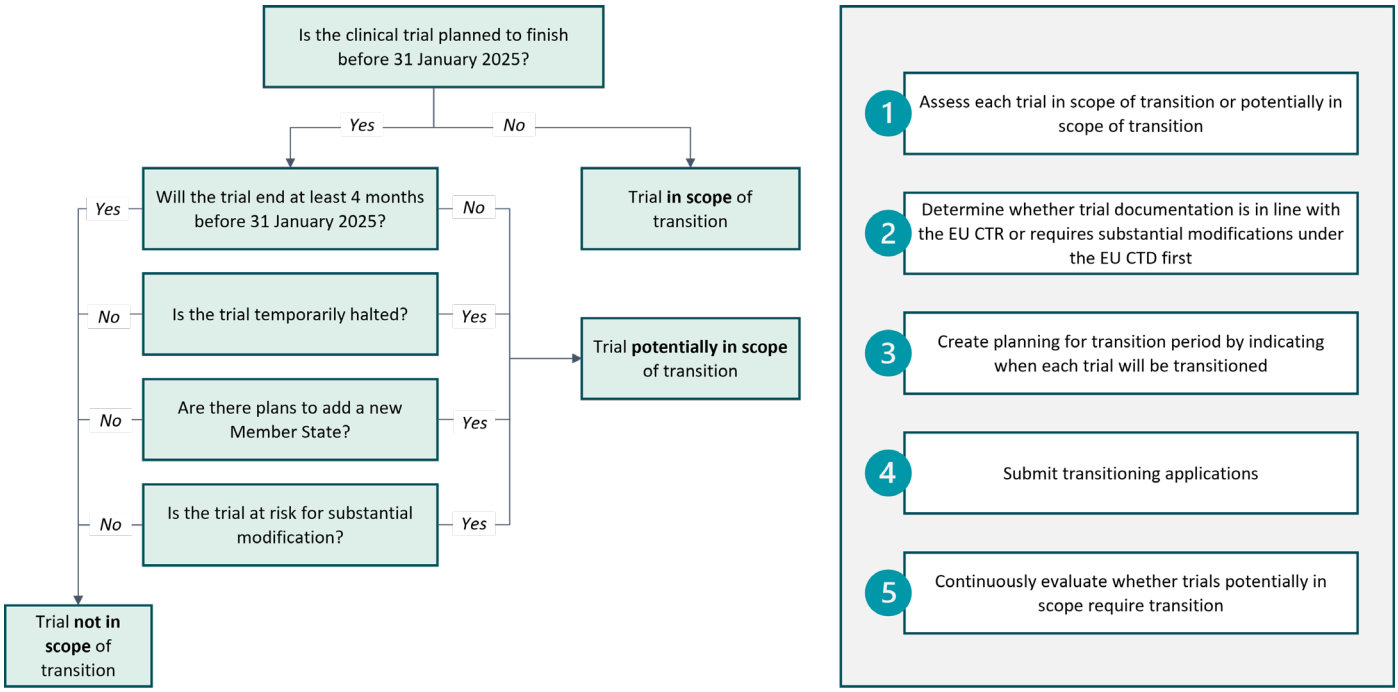


Figure 6. Flow chart to guide the strategy definition for transitioning clinical trials from the CTD to the EU CTR.

The following points are crucial for clinical trial sponsors to ensure clinical trials can be transitioned without risking delays in the submission and approval:

- Carefully assess the clinical trial pipeline to avoid unnecessary transition applications.
- Consider the time needed for the completion of the authorisation procedure and plan to submit the transitioning application early enough before the end of the three-year transition period. Submit the transitioning application latest in Q3 2024 to ensure approval before 31 January 2025.
- Even if a clinical trial is planned to end before the end of the three-year transition period, delays are always possible. A trial which is not transitioned and therefore does not comply with the EU CTR cannot run beyond 31 January 2025.
- Plan for additional time in case the clinical trial currently does not conform with the requirements of the EU CTR. Substantial modifications under the CTD take time.
- Member States are expecting high peaks in the workload for the validation of transitioning application due to new coordination processes between NCAs and ECs. Therefore, additional processing time needs to be considered for transition planning.
- During the transition from the CTD to the EU CTR the clinical trial is not on hold; meaning, patients can receive treatment during the transition. However, it is not possible to apply for modifications until the transition procedure is complete. It is therefore recommended to select a stable moment in the trial to perform the regime switch.
- In the CTIS, the upload of blank documents is allowed for transitioning trials for documents that were previously not required. The sponsor needs to complete the clinical trial dossier in line with the EU CTR requirements, at the latest at the time of authorisation of the first substantial modification of a given document.
- As for any initial application in the CTIS, the selection of the Reporting Member State is mandatory also for transitioning trials. However, the selection of the EC is integrated in the EU CTR process and will no longer be part of sponsors' submission strategy

In terms of transparency, transitioning applications are falling under the same requirements as any other application under the EU CTR. These transparency rules (redaction and deferrals) do not apply retroactively for notifications and reports issued under the CTD, but any new notification as of the moment of the transition of a trial will fall under the transparency rules of the EU CTR.

