EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Instructor's Guide:

Supervise a CT – Corrective measures

CTIS Training Programme – Module 14

Version 1.2 – November 2021

What you will find

- Overall guidelines on how to disseminate the knowledge.
- Overview of the audiences targeted in Module 14.
- Overview of the training materials prepared as part of Module 14.
- Recommendations on how to prepare and deliver the training sessions.

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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 fourteenth **Module of the CTIS Training Programme** (hereafter referred to as 'CTTM14'). The Module provides an overview of the corrective measure processes during the supervision phase of a Clinical Trial Application (CTA). **This guide contains** an overview of the audiences targeted with CTTM14, 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.

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Course elements

Target audiences

CTTM14 targets **Member State users**.

CTTM14 learning objectives

The learning objectives of CTTM14 are:

1. Understand what a corrective measure is, when can be created and the types.
2. Understand how to create and cancel a corrective measure.
3. Understand how to consult other MSCs on an intended corrective measure.
4. Understand how to request the sponsor's opinion.
5. Understand how to apply a corrective measure and how to update and revert an existing one.
6. Understand the roles and permissions involved in the corrective measure functionality.

Materials available

- **CTTM14 eLearning:** Interactive presentation, used as the main reference material for the content covered in this Module, can be viewed and completed by users at their own pace, expanding on detailed information as needed.

- **CTTM14 video-clips:** Practical system demonstration on how to create corrective measures, how MSCs consult each other on corrective measures, how to request the sponsor's opinion in the context of a corrective measure, how to cancel a draft corrective measure, how to submit corrective measures, as well as how to update and revert existing corrective measures once they have been submitted.
    - **Clip 1:** How to create corrective measures (7 minutes 5 seconds).
    - **Clip 2:** How to submit, update and revert corrective measures (3 minutes 42 seconds).

- **CTTM14 FAQs:** List of Frequently Asked Questions regarding the processes regarding corrective measures such as definitions, types, timelines, actors involved, etc.

- **CTTM14 Step-by-step guide:** Document summarising the main steps of the corrective measure process.

03

Course preparation

To ensure that the learning objectives of CTTM14 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 CTTM14 eLearning and CTTM14 Step-by-step 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. This is a suggestion from the training team. However, instructors can share materials with the trainees as they consider appropriate.

- Second, we suggest that you organise **a webinar** around one week after having shared the eLearning 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.

- **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 eLearning presentation and Step-by-step 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 eLearning** 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 evaluation process, which establishes that MSCs can consult with the sponsor for additional information during the validation and assessment phases. We recommend you to read at least the following articles, which are related to aspects covered in this Module:
    - *Chapter XIII: Supervision by Member States, Union Inspections and Controls*
        - Article 77 – Corrective measures to be taken by Member States.
    - 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: Applications submitted limited to Part I (article 11 of the CT Regulation, Additional MSC CTAs, and other measures related to the application procedure). Specifically, take a look at the questions:
            - 2.8. *What should be understood by conditions?;*
            - 2.11. *Can the decision on part I of a clinical trial application be changed at the moment of the addition of a Member State Concerned (article 14)?*
        - Section 3: Substantial Modifications:
            - 3.3. *How the different changes to ongoing clinical trials are classified in the Clinical Trials Regulation?*
        - Section 10: Start, End, Temporary Halt, and early termination of a clinical trial (Articles 36-38 of Regulation (EU) No 536/2014):
            - 10.9. *How is "suspension of a clinical trial" defined?*
        - Section 12: Miscellaneous:
            - 12.2. *Can a corrective measure be taken by a Member State after the end of a clinical trial?*
- **Review other relevant modules available in the CTIS Training Catalogue**. In particular, we advise you to review Modules 5 (How to manage a Clinical Trial (Notifications, Ad hoc assessment, Corrective measures, and Trial results) where you can find information about corrective measures and how your sponsor counterparts will manage them in terms of responsibilities, use of notifications, processes for ad-

[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

hoc assessments and corrective measures, etc.

- **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 three 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.

