EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Instructor's Guide:

Clinical Study Reports submission

CTIS Training Programme – Module 13

Version 1.0 – March 2021

What you will find

- Overall guidelines on how to disseminate the knowledge.
- Overview of the audiences targeted in Module 13.
- Overview of the training materials prepared as part of Module 13.
- Recommendations on how to prepare and deliver the training sessions.

Table of Contents

01

Introduction

Scope and objectives

This instructor guide is designed to help you, as a trainer, to disseminate the knowledge and the training materials prepared as part of the Clinical Trials Information System (CTIS) Training Programme to your target audience.

More specifically, this guide is focused on the **13th Module of the CTIS Training Programme** (hereafter referred to as 'CTTM13'). The Module provides an overview of how to manage and submit Clinical Study Reports in CTIS. **This guide contains** an overview of the audiences targeted with CTTM13, the training materials available, and a suggested methodology for disseminating the materials.

The training activities proposed in this instructor guide are available in English. Please, feel free to enrich the course with your contributions and/or adapt it to your participants' needs, but always taking into account the learning objectives and key ideas presented.

For any questions regarding the materials, please contact the CTIS Training Programme team at CT.training@ema.europa.eu.

02

Course elements

Target audiences

CTTM13 targets **marketing authorisation holder** users within the **sponsor** workspace.

CTTM13 learning objectives

The learning objectives of CTTM13 are:

1. Remember what a Clinical Study Report (CSR) is.
2. Understand how to prepare and submit a CSR.
3. Understand how to view, download, update and withdraw a CSR.
4. Understand the roles and permissions involved in managing a CSR.

Materials available

- **CTTM13 Quick Guide:** A step-by-step reference document to explain in detail how to create, submit, update, download, and withdraw a CSR.
- **CTTM13 Step-by-step guide:** Document summarising the main steps to submit and update a CSR.
- **CTTM13 FAQs:** List of Frequently Asked Questions regarding information and timelines of CSR; the management of CSR; the publication of CSR; and the roles and permissions involved in CSRs.

03

Course preparation

To ensure that the learning objectives of CTTM13 are met and that the training materials are optimally disseminated and consumed, we suggest that you follow a **blended learning approach** combining an activity where participants interact with the content individually and at their own pace and preferred timing (**asynchronous** learning), with an activity bringing together all participants at the same time (**synchronous** learning). For more information on this approach to learning, please refer to our general dissemination guidelines.

- First, we suggest that you **share the CTTM13 Quick guide** with the participants. This will allow them to understand the contents of the Module at their own pace and reflect on questions they may have.

- Second, we suggest that you organise **a webinar** around one week after having shared the Quick guide with the participants. This will allow you to check participants' understanding of the processes explained, address any questions they may have, and collect input on the training materials and methodology.

As the instructor, you are the **sole responsible for organising and hosting the webinar** with the materials provided by the CTIS Training Programme team. You may, of course, prefer to arrange a face-to-face session if the resources and the availability allow you to do so.

Please note that this guide only provides recommendations and suggestions on how to convey the knowledge to the participants. Do not hesitate to adapt it to your needs and preferences, including the possibility to combine one or more modules in the same webinar.

Preparation of a webinar

This section summarises some useful tips to help you organise a webinar successfully. For further details and recommendations on such activities, please refer to the dissemination guidelines.

- **Prepare an online quiz** to be launched during the webinar with some questions for the participants as an 'icebreaker' and to check whether the participants have understood the key concepts of the Quick Guide. The purpose of this activity is to start the webinar in an interactive manner and see if participants have acquired some basic information beforehand. The feedback gathered in this exercise will help you to better adapt your speech and presentation to the participants' knowledge level. Make sure to

include at least one test question to get participants familiarised with your chosen tool.