Optimisation of EU CTR readiness – What does that mean?

With the first year of transition behind us, stakeholders including EMA, clinical trial sponsors, and Member States have had a chance to prepare for EU CTR and have gained experience with the Regulation and specifically the Clinical Trial Information System. Numerous new guidelines and Frequently Asked Questions documents have been published to provide additional guidance. As additional information has become available over the past year, and with submissions of new CTAs under EU CTR in CTIS being mandatory since of 31 January 2023, it is a crucial moment to re-evaluate and refine previously defined EU CTR processes within organisations. **Additionally, clinical trial sponsors must ensure all studies in scope of transition can be transitioned within the next two years.**

In a previously published article "EU Clinical Trial Regulation & the Clinical Trial Information System: Preparing for the implementation of EU CTR and CTIS go-live", an EU CTR implementation programme was proposed consisting of three different strata[10]:

- Foundational = minimum viable product (MVP)
- Managed = foundation + data management and monitoring
- Automation = foundation & managed + automated processes and intelligent digitalisation.

This programme remains relevant, albeit with a slight shift in focus. Most sponsors will have gone through the foundational steps in order to prepare their organisation for EU CTR, adjusting internal processes to be compliant with EU CTR and suitable for interactions with CTIS. Although these initial steps have been taken, a re-evaluation of processes is advisable to ensure that clinical trial applications can continue to be submitted after 31 January 2023 and can continue to run following 31 January 2025 when the transition period will come to an end.

