28 June 2024

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Clinical Trials Information System (CTIS) Programme

Clinical Trials Information System (CTIS) - Sponsor Handbook

A compilation of key guidance, technical information, recommendations, and references for getting ready for the use of CTIS

Executive summary

The aim of the EMA CTIS Sponsor Handbook ('Handbook') is to provide clinical trial (CT) sponsors representing pharmaceutical industry, SME (small and medium-sized enterprises), academia, research organisations and other clinical trial sponsor organisations with the information they need to navigate the Clinical Trials Information System (CTIS) - to create and submit clinical trial information to the member states of the European Union as required by the Clinical Trial Regulation [CTR: Regulation (EU) No 536/2014]. The Regulation harmonises the assessment and supervision processes for clinical trials throughout the EU/EEA, via CTIS. CTIS contains the centralised EU portal and database for clinical trials foreseen by the Regulation.

The Handbook addresses key questions on CTIS and provides a compilation and references to key guidance, technical information, recommendations, training materials, and supportive documentation to facilitate the submission and assessment of CTAs and additional information during the lifecycle of a trial.

It has been developed by the European Medicines Agency (EMA) in collaboration with representatives of industry stakeholders.

The Handbook will be revised as more information becomes available, or system functionalities are updated. It is best used in conjunction with the many references to which it points, for example, Volume 10 of the publication 'The rules governing medicinal products in the European Union' that contains guidance documents applying to clinical trials (EudraLex - Volume 10 - Clinical trials guidelines).

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Document evolution

Version	Version description	Date
1.0	This first version of the CTIS Sponsor Handbook contains prioritised topics. Additional topics will be inserted/completed in the document and updates will be provided in the next versions.	28 July 2021
2.0	Updated handbook sections: - Editorial changes across the document - OMS registration process (section 3.2.1) *updated* - User personas and organisation models (section 4.5) *updated with new links* - Product management in CTIS (section 5) *updated* - Transition from Directive to Regulation (section 6) *updated* - Data fields and documents specifications (sections 7.1.3) *new* - SUSARs reporting (section 8.1) *updated* - Training environment for user training and organisation preparedness (section 10.4) *new*	30 November 2021
3.0	This document has been revised to its third version since CTIS went live. Updated handbook sections follow: - Editorial changes and reference updates across the document - Executive summary *updated* - Overview of Clinical Trial Application (CTA) process in CTIS – from submission to decision and reporting (section 1.2) *updated* - CTIS go-live date (section 1.3) *updated* - Organisation and Sponsor Administrator registration (section 2.2) *updated* - Key user management concepts in CTIS (section 3.1) *updated*	29 November 2022

Version	Version description	Date
	- Marketing Authorisation Holder (MAH) group of users (section 3.5) *new* - How to get a clinical trial application started in CTIS (section 4) *new* - Transition from Directive to Clinical Trial Regulation (section 5) *updated* - How to create a transitional trial in CTIS (section 5.3) *new* - How to manage trials transitioned to the CTR in CTIS (section 5.4) *new* - Data, documentation, and processes (section 7) *updated* - Safety reporting obligations (section 9) *updated* - Support (section 10) *updated* - Other references (section 11) *updated*	
3.01	- Minor editorial changes - Update of timelines due dates in CTIS in Section 4.1 - Update of document upload size (section 7.1.3.2) - Clarifications on dates for the transition period (section 5.1, 5.2.2)	December 2022
3.02	- Recording sites locally in CTIS (section 2.2.2) *new* - CTIS Bitesize Talks links *(multiple sections) new* - Multi-factor authorisation in CTIS (section 2.1.1) *new* - Multiple Q&A reference links added (section 10.6) *updated* - Glossary (section 12) *updated*	April 2023
3.03	- Module 7 video links (section 2.2.3) *updated* - Note added to Part II document 'Proof of insurance cover or identification' (section 4.2, table 4.2.5) *updated* - Additional reference materials for CTIS users link (section 4.2) *updated*	October 2023

Version	Version description	Date
	- CTCG guidance on transitional trials link (section 5.1) *updated* - Added link to CTCG Cover letter template for transitional trials (section 5.1) *new* - added link to the Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation *new* - Link Eudralex 10 page - Set of documents applicable to clinical trials authorised under Regulation EU No 536/2014 (sections 5.1 and 9.1) *update* - Maximum number of documents upload in one batch (section 7.1.3.2, table 7.1.3.2.1) *new* - CT Highlights newsletter subscription link (section 10.2) *updated* - CTIS online training modules page (section 10.4) *updated* - CTIS Training Environment Support Service link (section 10.5) *updated* - Added link to Q&A on protection of CCI and personal data in CTIS (section 10.6) *updated* - added link to Conclusion of VHP Procedure (section 11) *update* - ACT EU website link added (section 11) *new* - Reference to EMA Medical Terms Simplifier added (section 12) *new*	
4.0	- Multi-factor Authentication (MFA) in CTIS (section 2.1.1) *updated* - Transition Period (section 5.1) *updated* - Reference document to Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation (section 5.1) *updated* - Trials that should not be transitioned (section 5.2.1) *updated* - Links throughout the document *updated*	June 2024

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1. What CTIS is and what it does

1.1. A brief introduction to CTIS

Digitalisation & Improved Efficiency

CTIS is the **single-entry point** for clinical trials information in the European Union *(*EU) and in the European Economic Area (EEA).

This includes a single clinical trial application dossier, covering clinical trial applications submitted to EU/EEA Member States, including submission to National Competent Authorities (NCAs) and Ethics committees (ECs) and registration of the clinical trial in a public register; all in one integrated submission.

CTIS provides harmonised and simplified **end-to-end electronic application procedures** over the lifecycle of clinical trials across the EU/EEA.

CTIS is, however, not a clinical trial management system. It should therefore not be relied upon by sponsors to store information on a clinical trial. CTIS provides a digital secured archive of documents, decisions, and information on a clinical trial, but sponsors should ensure they utilise their own information management system to store information needed for compliance purposes.

The exchange of information between sponsors and Member States is fully **electronic in CTIS.**

In CTIS, Member States collaborate and **coordinate amongst themselves for the evaluation and supervision of clinical trials resulting in** one single decision per Member State Concerned.

Documents can be uploaded but not created in CTIS.

Increased Transparency

CTIS offers searchable **clinical trial information** to the patient, the healthcare professional, and the general public. Clinical trial **results are available both as a technical summary and in lay language.**

Information can be retrieved by searching for a particular trial or across trials for treatment-related details.

Patient safety in clinical trials is enhanced as CTIS provides an end-to-end electronic solution for safety reporting of trials.

CTIS facilitates a harmonised safety assessment in Europe, supported by agreed assessment report templates.

The clinical trial module of EudraVigilance provides for the electronic reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs) by sponsors and re-routing to Member States.

CTIS delivers an electronic Annual Safety Reports (ASRs) repository.

Support to Innovation & Research

CTIS is a unique intuitive tool that facilitates the submission of clinical trial applications including those for multi-national trials and therefore facilitating investigation of *e.g.* rare diseases. It thereby also supports academic innovative work.

CTIS offers search and export of structured clinical trial data to allow efficient reporting for scientists.

A clinical trial can be extended to more Member States *e.g.* to enhance recruitment rates.

1.2. Overview of Clinical Trial Application (CTA) process in CTIS – from submission to decision and reporting

CTIS is structured in two restricted and secured workspaces (Sponsor and Authority), only accessible to registered users, and a website openly accessible to the general public.

The sponsor workspace provides clinical trial sponsors with the functionalities for submission of CTAs to Member States, and management of information throughout the lifecycle of clinical trials.

The sponsor functionalities include:

- assignment and management of users;
- compilation of clinical trial dossiers;
- receiving of alerts and notices for ongoing trials;
- compilation of responses to requests for information;
- view deadlines, search, and access clinical trials;
- compilation of notifications related to the life cycle of the trial including submission of a summary of clinical study results.

Registered users with the appropriate permissions are able to access the following tabs for their affiliated trials:

The ***clinical trials*** tab provides search functionalities that facilitate users to find specific trials and view information (see module 9 of the CTIS training programme).

The ***notices and alerts*** tab shows the messages triggered by activities that occur during the life cycle of a clinical trial (see module 4 of the CTIS training programme).

The tab for ***requests for information*** –*RFI*– tab provides access to such requests made by Member States Concerned (MSC) for clinical trials, and enables users to view their status, due dates, and other relevant information (see modules 4, 5 and 11 of the CTIS training programme).

The ***User administration*** tab allows management of roles and permissions for all users that are registered in the system (see modules 3 and 7 of the online CTIS training programme).

The CTIS Training Material Catalogue Module 2 provides a high-level overview of CTIS workspaces.

References	Location (area or document)
Clinical Trial Regulation (EMA website)	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation
CTIS Training Material Module 02 'High-level overview of CTIS workspaces and common system functionalities: User Quick Guide'	https://www.ema.europa.eu/documents/other/quick-guide-overview-ctis-workspaces-common-system-functionalities-ctis-training-programme-module-02_en.pdf
CTIS Training Material Module 02 'High-level overview of CTIS workspaces and common system functionalities: CTIS common functionalities, Part A'	https://youtu.be/EgIRpL17WaU
CTIS Training Material Module 03 'User access management'	https://www.ema.europa.eu/documents/other/quick-guide-user-access-management-ctis-training-programme-module-03_en.pdf
CTIS Training Material Module 04 'Support with workload management - Notices & Alerts'	https://www.ema.europa.eu/en/learning-module/workload-management-sponsor/story.html
CTIS Training Material Module 04 'Support with workload management -RFIs'	https://www.youtube.com/watch?v=6z-Q6-LK8Ws
CTIS Training Material Module 05 'Manage a clinical trial through CTIS'	https://www.ema.europa.eu/en/learning-module/manage-ct/story.html
CTIS Training Material Module 09 'Search, view and download information on clinical trials and clinical trial applications: User Quick Guide'	https://www.ema.europa.eu/en/documents/other/quick-guide-how-search-view-download-clinical-trial-clinical-trial-application-sponsors-ctis_en.pdf
CTIS Training Material Module 11 'Respond to requests for information received during the evaluation of a clinical trial application'	https://www.ema.europa.eu/documents/other/step-step-guide-how-respond-requests-information-received-during-evaluation-clinical-trial_en.pdf

1.3. CTIS go-live date

CTIS was launched on 31 January 2022, and the Clinical Trial Regulation has been applicable since then.

In April 2021, the EMA's Management Board confirmed that the system met the agreed requirements following an independent audit of CTIS. On 31 July 2021, the European Commission confirmed 31 January 2022 as the date of entry into application of the Clinical Trials Regulation, and the go-live of CTIS, via publishment of a notice in the Official Journal of the European Union.

Since the launch of CTIS, there has been a 3-year transition period; this is covered in more detail in Section 5 'Transition from Directive to Clinical Trial Regulation'.

References	Location (area or document)
Information on clinical trials in the context of Regulation EU No 536/2014, including the notice published in the OJ (European Commission website)	https://ec.europa.eu/health/human-use/clinical-trials/regulation_en
Information in the context of Regulation EU No 536/2014 (EMA website)	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trial-regulation

2. Getting access to CTIS – registrations

2.1. User self-registration

In order to access the CTIS Sponsor workspace, a user needs to have an active EMA Account.

If the user already uses other EMA applications (e.g. Eudralink, SPOR, IRIS, EudraVigilance, OMS), the user already has an EMA Account and could access the CTIS Sponsor workspace using his/her existing EMA Account credentials.

If the user does not have an active EMA Account, (s)he needs to create one, by self-registration.

The self-registration process is described on the EMA Account Management (IAM) homepage and in Module 03 of the CTIS Training Material Catalogue.

References	Location (area or document)
EMA Account Management homepage	https://register.ema.europa.eu/identityiq/home.html
Getting Started with CTIS: Sponsor Quick guide	https://www.ema.europa.eu/documents/other/getting-started-ctis-sponsor-quick-guide_en.pdf
CTIS Training Material Module 03 'User Access Management: Quick Guide'	https://www.ema.europa.eu/en/documents/other/quick-guide-user-access-management-ctis-training-programme-module-03_en.pdf
CTIS Training Material Module 03 'User Access Management: Frequently Asked Questions (FAQs)'	https://www.ema.europa.eu/en/documents/other/faqs-user-access-management-ctis-training-programme-module-03_en.pdf
CTIS Training Material Module 03 'User Access Management: Videoclip'	https://www.youtube.com/watch?v=VSLYv9l-LcE&ab

2.1.1. Multi-factor authentication in CTIS

The multi-factor authentication (MFA) strategy for user logins to CTIS, for both Sponsor and Member State workspaces, was launched on **1 June 2023**. This process reinforced the security of CTIS user accounts.

For the MFA, it is recommended that each user is equipped with a mobile or an office phone that can be used for second factor authentication. Instructions on setting up MFA for EMA systems are available here.

Please note that MFA is not activated in the CTIS Training Environment.

2.2. Organisation and Sponsor Administrator registration

2.2.1. Organisation registration in OMS

CTIS utilises organisation data from Organisation Management Service (OMS). OMS provides a single source of validated organisation data that can be used as a reference to support EU regulatory activities and business processes. It stores master data comprising organisation name and location address for organisations such as marketing authorisation holders, sponsors, regulatory authorities, trial sites and manufacturers.

If an organisation has already been successfully registered in OMS, its information is public and a user can search and retrieve its details within CTIS to populate the CTA, submit notifications, or to use it for other sponsor-related activities in CTIS (e.g. populate employer's details in personal profile).

The possibility to search and retrieve an organisation in CTIS is available in different areas across CTIS, and these areas are provided in the following table. Users are recommended to register in OMS the organisations in advance to the population of their initial CTA.

Table 2.2.1.1. Search and retrieval of an organisation from OMS in CTIS.

CTIS Location/Situation	OMS data search & retrieval (*through pop-up windows*)
Personal profile	Update employer information
Request a role	Add sponsor organisation
Create new trial	Add sponsor organisation
Part I: 'Trial details' → 'Scientific advice and Paediatric Investigation Plan (PIP)' section	Add a Competent Authority
Part I: 'Sponsor' section	Add Sponsor Legal contact / Add Third party organisation
Part II: Trial Sites	Add site
Serious Breach notification form	Add site (where the breach occurred)

If an organisation is not yet registered in OMS when starting to use CTIS, it is required first to register the organisation via a 'change request'[1] directly on the OMS portal. OMS can register organisations included in a National Business Registry.

It is paramount that requests are supported by valid documentation to achieve a successful OMS validation. Therefore, it is expected that the entity in possession of the valid documentation proceeds with the registration in OMS. Users are urged to access the OMS related training material stored in OMS portal document repository and view the document requirements to submit a change request found in the document 'E - OMS Change Requests'.

Sponsor organisations that are not registered in any National Business Registry and cannot provide EMA with sufficient documentation for their requests as per document 'E - OMS Change Requests', shall attach to their requests a '**CT registration Headed letter'** found as a template in OMS portal document repository.

In case the request raised is incorrect, or it is not supported by the appropriate accompanying documentation, this will result in the OMS validation failing, and the organisation's details will not be retrievable in a subsequent search in OMS for that organisation.