- **Send the Quick Guide** to the training participants one week in advance.
- **Review relevant documentation in advance.** In addition to reviewing all the training materials of this Module, including the FAQs, we recommend you to familiarise yourself with the articles of the Clinical Trials Regulation[1] related to the Clinical study report. We recommend you to read at least the following articles, which are related to aspects covered in this Module:
    - *Chapter I: General provisions*
        - Article 2(35) – Definitions.
    - *Chapter VI: Start, end, temporary halt, and early termination of a clinical trial*
        - Article 37(4) - End of a clinical trial, temporary halt and early termination of a clinical trial, and submission of the results.
    - We also recommend you take a look at the latest version of the European Commission's Clinical Trials Regulation Q&A[2], concretely:
        - Section 2: Start, end, temporary halt, and early termination of a clinical trial. Specifically, take a look at the question:
            - 10.12. *How is the "end of a clinical trial" defined? What are the sponsor's obligations after the clinical trial ends?.*

- **Choose the right platform** to host your webinar, and make sure the participants are aware of the connection requirements by sharing with them the instructions.

- **Limit participation** to a maximum of 20 participants and up to a maximum of two hours duration, to maintain optimal interaction and keep the participants focused. If you choose to go for a longer webinar, make sure to foresee a break at least every 60 minutes.

[1] Regulation (EU) No 536/2014 of the European Parliament and of the Council on clinical trials on medicinal products for human use, *EU Official Journal* L158. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

[2] European Commission, Clinical Trials Regulation (EU) No 536/2014 Questions & Answers DRAFT, Version 3, February 2021. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/regulation5362014_qa_en.pdf

04

Course development

In this section, we describe the proposed timings for each activity, the material to be used, the objective of the activity, and the steps to be followed by you as a trainer:

Activity 1: Reviewing the Quick Guide individually

Time: One week before the webinar

Material: CTTM13 Quick Guide

Objective:

This activity consists of the individual review by participants of the CTTM13 Quick Guide by themselves, so they can have an overview of the process and make a note of questions that are not clear to them.

Steps:

1. Send the Quick Guide to the participants and ask them to review it before the webinar day.

2. Send an email reminder one or two days before the webinar, asking them to write down any questions they may have ahead of the webinar.

Activity 2: Webinar

Time: Ca two hours

Material: CTTM13 Quick Guide, CTTM13 Step-by-step guide, CTTM13 FAQs, and password-protected feedback form built by the CTIS Training Programme team with EU survey tool for participants to provide feedback anonymously.

Objective:

This proposed activity consists of the organisation of a webinar to:

- Assess if participants have gathered the knowledge presented in the CTTM13 Quick Guide.
- Present the additional materials for the CTTM13 (FAQs document).
- Answer any questions regarding the content of the CTTM13.
- Receive feedback regarding the learning materials and the training delivery methodology.

We propose to structure this activity in seven parts described below:

1. **Part 1:** Introduction to the webinar (*approximately 15 minutes*).
    a. Introduce yourself as a trainer and remind participants of the basic rules of the session, as well as any practicalities regarding the software used for the webinar, as applicable.
    b. Explain the aim of the webinar and describe briefly the materials that will be used for the session.
    c. Open a quick roundtable to allow participants to introduce themselves briefly.
2. **Part 2**: Questions on the material reviewed and interactive knowledge check (*approximately 25 minutes*).
    a. Ask if participants have any questions regarding the CTTM13 Quick Guide.
    b. Launch an online quiz to check if participants understood the key concepts from the CTTM13 Quick Guide. Refer to the general dissemination guidelines for examples of tools that you can use for that purpose.
3. **Part 3:** "Fill in the blanks" exercise (approximately 15 minutes).
    a. Display the CTTM13 Quick guide with certain missing words that the participants will have to fill (maximum 10 blanks throughout the document).
    b. Share the original version of the quick guide with the participants and explain its purpose.