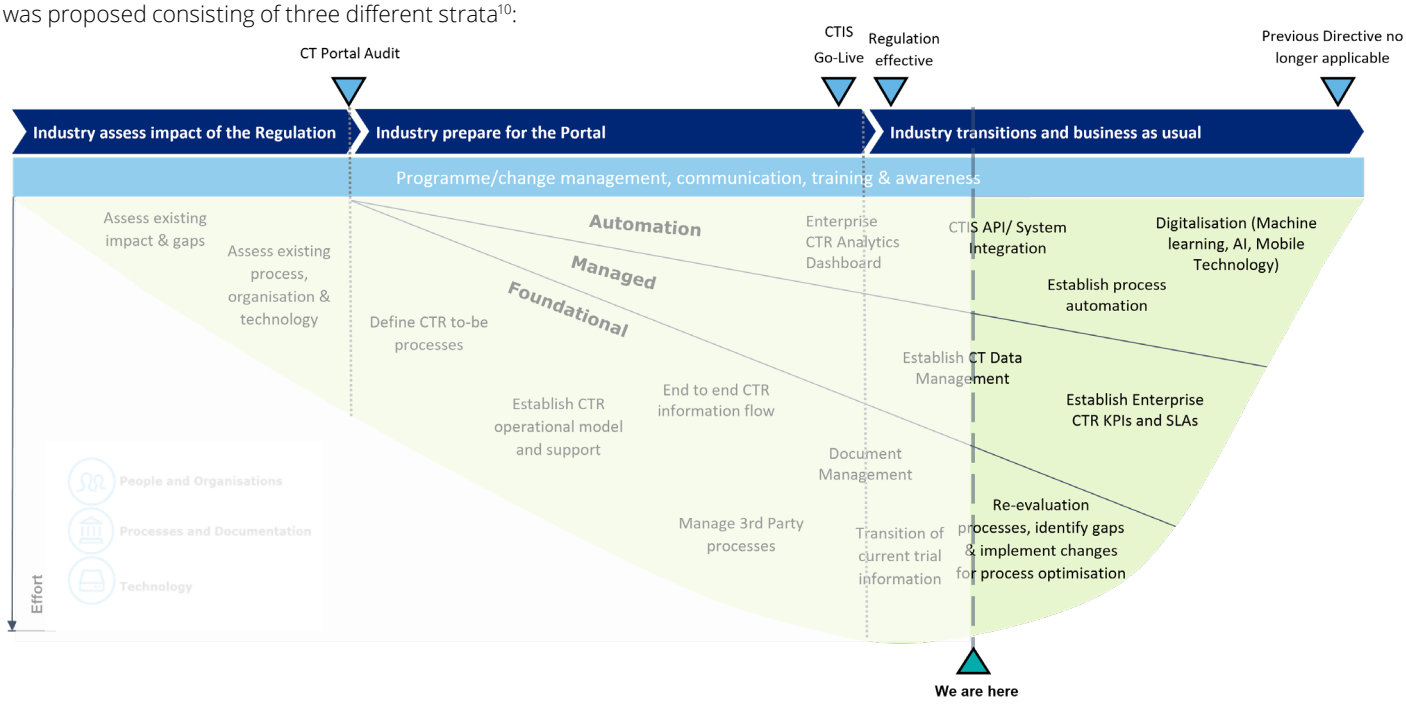


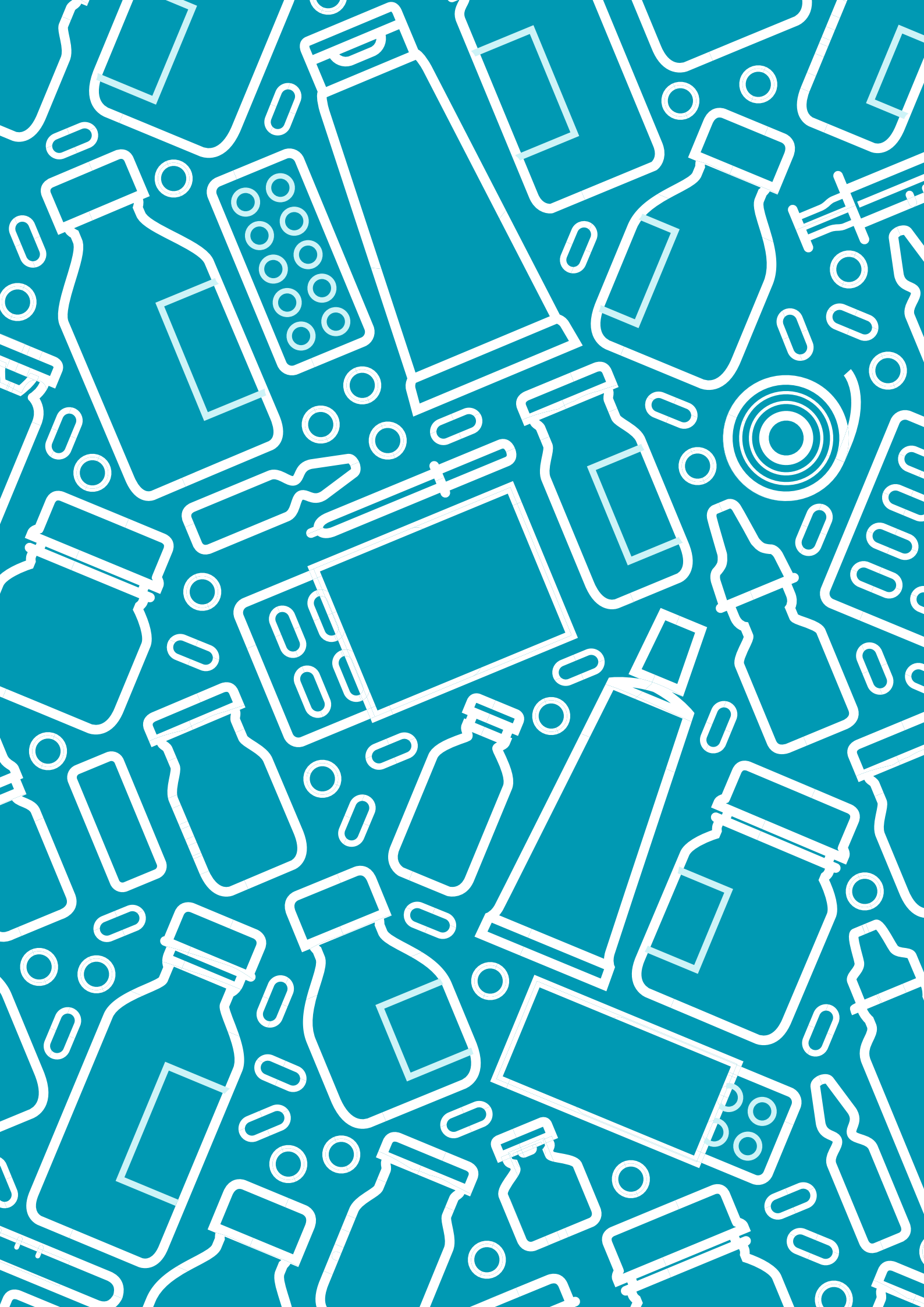
Figure 7. Overview of EU CTR implementation programme.