Of note, any party can create a new organisation record in OMS e.g., for a clinical investigator site, CROs, vendors or other facilities etc., that would be required when completing a CTA or submitting a notification in CTIS. Any request should be supported by valid documentation, as explained above, otherwise it will not be possible for the sponsor user to search, select and find that organisation's details again if the OMS request has failed (e.g. to support the registration in OMS of a clinical investigator site/facility, a headed letter document signed and dated by a representative of that organisation, stating the full company name and address, should be provided).

Sponsors should refer to OMS process to ascertain the validation timelines of change requests to be able to search and select the organisation with the address of interest in CTIS. Note that an organisation can have several addresses (linked to the same main ORG-ID) and only one can be selected in CTIS.

References	Location (area or document)
EMA Organisation Management Service (OMS) homepage	https://www.ema.europa.eu/en/human-regulatory/research-development/data-medicines-iso-idmp-standards/spor-master-data/organisation-management-service-oms
Submission of change requests in OMS	https://www.ema.europa.eu/en/human-regulatory/research-development/data-medicines-iso-idmp-standards/spor-master-data/organisation-management-service-oms#submitting-change-requests-section
Industry Webinar Introduction to OMS services and activities	https://www.youtube.com/watch?v=fxMpsgDnWZY&ab

[1] The term 'change request' for OMS refers to an addition of new or modification of existing records in OMS.

2.2.2. Organisation registration locally in CTIS for use in CTIS

If users do not retrieve an organisation further to a search in OMS or in CTIS, they can opt to create the site in CTIS by clicking the button 'New Organisation', which will now appear enabled. It should be noted that this functionality is only available for:

- Part I Sponsor section – Third-party organisations
- Part II – Trial sites
- Serious Breach notifications – Details of the site where the serious breach occurred
- Third Country Inspectorate Inspection – Third country inspection site
- MS Inspections – Inspected site

Organisations that are created locally in CTIS are not validated by EMA. But users are encouraged to keep in mind the OMS data quality standard set when they create their organisations in CTIS, reducing then the possibility to receive RFIs from assessing authorities regarding inaccurate data.

Once users initiate the registration of an organisation in CTIS, it is in DRAFT status and the draft organisation is visible only within the scope of the draft CTA or draft notification, i.e. it does appear when other sponsors (or even the same sponsors who created the organisation) search in CTIS.

Once the CTA or notification, which contains this organisation registered in CTIS (still in DRAFT status) is submitted, the locally registered organisation in CTIS changes from DRAFT status to ACTIVE status. This implies that the organisation is now searchable by other users, including users from different organisations such as other sponsors. Organisations registered locally in CTIS with ACTIVE status are no longer editable (to edit details of the organisation such as address or name or country etc). If users need to update the organisation details whilst responding to an RFI or drafting a substantial modification, they will need to remove the initially created organisation from their application/notification and add a new one by following the process described above.

More details can be found in the Module 03 of the CTIS Training Material Catalogue in Step-by-step guide (Create organisations locally in CTIS).

2.2.3. Sponsor Administrator registration in EMA Account Management portal for use in CTIS

The CTIS Sponsor Administrator is a high-level administrator role requested and managed through the EMA Account Management portal.

A sponsor administrator is required to initiate the management of users in the sponsor workspace.

The request for the Sponsor Administrator role is submitted by the user that will become the Sponsor Administrator for an organisation with a specific organisation identifier (ORG-ID) and will be handled via EMA Account Management portal.

The registration process for the Sponsor Administrator ('Sponsor Admin') role, via the EMA Account Management portal, started on 1 September 2021 and needs to be supported by an appropriate 'Affiliation letter' submitted to EMA at the time of registration. There is also the alternative route of the

External Organisation Administrator, described in the EMA Account Management portal (last link in 'References' table below).

It should be noted that the appointment of the high-level administrator for a sponsor, namely the Sponsor Admin for an organisation, is processed in IAM based on the organisation identifier (Org-ID).

If different Org-IDs for the same organisation exist, they cannot be grouped together in the request to appoint a Sponsor Admin for the purpose of using CTIS, and therefore, each request should be raised individually. However, the same affiliation letter can be used and attached for each individual request.

Once the Sponsor Administrator role is assigned to one person by EMA (or by the External Organisation Administrator of the organisation) on the basis of the validation of the request, the Sponsor Administrator (or the External Organisation Admin) receives automated e-mail notifications of requests from other users wishing to become Sponsor Administrators for the same organisation. The first Sponsor Admin (or the External Organisation Admin) manages such requests in the EMA account Management portal.

EMA does not handle these requests once the first Sponsor Administrator (or an External Organisation Administrator) has been assigned by EMA. The necessity of an 'Affiliation letter', or any other supporting documentation, for these subsequent requests are decided by each organisation internally[2].

Explanatory training material is available in the CTIS Training Material Catalogue, in Module 07 'Management of registered users and Role matrix' and on the EMA Account Management homepage.

References	Location (area or document)
EMA Account Management homepage	https://register.ema.europa.eu/identityiq/home.html
Affiliation letter template	https://register.ema.europa.eu/identityiq/help/affiliation template.docx
CTIS Training Material Module 07 'Management of registered users and Role matrix: Step-by-step Quick Guide (high level Admin)'	https://www.ema.europa.eu/en/documents/other/step-step-guide-high-level-ctis-administrator-management-roles-permissions-ctis-training-programme_en.pdf
CTIS Training Material Module 07 'Management of registered users and Role matrix: Frequently Asked Questions (FAQs) – specific ones'	https://www.ema.europa.eu/en/documents/other/faqs-management-roles-permissions-ctis-training-programme-module-07_en.pdf
CTIS Training Material Module 03 'Frequently Asked Questions (FAQs)'	https://www.ema.europa.eu/documents/other/faqs-user-access-management-ctis-training-programme-module-03_en.pdf
CTIS Training Material Module 07 'How to request roles and how to assign roles to registered users in CTIS' and 'How to amend	https://www.youtube.com/watch?v=CBLVMFC4JeA https://www.youtube.com/watch?v=1CUyQcICyl8

[2] However, proof of affiliation letter is not required once an External Organisation Administrator has been validated in EMA Account Management for a certain organisation.

and revoke roles of registered users in CTIS' Videoclips	
External Organisation Administrator	https://register.ema.europa.eu/identityiq/help/useradmin.html#OrganisationAdmin

3. Management of users and organisations in CTIS

3.1. Key user management concepts in CTIS

There are two approaches to user management in CTIS: the organisation-centric approach and the trial-centric approach.

These approaches have been designed according to the needs of the different types of sponsor organisations that will use CTIS.

Before using CTIS, sponsors should carefully consider which user management approach best fits their organisation.

A full description of each of these approaches, including their advantages and disadvantages, are explained in the reference documents listed below, as well as in Section 3.3 ('Organisation-centric approach - Sponsor Administrator') and section 3.4. ('Trial-centric approach – Clinical Trial Administrator') of this document. Based upon the current experience with user administration for non-commercial sponsors, we recommend considering following the organisation centric approach and to request the help of your Clinical Trial Centre for CTIS operations and CTR compliance.

References	Location (area or document)
CTIS Training Material Module 07 'Creating a clinical trial: Clinical trial centric approach vs organisation centric approach' (Video)	https://www.youtube.com/watch?v=hfzZxwX2W-Y
CTIS Training Material Module 07 'Management of registered users and role matrix'	https://www.ema.europa.eu/en/learning-module/management-roles/story.html

3.2. User roles concept in CTIS

In order to perform an action in CTIS, such as preparing, submitting or viewing a CTA, notifications, summary of results or clinical study reports, a user must be assigned with a CTIS user role to obtain appropriate permissions.

Up to 18 sponsor user roles are foreseen for CTIS. The profile of a user can be built with a combination of different roles, to allow the user to complete various actions in CTIS. Users with administrator roles (high-level administrator, clinical trial administrator) can assign roles to other users, enabling them to perform actions.

Each role in CTIS comes with a specific set of permissions, which are predefined levels of actions that users can perform on data and documents stored in CTIS. These permissions are at user management level (reserved for administrator user roles) and access level, ranging from viewing to creating, preparing and submitting clinical trial information in CTIS.

EMA has prepared a document to describe the concept of user roles and permissions in detail, a Role Matrix, which outlines the permissions linked to each user role, and a summary of roles document. These documents can be found at the links below.

References	Location (area or document)
CTIS Training Material Module 07 'Management of registered users and role matrix'	https://www.ema.europa.eu/en/learning-module/management-roles/story.html
Sponsors Business Processes and Roles	https://www.ema.europa.eu/documents/other/sponsors-business-processes-roles-ctis-training-programme-module-07_en.pdf
Sponsor workspace: summary of role permissions - Sponsor Workspace Roles - permission matrix summary	https://www.ema.europa.eu/documents/other/roles-permissions-matrix-summary-sponsors-workspace-ctis-training-programme-module-07_en.pdf

3.3. Organisation-centric approach - Sponsor Administrator

The organisation-centric approach is one of two user management approaches in CTIS that can be used by sponsors of a clinical trial. It is intended to serve the needs of organisations and/or sponsors that run multiple clinical trials.

The organisation-centric approach means that user management is done at organisation level.

Under the organisation-centric approach, the sponsor needs to appoint a high-level administrator (Sponsor Administrator). The Sponsor Administrator must be registered in EMA Account Management platform (see Section 2.2.2 on 'Sponsor Administrator registration in EMA Account Management portal for use in CTIS').

Before a user can register as a high-level administrator for a sponsor organisation, this organisation needs to be registered with the Organisation Management Service (OMS); see Section 2.2.1 on 'Organisation registration in OMS for use in CTIS'.

Management of users within the organisation is done at the organisation level with a top-down model. Once appointed, sponsor administrators can assign medium-level administrator (i.e. clinical trial administrator) and business roles to users in CTIS to perform user management or business activities. In the organisation-centric approach, users become affiliated to the organisation (in particular, the user becomes affiliated to the ORG-ID number as registered in OMS) of the sponsor administrator in CTIS when they are assigned with a role by this administrator.

The organisation-centric approach is particularly useful for organisations that (will) conduct trials on a regular basis, even if the frequency is low. The advantages of this approach are that it allows the

management of access and roles across trials within one organisation thus, supporting data quality and integrity through a top-down validation process, as well as ensuring security as a user can only create a new CTA for that organisation-ID, as registered in OMS, if it has been previously assigned the clinical trial administrator (CT Administrator) role by the sponsor administrator.

Note: a user needs to be given the role of CT Administrator with scope 'all trials' in order to be able to create one or more new CTAs, copy or resubmit a trial for that organisation-ID.

Additional information is published on the EMA Corporate website under the Training Programme - User access management (Module 03).

References	Location (area or document)
EMA Account Management homepage	https://register.ema.europa.eu/identityiq/home.html
CTIS Training Material Module 03 'User access management: User Quick Guide'	https://www.ema.europa.eu/en/documents/other/quick-guide-user-access-management-ctis-training-programme-module-03_en.pdf

3.4. Trial-centric approach – Clinical Trial Administrator

The trial-centric approach is one of two user management approaches in CTIS. A user is automatically guided to use this approach in CTIS only in the case a sponsor administrator has not been registered and appointed in the EMA account management system for a specific organisation.

In this approach, when the user initiates the creation of a new CTA, the system checks if a sponsor administrator has been appointed for the sponsor organisation selected for that initial CTA. If that is not the case, the user will be able to proceed becoming the clinical trial administrator for that particular trial.

Further allocation of other CT Administrator or business roles to users is then done at trial level. The clinical trial administrator can manage users only for the trial(s) of his/her concern and can perform all sponsor business activities in CTIS related only to that particular trial(s).

In the trial-centric approach, users follow a bottom-up model that supports an easy way of submitting a limited number of CTAs and straightforward management of a small number of users at trial level, not organisation level.

This approach is intended to serve the needs of small organisations and specifically academic sponsors, which may initiate trials on an *ad hoc* basis. It allows for the management of a smaller number of users and one or very limited numbers of clinical trials. This allows a faster process (no need for registration of a high-level sponsor administrator) when submitting a first initial, and subsequent applications, as applicable. However, it is less secure as any user can, potentially, create a trial on behalf of a sponsor organization that has not previously registered a sponsor administrator. Moreover, no individual user will have a centralised oversight of the trials being conducted for that sponsor organization nor the users involved.

Additional information is published on the EMA corporate website under the Training Programme - User access management (Module 03).

References	Location (area or document)
CTIS Training Material Module 03 'User access management: User Quick Guide'	https://www.ema.europa.eu/en/documents/other/quick-guide-user-access-management-ctis-training-programme-module-03_en.pdf

3.5. Marketing Authorisation Holder (MAH) group of users

A MAH Administrator role is also available to support the submission of clinical study reports into CTIS when a trial has been included in a marketing authorisation application. The registration process for MAH Administrator takes place via CTIS Service Desk, with the submission of a valid cover letter, including the required information. More details on this process can be found in the CTIS Training Material Module 13 'Clinical study reports submissions'.

References	Location (area or document)
CTIS Training Material Module 13 'Clinical study reports submissions'	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-ctis-online-modular-training-programme#sponsor-workspace-section

3.6. CTIS user personas and organisation models

Sponsors have various processes, structures and partnerships for managing clinical trials. In order to facilitate the completion of processes in CTIS, sponsors must understand the CTIS User Management functionalities and how to best make use of these functionalities in their organisational environment. Sponsors also need to understand user roles so that they can ensure that they have the correct confidentiality agreements in place.

To assist sponsors in understanding the CTIS User Management functionalities and how to organise in CTIS, EMA has published CTIS user personas linked to CTIS user roles and permissions, and example sponsor organisation models in CTIS.

References	Location (area or document)
CTIS sponsor user personas	https://www.ema.europa.eu/documents/other/clinical-trial-information-system-ctis-sponsor-user-personas_en.pdf
Principles for sponsor organisation modelling in CTIS	https://www.ema.europa.eu/documents/other/principles-sponsor-organisation-modelling-ctis_en.pdf

4. How to get a clinical trial application started in CTIS

4.1. Introduction

Under the organisation-centric approach, the Sponsor Administrator needs to organise access for the users based on the interactions that they will have in the system. It is essential that the permissions granted, and the scope of the role (trial specific or all trials) are understood to enable the relevant navigation, access to data and documents accordingly but also to enable activities in the system as required. Refer to Sections 2. and 3.

In case, the trial centric approach is selected, the CT administrator needs to organise user access based on the interactions users should have in the system to fulfil the sponsor's obligations.

It is important that in advance of any interactions with the system, sponsor users get familiarised with the use and navigation in CTIS. It is recommended that initially a small team of users is assigned to navigate to perform activities in CTIS for a given trial/application. These users are strongly recommended to get experience first on the CTIS Training environment (see Section 10.5.).

This approach enables familiarisation with CTIS and facilitates readiness and preparation of dossier to ease member state assessment.

To create and prepare any type of clinical trial applications in CTIS, several training materials including step-by-step, e-learning and videos can be consulted (module 10). Section 4.2 presents the various subsections of the clinical trial application tab as they need to be completed and their corresponding dedicated training materials. An overview of the documents available to be submitted in CTIS is also presented. Section 4.3 presents the navigation of the evaluation tab and the timelines that provide information on the assessment activities once the clinical trial application has been submitted. All timelines due dates in CTIS follow Central European Time (CET), regardless of the seasons of the year.