Break: (10 minutes)

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4. **Part 4**: Questions and answers (*approximately 20 minutes*).
    a. Present the CTTM13 FAQs document and explain what type of questions they will find there (*approximately 5 minutes*)

b. Give some time to the participants to think and ask the questions they have on the materials.

c. Note the questions of the participants. Allow them to ask them orally or via chat. *We suggest gathering all questions at the beginning of this exercise to make sure that all questions are captured without time constraints.*

d. Answer the questions using the CTTM13 FAQs. *We suggest that you note the questions of the participants that you are not able to answer surely. After the training session, you are encouraged to send all your questions, including the ones you were unable to answer to the CTIS Training Programme Team (CT.Training@ema.europa.eu), who can support you with preparing the answers. You should disseminate the answers to all the participants of the webinar.*

5. **Part 6:** Gather feedback about the training materials and methodology (*approximately 15 minutes*).

   a. Share the link of the feedback form on EU Survey and the credentials to access it with the participants.

   b. Give them 15 minutes to complete it. *If time is not enough, you may decide to share the link to the survey with the participants via email and ask them to complete it after the webinar. However, it is recommended to do it at the session for a higher response rate and to spare the need for follow-up.*

6. **Part 7:** Wrap up the webinar (*approximately 5 minutes*).

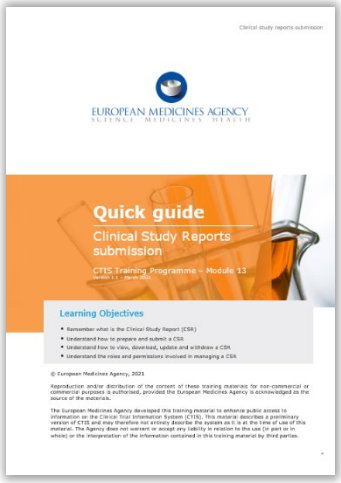
   a. Conclude the webinar and reference for future training modules and/or training sessions.

   b. Allow participants to ask final questions.

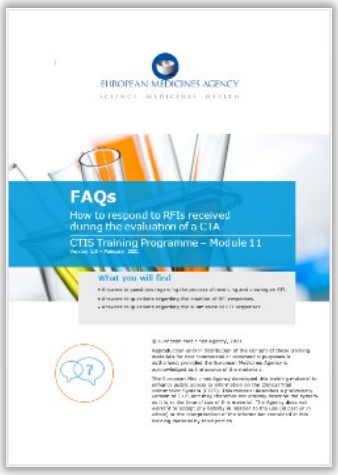
05

Annex

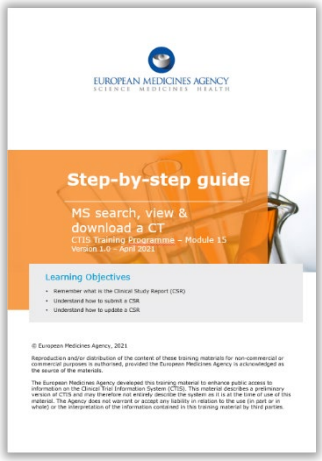
Quick guide



FAQs



Step-by-step guide



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Quick guide

Clinical Study Reports submission

CTIS Training Programme – Module 13

Version 1.0 – March 2021

Learning Objectives

- Remember what a Clinical Study Report (CSR) is
- Understand how to create and submit a CSR
- Understand how to view, download, update and withdraw a CSR
- Understand the roles and permissions involved in managing a CSR

The European Medicines Agency developed this training material to enhance public access to information on the Clinical Trial Information System (CTIS). This material describes a preliminary version of CTIS and may therefore not entirely describe the system as it is at the time of use of this 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.