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 eLearning individually

Time: One week before the webinar

Material: CTTM14 eLearning and CTTM14 Step-by-step guide

Objective:

This activity consists in the individual review by participants of the CTTM14 eLearning and CTTM14 Step-by-step guide presentation 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 eLearning and Step-by-step 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 and a half

Material: CTTM14 eLearning, CTTM14 video-clips, CTTM14 FAQs, CTTM14 Step-by-step guide 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 CTTM14 eLearning and CTTM14 Step-by-step guide.
- Present the additional materials for the CTTM14.
- Answer any questions regarding the content of the CTTM14.
- 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 CTTM14 eLearning presentation and CTTM14 Step-by-step guide.
    b. Launch an online quiz to check if participants understood the key concepts from the CTTM14 eLearning and CTTM14 Step-by-step guide. Refer to the general dissemination guidelines for examples of tools that you can use for that purpose.
3. **Part 3:** Screening of CTTM14 video-clips (*approximately 20 minutes*).
    a. Make a brief introduction to the CTTM14 video-clips, so that participants have an understanding of the content they are about to watch. Explain that the video-clips aim to show them how the functionalities of Module 14 work in practice in the system.
    b. You may want to prepare a short slide deck with key concepts to display on the screen before playing the video-clips.
    c. After each video-clip, allow five minutes so that participants can ask questions. Be ready to have CTIS open to be able to show how something works on the system in practice, or show any particular aspect of the eLearning presentation. Be also ready to replay a video-clip if an aspect was not clear enough.

Break: (10 minutes)

4. **Part 4**: 'Case scenarios activity' (approximately 40 minutes).

    a. This activity is an exercise in which participants will have to read a series of scenarios about the processes of corrective measures. The activity focuses on selecting the corresponding items regarding the activities, timelines and user roles that would match what each scenario proposes.

    b. Send out to the participants a PDF file containing the pages regarding the exercise (pages 14 and 15 of the Annex), and explain it during the session.

    c. Give participants 20 minutes to select the corresponding items that would match what each scenario proposes (*use breakout rooms within the webinar if allowed by the online tool chosen, so that participants may discuss the exercise among themselves*).

    d. Use approximately 20 minutes to discuss the outcome of the exercise. You can use the possible solution to the case scenarios provided on pages 16 and 17 of the Annex. This activity can be performed in different settings. Here are some tips on how to handle them:

        i. In a virtual meeting where participants cannot share their screen, you should share your screen and start clicking on the possible correct answers based on the participants' input.

        ii. In a virtual meeting where participants can share the screen, you can ask for volunteers to present their document with the correct answers.

        iii. In a face-to-face session, you can organise participants in groups and request them to do the exercise together. You may decide to add complexity with new scenarios that you can develop yourself. Give a couple of minutes to each group to present their exercise.

    e. To engage with participants while they are presenting the outcome of the exercise, you can ask specific questions such as:

        i. What other scenarios can be envisaged?

        ii. What other steps/actions do you consider important to be included?

        iii. Do you find this exercise difficult?

5. **Part 5:** Questions and answers (*approximately 20 minutes*).

    a. Present the CTTM14 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. Prepare a blank slide as an empty whiteboard where participants can add relevant information, raise questions or pinpoint different logics on the ways to respond to an RFI received during the evaluation of a CTA.

d. 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.*

e. Answer the questions using the CTTM14 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.*

6. **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.*

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

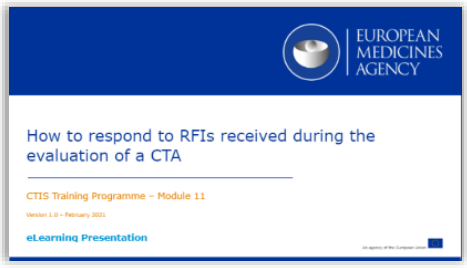
    a. Conclude the webinar and reference for future training modules and/or training sessions.

    b. Allow participants to ask final questions.

05

Annex

eLearning



FAQs

Video-clips

Step-by-step guide

Case scenarios activity

Activity objectives

This exercise will help you think about the corrective measure steps and processes you have learned with the materials of this module. Your task is focused on **reading the three scenarios** and **selecting the items via the checkboxes** ☐ on the left that you think match or are relevant for the scenario in each of the categories of the table below. The categories refer to actions to be taken, relevant timelines or moments to perform an action, and specific users/roles involved in the Corrective Measure (CM) processes. Be aware that, for some categories, selecting more than one option is correct. Also, this is a flexible exercise; therefore, there may be different combinations of correct answers.

Scenarios

Austria is the RMS of an authorised trial, and Germany is the other MSC. The sponsor has sent a notification of an unexpected event. The RMS deems it necessary to submit a CM that requires immediate action: revoking the application authorisation.