4.2. Drafting of the clinical trial application dossier

Table 4.2.1. Create a CTA

Step process 1: Create a CTA	Location (area or document)
Create a clinical trial application (Step-by-step guide)	https://www.ema.europa.eu/en/documents/other/step-step-guide-create-submit-withdraw-clinical-trial-application-nonsubstantial-modifications-ctis_en.pdf
Create a clinical trial application (E-learning)	https://www.ema.europa.eu/en/learning-module/create-ct-application/story.html

Table 4.2.2. Populate MSC & Form sections

Step process 2: Populate MSC & Form sections	Location (area or document)
Complete the MSC and Form sections (video)	https://www.youtube.com/watch?v=1du3VUq4K5g

Table 4.2.3. Populate Part I section

Step Process 3: Populate Part I section	Location (area or document)
Complete the Part I section (video)	https://www.youtube.com/watch?v=piRl9ZGTe-Y
Fill in the trial details of Part I section (video)	https://www.youtube.com/watch?v=q2Qn6p9VnXs
Complete sub section Sponsor details (video)	https://www.youtube.com/watch?v=4HtR_Xtn7pc
Complete sub section Product details (video)	https://www.youtube.com/watch?v=e-JTvFoBlCs Sponsor Handbook v.3.0.3: Section 6 'Product management in CTIS'

Table 4.2.4. Populate Part II section

Step Process 4: Populate Part II section	Location (area or document)
Complete Part II section (video)	https://www.youtube.com/watch?v=jmylMwZFroc

Table 4.2.5. Overview of documents and data available to be submitted in CTIS for an initial CTA.

CTA tabs subsections	CTA placeholders	Document types available for upload[3,4,5]	Note
Form	Cover letter	Cover letter	Refer to the EudraLex vol.10 CTR Q&As and CTR document on content requirements
	Proof of payment	Proof of payment	Where applicable
	Compliance with regulation	Compliance with Regulation (EU) 2016/679	
	Trial category		Complete the relevant data field, see section 7.2.
MSC	Member states concerned		Indicate the proposed RMS
Part I	Trial specific information (Part I) – Trial details		
	Trial identifiers		Provide identifiers of the trial
	Trial information	Low Intervention justification	
	Protocol information	• Protocol • Protocol synopsis • DSMB • Study design	
	Scientific advice and Paediatric Investigation Plan (PIP)	• Summary of scientific advice • Scientific advice–Quality • PIP opinion	
	Associated clinical trials	Sponsor agreement	

[3] Include a document 'not for publication' alongside the document 'for publication' is needed.

[4] Include translations if required; refer to the CTR Q&As (Eudralex vol.10 chapter V)

[5] Only include signed documents if required as per the CTR Q&As (Eudralex vol.10 chapter V)

CTA tabs subsections	CTA placeholders	Document types available for upload[3,4,5]	Note
	References		Provide the PMID[6] number if available
	Countries outside the EEA		Add non-EEA country if applicable
	Trial specific information (Part I) – Sponsor details		Refer to the Eudralex vol.10 CTR Q&As on content requirements
	Trial specific information (Part I) – Product details		Reference to content (CTA)
	Role: test	• IB or SmPC • IMPD safety and efficacy • IMPD Quality	Include comparator, placebo or auxiliary product as necessary
	Content labelling	Content labelling of IMP	
Part II	Trial site		
	Recruitment arrangements	Recruitment arrangements	Refer to 'Part II application document templates', available under chapter I of Eudralex vol.10
	Subject information and informed consent form	Subject information and informed consent form	Refer to national requirements
	Suitability of the investigator	• Investigator CV • Suitability of the investigator • Declaration of Interest	
	Suitability of the facilities	Suitability of the facilities	If signed, consider redaction

[6] PubMed Identifier

CTA tabs subsections	CTA placeholders	Document types available for upload[3,4,5]	Note
	Proof of insurance cover or indemnification	Proof of insurance cover or indemnification	Only the certificate of insurance (avoid adding CCI in these documents)
	Financial and other arrangements	Financial and other arrangements	National requirements, e.g. some MS require signed Clinical Trial agreements
	Compliance with national requirements on Data Protection	Compliance with national requirements on Data Protection	Optional only, required by some countries
	Compliance with use of Biological samples	Compliance with use of Biological samples	Optional, only if biological samples are collected

References	Location (area or document)
Technical requirements for optimal use of CTIS	https://www.ema.europa.eu/en/documents/other/clinical-trials-information-system-ctis-technical-requirements-optimal-use_en.pdf
CTIS training material module 10 ‘Create, submit, and withdraw a clinical trial'	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-ctis-online-modular-training-programme#sponsor-workspace-section
Additional reference materials for CTIS users	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support#additional-reference-materials-for-ctis-users-section
CTIS Structured data form Instructions - initial application, additional MSC, substantial and non-substantial modifications	https://www.ema.europa.eu/documents/template-form/clinical-trial-information-system-ctis-structured-data-form-initial-application-additional-member_en.xlsx
List of data and documents requested as a minimum in CTIS to proceed with submission of the different application types	https://www.ema.europa.eu/en/documents/other/checklist-required-fields-application-type-ctis-training-programme-module-10_en.pdf

4.3. Clinical Trial Application under evaluation

Table 4.3.1. Evaluation Tab

The Evaluation tab includes several subsections presenting the assessment overview for the validation, the Part I and the Part II, and the decision for each MSC. The validation, Part I, and Part II sections include an RFI and a conclusion subsection.

Evaluation tab	Location (area or document)
View the tabs for validation, Part I conclusion, Part II conclusion, and decision of a clinical trial application Search, view, and download information on a clinical trial	https://www.ema.europa.eu/en/documents/other/quick-guide-how-search-view-download-clinical-trial-clinical-trial-application-sponsors-ctis_en.pdf
Access, view, and respond to an RFI	https://www.youtube.com/watch?v=vbQVkYi3pGI

The timetables give an overview and progress on the assessment of the particular clinical trial application.

Table 4.3.2. Timetables and Timelines for CTA Assessment

CTA Assessment: Timetables and Timelines	Location (area or document)
View Timetable (video)	https://www.youtube.com/watch?v=HN7zcQW81P0
CTIS Evaluation timelines	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support#evaluation-timelines-section

4.4. Clinical Trial Application after decision

Once the clinical trial application has been authorised, the conclusion to the validation and the assessment phases can be viewed in the evaluation tab. At the bottom of the page, in the assessment overview table, the information is recorded for each member state and includes each MSC's respective decision.

In the event that a MSC would have disagreed to the conclusion 'acceptable' or 'acceptable with conditions' to Part I, this information would be also recorded in that section.

All documents and data authorised for the trial, as a result of the authorisation of the latest application, can be consulted in the tab 'Full Trial Information'.

5. Transition from Directive to Clinical Trial Regulation

5.1. Transition period

There is a 3-year transition period that started on the CTIS go-live date.

Year 1 (31 January 2022 to 30 January 2023):

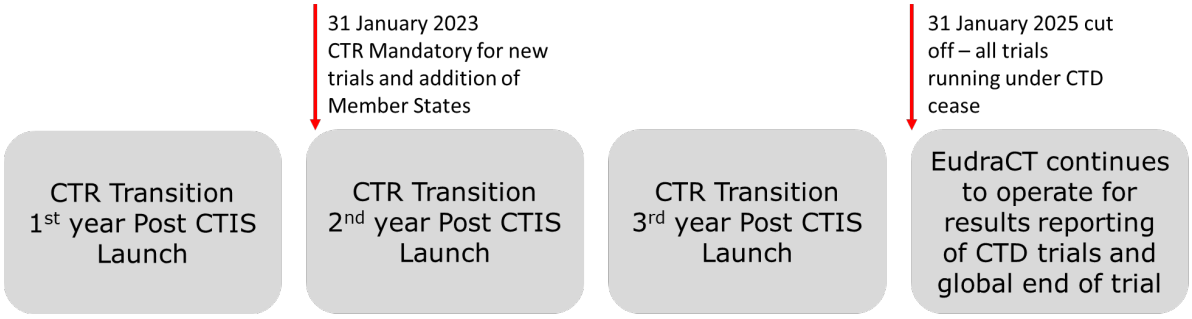
During the first year after CTIS go-live, sponsors could choose whether to apply for a new CTA under the Clinical Trial Directive (CTD: Directive 2001/20/EC), or to apply under the new legislation, the Clinical Trial Regulation (EU) No 536/2014, using CTIS.

Member States were ready to use CTIS and accept applications under the new legislation (CTR) from day 1 of CTIS go-live.

Years 2 and 3 (31 January 2023 to 30 January 2025):

From 31 January 2023, all new CTAs must be submitted under the new legislation (CTR) using CTIS. Submission of new CTAs under the CTD in EudraCT is no longer be available for new CTAs. The addition of new member states is also no longer be possible under the CTD as from 31 January 2023. Trials under the CTD must first be transitioned, and then an Additional Member Stated Concerned Application can be submitted only once the clinical trial dossier has been updated through a substantial modification using CTIS.

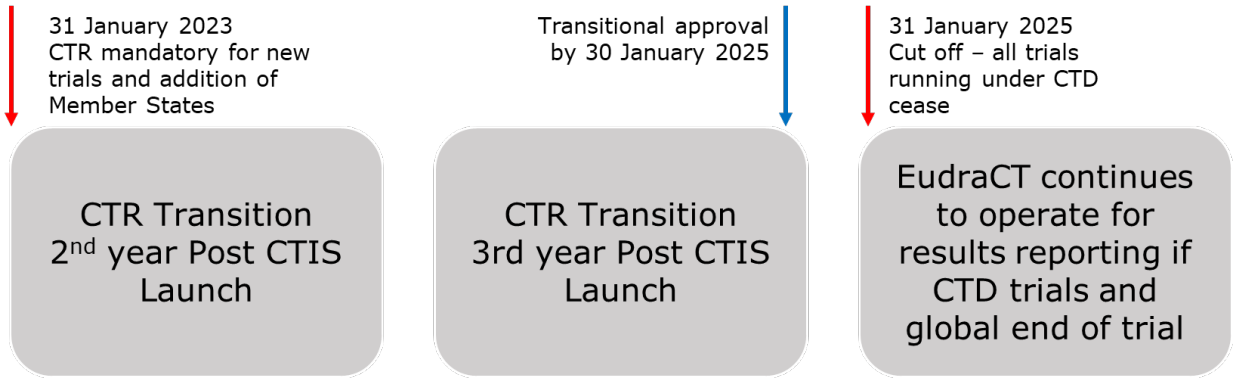
Figure 5.1.1. Schematic representation of the Clinical Trial Regulation transition period.



CTAs that were submitted under the old legislation (CTD), utilising EudraCT, prior to 30 January 2023, will be able to continue to run until completion under that Directive until 30 January 2025. Processes will remain unchanged, and sponsors will therefore be able to submit substantial amendments and end of trial notifications as needed under the Directive. EudraCT will remain operational throughout the transition period to enable these trials to continue.

As from 31 January 2025, clinical trials authorised under the CTD must either have ended in the EU/EEA or have been transitioned. They cannot continue operating under the old legislation utilising EudraCT beyond the end of the 3-year transition period (30 January 2025). Thus, if sponsors are running trials that they expect to continue in EU/EEA beyond 30 January 2025, sponsors need to transition them to the CTR before the transition period expires.

Figure 5.1.2. Schematic representation of the Clinical Trial Regulation transition period from 31 January 2023.



EudraCT will remain active beyond the end of the transition period for sponsors to notify global end of the trial and submission of summary results of trials completed under the Directive.

Transition applications can be submitted at any time during the 3-year transition period and sponsors are urged to ensure that they complete the process early enough in the transition period to ensure continuity of the clinical trial beyond 30 January 2025, taking account of statutory holidays and the two-week winter clock stop.

References	Location (area or document)
Link to EudraLex - Volume 10 - Clinical trials guidelines - Set of documents applicable to clinical trials authorised under Regulation EU No 536/2014[7]	https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1
Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation	https://health.ec.europa.eu/document/download/10c83e6b-2587-420d-9204-d49c2f75f476_en?filename=transition_ct_dir-reg_guidance_en.pdf
CTCG Best Practice Guide for sponsors of multinational clinical trials with different Part I document versions approved in different Member States under the Directive 2001/20/EC that will transition to the Regulation (EU) No. 536/2014	https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2024_03_CTCG_Best_Practice_Guide_for_sponsors.pdf
Annex Cover Letter Template Declaration vs. 4.0	https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2024_03_CTCG_Annex_cover_letter_template_-

[7] The latest published European Commission Clinical Trials Regulation No 536/2014 Q&A document can be found under the 'Set of documents applicable to clinical trials authorised under Regulation EU No 536/2014' section.

	_CTCG_Best_Practice_Guide_for_sponsors_on_transition_vs4.docx

5.2. Points to consider on transitional arrangements

Some aspects have been included here of what the sponsor should consider when defining a submission strategy for CTIS during the transition period.

5.2.1. What trials should not be transitioned

- Trials that have already ended or will end before the end of the transition period in the EU/EEA should not be transitioned.
- If an end of trial notification has been submitted in all EU/EEA member states, but the global end of the trial has not been notified, the trial should not need to be transitioned. Global end of the trial and trial summary results should be posted via EudraCT under the Directive.
- Trials that are old and started prior to the Directive 2001/20/EC coming into application do not benefit from the transition process. If they are truly interventional and need to continue to run after the end of the CTR transition period, then a new CTA under the CTR needs to be submitted.
- Paediatric trials that are being conducted entirely outside the EU/EEA but for which a EudraCT number has been created should also not be transitioned.

5.2.2. Can the trial be transitioned?

Only trials submitted under the CTD and likely to be ongoing beyond 30 January 2025 need to be transitioned if they meet these criteria:

- are interventional clinical trials in humans;
- involve at least one active site in the EU/EEA where the trial is still ongoing;
- there are no substantial amendments ongoing in any Member State Concerned (MSC) under the Directive.

Details of the requirements for transitioning of mono-national and multi-national trials are provided in the EudraLex Volume 10 Q&A mentioned in the References table above.

General considerations:

Sponsors need to ensure that all current approved documents under the Directive are available in electronic format in compliance with CTIS upload requirements (see section 7.1.3. ‘Data fields and document specifications’).

Retrospective documents do not need to be submitted to CTIS (e.g. earlier versions of IBs or Protocols that have been superseded under the CTD). Only current approved versions should be included in the transition application.

Where a mandatory document is expected to be uploaded into the CTIS that does not exist for the transitioning trial (e.g. site suitability documentation), then a blank document is expected to be uploaded with a comment that the document does not apply and it has been provided to allow transition from the CTD to the CTR Regulation.

When completing the CTA, and providing the CT data and documents in CTIS, consideration should be given to the transparency requirements of the CTR, including the need to remove personal data from submitted documentation, if applicable: see chapter 8. on transparency of data.

Mono-national trials:

The trial is transitioned from the CTD to the CTR by submitting a new application in CTIS that reflects the content of the dossier that is currently approved and has been assessed by the MSC. Documentation required is specified in the question 9 to the Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation the available in the EudraLex Volume 10

Multi-national trials:

Multi-national clinical trials (trials conducted under the same EudraCT number in different Member States) should be transitioned as a single multi-country CTA under the CTR, utilising a harmonised or at least consolidated protocol Sponsors may need to consider harmonising the protocol by substantial amendments under the CTD before they transition them as one trial under CTR with one EU Clinical Trial number Consolidation of a protocol, to reflect only what is already approved in each MSC prior to submission of a transition application, does not require prior approval via submission of a substantial amendment under the Directive since no changes to the protocol content are made during the consolidation process.