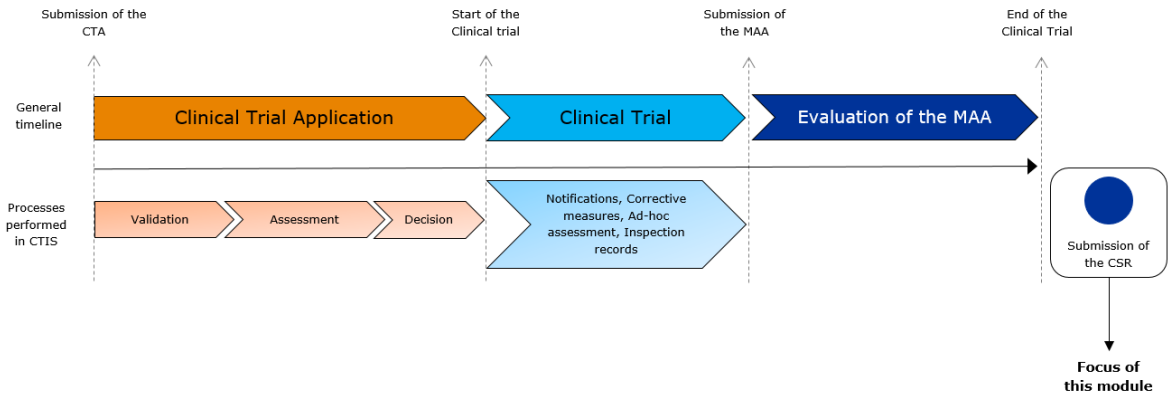
Introduction

Where a clinical trial is intended to be used for obtaining a marketing authorisation for an investigational medicinal product, the sponsor must submit a _____ _____ _____. The European Regulatory Authorities are responsible for evaluating those applications in the European Union (EU). Once granted, the authorisation allows to commercialise a medicine and make it available to patients and healthcare professionals across the European Economic Area. The process for evaluation of the MAA is not performed in CTIS and therefore it will not be the focus of this module.

As per Article 37 of the CT Regulation, the marketing authorisation applicants/holders must submit a _____ _____ _____ to CTIS, within **30 days** after the day the marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed, or the applicant for the marketing authorisation has withdrawn the application.

A CSR is a report of an individual study of an investigational medicinal product, in which the clinical and statistical description, presentations, and analyses are integrated[1]. The CSR includes a title page; a synopsis; a table of contents for the individual clinical study report; a list of abbreviations and definitions of terms; the ethics of the clinical study; the investigators and study administrative structure; the study objectives; the investigational plan; the study patients; the efficacy evaluation; and the safety evaluation. **At the moment of the submission, the information contained in the CSR will become public**.

In CTIS, the users responsible for this action are the **Marketing Authorisation Holder users (MAH)** within the sponsor workspace**.**



Article 37(4) of the CT Regulation also describes that irrespective of the outcome of a clinical trial, the sponsor must submit to CTIS a summary of the results of the trial, within one year from the end of a clinical trial in all Member States concerned or within six months for a trial in paediatric population. The summary of results shall be accompanied by a summary written in a manner that is understandable to laypersons.

[1] ICH Topic E 3 Structure and Content of Clinical Study Reports, July 1996, European Medicines Agency. Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-3-structure-content-clinical-study-reports-step-5_en.pdf

It should be noted that while the summary of results and the layperson summary are to be provided by the sponsor users after the end of each clinical trial in the EU, the CSRs are to be submitted by the MAH users only, in the case that a clinical trial is intended to be used for obtaining a marketing authorisation for the investigational medicinal product. As these processes are independent and performed by different users, they are explained in dedicated modules: **the focus of this module is the submission of the CSR**, while for more information regarding the summary of results, users can refer to *Module 5: How to manage a CT (Notifications, Ad Hoc assessment, Corrective measures, and Trial results).*

Sections of this quick guide

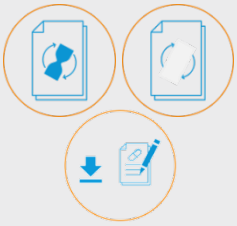
This quick guide is structured in four sections:

Create and submit a CSR

This section outlines the steps that users need to follow to create and submit new CSRs.

Search for a CSR

This section outlines the steps that users need to follow to search for a CSR (including an explanation of the different fields of search).



Update, download and withdraw a CSR

This section outlines the steps that users need to follow to update, download or withdraw a CSR.

Roles and permissions

This section provides an explanation of which roles can view, submit, update and withdraw a CSR.

Create and submit a CSR

A new CSR for an already existing Clinical Trial can be created and uploaded from the Clinical study reports tab using the '+ New' button.

If users want to cancel the submission they need to select the button 'Close'.

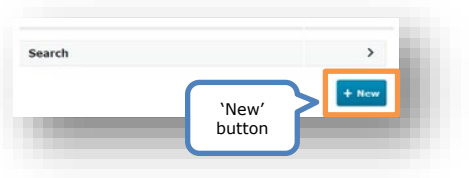
#CTIS insights

Users can create a CSR for _____ Clinical Trials only.