[10] EU Clinical Trial Regulation & the Clinical Trial Information System: Preparing for the implementation of EU CTR and CTIS go-live, https://www2.deloitte.com/nl/nl/pages/risk/articles/eu-clinical-trials-regulation-go-live.html

With re-evaluation in mind, the following foundational steps should be taken in order to ensure optimisation of EU CTR readiness.

Foundational steps for optimisation of EU CTR readiness	
Lessons Learnt Workshop	Lessons Learnt Workshop(s) can be organised with internal and external stakeholders to discuss the current clinical trial operations under EU CTR and the key challenges faced so far. This workshop or workshops may engage stakeholders that have been involved in EU CTR preparedness so far, representatives of stakeholders impacted by the changes, and possibly third parties such as CROs and translators. Inclusion of experience shared by other clinical trial
Gap Analysis	Based on the findings from the Lessons Learnt Workshop(s) and the most recent information from the EMA, identify any gaps in the current processes. To determine the gaps, questions regarding organisational structure, types of submissions and tooling for CTIS submission should be considered.
Identification of Needs & Actions	Based on identified gaps, determine the needs and potential required actions to address the gaps and to ensure future-proof clinical trials
Implementation of changes to optimise processes	Address needs and implement defined actions to optimise processes and ensure clinical trial applications can be submitted via CTIS in a timely manner and ongoing trials can continue to run post 31 January 2025.

Table 3. Foundational steps for optimisation of EU CTR readiness.



Conclusion

The first year of the transition period was a valuable learning experience for sponsors who had already submitted trials under the EU CTR, as well as for Member States. In 2023, the choice between the CTD and EU CTR for new clinical trials is no longer be an option. The focus of the second phase of the transition period, between January 2023 and January 2025, will be the complete transition of ongoing trials in scope of transition.

This period provides an opportunity for sponsors to turn their achieved EU CTR readiness into an optimised strategy to fully benefit from the EU CTR. It is important that the known challenges of the EU CTR and any issues discovered through the first year of CTIS operation be addressed and reflected in designing the updated approach.

Three essential considerations to navigate transition

01. Be proactive and take action now

The first transition year was rich in industry experience. Waiting for still more information to be revealed will deliver diminishing returns and potentially further increase the time pressure on your organisation to adjust.

02. Review the current EU CTR process solutions already implemented by your organisation

and search for opportunities for optimisation. Refine and monitor your transition strategy to ensure that the plan remains realistic and allows for timely transition.

03. Consider opportunities for implementing (semi-) automated process elements

to increase efficiency in submission preparation. Planning for leaner processes now could prevent time and resource strain in the long run.

If you have any questions do not hesitate to reach out to our authors and contacts with any questions should your organisation seek support for this critical transition.

Useful links

1. Regulation (EU) No 536/2014, https://health.ec.europa.eu/system/files/2016-11/reg_2014_536_en_0.pdf
2. Clinical Trials highlights, https://www.ema.europa.eu/en/news-events/publications/newsletters#clinical-trials-highlights-section
3. Part II application document templates, https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014
4. Handbook for clinical trial sponsors, https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support#handbook-for-clinical-trial-sponsors-section
5. Reference materials for clinical trial sponsors, https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support#reference-materials-for-clinical-trial-sponsors-section
6. Regulation (EU) No 536/2014: Questions & Answers (version 6.3, December 2022), https://health.ec.europa.eu/system/files/2022-12/regulation5362014_qa_en.pdf
7. Guidance document on how to approach the protection of personal data and commercially confidential information in documents uploaded and published in the Clinical Trial Information System (CTIS), https://www.ema.europa.eu/en/documents/other/draft-guidance-document-how-approach-protection-personal-data-commercially-confidential-information_en.pdf
8. Industry Webinar Introduction to OMS services and activities, https://www.youtube.com/watch?v=fxMpsgDnWZY
9. CTIS training and information events, https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support#training-and-information-events-section

Authors and contacts

Speak to our experts

We have extensive experience in supporting regulators and top pharmaceutical companies to prepare for new Life Science Regulations, and since 2014 we have been helping organisations prepare for the implementation of the Clinical Trials Regulation. We are skilled with differentiating and setting up regulatory frameworks in challenging and diverse jurisdictions. We pride ourselves in supporting organisations in defining and executing optimal strategies for CTR implementation and ensuring they are and remain responsible businesses.

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