In addition, if a sponsor intends to transition a multi-national clinical trial as a multi-country CTA under the CTR, only data field information and documents for the MSCs where the trial is still ongoing need to be entered in CTIS.

The trial is transitioned from the Directive to the Regulation by submitting a new application in CTIS that reflects the dossier that is currently approved and has been assessed by all the MSCs. If the protocol is not consolidated, the sponsor should first submit a substantial amendment under the Directive in order to align and obtain a harmonised protocol authorised by all Member States before submitting a transition application under the CTR.

Alternatively, for trials where full harmonization of the protocol to be submitted in the Part I of the application cannot be achieved due to different national requirements, a sponsor needs to prepare a consolidated protocol, reflecting the common core provisions and capturing the minor differences as regards the nationally authorised trials (see Reference table above for CTCG's 'Best Practice Guide for sponsors of multinational clinical trials'). The consolidated protocol must correspond to what is authorised in each of the Member States concerned.

For VHP trials being transitioned, the sponsor should propose as the RMS the country that acted as the VHP Reference MS.

For more information regarding the conditions for the transition of multi-national trials refer to the question 10 to the Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation the available in EudraLex Volume 10.

5.2.3. What are the assessment timelines of transitional trials

In CTIS after submission of the dossier, the assessment workflow is triggered and the MSC need to select the RMS in the event of multi-national trials. The validation, assessment Part I, Part II and decision milestones are triggered in the system with the need for MSC to proactively record their conclusions and decisions. Therefore, transitioning a trial from the Directive to the Regulation can take up to a period of 60 days.

It is unlikely that RFI are raised for transitional trials unless the documentation submitted does not correspond with the documents approved under the CTD. In such a case, the timelines would be extended by 15 days in the validation or 31 days in the assessment phase.

5.3. How to create a transitional trial in CTIS

To transition a trial from EudraCT to CTIS, sponsors need to submit an initial CTA marked as a transitional trial. On how to mark their initial CTA as transitional trial, users may follow the instructions of the Quick Guide of CTIS Training Module 23 that is dedicated to transitional trials. Once an initial trial is marked as transitional, additional fields will appear in the application dossier, allowing users to add in their transitional trial the corresponding EudraCT trial number. If sponsors create the trial without marking it as transitional, they cannot correct it at a later stage. They shall create the trial from scratch, marking it this time as transitional.

References	Location (area or document)
CTIS Training Material Module 23 – Transitional trials: 'Quick guide Transitional trials from EudraCT to CTIS'	https://www.ema.europa.eu/en/documents/other/sponsors-guide-transition-trials-eudract-ctis-ctis-training-programme-module-23_en.pdf
CTIS Training Material Module 23 – Transitional trials: 'FAQs Transitional trials from EudraCT to CTIS'	https://www.ema.europa.eu/en/documents/other/faqs-transition-trials-eudract-ctis-ctis-training-programme-module-23_en.pdf

5.4. How to manage trials transitioned to the CTR in CTIS

Once the trial has a recorded authorisation in CTIS, all the requirements of the CTR apply from the date of approval of the transition application under the CTR. The sponsor needs to comply with their CTR obligations for the management of the trial and submit notification information as required. These include start of trial notification and start of recruitment that can have occurred prior to authorisation, but could include further events as they are likely to take place.

Also, any changes to the dossier need to be reflected in line with the requirements of the CTR. Therefore, any subsequent substantial modifications submitted to the MSC need to comply with the requirements of the CTR.

6. Product management in CTIS

6.1. Medicinal product registration in XEVMPD

Before completing the CTA in CTIS, the sponsors should ensure that the details of the medicinal products used in the clinical trials are already registered in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD). It should be noted that a placebo can be added manually in CTIS directly; sponsors do not need to submit placebo's information on the XEVMPD.

The dictionary includes all medicinal products that are authorised in the EU/EEA and unauthorised medicinal products (referred to in the XEVMPD as 'development' products) that are associated with clinical trials. Unauthorised products include those that have not received a marketing authorisation in the EU/EEA for the strength and/or pharmaceutical form.

To submit medicinal product data in the XEVMPD, sponsor organisations must be registered in the Organisation Management Service (OMS) and also with EudraVigilance either via Gateway or the EudraVigilance web application (EVWEB). This application allows registered users to create and send Extended EudraVigilance Product Report Messages (XEVPRMs), receive XEVPRM acknowledgements, view medicinal product information and perform queries.

Consolidated guidance on the electronic submission of information on unauthorised medicinal products for human use in the XEVMPD is now available on the 'Data submission on investigational medicines: guidance for clinical trial sponsors' webpage. The guidance was prepared based on the processes already in use and on information available in existing documentation.

Some high-level details specific for the registration of medicinal products in XEVMPD, to then be used in CTIS, are also presented below to describe the business flow.

The active substance for the development medicinal product must be available in EMA SMS (Substance Management Service).

Substance data is entered and maintained in the XEVMPD by the EMA; when substance information is successfully inserted in the XEVMPD, a substance EV Code is generated by the XEVMPD.

To request the addition of new substance information, or an amendment of existing substance information, in the XEVMPD, sponsors should follow the process described in the 'Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)' document. EMA will validate the request and the substance EV Code will be provided to the sponsor via an e-mail confirmation from the EMA ServiceNow within 4 working days.

If a development medicinal product needs to be entered in the dictionary by the sponsor, the sponsor should submit the medicinal product data in the XEVMPD via an XEVPRM with the operation type 'Insert'.

The medicinal product data must be submitted in accordance with the principles described in section 1 '*Initial submission of a development medicinal product'* of the 'Guidance on the electronic submission of information on investigational medicinal products for human use in the Extended EudraVigilance medicinal product dictionary (XEVMPD)' document. The document also includes information on how to add missing information (for example substance or sponsor details) in the XEVMPD. Providing that the insertion was successful, an EV Code will be assigned to the medicinal product record by the XEVMPD and sent automatically to the sponsors' sender organisation ID via an XEVPRM acknowledgement.

Once the EV Code assigned to the medicinal product record is available in the XEVMPD, the sponsor can search and retrieve the product details in CTIS. More information on associating an unauthorised medicinal product to a CTA can be found in Section 6.4. 'Adding an unauthorised medicinal product in CTIS' of this handbook.

When registering medicinal products in the xEVMPD, sponsors are advised to take into account the publication requirements of the relevant CTIS product data fields, as specified in CTIS application fields. The publication modality and timelines of product-related fields is defined in Annex I of the Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS). Note that fields taken from xEVMPD cannot be further amended in CTIS before publication. As per the xEVMPD guidance, due to the CTIS publication rules **it is recommended that the product name created and entered in xEVMPD does not include the pharmaceutical form nor the strength of the product**.

Training for clinical trial sponsors on how to enter and maintain product information into the XEVMPD is also available (links in the 'References' table below).

References	Location (area or document)
Data submission on investigational medicines: guidance for clinical trial sponsors webpage	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/data-submission-investigational-medicines-guidance-clinical-trial-sponsors
Guidance on the electronic submission of information on investigational medicinal products for human use in the Extended EudraVigilance medicinal product dictionary (XEVMPD)	https://www.ema.europa.eu/en/documents/other/guidance-electronic-submission-information-investigational-medicinal-products-human-use-extended_en.pdf
Electronic submission of investigational medicinal product (IMP) data to the Extended EudraVigilance medicinal product dictionary (XEVMPD) - Frequently asked questions and answers (FAQs)	https://www.ema.europa.eu/en/documents/other/electronic-submission-investigational-medicinal-product-imp-data-extended-eudravigilance-medicinal_.pdf
Extended EudraVigilance medicinal product dictionary (XEVMPD) training webpage	https://www.ema.europa.eu/en/human-regulatory/post-authorisation/data-medicines-iso-idmp-standards/extended-eudravigilance-medicinal-product-dictionary-xevmpd-training
eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) Data-Entry Tool (EVWEB) user manual	https://www.ema.europa.eu/en/documents/other/extended-eudravigilance-medicinal-product-dictionary-xevmpd-data-entry-tool-user-manual_en.pdf
eXtended EudraVigilance Medicinal Product Report Message (XEVPRM) Step-by-Step	https://www.ema.europa.eu/en/documents/other/extended-eudravigilance-medicinal-product-report-message-step-step-guide-insert-development_en.pdf

Guide: Insert of a Development Medicinal Product (DMP)	

6.2. Medicinal product in CTIS extracted from XEVMPD

For each trial in CTIS, the sponsor has to associate at least one medicinal product with the role as 'test' and populate this information in the Part I of an initial CTA.

Other product roles that can be associated to a CTA, as applicable, are: comparator, placebo and auxiliary medicinal product.

In CTIS, the product information (for test product, comparator and auxiliary medicinal product) is retrieved from the XEVMPD and this is enabled by a search and selection functionality available for an authorised product (i.e. a product with a marketing authorisation in the EU/EEA), an active substance, an Anatomical Therapeutic Chemicals (ATC) code and an unauthorised product.

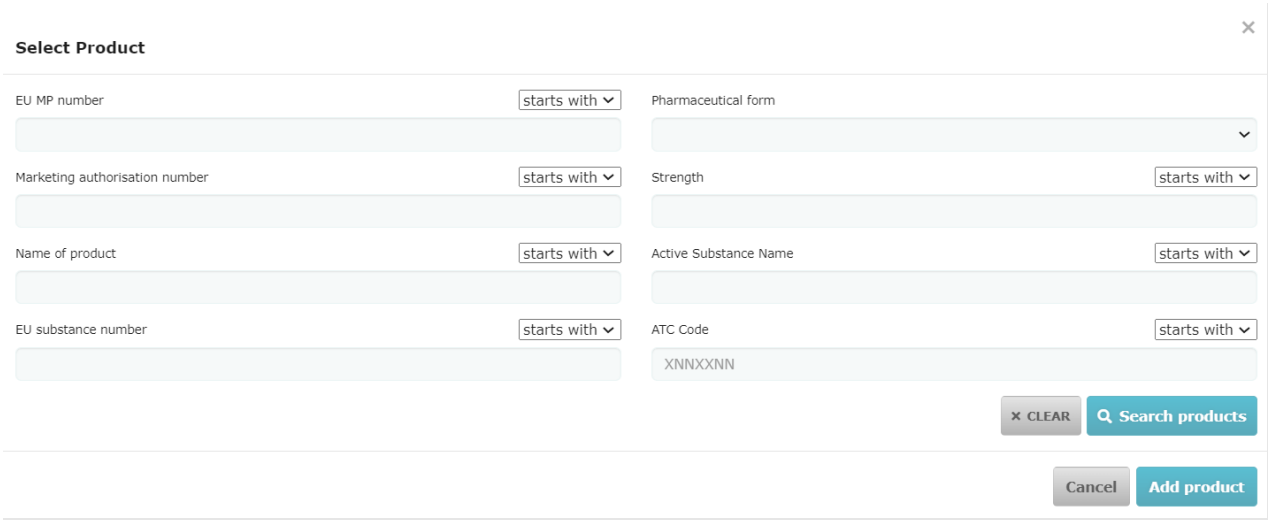
6.3. Adding an authorised medicinal product in CTIS

Medicinal product details in an application form are mandatory. The users can add product details in a CTA for any product role in the trial (test, comparator, auxiliary) by searching and selecting the product details from XEVMPD. Only for placebo, the product details can be specified locally in CTIS.

A user can add an authorised product by searching per product details, active substance, or ATC code, as applicable.

The following parameters are displayed to a user that can search in XEVMPD, via CTIS, for an authorised medicinal product:

Figure 6.3.1. Search for an authorised medicinal product.



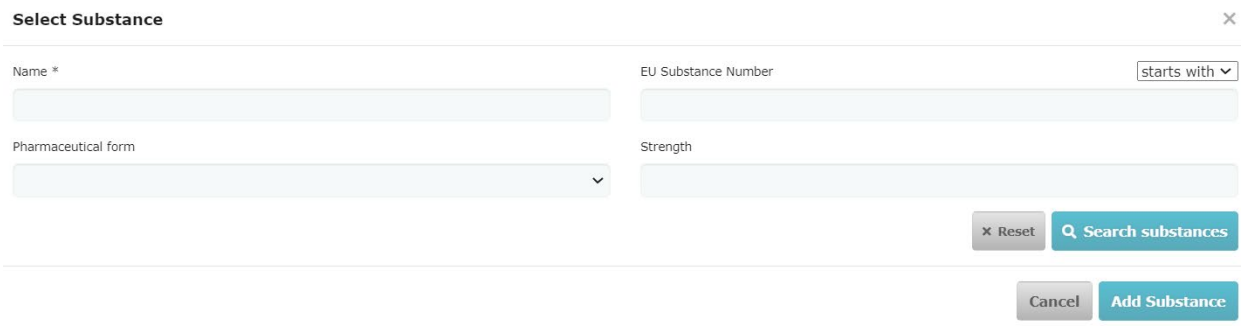
Depending on the parameters used to run the search, the user can get a unique search result returned, or multiple results can be retrieved.

For example, in case of search by EU MP number (i.e. EV Code assigned to a specific medicinal product record) only one result will be returned.

However, if the user is searching for an active substance, a pharmaceutical form or strength of a medicinal product, then multiple results may be returned.

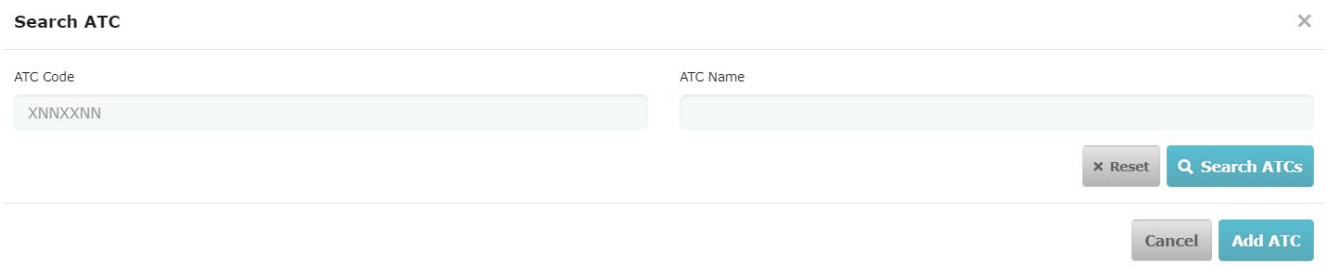
The following parameters are displayed to a user that can search in XEVMPD, via CTIS, for an active substance used in an authorised medicinal product:

Figure 6.3.2. Search for an active substance.



The following parameters are displayed to a user that can search in XEVMPD, via CTIS, for an ATC code (level 3, 4 or 5) associated with an authorised product:

Figure 6.3.3. Search for ATC code (level 3, 4 or 5) associated with an authorised medicinal product.



6.4. Adding an unauthorised medicinal product in CTIS

Unauthorised medicinal product details may contain confidential information and therefore access to this information is restricted.

As explained in Section 6.1 'Medicinal product registration in XEVMPD' above, unauthorised products include those that have not received a marketing authorisation in the EU/EEA for the strength and/or pharmaceutical form.

If an active substance is used in a clinical trial in a new pharmaceutical dose form and/or new strength, a new development medicinal product must be entered in the XEVMPD by the sponsor organisation.