Create and submit a CSR

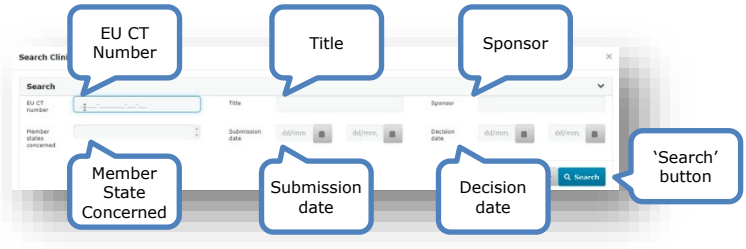
MAH users can access the _____ _____ _____ tab from the sponsor workspace. Within this tab, users with specific roles (*see section 4: Roles and permissions*) can **create and submit** a new CSR.

1. To do so, they need to select the 'New' button displayed on the left of the screen.

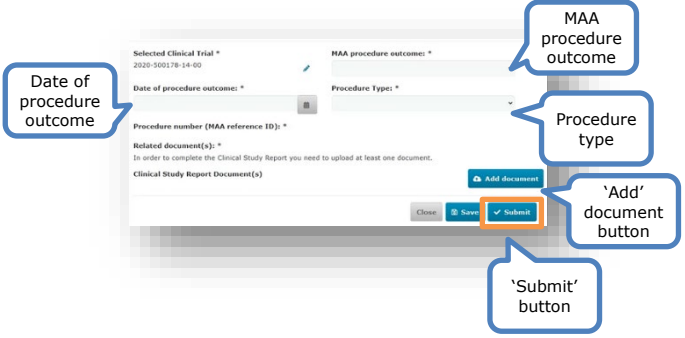


2. After users have clicked on the 'New' button, a **search** interface is displayed where users can search for the **Clinical Trial** (CT) for which they intend to submit the CSR. This search functionality allows users to find the CT by populating one or more of the following fields:

- **EU CT Number:** Number assigned by the system to a specific CT.
- **Member State Concerned:** Member State of the European Union in which the CT was carried out.
- **Title:** Title of the CT.
- **Submission date:** Date of submission of the Initial application dossier.
- **Sponsor:** Organisation submitting the Initial application dossier.
- **Decision date:** Date in which the MSCs provided a decision on the authorisation of the CT in question.



3. After the search is launched, users are able to select one trial and then click on the '**Confirm'** button at the end of the results page.
4. Once confirmed, a pop-up window is displayed in which users can populate the CSR form (including the fields MAA procedure outcome, procedure type, date of the outcome, and MAA reference ID), upload the appropriate document(s) and click on the 'Submit' button.

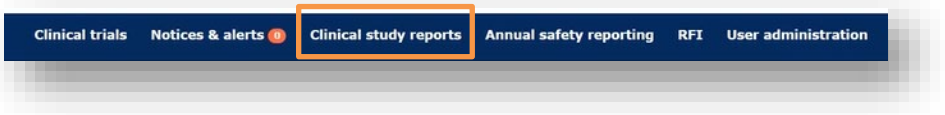


Search for a CSR

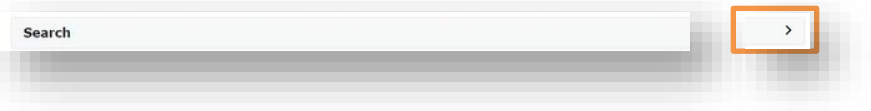
MAH users can search for a specific CSR managed by their organisation, from the Clinical study reports tab.

Search for a CSR

MAH users of the sponsor workspace have the **Clinical study reports tab available** in CTIS.