Relevant activities	Timelines	User roles involved
☐ Create a new "suspend" CM		☐ Decision Maker Submitter ☐ Supervisor Submitter ☐ Sponsor Notifications Submitter ☐ EC Admin ☐ CT coordinator
☐ Create a new "revoke" CM		
☐ Consult with sponsor	☐ Wait 7 days for the sponsor to respond to the request for opinion ☐ No timeline fixed	
☐ Consult with other MSC	☐ Wait 7 days for the MSCs to respond to the consultation ☐ No timeline fixed	
☐ Submit the CM		

Germany wants to create a CM to suspend an authorised trial because they consider the trial is no longer meeting the CT Regulation requirements. The MSC decides to create a CM that does not require immediate action.

Relevant activities	Timelines	User roles involved
☐ Create a new "suspend" CM		☐ Decision Maker Submitter ☐ Supervisor Submitter ☐ Sponsor Notifications Submitter ☐ EC Admin ☐ CT coordinator
☐ Create a new "revoke" CM		
☐ Consult with sponsor	☐ Wait 7 days for the sponsor to respond to the request for opinion ☐ No timeline fixed	
☐ Consult with other MSC	☐ Wait 7 days for the MSCs to respond to the consultation ☐ No timeline fixed	
☐ Submit the CM		

Austria has submitted a CM to suspend and require modification of a trial. The sponsor has submitted a substantial modification and Austria has authorised it. Now Austria considers that this trial can be authorised with conditions and wants to change the MSC decision.

Relevant activities	Timelines	User roles involved
☐ Update the CM	☐ Wait 7 days after having the CM submitted before updating it ☐ No timeline fixed	☐ Decision Maker Submitter ☐ Supervisor Submitter ☐ Sponsor Notifications Submitter ☐ EC Admin ☐ CT coordinator
☐ Revert the CM	☐ Wait 7 days after having the CM submitted before reverting it ☐ No timeline fixed	
☐ Consult with sponsor	☐ Wait 7 days for the sponsor to respond to the request for opinion ☐ No timeline fixed	
☐ Consult with other MSC	☐ Wait 7 days for the MSCs to respond to the consultation ☐ No timeline fixed	

Case scenarios activity possible solutions

Activity objectives

This exercise will help you think about the corrective measure steps and processes you have learned with the materials of this module. Your task is focused on **reading the three scenarios** and **selecting the items via the checkboxes** ☐ on the left that you think match or are relevant for the scenario in each of the categories of the table below. The categories refer to actions to be taken, relevant timelines or moments to perform an action, and specific users/roles involved in the Corrective Measure (CM) processes. Be aware that, for some categories, selecting more than one option is correct. Also, this is a flexible exercise; therefore, there may be different combinations of correct answers.

Scenarios

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☒ Create a new "revoke" CM		
☐ Consult with sponsor	☐ Wait 7 days for the sponsor to respond to the request for opinion ☐ No timeline fixed	
☒ Consult with other MSC	☐ Wait 7 days for the MSCs to respond to the consultation ☒ No timeline fixed	
☒ Submit the CM		

Germany wants to create a CM to suspend an authorised trial because they consider the trial is no longer meeting the CT Regulation requirements. The MSC decides to create a CM that does not require immediate action.

Relevant activities	Timelines	User roles involved
☒ Create a new "suspend" CM		☒ Decision Maker Submitter ☒ Supervisor Submitter ☒ Sponsor Notifications Submitter ☐ EC Admin ☐ CT coordinator
☐ Create a new "revoke" CM		
☒ Consult with sponsor	☒ Wait 7 days for the sponsor to respond to the request for opinion ☐ No timeline fixed	
☒ Consult with other MSC	☐ Wait 7 days for the MSCs to respond to the consultation ☒ No timeline fixed	
☒ Submit the CM		

Austria has submitted a CM to suspend and require modification of a trial. The sponsor has submitted a substantial modification and Austria has authorised it. Now Austria considers that this trial can be authorised with conditions and wants to change the MSC decision.

Relevant activities	Timelines	User roles involved
☐ Update the CM	☐ Wait 7 days after having the CM submitted before updating it ☐ No timeline fixed	■ Decision Maker Submitter ■ Supervisor Submitter ☐ Sponsor Notifications Submitter ☐ EC Admin ☐ CT coordinator
■ Revert the CM	☐ Wait 7 days after having the CM submitted before reverting it ■ No timeline fixed	
☐ Consult with sponsor	☐ Wait 7 days for the sponsor to respond to the request for opinion ☐ No timeline fixed	
☐ Consult with other MSC	☐ Wait 7 days for the MSCs to respond to the consultation ☐ No timeline fixed	

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Clinical Trials Information System (CTIS)

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