If a medicinal product not yet authorised in the EEA is used in a clinical trial for different indications and/or routes of administration(s), the sponsor can update their existing development medicinal product in XEVMPD with the new indication/route of administration.

Registration of development medicinal products in XEVMPD is independent of the role of the medicinal product in the clinical trial (i.e. test, comparator etc.) before they can be used to populate dossier part I of the CTA in CTIS.

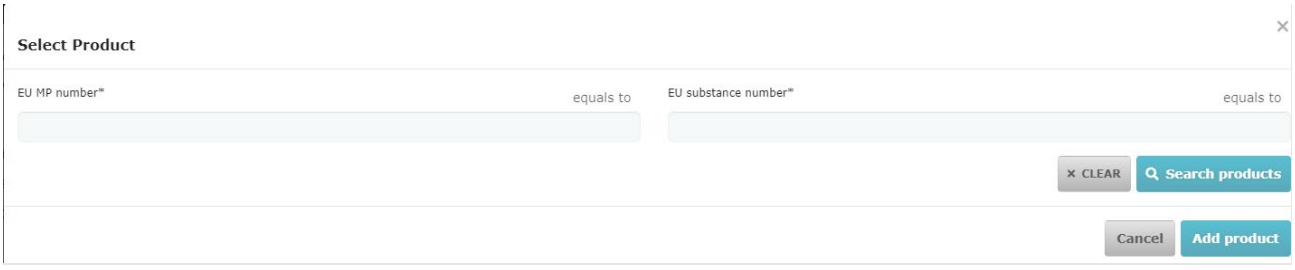
Users can retrieve unauthorised products information in CTIS only by searching for EU MP number (medicinal product EV Code) together with the EU substance number (substance EV Code) referenced in this product in the XEVMPD.

A medicinal product EV Code is a unique number assigned by the XEVMPD to each medicinal product record successfully inserted in the dictionary; it is used to identify this medicinal product in the XEVMPD.

It should be noted that both parameters, namely the medicinal product EV Code and the substance EV Code, are mandatory to run the search in CTIS for unauthorised medicinal product data.

Users have to be cognisant of the required information in order to be able to run the search for development products in XEVMPD and add the product in the CTA of CTIS.

Figure 6.4.1. Search for an unauthorised medicinal product.



Once the medicinal product of interest is identified, the user will see some pre-populated data, as it is available in the XEVMPD. **The strength and pharmaceutical form of the retrieved unauthorised product are not displayed in the draft CTA dossier Part I. This information only becomes visible following the submission of the application to the MSCs.**

More details on the registration of medicinal products in XEVMPD are provided in Section 6.1. of this handbook.

6.5. Medicinal product details in CTIS

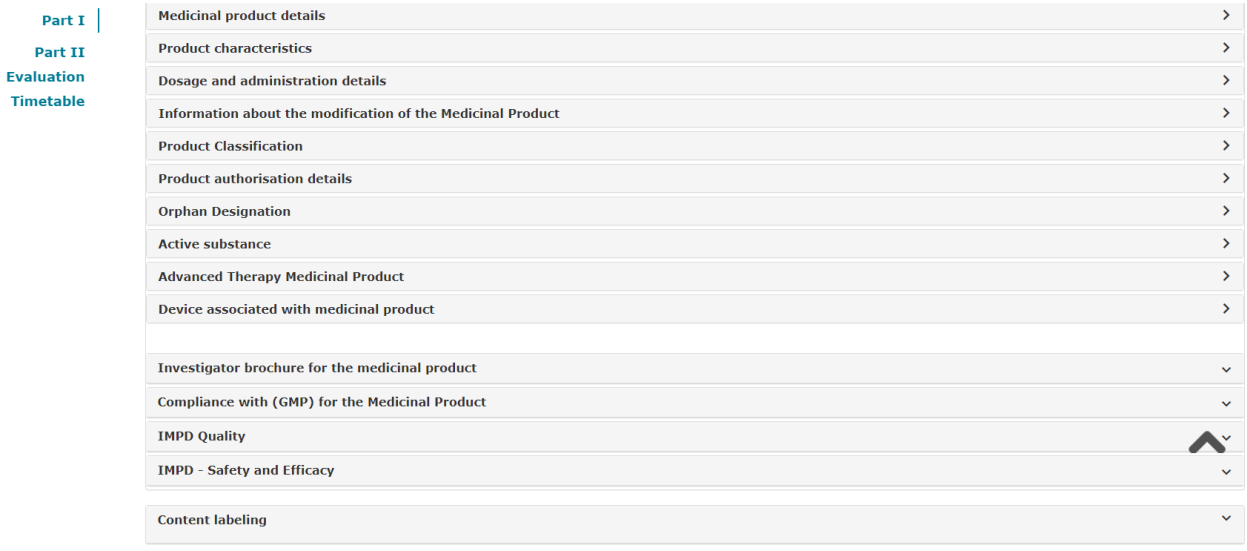
For both authorised and unauthorised products, once the desired medicinal product details are retrieved from XEVMPD, users will see some pre-populated data in CTIS extracted from XEVMPD.

Some additional details, such as the dosage and administration details, information about the medicinal product, Advance Therapy Medicinal Product (ATMP) details (as applicable), and combination with medical device (as applicable), will have to be populated in CTIS.

In addition to the population of the structured data fields in CTIS, for each product, users also have to provide the documents foreseen in the Clinical Trials Regulation, as applicable, namely:

- Investigator Brochure (IB) or the Summary of Product Characteristics (SmPC);
- Investigational Medicinal Product Dossier (IMPD) Quality;
- Investigational Medicinal Product Dossier (IMPD) Safety and Efficacy;
- GMP documentation ;
- Content labelling.

Figure 6.5.1. Additional details for medicinal products (Part I).



For more information, see also training module 10.

References	Location (area or document)
CTIS Training Material Module 10 'Create, submit and withdraw a clinical trial'	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-ctis-online-modular-training-programme#sponsor-workspace-section
'How to submit an initial CTA in the CTIS Sponsor workspace – Fill in the Part I section' (video) - CTIS Training Material Module 10	https://www.youtube.com/watch?v=e-JTvFoBlCs

7. Data, documentation and processes

7.1. Clinical Trial Application (CTA) and Notification Forms

This section intends to provide information on the data fields and documents that sponsors need to complete, as applicable, in the context of clinical trial applications and notifications to be submitted to CTIS. These forms provide an overview of the data fields to be completed, and documents to be provided with the aim to help sponsors prepare in advance, the information required for the submission of an initial CTA, adding Member State Concerned application (MSC), Substantial Modification (SM), non-Substantial Modification, (non-SM) and notifications.

The forms referred to in this document include the attributes of the fields (e.g. character limit).

7.1.1. Clinical Trial Application Form overview of the data fields to be completed and documents to be provided

In the table below, there are references to four Excel documents that list the structured data fields and the documents to be completed. Each data form addresses the information to be provided for any type of clinical trial application, for a multi-trial substantial modification, for the response to a request for information, or for an annual safety report. Each document contains an overview with some relevant instructions followed by the list of the data fields to be completed, and documents to be uploaded for each of the CTIS sections to be prepared for an application: the 'Form' section (4 tabs included, one per application type), 'MSC', 'Part I' and 'Part II' sections. Moreover, the documents include the different searches that the sponsor will need to perform through interfaces with other systems.

References	Location (area or document)
CTIS structured data form - Applications (IN, AMSC, SM, non-SM)	https://www.ema.europa.eu/documents/template-form/ctis-structured-data-form-initial-application-additional-member-state-concerned-substantial_en.xlsx

CTIS structured data form - Applications (Multi trial SM)	https://www.ema.europa.eu/documents/template-form/ctis-structured-data-form-multi-trial-substantial-modification_en.xlsx
CTIS structured data form – Requests for Information	https://www.ema.europa.eu/documents/template-form/clinical-trial-information-system-ctis-structured-data-form-request-information-rfi_en.xlsx
CTIS structured data form – Annual Safety Report	https://www.ema.europa.eu/documents/template-form/clinical-trial-information-system-ctis-structured-data-form-annual-safety-report-asr_en.xlsx

7.1.2. Notification and Results: overview of the data fields to be completed and documents to be provided

The document provided in the table below contains an overview with some relevant instructions followed by the overview of the data fields to be completed and to be uploaded for each notification form present in the 'Notifications' section implemented in the system: start of trial, start of recruitment, end of recruitment, end of trial, global end of trial, temporary halt, restart of trial, restart of recruitment, anticipated date of summary of results, unexpected event, serious breach, urgent safety measure and 3rd country inspectorate inspection.

Details on the submission of results documents are also provided.

References	Location (area or document)
CTIS structured data form – Notifications and Results	https://www.ema.europa.eu/documents/template-form/ctis-structured-data-form-notifications_en.xlsx

7.1.3. Data fields and document specifications

Data fields and document specifications can be found in the overview section of each CTIS Structured data form.

When populating clinical trial information in CTIS, the following points should be considered:

7.1.3.1. Limits of characters for free-text fields

Generally, there is a limitation of 4000 characters for manual data free-text fields. Nevertheless, there are certain fields following masked values, i.e. PIP number (EMEA-111111-PIP11-11) or fields with smaller sizes. These are further detailed below.

Table 7.1.3.1. Number of characters allowed in free text fields in CTIS

Text field	Character limitation
Manual data free-text fields (general rule)	4000
Phone number	15
Protocol code, registry identifier, designation number for orphan drug, CAT reference number	20
Sponsor internal identifier for unexpected event, serious breach, urgent safety measure, 3rd country inspectorate inspection notifications	20
Registry name, source of monetary support, period title, arm title, sponsor contact person first name and last name, address, town/city, department, email address, product code, gene of interest, species origin for the xenogeneic cells, tissue-engineered xenogeneic species of origin, device trade name, device notified body, authorisation number of manufacturing and import	100
Primary and secondary end points	500
Description of the device	2000

7.1.3.2. Characteristics of documents upload

Every time users upload a document in CTIS, they should keep in mind that the system allows for storage of clinical trial data with a maximum size of 220 GB and particularly permits the following characteristics for document upload:

Table 7.1.3.2.1. Characteristics of document upload in CTIS

Document details	System limitation
Document file name	100 characters. None of these 7 special characters (/,.;|) allowed
Document version	10 characters, it can be numerical or not
Document comment free text field	4000 characters
Document file size	50 MB
Maximum number of documents uploaded in one batch	25

References	Location (area or document)

Guide on CTIS Common features	https://www.ema.europa.eu/documents/other/clinical-trials-information-system-ctis-common-features-ctis-training-programme-module-02_en.pdf
CTCG's 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

7.2. Trial categorisation

The trial category is chosen by the sponsor when filling in the 'form' section of the application, based on definitions provided in table V of Annex I of the Guidance document on how to approach the protection of personal data and commercially confidential information while using the CTIS. Refer to CTIS training Module 10 e-learning presentation and FAQs for instructions on how to change the category of a trial.

References	Location (area or document)
CTIS Training Material Module 10 'Create, submit and withdraw a clinical trial'	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-ctis-online-modular-training-programme#sponsor-workspace-section

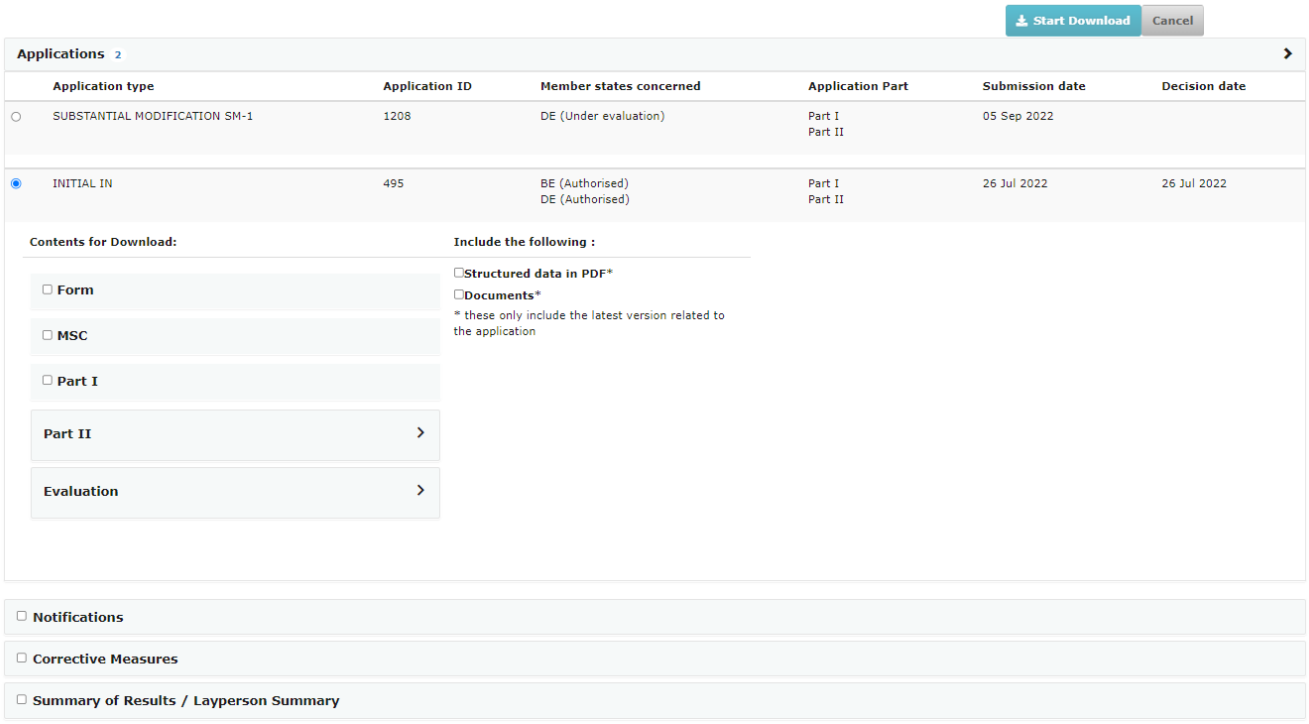
7.3. Download options

There are two ways for downloading CT and CTAs information; either from the clinical trial page or from the clinical trial application(s) of the trial. There is also an option for CTIS sponsor users to download search results when searching for clinical trials. The subsections below provide users with more details for each download option.

7.3.1. Clinical trial page

By clicking on the trial number, users open the clinical trial page and may access all related information submitted via the application(s) of the trial. On the upper right corner, users can use the download button and retrieve a zip file that includes any information related to the trial and its applications. The users, once click on the 'Download' button, can view a tree menu from which they can select which data (application dossier –Form, MSC, Part I and Part II– or Evaluation related) of an application (only one application per time can be selected) they wish to include in the downloading zip file. Besides application related data, users may include in the zip file additional information regarding Notifications, Corrective Measures and Trial results.

Figure 7.3.1.1: Downloading application data from the clinical trial page.