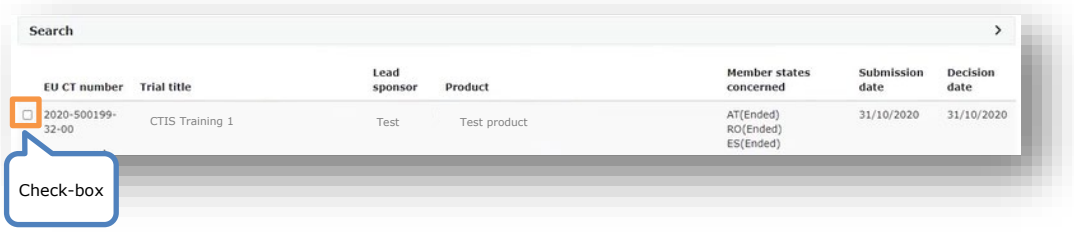
1. From the Clinical study reports tab, users can open the search functionality by clicking on the **drop-down** button displayed on the right side of the 'Search' field.



2. Once the search functionality is opened, users can search for a specific CSR that has been already submitted, withdrawn or that is in draft status, by populating one or more of the available search fields. The fields include:

   - **EU CT Number:** Unique identifier of the clinical trial to which the CSR corresponds to.
   - **Title**: Trial title.
   - **Procedure number (MAA reference ID)**: MAA procedure number.
   - **MAA procedure outcome:** Decision that the awarding body has provided to the applicant for the application. These can be: MA granted, Procedure for MA completed, and MA withdrawn by the applicant (*see section 3: Update and withdraw a CSR for more information*).
   - **Submission date**: Date when CSR was submitted, as applicable.
   - **Status**: This shows the status of a given CSR. These can be submitted, draft, or withdrawn.

3. Once the search is launched, a list of the CSRs matching the populated fields is displayed. Users can select a specific CSR from the results page by clicking on the checkbox located on the left of each CSR.



#CTIS insights

The search interface of the CSR differs from the search interphases of other tabs as it only includes an Advanced search functionality.

Update a CSR

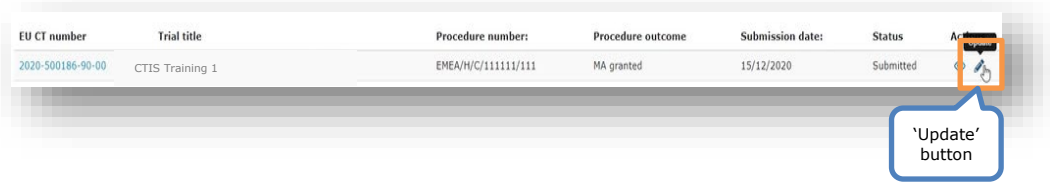
CSRs data can be updated from the Clinical study reports tab using the _____ _____.

Update a CSR

MAH users (with specific roles) con also **update** an existing CSR.

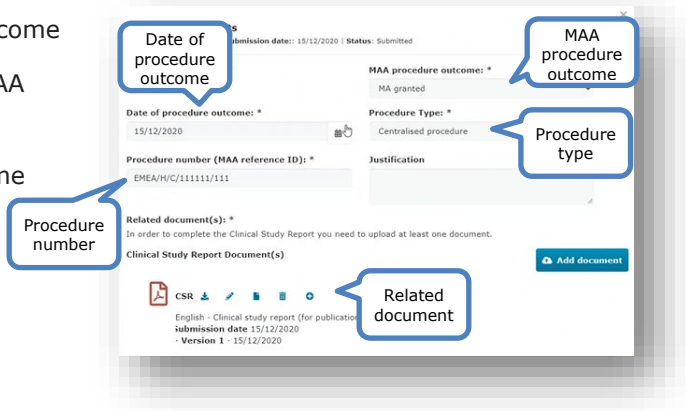
1. To do so, they need to search for a CSR (*see section 2: Search for a CSR*). Once the search is launched, the CSR matching the data populated in the search fields is displayed.

2. Once users have identified the CSR to be updated, they can click on the 'Update' icon (pencil) on the right side of the CSR.