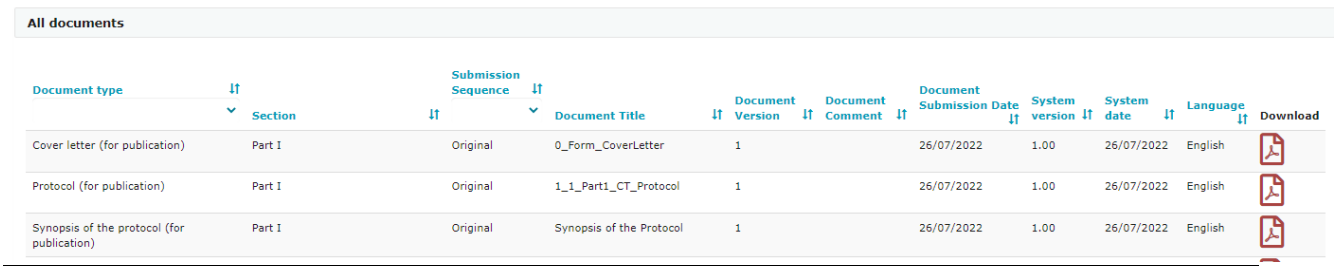


By using the 'Download' button, users can download the latest version of the structured data and documents that have been submitted per application, provided they have permission to access. They can access and retrieve previous submitted versions of data and documents, by navigating through the CTA pages, as it is described in the following subsection (second download option).

7.3.2. Clinical trial application page

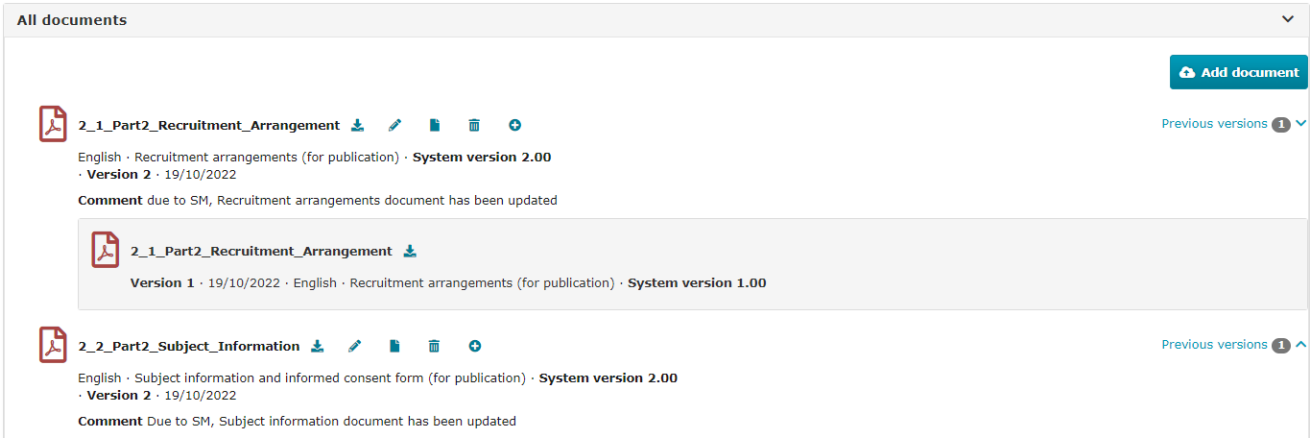
Users can download the documents submitted in the various sections of a CTA or a non-SM. They can download the files from the sections Form (e.g. cover letter), Part I (e.g. protocol) and Part II (e.g. Recruitment arrangements), using the 'Download' icon, found on the right side of each document in its placeholder. Another way to download the documents from the CTA page is to access them from the 'All documents' tile, found in the end of the Part I and II sections and use the respective PDF icons, found on the right side of all documents.

Figure 7.3.2.1: Downloading documents from the clinical trial application page ('All documents' tile).



Previous versions of the documents (if any) can be downloaded also. You may access them using the arrow next to ‘Previous versions’ found on the right side of the documents, and then the ‘Download’ icon.

Figure 7.3.2.2. Downloading previous document versions.



Previous versions of the application and their respective data can be accessed by using the ‘Versions’ button, found on the upper right corner of the CTA page.

Figure 7.2.3.2.3: Accessing previous versions of a CTA and respective data.

7.3.3. Clinical Trial Search Download of results

Within the clinical trial overview page, users can use the subtabs to access and view any data and information related to that clinical trial. One of them, labelled ‘Trial results’, contains the placeholders for summary of results, for lay person summary of results and for related clinical study reports. The documents attached to those placeholders can be downloaded by users who have the appropriate access, by using the respective download icons. Users may download the data related to clinical trial results by using the download functionality, found on the CT overview page. By clicking the download button, found on the upper right corner, users can select which data to include in their download zip file. Among the main data groupings, users may retrieve the summary of results/Layperson summary.

References	Location (area or document)

Search, view and download information on clinical trials and clinical trial applications – Sponsor users	https://www.ema.europa.eu/documents/other/step-step-guide-how-search-view-download-clinical-trial-clinical-trial-application-authority-ctis_en.pdf

7.4. How to apply a change to a clinical trial dossier

7.4.1. During the drafting of the initial clinical trial application

Users can edit the application while it is in draft status (i.e. until it has not been submitted). To do so, users can access the application, from the CT summary page and select the 'Application ID' under the column' ID' of the 'Application and Non-Substantial Modification' section. In order to populate and upload the relevant information and documentation of an application, users need to click on the padlock button of each subsection. If users need to update documents of an application that is still in draft, they need to remove the already attached document and re-upload the new version. They can also edit the details pertaining to a document. By using the pencil icon, they can make many of the placeholder fields editable (title, date, version, comment), and the values populated to them may change. Afterwards, they can either save the application by clicking on the 'Save' button in the upper-right corner of the page or, if all the required fields are completed, submit the application.

References	Location (area or document)
'High-level overview of CTIS workspaces and common system functionalities' – CTIS Training Material Module 02	https://www.ema.europa.eu/documents/other/clinical-trials-information-system-ctis-common-features-ctis-training-programme-module-02_en.pdf

7.4.2. Once the initial clinical trial application has been submitted

After submitting the CTA, if users want to update the dossier, they need to create a substantial modification (SM) CTA or a non-substantial modification (non-SM), as applicable.

A sponsor can draft and submit a substantial modification (SM) or a non-substantial modification (non-SM) to a MSC that does not have an assessment on-going in relation to this clinical trial (see next table).

Table 7.4.2.1. Allowed submissions whilst ongoing evaluation of a CTA.

	Submission of an SM to Part I and Part II	Submission of an SM to Part I	Submission of an SM to Part II	Submission of a non-SM	Submission of an application for additional MSC
Initial application	Not until a decision is issued by all MSCs	Not until a decision is issued by all MSCs	Not until a decision is issued by all MSCs	Not until a decision is issued by all MSCs	Not until a decision is issued by all MSCs
Evaluating Part I & Part II SM application	No	No	No	No	No
Evaluating Part I only SM application	No	No	No	No	No
Evaluating Part II only SM application	No	No	Only to MS who did not receive the Part II SM	No	yes
Evaluating add additional member state	No	No	Only to MS not evaluating the application to add an additional MSC	No	Only to MS that is not an MSC or evaluating an assessment to become an MSC

Substantial modification (SM) - request by the sponsor for a change of a CT that is likely to substantially impact the subjects' safety or rights or the reliability/robustness of the generated data. A substantial modification will be evaluated by the MSC after it has been submitted.

The scope of a substantial modification can be Part I only, Part II only, or Part I and Part II. After selecting the scope of the SM, users need to prepare the dossier of the SM, adding required information, editing already submitted structured data and updating submitted documents. They can update a document, using the ‘update’ icon. Once click on the update icon, users can attach the new version of the document, indicating their version reference and adding any relevant comment (if needed) in the dedicated free text field. They can change the information pertaining to the document by using the pencil icon and even empty the document placeholder, by using the remove icon.

Non-substantial modification (non-SM) - any change to the CT dossier that is not likely to substantially impact the safety or rights of the subjects, or the reliability and robustness of the data generated in the CT but is relevant for the supervision.
Sponsors can submit non-SMs to keep the information of the dossier up to date. Non-SM changes can also be provided as part of RFI responses where so required.

A sponsor can only submit an SM or a non-SM to an MSC that **does not have an on-going assessment** of an application for the concerned trial. If users need to upload new versions of documents, they can submit a clean version of the updated document, as well as the original document with tracked changes, to facilitate the assessment of CTAs.

Table 7.4.2.2. Documents and Structured Data Fields that may be populated with an SM application type.

	Form	MSC	Part I[a]	Part II[a]
Document for upload	Cover letter		Documents	Documents
	Modification description		Document translations	Document translations
	Supporting information			
	Proof of payment			
Structured data field	Supporting information	Number of subjects per MSC	Data	Trial site
	SM reason		Data translations	PI contact details
	SM scope		Third party entity	
			Sponsor contact details	
			Description of changes	

[a]*If there are any changes to the dossier*

Table 7.4.2.2.3. Documents and Structured Data Fields that may be populated with a non-SM application type.

	Form	MSC	Part I[a]	Part II[a]
Document for upload			Documents[b]	Documents
			Document translations	Document translations
Structured data field	Modification description	Number of subjects per MSC	Data[b]	PI contact details
			Data translations	
			Third party entity	

	Form	MSC	Part I[a]	Part II[a]
			Sponsor contact details	
			Description of changes	

[a]*If there are any changes to the dossier*

[b]*Document/Field can be modified with limitations*

References	Location (area or document)
How to Manage a CT – CTIS Training Material Module 05 eLearning *Section 3 - Update and withdraw other types of notifications slide*	https://www.ema.europa.eu/en/learning-module/manage-ct/story.html https://www.ema.europa.eu/en/documents/other/step-step-guide-how-search-view-download-clinical-trial-clinical-trial-application-sponsors-ctis_en.pdf
Create, submit and withdraw a CTA – CTIS Training Material Module 10 eLearning *Section 2 – Edit and upload*	https://www.ema.europa.eu/en/learning-module/create-ct-application/story.html
'Step-by-step guide' – CTIS Training Material Module 10 *Page 4*	https://www.ema.europa.eu/en/documents/other/step-step-guide-create-submit-withdraw-clinical-trial-application-nonsubstantial-modifications-ctis_en.pdf
FAQs - CTIS Training Material Module 10 *Questions* *1.6. How can users edit a CTA?* *2.3. How can users create & edit an Initial CTA?*	https://www.ema.europa.eu/en/documents/other/faqs-how-create-submit-withdraw-clinical-trial-application-ctis-training-programme-module-10_en.pdf

7.5. Handling of Requests for Information (RFIs) in CTIS

During the evaluation of CTAs, MSC have the possibility to require clarifications from the sponsors by raising RFIs that should be addressed within the defined timelines. **It should be noted that failing to provide responses within the timelines will lead to the application being lapsed.** It is encouraged that high-quality dossiers are submitted in CTIS with each application, to minimise, where possible, the need to raise a request for information.

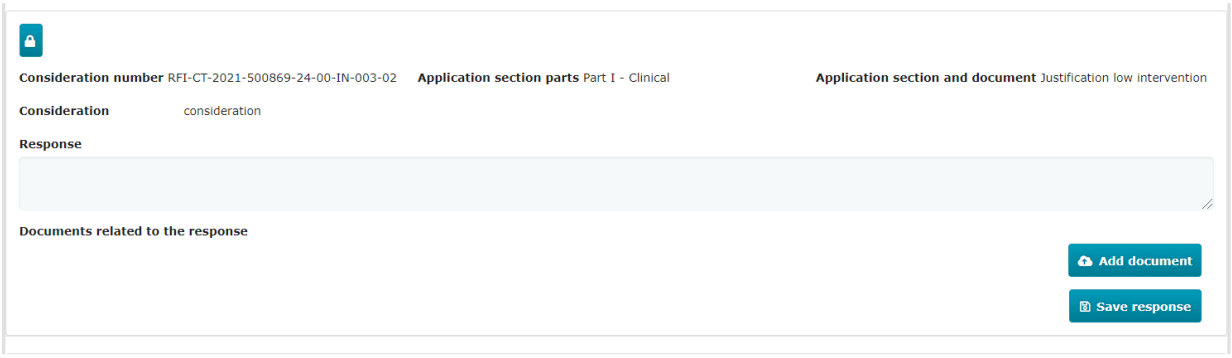
RFI can be identified by the sponsors via monitoring the notices and alerts tab and the RFI tab in CTIS Sponsor workspace. For example, in an initial application with Part I and Part II, an RFI can be raised by the RMS as part of the validation and assessment of Part I and by each MSC following art II assessment. RFI can be raised by the RMS and MSC at any point in time during the evaluation phase. There are no predicted timelines and period of time when RFI can be raised, therefore the sponsors should be vigilant in monitoring the notices and alerts and the RFI tab.

RFIs are raised by the RMS/MSC via the considerations documented in the system as part of the evaluation. Documented considerations are then consolidated by the RMS/MSC (accepted/merged/adapted or rejected) directly in CTIS and used as the basis for the RFI. RMS/MSC can also upload documents into CTIS as supporting documentation to the RFI being raised.

Sponsors have the possibility to download from CTIS the considerations part of the RFI, as well as any supporting documentation, so the RFI can be allocated to relevant team members to be addressed. Users can also have access to the considerations in the RFI and any documents directly from CTIS and provide their reply directly in the system.

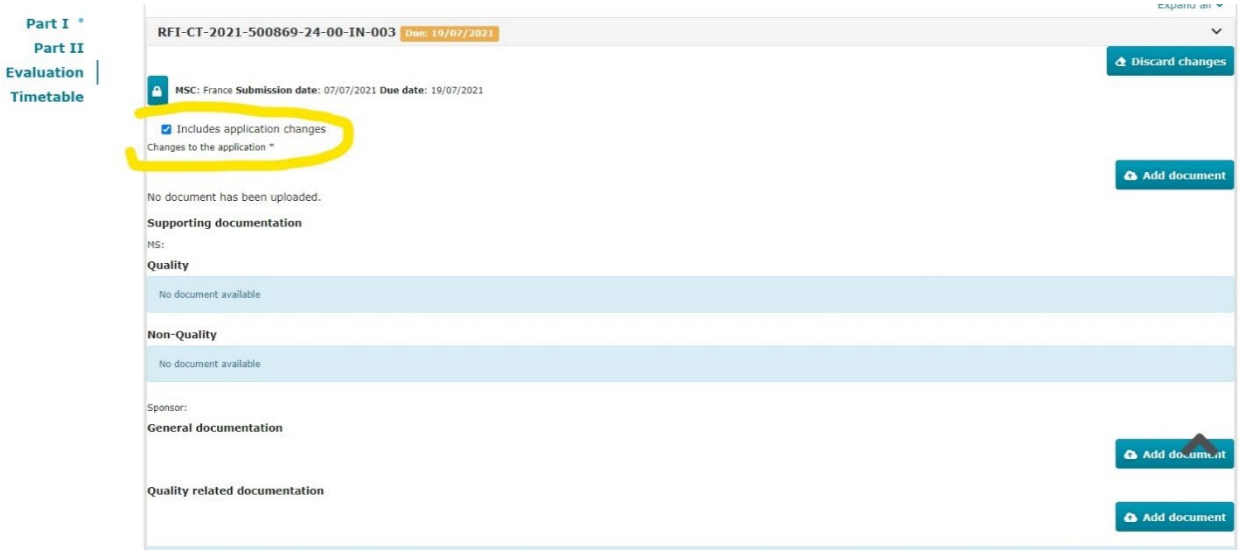
In order to address an RFI, the sponsor has to provide a response in the free text displayed after each consideration raised by the RMS/MSC as part of the RFI, that can be complemented by supporting documents. RFI responses can be saved as drafts before submission.