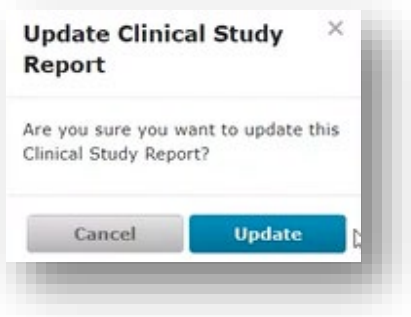
3. After users click on the update icon, a pop-up window is displayed where the fields that are required to complete are marked with an asterisk (*). These fields include:

   - Date of procedure outcome
   - Procedure number (MAA reference ID)
   - MAA procedure outcome
   - Procedure type
   - Related documents



4. After users have updated the necessary fields, they can click on the 'Update' button on the bottom left corner of the pop-up window.

5. The system will display a message requesting active confirmation of the update of the CSR.



#CTIS insights

Users can save drafts of uncompleted CSRs by selecting the 'Save' button. They can access those draft versions and complete them via the 'Clinical study reports' tab.

Download a CSR

CSRs data can be downloaded through three paths:

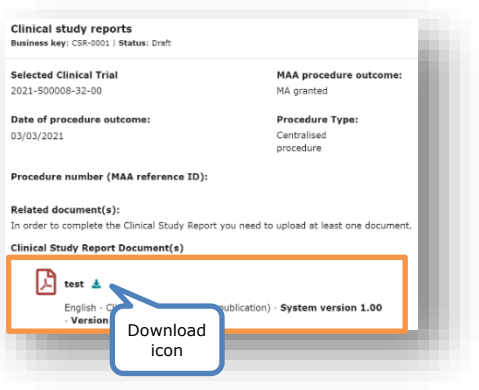
1) From the overview page of the CSR
2) From the Trial results sub-tab of the Clinical trial page
3) Downloading all the documentation from the CT

Download a CSR

Users have three options to download a CSR:

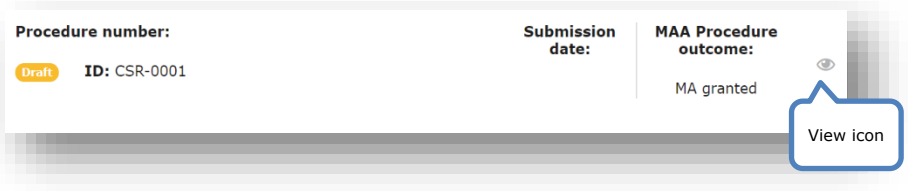
I. From the overview page of the CSR:

1. Search the CSR from the search functionality of the Clinical study reports tab.
2. Select the 'View' icon on the right side of the CSR.
3. After selecting the 'View' icon, a pop-up window is displayed with all the information of the CSR included the uploaded document(s).
4. Users can download the documents by selecting the 'Download' icon.



II. From the Trial results sub-tab of the Clinical trial page:

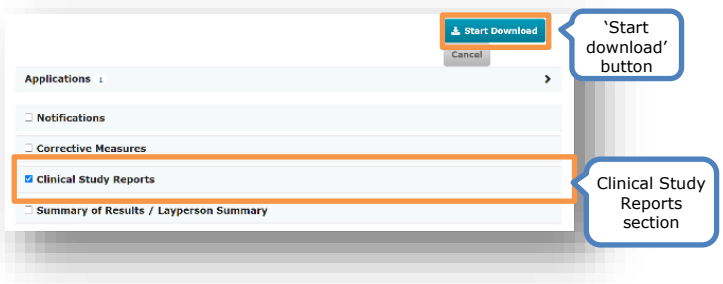
1. Search a specific CT from the Clinical trials tab and click on the [redacted].
2. Select the Trial results sub-tab of the Clinical trial page.
3. Go to the section 'Clinical Study Reports'.
4. Select the 'View' icon on the right side of the CSR.



5. After selecting the view icon, a pop-up window is displayed with all the information of the CSR, including the uploaded document(s).
6. Users can download the documents by selecting the 'Download' icon.

III. Downloading the documentation from the CT:

1. Search a specific CT from the Clinical trials Tab and click on the EU CT number.
2. Select the download Download button on the top-right corner of a Clinical trial page.
3. Select the 'Clinical Study Reports' section.
4. Click on the Start Download button.