Figure 7.5.1. Response to an RFI consideration (free text with optional supporting documents) can be saved as draft before submission.



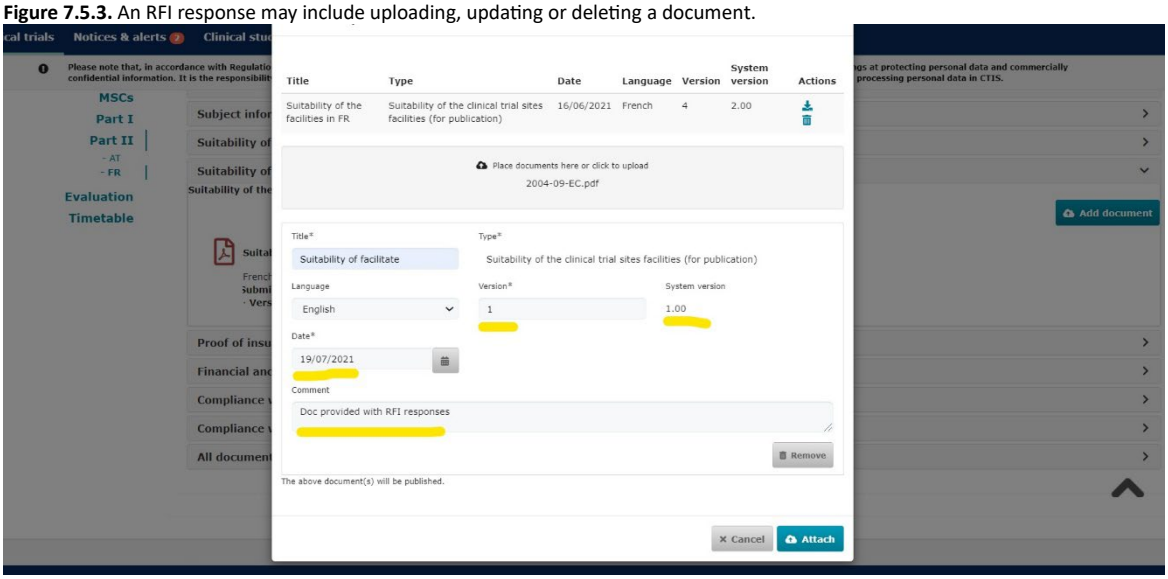
The sponsor also has the possibility to apply changes to the dossier, both structure data and documents, depending on the nature of the request raised. If changes to the dossier are applied, the sponsor should also provide a document containing a description of the changes made.

Figure 7.5.2. Changes to a CTA dossier shall be described in a document.



Previously uploaded documents can be deleted when responding to an RFI or a new version of a document can be provided (in this case documents will have the same document type, language and title). When uploading a new document, the sponsor can specify the date and the version of the file, and a system version will also be generated sequentially by the system, independently of the sponsor's version number.

Figure 7.5.3. An RFI response may include uploading, updating or deleting a document.



Completely new documents can also be submitted when replying to an RFI, for the section of the application dossier in question and subject to the RFI.

Access to the RFI, as well as download functionality, depends on the user profile. For example, in Part I users will only have access to RFI pertaining to Part I of the dossier. Each user can download the RFI and RFI responses that the user has access to. It should be noted that CT Administrators can assign to themselves access to Part I and Part II and therefore can have access to all RFIs.

CTIS enables sponsors users to address RFIs simultaneously in the different sections of the CTA, namely a user can work on Part I RFI at the same time as users working on Part II RFI. Also, Part II RFIs raised by different MSCs can be addressed simultaneously by different users, if needed. In case of simultaneous RFIs, users should be mindful to work on their respective RFIs.

Figure 7.5.4. New CTA drafts are created to respond to RFIs simultaneously.

RFI raised in the course of evaluating a Clinical Trial Application (CTA) and the responses provided are subject to publication rules, except for RFI raised for sections of the application that are exempted from publication, such as the quality section of the dossier or questions related to quality in general.

Training material on how to address incoming RFIs related to the evaluation of a CTA has been published on the CTIS Training Material Catalogue, Module 11.

As part of an ad hoc assessment, in case of evaluation of an annual safety report (ASRs), or when a sponsor opinion needs to be provided in the context of a corrective measure, an RFI can also be raised. That RFI and its response are exempt from publication.

Training material on how to address other types of incoming RFIs (Ad hoc assessment, Corrective measures) has been published in the CTIS Training Material Catalogue, Modules 04 and 05. Training material on how to address incoming RFIs related to ASR is published in the CTIS Training Material Catalogue, Module 18.

References	Location (area or document)
CTIS Training Material Module 04 'Support with workload management in the sponsor workspace: eLearning – RFI section'	https://www.ema.europa.eu/en/learning-module/workload-management-sponsor/story.html
CTIS Training Material Module 04 'Support with workload management in the sponsor workspace: FAQs – RFI section'	https://www.ema.europa.eu/en/documents/other/faqs-support-workload-management-workspace-ctis-training-programme-module-04_en.pdf
CTIS Training Material Module 04 'Support with workload management in the sponsor workspace: Videoclip'	https://www.youtube.com/watch?v=6z-Q6-LK8Ws&ab
CTIS Training Material Module 05 'Manage a CT through CTIS: eLearning – various references to types of RFI'	https://www.ema.europa.eu/en/learning-module/manage-ct/story.html
CTIS Training Material Module 05 'Manage a CT through CTIS: FAQs – various references to types of RFI'	https://www.ema.europa.eu/en/documents/other/faqs-how-manage-ct-ctis-training-programme-module-05_en.pdf
CTIS Training Material Module 11 'Respond to requests for information received during the evaluation of a clinical trial application: eLearning'	https://www.ema.europa.eu/en/learning-module/respond-to-rfis-ctis/story.html
CTIS Training Material Module 11 'Respond to requests for information received during the evaluation of a clinical trial application: FAQs'	https://www.ema.europa.eu/en/documents/other/faqs-how-respond-requests-information-received-during-evaluation-clinical-trial-application-ctis_en.pdf
CTIS Training Material Module 11 'Respond to requests for information received during the evaluation of a clinical trial application: Videoclips'	https://www.youtube.com/watch?v=vbQVkYi3pGI&ab https://www.youtube.com/watch?v=DXrQMStp2a0&ab https://www.youtube.com/watch?v=sO8YRSatsDA&ab
CTIS Training Material Module 18 'How to create and submit an annual safety report	https://www.ema.europa.eu/en/documents/other/step-step-guide-how-create-submit-annual-safety-report-respond-related-requests-information-ctis_en.pdf

and respond to related requests for information: Step by Step guide'	

7.6. Submitting the Clinical Study Report (CSR)

Refer to the following Quick guide for information on how to submit a CSR.

References	Location (area or document)
CTIS Training Material Module 13 'Clinical Study Reports submission Quick guide'	https://www.ema.europa.eu/en/documents/other/quick-guide-clinical-study-reports-submission-ctis-training-programme-module-13_en.pdf

8. Data transparency

The clinical trial information processes and flows in CTIS start with a CTA submitted by the sponsor, or delegated entities, via CTIS secure domain (see Section 4. 'How to get a clinical trial application started in CTIS '), to carry out a clinical trial in the EU/EEA, and the corresponding evaluation performed by the MSCs.

Following this evaluation, a decision is issued by each MSC for the CTA, on whether the trial is authorised, authorised with conditions, or not authorised. After a decision of any kind has been issued by the MSC, data and documents submitted to CTIS for the trial will be made available to the public as per the modality and timelines defined in the Annex 1 to the Guidance document on how to approach the protection of personal data and commercially confidential information while using the CTIS. The detailed list of structured data that are, or are not subject to publication is specified in the files mentioned in Section 7.1. of this document (specifically: CTIS application fields and Notifications and Results). A useful summary of the rules can be found in the quick user guide. All the mentioned reference documents reflect the current publication rules for CTIS, defined in the Revised CTIS transparency rules, and provide guidance on the protection of personal data and commercially confidential information (CCI) submitted to the system, in accordance with the requirements of Article 81(4) of Regulation (EU) No 536/2014 (CTR). A Questions and Answers (Q&A) document on this topic is also available to users, see Q&A on the protection of Commercially Confidential Information and Personal Data while using CTIS.

The disclosure timelines of data in CTIS depend on the trial category, on the population age (in case of category 1 trials) and on the trial phase (in case of category 2 trials that are integrated phase 1 and 2). The trial category is chosen by the sponsor when filling in the 'form' section of the application, based on definitions provided in Table V of Annex I. Exceptions to these disclosure rules apply to all trials submitted before 18 June 2024 (referred to as 'historical trials'), which have only their structured data published; moreover, for those trials documents submitted through part I Non-Substantial Modifications and additional member state applications are also not published: see section 2.3 of Guidance document and table IV of its Annex I.

For all documents that are in scope of publication (see Table II of Annex I of the guidance document), users need to provide a document version 'for publication', where personal data and CCI should be properly redacted or should not appear (see chapter 3 and 4 of the Guidance document). Please note

that **any document inadvertently uploaded 'for publication' into the relevant CTIS document upload sections will be published**. For example, if an IB is uploaded into the SmPC section of a Category 2 or 3 trial, the IB will be made public if the sponsor does not correct this oversight before the decision on the application.

The ability to upload a version 'not for publication' is made available to the sponsor, in order to provide information on personal data and CCI that are deemed necessary for the assessment by the RMS/MSCs. It is not expected that such a version is provided by the sponsor for all document types: this need depends on the document content. This functionality allows the exchange of information in the CTIS secure domain between users with regulated access depending on their profile, while at the same time protecting personal data and the legitimate interest of sponsors for what concerns CCI.

With respect to those documents that are not subject to publication, note that quality and non-quality documents need to be submitted as separate documents. This includes the IMPD-Q, Scientific Advice - Quality and Quality RFI response documents. CTIS user roles depend on maintaining separate quality documents to ensure only authorised users can view quality information.

References	Location (area or document)
Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014R0536
Revised CTIS transparency rules	https://www.ema.europa.eu/en/documents/other/revised-ctis-transparency-rules_en.pdf
Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS)	https://accelerating-clinical-trials.europa.eu/document/download/6a0b836f-4779-4bb9-9584-1ce504a9ae38_en?filename=guidance-document-how-approach-protection-personal-data-commercially-confidential-information-while_.pdf
Annex I to the Guidance document	https://accelerating-clinical-trials.europa.eu/document/download/824905dd-3033-41e6-a871-67b20c4f4c94_en?filename=annex-i-guidance-document-how-approach-protection-personal-data-commercially-confidential_.pdf
Q&A on the protection of Commercially Confidential Information and Personal Data while using CTIS	https://accelerating-clinical-trials.europa.eu/document/download/33702a5d-13be-4c4f-936d-3627dd73085b_en?filename=ACT%20EU_Q%26A%20on%20protection%20of%20Commercially%20Confidential%20Information%20and%20Personal%20Data%20while%20using%20CTIS_v1.3.pdf

Quick user guide	https://accelerating-clinical-trials.europa.eu/document/download/a101771b-0be7-492f-b8bd-7f551ffbb7a7_en?filename=Revised%20CTIS%20transparency%20rules%2C%20Interim%20period%20%26%20Historical%20trials_quick%20guide%20for%20users_1.pdf
CTIS structured data form - Applications (IN, AMSC, SM, non-SM)	https://www.ema.europa.eu/documents/template-form/ctis-structured-data-form-initial-application-additional-member-state-concerned-substantial_en.xlsx
CTIS structured data form – Notifications and Results	https://www.ema.europa.eu/documents/template-form/ctis-structured-data-form-notifications_en.xlsx
CTIS Training Material Module 12 'Data protection: e-learning course'	https://www.ema.europa.eu/en/learning-module/data-protection-ctis/story.html

9. Safety reporting obligations

9.1. Suspected Unexpected Serious Adverse Reactions (SUSARs)

The reporting of SUSARs by the sponsor to the European Medicines Agency in the context of the CTR is outlined in Article 42. The most relevant change for sponsors is the legal obligation for the electronic reporting of SUSARs to the clinical trial module of EudraVigilance for a CT performed in at least one Member State (Art 42.1).

Where a sponsor, due to a lack of resources, does not have the possibility to report to EudraVigilance, and the sponsor has the agreement of the MSC, it may report to the Member State where the SUSARs occurred. That Member State shall then report the SUSARs to EudraVigilance (Art 42.3).

Since CTIS was launched, CT-3 final arrangement for SUSARs applies also to all trials approved through the CTD, as announced by the Clinical Trials Expert Group (CTEG) in April 2021. This means that from 31 January 2022, **sponsors report SUSARs to EudraVigilance only and it is no longer required to send them to member states**, regardless of whether the trial has been approved through the CTR or CTD. This brings the benefit of a single submission process and harmonised procedures to the area of SUSAR reporting. Member states have the ability to set up SUSAR rerouting rules in EudraVigilance if they wish to receive copies of SUSARs for their national systems. This applies for all trials approved under the CTD or CTR.

For some member states, continued direct SUSAR reporting to ethics committees for clinical trials under the CTD is still also required under their national law; thus, this may be considered on top of the direct reporting to EudraVigilance. In case of doubt, liaise directly with the member state concerned (for a link to the member states contact points, refer to Section 11 'Other references').

Updated information regarding reporting safety information on clinical trials can be found on the EMA webpage.

Section 7c (REPORTING OF ADVERSE EVENTS/REACTIONS) of the EudraLex Volume 10 Q&A published by the Commission addresses some additional questions in the context of SUSAR reporting.

References	Location (area or document)
Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014R0536
Link to EudraLex - Volume 10 - Clinical trials guidelines - Set of documents applicable to clinical trials authorised under Regulation EU No 536/2014[8]	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
Detailed guidance on the collection, verification and presentation of adverse events/reactions arising from clinical trials on medicinal products for human use ('CT-3')	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52011XC0611(01)
CTEG announcement that CT-3 final arrangements for SUSAR reporting will apply since CTIS launch	https://ec.europa.eu/transparency/expert-groups-register/core/api/front/document/56534/download
Reporting safety information on clinical trials	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/reporting-safety-information-clinical-trials
EudraVigilance: electronic reporting	https://www.ema.europa.eu/en/human-regulatory/research-development/pharmacovigilance/eudravigilance/eudravigilance-electronic-reporting

9.2. Annual Safety Report (ASR)

The reporting of ASRs by the sponsor to the Agency in the context of the CTR is outlined in Article 43, applicable to trials registered in CTIS and managed under the CTR. The sponsor shall submit annually through CTIS a report on the safety of each investigational medicinal product (IMP) used in a clinical trial, other than placebo, for which it is the sponsor. This obligation referred to in paragraph 1 starts with the first authorisation of a clinical trial in accordance with the CTR and it ends with the end of the last clinical trial conducted by the sponsor with the IMP.

Section 7d (ANNUAL SAFETY REPORTS) of the Q&A published by the Commission in EudraLex Volume 10 (see 'References' table above) may address some of the questions in the context of ASR reporting.

[8] The latest published European Commission Clinical Trials Regulation No 536/2014 Q&A document can be found under the 'Set of documents applicable to clinical trials authorised under Regulation EU No 536/2014' section.