#CTIS insights

Users can download a specific CSR from the Trial summary sub-tab of the CT page, by clicking on the EU CT number listed on the search results from the Clinical trials tab.

Withdraw a CSR

Users can withdraw a submitted CSR. To do so, they are required to provide a suitable _____ for the withdrawal.

#CTIS insights

A notice will be generated informing the sponsor responsible of the CT that a CSR corresponding to it has been submitted or withdrawn in CTIS.

Withdraw a CSR

MAH roles can also **withdraw** a CSR[2]:

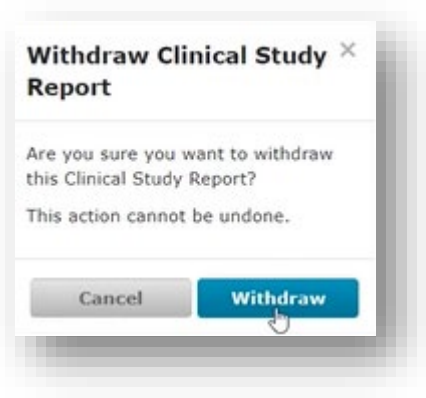
1. To do so, they need to search for a CSR (*see section 1: Search for a CSR*). Once the search is launched, the CSR matching the data populated in the search fields is displayed.

2. Once users have identified the CSR to be withdrawn, they can click on the 'Update' icon on the right side of the CSR.

3. After users click on the update button, a pop-up window is displayed. In order to withdraw a CSR, a justification for its withdrawal is required.

4. After providing the justification users can click on the 'Withdraw' button at the bottom right corner of the pop-up window.

5. After users have clicked on the 'Withdraw' button, a message requesting the active confirmation for the withdrawal will appear.



[2] *For more information on the implications of the withdrawal of a CSR, refer to the FAQs document of this module.*

Roles and permissions

There are three roles in the MAH user group:

1) MAH Admin
2) CSR Submitter
3) CSR Viewer

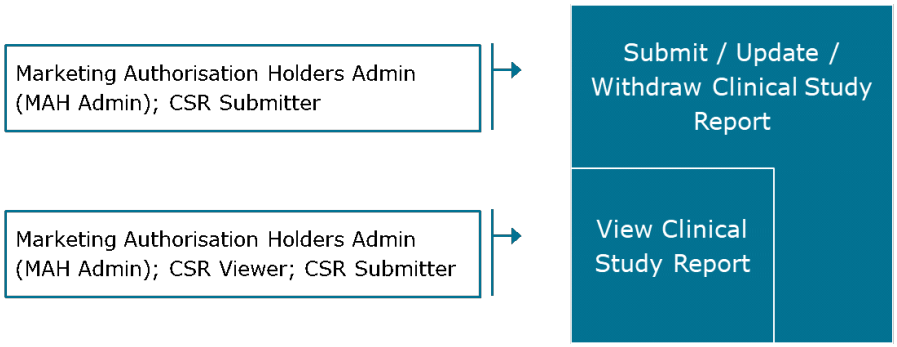
Roles and permissions

CTIS is a **role-based system** that enables users to perform different actions depending on the **permissions** attached to the **roles** assigned to them by a user from their organisation with administrator permissions.

In relation to the CSR process, three roles (from the MAH user group) are involved: Marketing Authorisation Holder Admin (MAH Admin), CSR Viewer, and CSR Submitter.

MAH Admin role needs to be assigned by the _____ _____via CTIS. The MAH Admin user is able to assign the roles of CSR Submitter or Viewer to users within its organisation. This can be done for one or several trials.

The CSR Submitter can then submit the CSR for the trials for which the role has been granted as well as update or withdraw of the CSR(s) in question. The CSR Viewers can only view CSRs (including the drafts) but cannot submit, update or withdraw CSRs.



Matching of roles and permissions with the actions to be performed in CTIS

#CTIS insights

The permission levels are structured in a cascade system where the lowest level is viewing permissions, and the highest level is submitting permissions.

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Clinical Trials Information System (CTIS)

Instructor's guide: Clinical study reports submission