The documents referred to in this handbook's Section 9.2. apply also to this section. In addition, you can find the link to the ASR submission training module below:

References	Location (area or document)
CTIS Training Material Module 18 'How to create and submit an annual safety report and respond to related requests for information'	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-ctis-online-modular-training-programme#sponsor-workspace-section
CTIS Training Material Module 18 'How to create and submit an annual safety report and respond to related requests for information: Step by Step Guide'	https://www.ema.europa.eu/en/documents/other/step-step-guide-how-create-submit-annual-safety-report-respond-related-requests-information-ctis_en.pdf

10. Support

10.1. Release notes and known issues

EMA regularly performs technical updates to CTIS to improve its features and functionality. When significant updates are made to CTIS, EMA publishes release notes that outline what has changed in the system. Updates may include improvements to existing features and functionality, the addition of new features as well as functionality and technical improvements.

In addition, EMA publishes known issues that sponsor and authority users may encounter when using the CTIS secure workspaces. Where possible, workarounds to apply are proposed.

All versions of the release notes and known issues documents can be found on the 'Website outages and system releases' page of EU Clinical Trials. CTIS users are advised to make use of **the latest version** of the lists of known issues published on this page.

References	Location (area or document)
EU Clinical Trials Website – Website outages and system releases	https://euclinicaltrials.eu/website-outages-and-system-releases

10.2. CTIS Highlights Newsletters

To stay up to date with developments and plans, see EMA Clinical Trials Highlights Newsletters on EMA corporate website: subscribe at https://ec.europa.eu/newsroom/ema/user-subscriptions/3201/create

References	Location (area or document)

Clinical Trials Highlights Newsletter	https://www.ema.europa.eu/en/news-events/publications/newsletters#clinical-trials-highlights-section

10.3. CTIS information events

The events page on the EMA corporate website displays information events organised by EMA on CTIS (search words e.g. CTIS; SME).

In order to further support CTIS sponsor users after CTIS go-live, EMA has launched series of virtual events where sponsors can ask their questions live to CTIS experts. CTIS walk-in clinics provide an opportunity for sponsors to receive practical guidance about the Clinical Trials Information System by asking questions to CTIS experts in real-time. CTIS bitesize talks are themed events offering users live system demonstrations on a specific CTIS functionality on each session, and questions are also received and answered by CTIS experts in real-time. In addition, EMA introduced OMS troubleshooting sessions for CTIS users, another series of virtual events aiming to address and clarify outstanding issues and questions related to registering organisation and/or location data in OMS for use in CTIS CTAs.

All of these events are open to everyone. The recorded videos of past events become available for the public on EMA's YouTube channel and can be accessed also through the dedicated event pages.

For a complete list of the CTIS-related virtual events, sessions and webinars, visit the EMA's webpage on CTIS Training and information events.

References	Location (area or document)
EMA corporate website Events page	https://www.ema.europa.eu/en/events/upcoming-events
EMA CTIS Training and information events page	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support#training-and-information-events-section

10.4. CTIS training

Training from EMA on how to use the Clinical Trials Information System (CTIS) is available. The EMA's training resources are tailored for clinical trial sponsors and staff of the European Union (EU) Member States, European Commission and other organisations who will use the system.

The EMA CTIS training programme is mainly composed of **online training modules** published on the CTIS training programme page on the EMA corporate website. A wide selection of materials in different formats are available on introductory modules, common functionalities for all registered users, modules on the authority (Member States, EMA and European Commission) workspace and on the sponsor workspace. It also includes recordings from virtual training sessions organised by EMA as well as a section with information about the Master trainer programme.

When starting to use the training materials, it is advised that organisations and users first make use of the Guide to CTIS Training Material Catalogue.

Reproduction and/or distribution of the content of the published training materials is authorised for non-commercial or commercial purposes, provided that the EMA is acknowledged as the source of the materials.

EMA has developed the training materials to enhance public access to information on CTIS. The training materials describe initially a preliminary version of CTIS and while the material will undergo revision it may therefore, not entirely describe the system as it is at the time of use of the material. The Agency does not warrant or accept any liability in relation to the use (in part or in whole) or the interpretation of the information contained in this training material by third parties.

Limited end user training events are organised by EMA and announcements are made on the events page (see 'References' table in 10.4) of the EMA corporate website (search e.g. with word 'CTIS' or 'SME').

References	Location (area or document)
Clinical Trials Information System (CTIS) online training modules page (EMA corporate website)	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/training-support/clinical-trials-information-system-ctis-online-training-modules
Guide to CTIS Training Material Catalogue (EMA corporate website)	https://www.ema.europa.eu/en/documents/other/guide-ctis-training-material-catalogue_en.pdf

10.5. CTIS training environment for user training and organisation preparedness

The Clinical Trial Information System training environment (CTIS Sandbox) is a copy of a recent version of CTIS albeit not always identical to the latest version. The purpose of CTIS Sandbox is to enable knowledge acquisition of the already implemented functionalities of CTIS, by the future CTIS users and their organisations in a practical way and in a safe environment. CTIS Sandbox use is directed by conditions, instructions and guidance, and is made available by EMA. EMA will maintain support for the CTIS Sandbox users through a CTIS Training Environment Support Service (TESS).

Access to CTIS Sandbox is based on need and is therefore intended for, and limited to, those individuals and organisations that are the already using or intending to use the secure workspaces of CTIS (authority and sponsor workspace).

A phased rollout of the CTIS Training Environment is provided to defined user groups in sequence, started with Member States and the European Commission and followed by Sponsors.

Currently, access to the CTIS Training Environment is provided to representatives of sponsor organisations based on the need to create an initial clinical trial application. Organisations have been offered the opportunity to access the CTIS Training Environment in several phases before and after CTIS go-live.

Access to the CTIS Training Environment can be requested by completing a self-assessment through a survey (Survey) that collects information on contact details of individuals, the organisations that they represent, and their plans/need for the use of CTIS. The data collected allows EMA to understand the need for access to CTIS Training Environment and to consider when access will be granted to ensure that the Agency is able to support the CTIS Training Environment users effectively. Organisations wishing to express interest for access to the CTIS Training Environment after the closure of the Survey,

can stay tuned for latest updates on the Survey by subscribing to the Clinical Trials Highlights Newsletters (see Section 10.2).

Before accessing the CTIS Training Environment, users need to be thoroughly trained on CTIS to get the best out of their access. The EMA's published online modular training program can be used for such preparation purposes.

Version deployments and planned downtimes of the CTIS Training Environment are communicated to users as required.

References	Location (area or document)
CTIS Training Environment Survey	https://ec.europa.eu/eusurvey/runner/2abb5ba8-0ec4-9979-b692-0c63f4508b9b
CTIS Training Environment Support Service (TESS)	https://support.ema.europa.eu/

10.6. Questions and answers on CTR, CTIS and other EMA IT systems

Questions and answers on the Clinical Trials Regulation are available in EudraLex Volume 10 Q&A.

Frequently Asked Questions on CTIS functionalities are available as part of the published online training material modules.

If answers cannot be found, sponsors with an EMA account can direct their queries to the **EMA's Service Desk on CTIS**. For sponsors that have not yet created an EMA account, general questions on CTIS functionalities can be directed through **AskEMA** by use of the general form.

For technical support with other EMA IT systems (e.g. EudraVigilance, IRIS, EudraCT), use the **EMA ServiceNow portal** (see table below for links).

References	Location (area or document)
Questions & Answers on CTR - EudraLex Volume 10 - Clinical trials guidelines[9]	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
Frequently Asked Questions (FAQs) on CTIS functionalities	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-ctis-online-modular-training-programme *FAQs are available within each respective training module*

[9] The latest published European Commission Clinical Trials Regulation No 536/2014 Q&A document can be found under the 'Set of documents applicable to clinical trials authorised under Regulation EU No 536/2014' section.

EMA Service Desk for CTIS: Questions on CTIS functionalities - for EMA account holders	https://support.ema.europa.eu/esc?id=emp_taxonomy_topic&topic_id=2111dcb6c39d9d10e68bf1f4e40131ee
AskEMA: Questions on CTIS functionalities - for non-EMA account holders	https://www.ema.europa.eu/en/about-us/contact/send-question-european-medicines-agency
EMA ServiceNow: Assistance with information technology (IT) systems	https://support.ema.europa.eu/esc
Q&A on the protection of Commercially Confidential Information and Personal Data while using CTIS	https://accelerating-clinical-trials.europa.eu/document/download/33702a5d-13be-4c4f-936d-3627dd73085b_en?filename=ACT%20EU_Q%26A%20on%20protection%20of%20Commercially%20Confidential%20Information%20and%20Personal%20Data%20while%20using%20CTIS_v1.3.pdf
Questions and answers – Clinical Trials Information System (CTIS) and Clinical Trials Regulation (CTR)	https://www.ema.europa.eu/en/documents/other/questions-answers-query-management-working-group-ctis-ctr_en.pdf
CTCG Q&A on submission Complex Clinical Trials in CTIS, vs 1.0, dd 14 March 2023	https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2023_03_CTCG_QA_complex_clinical_trials_and_CTIS_v1.0.pdf
Complex clinical trials – Questions and answers	https://health.ec.europa.eu/system/files/2022-06/medicinal_qa_complex_clinical-trials_en.pdf

10.7. Support for SME and academia sponsors

Specific events and dedicated training materials are organised for SME and academia sponsors. For more information on future events and past recordings, users can visit 'CTIS Training and information events' webpage.

References	Location (area or document)
CTIS Training Module 19 'CTIS for SMEs and academia'	https://www.ema.europa.eu/en/documents/other/quick-guide-introduction-ctis-smes-academia-ctis-training-programme-module-19_en.pdf
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

11. Other references

References	Location (area or document)
Clinical Trials Information System – EMA webpages	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support
Clinical Trials in the European Union	https://euclinicaltrials.eu/home
Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014R0536
Link to Commission website containing information on clinical trials in the context of Regulation EU No 536/2014	https://ec.europa.eu/health/human-use/clinical-trials/regulation_en
Link to EudraLex - Volume 10 - Clinical trials guidelines	https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1
List of national contact points (frequently updated)	*Last document in Chapter V of Eudralex vol.10 CTR (see above)*
EudraCT (European Union Drug Regulating Authorities Clinical Trials Database)[10]	https://eudract.ema.europa.eu/
CTIS website outages and system releases	https://.eu/website-outages-and-system-releases
Conclusion of VHP Procedure - Deadline for submissions to VHP in the context of the Christmas Break 2021/2022 and transition to CTIS/CTR starting with the CTR application	https://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2021_07_CTFG_Conclusion_VHP_Deadlines_for_VHP_Submissions.pdf
ACT EU website: Implementation of the Clinical Trials Regulation	https://accelerating-clinical-trials.europa.eu/priority-action-areas/implementation-clinical-trials-regulation_en

[10] EudraCT is the European database for interventional clinical trials on medicinal products authorized in the European Union (EEA) and outside the EU/EEA if they are part of a Paediatric Investigation Plan (PIP) from 1 May 2004 onwards; established in accordance with Directive 2001/20/EC.

12. Acronyms and Glossaries

References	Location (area or document)
CTIS Training: List of Acronyms	https://www.ema.europa.eu/en/documents/other/ctis-training-list-acronyms_en.pdf
EMA General Glossary of regulatory terms	https://www.ema.europa.eu/en/about-us/about-website/glossary
EMA Medical Terms Simplifier	https://www.ema.europa.eu/en/documents/other/ema-medical-terms-simplifier_en.pdf

Acronym	Term	Definition
CAT	Committee for Advanced Therapies	The committee that is responsible for assessing the quality, safety and efficacy of advanced therapy medicines, including medicines classified as gene therapy, somatic cell therapy or tissue-engineered products.
CCI	Commercially confidential information	Information whose publication might prejudice the commercial interests of individuals or companies to an unreasonable degree. The Agency cannot disclose commercially confidential information unless there is an overriding public interest in disclosure.
CTD	Clinical Trial Directive 2001/20/EC	Introduced to simplify and harmonise the administrative provisions governing clinical trials in Europe. It was repealed by the Clinical Trial Regulation application.
CTEG	Clinical Trials Experts Group	
CTFG & CTFG	Clinical Trials Facilitation Group	Acts as a forum for discussion to agree on common principles and processes to be applied throughout the European medicines regulatory network (EMRN). It also promotes harmonisation of clinical trial assessment decisions and administrative processes across the national competent authorities (NCAs).
CTR	Clinical Trial Regulation	European Union (EU) pharmaceutical legislation known as the Clinical Trials Regulation entered into application on 31 January 2022. It aims to ensure the EU offers an attractive and favourable environment for carrying out clinical research on a large scale, with high standards of public transparency and safety for clinical trial participants.

DMP	Development Medicinal Product	A medicinal product under investigation in a clinical trial in the EEA which does not have a marketing authorisation in the EEA and to which special confidentiality arrangements need to be applied.
DSMB	Clinical Trial Data Safety Monitoring Board	A group of independent individuals, external to the trial, who are experts in relevant areas. They review the accumulated data from one or more ongoing clinical trials on a regular basis and advise the sponsor about the continued safety of the trial participants, the continued validity of the trial, and the continued scientific merit of the trial.
EMA	European Medicines Agency	Agency of the European Union in charge of the evaluation and supervision of pharmaceutical products.
EU	European Union	Supranational political and economic union of 27 member states that are located primarily in Europe.
EU MP number	EU Medicinal Product number	Identifier issued by the European Medicines Agency for treatments approved in the European Union.
EUDRACT	European Union Drug Regulation Authorities Clinical Trials Database	EudraCT (European Union Drug Regulating Authorities Clinical Trials) is the European Clinical Trials Database of all interventional clinical trials of medicinal products commencing in the European Union from 1 May 2004 onwards. The EudraCT database has been established in accordance with Directive 2001/20/EC.
EV code	EudraVigilance code	EudraVigilance Code
EVWEB	EudraVigilance web-based tool	EVWEB allows the sending and receiving of safety and acknowledgement messages in compliance with the latest ICH M2 standards.
FAQ	Frequently Asked Questions	A question in a list of questions and answers intended to help people understand a particular subject.
IB	Investigator Brochure	A multifunctional regulatory document essential for the conduct of clinical trials that summarises the physical, chemical, pharmaceutical, pharmacological, and toxicological characteristics of an investigational medicinal product (IMP) as well as any clinical experience.
MAA	Marketing Authorisation Application	An application made to a European regulatory authority for approval to market a medicine within the European Union.

PI	Principal Investigator	The person(s) in charge of a clinical trial or a scientific research grant. The PI prepares and carries out the clinical trial protocol (plan for the study) or research paid for by the grant. The PI also analyses the data and reports the results of the trial or grant research.
PIP	Paediatric investigation plan	A development plan aimed at ensuring that the necessary data are obtained to support the authorisation of a medicine for children, through studies in children. All applications for marketing authorisation for new medicines have to include the results of studies as described in an agreed paediatric investigation plan, unless the medicine is exempt because of a deferral or waiver.
SME	Micro, Small to Medium-size Enterprise	
SmPC	Summary of Product Characteristics	This is the product information document which is made available to all prescribing physicians in the EU for marketed products.
SUSAR	Suspected Unexpected Serious Adverse Reactions	Suspected Unexpected Serious Adverse Reaction is the term used to refer to an adverse event that occurs in a clinical trial subject, which is assessed by the sponsor and or study investigator as being unexpected, serious and as having a reasonable possibility of a causal relationship with the study drug.
TESS	CTIS Training Environment Support Service	
VHP	Voluntary Harmonisation Procedure	
XEVPRM	eXtended EudraVigilance Medicinal Product Report Message	